Protocol

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AMERICAN COLLEGE OF RADIOLOGY IMAGING NETWORK
ACRIN #6654
CONTEMPORARY SCREENING FOR THE DETECTION OF LUNG CANCER

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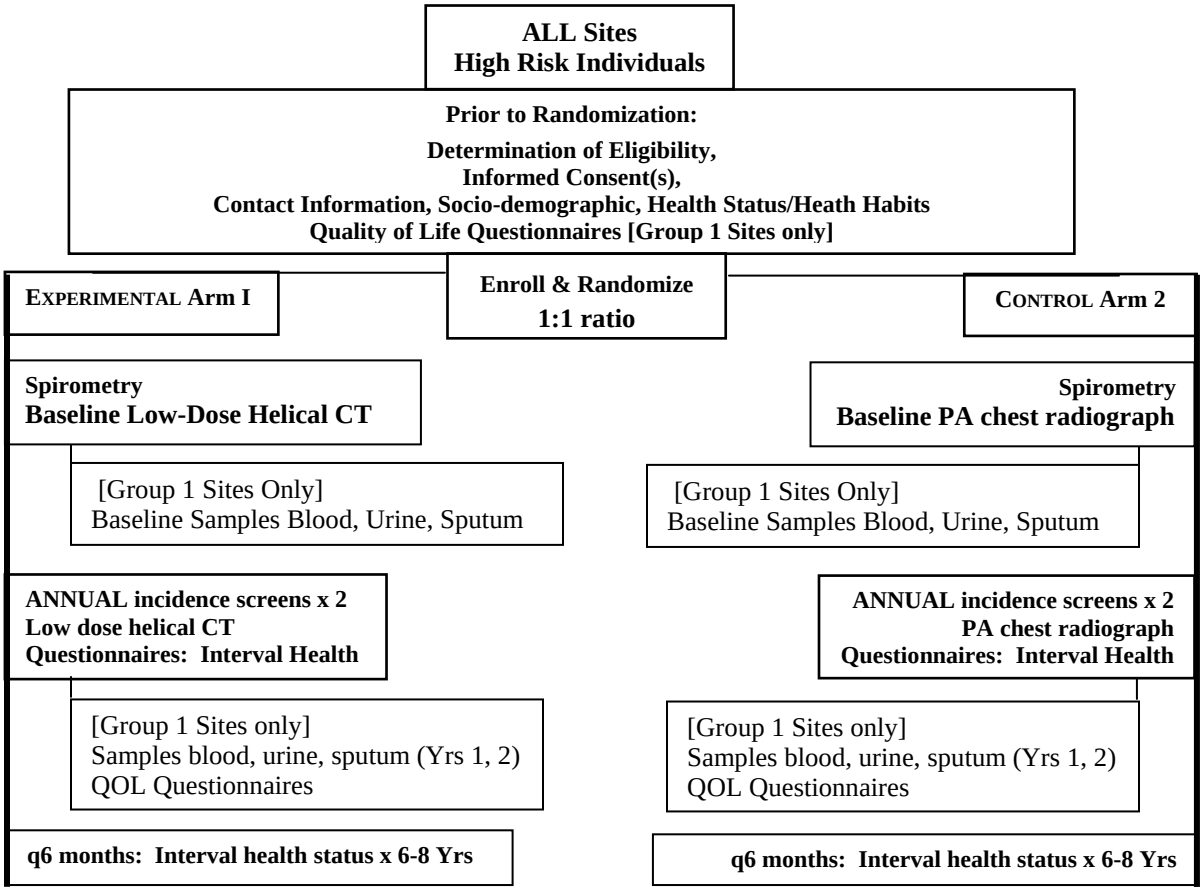
ACRIN 6654: CONTEMPORARY SCREENING FOR LUNG CANCER SCHEMA



Eligibility: *(see Section 4.0 for details)*

- Age 55-74 years and 364 days.
- Current or previous cumulative cigarette smoking history of ≥ 30 pack years *(packs per day x years smoked)*.
- Former smokers must have quit smoking within the previous 15 years.
- No medical or psychiatric condition precluding informed medical consent.
- Ability to lie on the back with arms raised over the head.
- No metallic implants or metallic devices in the chest or back *(pacemakers or Harrington fixation rods, etc.)* that would cause sufficient beam hardening artifact so as to degrade image quality in the lungs.
- No prior history of lung cancer.
- No treatment for, or advisement by a physician of evidence of *any* cancer within the past five years, with the exceptions of non-melanoma skin cancer and most in-situ carcinomas. (Treatment for, or evidence of, melanoma or in-situ bladder/transition cell carcinomas within the preceding five years renders the potential participant ineligible.)
- No prior removal of any portion of the lung, excluding percutaneous lung biopsy.
- No requirement for home oxygen supplementation for respiratory conditions.
- No participation in another cancer screening trial, [e.g., the PLCO, ELCAP, or single arm trials such as those of the Mayo Lung Trial, Jewish Heart and Lung Institute, or the Moffitt Lung Trial].
- No participation in a cancer prevention trial, other than smoking cessation programs.
- No present symptoms suggestive of current lung cancer, including: unexplained weight loss of over 15 pounds within the past 12 months or unexplained hemoptysis.
- No medical conditions that pose a significant risk of mortality during the trial period.
- No pneumonia or acute respiratory infection within 12 weeks of enrollment that was treated with antibiotics under physician supervision. *(These individuals would be eligible 12 weeks from the first dose of antibiotics.)*
- No individuals within 6 months of receipt of cytotoxic agents for any condition. *(These individuals would be eligible 6 months from the last dose of the drug from the final cycle.)*
- No chest CT scan within the preceding 18 months. *(These individuals would be eligible 18 months after chest CT.)*
- Signed study-specific informed consent prior to study entry.

Required Sample Size: Up to 25,000 participants

1.0 ABSTRACT

Lung cancer is now the most common cause of cancer death among women and men. Despite considerable clinical research in multi-modality cancer treatment, there has been no significant decrease in lung cancer-specific mortality over the past three decades. Approximately 80% of lung cancers are of non-small cell histology, for which prognosis depends primarily upon tumor stage at the time of diagnosis. Although overall survival rates with non-small cell carcinoma are dismal, patients with surgical stage I disease may have 10-year survivals of up to 70%. This has formed the rationale for early detection programs. Both chest radiographs and spiral computed tomography (CT) have been used to screen for lung cancer. Thus far, however, neither test has been shown to reduce lung cancer mortality. This project is a multicenter, randomized controlled trial involving 23 sites across the nation and will enroll up to 25,000 individuals at high risk of developing lung cancer. High risk will be defined by age 55-74 years with a current or previous heavy smoking history equaling at least 30 pack years; former smokers must have quit within the preceding 15 years. Prior to randomization, all sites will collect standardized eligibility data, including health histories, smoking behavior, and sociodemographic data, and will complete spirometry. The Experimental group at all sites will undergo screening with low dose helical CT. The Control group at all sites will undergo screening with chest radiographs. Experimental and Control arms will be screened annually for at least two incidence screens and will be followed thereafter for up to a total of eight years to determine outcomes. All participants will be contacted at six-month intervals to document interval health status and changes in smoking behaviors. The primary endpoint of the trial is to determine which screening test is better at reducing lung cancer-specific mortality. Secondary endpoints include: all cause mortality, differences in stage distribution at diagnosis, and differences in cost and medical resource utilization between the two arms. At some of the participating institutions, three additional study aims will include: [1] the creation of a bank of specimens from well-characterized high-risk cohorts that can be used to test future potential biomolecular markers of lung cancer; [2] evaluation of the influence of screening on smoking behaviors; and [3] the evaluation of screening on various issues of quality of life and anxiety.

2.0 BACKGROUND AND SIGNIFICANCE

Lung cancer is now the most common cause of cancer death in men and women in the United States.[1,2,3] Despite considerable research in treatment, mortality from primary lung cancer has risen over the past three decades, and approximately 85% of individuals who acquire lung cancer will die from it.[3,4] More Americans will die from lung cancer than colon, breast, and prostate cancers combined.

Small-cell lung cancer accounts for roughly 20% of lung cancers. Small-cell lung cancer behaves aggressively with early and wide dissemination and is not favorably influenced by existing screening or treatment methods. Non-small cell lung cancer *(NSCLC)* accounts for about 75% of all lung cancers. The prognosis in patients with NSCLC relates primarily to surgical stage at the time of diagnosis, although performance status, ethnicity, and histologic type are lesser determinants. Overall 5-year survival from lung cancer is less than 15%[3]; however, patients with surgical early stage NSCLC who undergo curative resection have 5-year survival rates of 40-70%. Survival in a cohort of 598 patients with surgically resected stage I tumors was recently reported.[5] The overall 5-year survival rate was 75%; however, when stratified by TNM tumor classification, patients with T1 tumors fared better than those with T2 tumors, with 5-year survival rates of 82% and 68%, respectively.[5,6] Tumor size also influenced survival, which was best in those with tumor diameters less than 1 cm and poorest in those with diameters greater than 5 cm. The improved survival seen with the early detection of NSCLC has formed the rationale for lung cancer screening.

2.1 Risk Factors for Lung Cancer

Cigarette smoking is the single most important risk factor for lung cancer; 85% of lung cancer deaths are attributable to smoking.[7-11] Three decades have passed since the first report by the United States Surgeon General on the causal relationship between smoking and lung cancer in men. Although smoking prevalence has considerably decreased over this period, annual cancer statistics of the American Cancer Society show a significant increased incidence in lung cancer owing to persistent risk among former smokers of advancing age. Indeed, lung cancer is increasingly a disease of former smokers. While primary prevention is rightfully an important focus for reducing lung cancer, it is an incomplete preventive solution for the population at risk. Former smokers have already achieved smoking cessation, but will continue to be the source of an increasing fraction of lung cancer in the future.

The relative risk of lung cancer is influenced by duration of smoking, intensity of exposure *(number of cigarettes smoked per day)*, and duration of smoking cessation in ex-smokers. Risk increases in rough proportion to the number of cigarettes smoked per day.[12,13] Duration-specific risks increase steadily, but are most significant beyond 20 years of smoking duration. Cancer risk remains elevated in former cigarette smokers, declining significantly beyond five years from cessation. The following table shows the calculated excess risk of lung cancer death in males due to smoking when stratified by age and smoking category. From these data, we can see that a 55 year old male who smokes 25 cigarettes or more per day has a 12.6% chance of dying from smoking-related lung cancer by age 75; and an 18.5% chance by age 85.

Table 1: Percent Probability of Dying from Lung Cancer Due to Smoking Based on Age and Smoking Status[14]

Age	Smoking Category	Percent Probability of Lung Cancer Death		
		Age 65	Age 75	Age 85
35	Former	1.9	4.4	6.5
	Current < 25 cigarettes/day	2.5	6.3	9.3
	Current > 25 cigarettes/day	6.3	13.0	17.9
45	Former	1.9	4.4	6.7
	Current < 25 cigarettes/day	2.5	6.4	9.5
	Current > 25 cigarettes/day	6.4	13.3	18.5
55	Former	1.6	4.3	6.6
	Current < 25 cigarettes/day	2.1	6.4	9.8
	Current > 25 cigarettes/day	4.6	12.6	18.5
65	Former		3.2	5.9
	Current < 25 cigarettes/day		5.2	9.4
	Current > 25 cigarettes/day		10.4	18.0

Lung cancer occurs primarily in patients between ages 50 and 80 years. The relative risk of lung cancer is also influenced by other host factors, including gender, ethnicity, socioeconomic status, family history, occupational exposures, and the presence of airflow obstruction.[15,16,17] Statistics from the Surveillance, Epidemiology, and End-Results *(SEER)* program show that the age-adjusted lung cancer incidence is higher among African-Americans than Caucasians of the same gender and is also greater in lower socioeconomic classes, relating to differences in access to medical care, smoking patterns, and diet. Lung cancer prevalence is particularly high among individuals smoking 30-40 pack years or more with airflow obstruction, defined by FEV1/FVC less than 70% and an FEV1 less than 70% predicted.[18] Indeed, airflow obstruction is associated with a 4-5-fold increase in lung cancer when all other risk factors are controlled.[15,16,17] In a recent study of 148 emphysema participants being evaluated for lung volume reduction, the prevalence of asymptomatic lung cancer was 5%.[19] Cancer risk presumably derives from poor clearance of carcinogens from the bronchial epithelium and peripheral airspaces. At the highest risk of lung cancer are individuals with previously surgically treated stage I NSCLC or supraglottic primary neoplasms.[5,20,21,22]

2.2 Historical Lung Cancer Screening Trials

At the present time, it is generally accepted that screening for lung cancer confers no mortality benefit. Several large randomized controlled trials, although differing in experimental design, concluded that screening did not reduce lung cancer-specific mortality. In four major prospective trials, screening was performed by some combination of chest radiography *(CXR)* and histologic sputum analysis at various frequencies as tabulated below.[23-27] The participants were all male smokers over 45 years of age at high risk of developing lung cancer *(smoking > 1 ppd):*

Table 2: Summary of Screening Protocols in Four Major Lung Cancer Screening Trials

GROUP	Johns Hopkins & Memorial Sloan-Kettering Lung Projects *(N = 10,000)*		Mayo Lung Project *(N = 10,000)*		Czech Study [1]	
	Screen	Frequency	Screen	Frequency	Screen	Frequency
Control	CXR	Annual	Recommendations: CXR[2] + Sputum Annually		None	
Experimental	CXR Sputum	Annual Q 4 months	CXR Sputum	Q 4 months	CXR Sputum	Q 6 months x 3 years

Note: [1] Both Czech groups underwent CXR + sputum at year 3; CXR at years 4,5,6
[2] Roughly half of Control subjects received annual chest radiographs

In the Johns Hopkins and Memorial Sloan-Kettering trials, both Experimental and Control participants underwent annual screening chest radiography.[23,24] The trials were designed to address the incremental benefit of sputum cytology analysis rather than chest radiographs per se. Although they found that sputum analysis did not favorably influence outcome, these studies achieved survival rates among all groups three times higher than predicted by epidemiological data, thus inviting the supposition that annual radiographic screen may indeed have improved outcome. The Mayo Lung and Czechoslovak trials showed advantages to the screened groups with respect to earlier stage at diagnosis, resectability, and survival. However, because the Experimental groups in both studies demonstrated *increases* in cumulative lung cancer incidence above that of Control groups *(p = 0.019)*, significant improvements in case fatality *(# cancer deaths / # individuals with cancer)* did not translate into significant reductions in lung cancer mortality *(# cancer deaths / # individuals screened)*.[25,26,27]

2.3 Early Detection Biases in Screening

The disparities in these trials between lung cancer mortality and the improvements realized in stage at diagnosis, resectability, and survival within the screened group have been ascribed to three biases peculiar to screening: lead-time, length, and overdiagnosis.[28,29,29b]

2.3.1 *Lead-Time Bias:* Lead-time bias pertains to comparisons between screening and non-screening cases that are not adjusted for the timing of diagnosis. If screening detects disease earlier, the patient will survive longer from the time of diagnosis even if death is not delayed. Although readily measurable, survival is an inadequate measure of the effectiveness of screening, and has no predictable relationship to mortality.

2.3.2 *Length Bias:* Length bias pertains to comparisons between screening and non-screening conditions that are not adjusted for the rate of cancer progression and the tendency of screening to detect slow-growing cancers. Screening ideally detects cancers in the detectable preclinical phase, that period in which the cancer is present but produces no symptoms. The likelihood of detection by screening is directly related to how quickly the cancer grows: the more slowly growing the neoplasm, the longer it is present without symptoms, and the greater the likelihood of detection. Fast-growing cancers have a commensurately shorter detectable preclinical period. Overall, screening tends to detect tumors of more indolent biology and growth potential.

2.3.3 *Overdiagnosis Bias:* Overdiagnosis bias refers to the phenomenon of detecting pseudodisease, e.g., a lung cancer that would otherwise have remained subclinical before death from other causes. There is contradictory evidence on the issue of pseudodisease. In small studies of individuals with clinical stage I lung cancer who have not been treated by surgical resection, mortality is 80% at ten years. However, high mortality does not imply that *all* lung cancers are lethal, only that *known* lesions are lethal.[30] Published reports have documented "surprise" lung cancers at autopsy/necropsy in individuals who have died of other conditions such as coronary

artery disease. Also, it is well known that small lung lesions less than 2 cm diameter may be easily overlooked at autopsy due to sampling error. The reported necropsy "surprise" detection rates suggest that there may be a significant reservoir of asymptomatic lung cancer.[31]

2.4 Analysis of the Influences of Screening Biases on the Mayo Lung Project

In the Mayo Lung Project *(MLP)*, the screened group demonstrated 46 excess lung cancers *(206 cases in screened group versus 160 cases in unscreened group)*. This excess was largely accounted for by a higher number of early stage lung cancers among screened participants. However, there was no proportionate *decrease* in late stage cancers[26] and ultimately, no decrease in lung cancer-specific mortality. The excess lung cancers in the screened participants have been explained by: [1] pseudodisease, e.g., overdiagnosis bias in the screened group, [2] underdiagnosis of lung cancer in the non-screened group; e.g., misclassification of cause of death; and [3] a fundamental flaw in the process of randomization whereby the Experimental group as a whole had a higher risk profile for lung cancer. These contentions are not supported by recent re-analysis of the risk-defining features of the two groups.[29b,32]

Ultimately, the results of the MLP do *not* prove that lung cancer screening with chest radiographs is futile. However, they *do* indicate that, as a matter of public policy, CXR screening cannot be endorsed without better demonstration of screening benefit. For this reason, the National Cancer Institute has initiated a large randomized controlled screening trial using chest radiographs for lung cancer screening as part of the Prostate-Lung-Colorectal-Ovarian *(PLCO)* trial, with one objective being the determination of whether screening reduces lung cancer-specific mortality by at least 10% relative to unscreened groups. It is hoped that this trial will resolve lingering questions about the utility of chest radiographic screening.[33]

2.5 Lung Cancer Screening with Helical CT

Although there is ongoing controversy regarding the utility of chest radiography in early lung cancer detection, it is generally acknowledged that helical CT represents an important advance in lung nodule detection and characterization.[34,35] Helical CT allows the whole chest to be surveyed in a single suspended breath-hold, reducing motion artifacts and eliminating respiratory misregistration and the potential to under sample the whole lung. Nodule detection increases in parallel with narrower slice thickness. The effective slice thickness, and therefore the in-plane resolution of axial reconstructions, is determined by the combination of beam collimation, table incrementation, and interpolation algorithm.[36,37,38] Because the resulting data set is volumetric, overlapping axial reconstructions can effectively increase z-axis resolution and the potential to detect small lung nodules *(between 5-10 mm diameter)*.[39]

In one recent retrospective review of missed lung cancers by incremental CT, the mean diameter of missed lesions was 1.2 cm *(range: 2-20 mm)*, whereas retrospective analysis on chest radiographs observed a mean diameter of missed lesions of 1.6 cm *(range 8-34 mm)*.[40,41] Although there is greater radiation exposure with CT than chest radiography, low dose techniques have achieved calculated exposure doses that are 17% that of conventional CT and 10 times that of chest radiograph.[42]

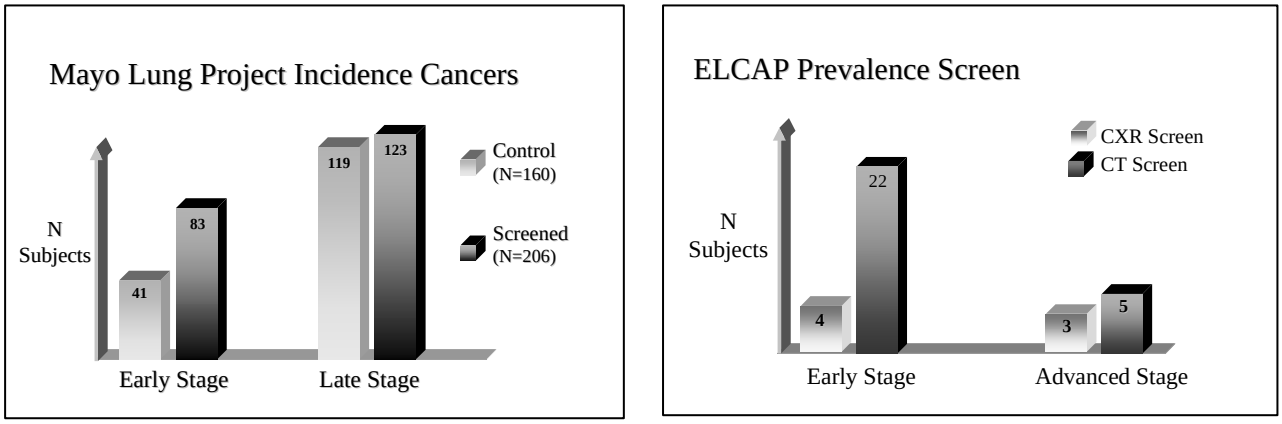
Screening trials using low-dose helical CT are in progress in both the United States and Japan.[42,43,44] These single-arm trials have demonstrated striking increases in the detection of early stage lung cancers. In Japan, where roughly 70% of lung cancers originate in the lung periphery[42,43] large trials in high-risk individuals have consisted of chest radiographs, low dose helical CT, and sputum cytology at six month intervals over a two year period.[42] Suspicious focal abnormalities detected on *any* screening modality were further characterized with high-resolution CT *(HRCT)*. Among 1,369 participants, 229 cases were referred for HRCT; of these, 19 were referred for tissue sampling. Overall, 18 lung cancers were found: 15 peripheral cancers by imaging *(CT alone or CT and chest radiography)* and 3 central lesions by sputum cytology alone. Low-dose helical CT depicted all peripheral lung cancers as well as one lung metastasis whereas only four of 15 peripheral cancers were seen on chest radiography; in no participant was chest radiography the sole method of detection. Fourteen of the 15 cancers were stage I at diagnosis with mean diameters on helical CT of 16 mm ± 7, versus 30 mm ± 14 on projectional radiography. These

findings confirm the sensitivity of CT over chest radiography in detecting smaller, early stage lung cancers.

The most heavily publicized CT screening trial in the United States, the Early Lung Cancer Action Project *(ELCAP)*, has reported its results of a prevalence screen of 1000 individuals at high risk of lung cancer who have been followed with annual low dose helical CT and chest radiographs.[44] In the ongoing ELCAP trial, the prevalence CT screen was positive in 233 participants, of whom 16 *(7%)* were lost to follow-up. Of the remaining 217 participants, 27 primary lung cancers were found *(2.7% prevalence of lung cancer)*. With low dose CT, 96% of cancers were resectable, and 81% were stage I at diagnosis. Relative to chest radiographs, prevalence CT screens detected three times more nodules, four times more cancers, six times more stage I lesions, but roughly equivalent numbers of advanced stage cancers. Incidence data show lower numbers of abnormal screening CT exams, a greater proportion of which reflect malignancies. These incidence screens, the stage distributions, and long-term follow-up will be important to observe.[44]

Figure 1: Distribution of Stage in the (a) MLP incidence screens and (b) ELCAP prevalence screen. In both trials, the primary screening intervention resulted in an increase in the number of cancers found, the excess cancers being mostly early stage tumors. In the MLP, screening conferred no mortality benefit. The effect of CT screening on mortality in ELCAP awaits follow-up.

(a) **(b)**



The ELCAP trial is a single-arm design; as such, it will be very difficult to determine whether CT screening will achieve a genuine decrease in lung cancer-specific mortality or merely an "improved survival" due to the screening biases of lead-time, length, and overdiagnosis. Unfortunately, the preponderance of early stage cancers found at screening CT, combined with optimistic survival predictions, have been promulgated in the lay press to predict *mortality* reductions of up to 80%. These conclusions are not supported by scientific data and overstate what is currently known about lung cancer screening with CT.

2.6 Tumor Size Relative to Tumor Behavior

Lesion size is one of the defining features of anatomic staging with the TNM classification. The T status of a primary lung cancer stratifies tumors by size, with T1 lesions defined as 3 cm or less in diameter and T2 lesions being greater than 3 cm diameter.[45,46] Nodules detected on CT are consistently smaller than those detected on CXRs; as such, it is natural to assume that CT screening will affect a mortality benefit over non-screening because the average size of the detectable lung cancers is smaller. However compelling the logic, a linear relationship between tumor size and mortality has not been shown for lesions within the T1 designation. Simply stated, it is not known whether the detection and treatment of a 5 mm diameter T1 cancer will affect a better outcome than the detection of a 20 mm diameter T1 cancer. A recent retrospective study found no survival advantage among T1 cancers based upon size.[47] This observation is somewhat counter-intuitive. It is possible that ascertainment bias and small sample size may have obscured a predictable relationship between tumor size and outcome. Alternatively, as

intimated by the investigators, there may be confounding biological variables that influence tumor aggressiveness beyond size.[48]

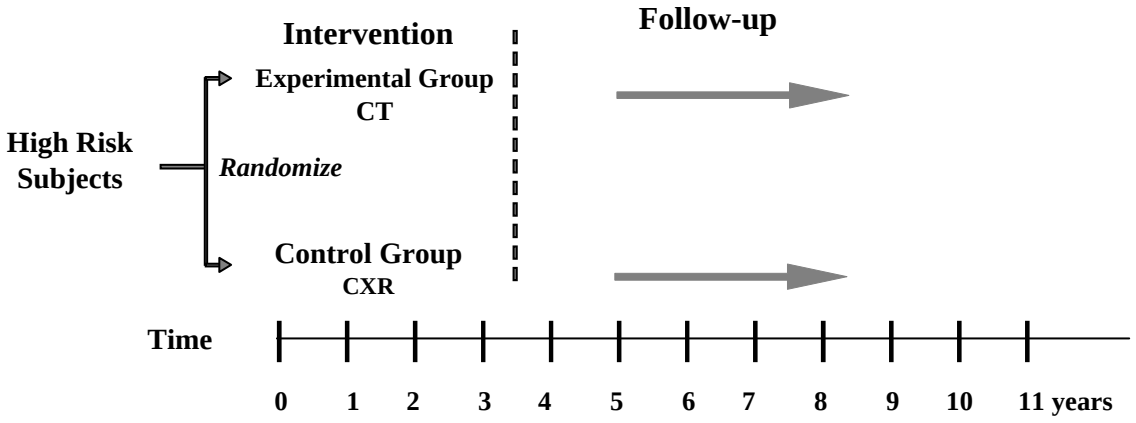
The latter contention is indirectly supported by other studies that show carcinocythemia and the potential for metastatic dissemination among T1 lung cancers. In patients with stage I lung cancer, peripheral blood samples taken before, during, and after curative surgical resection showed circulating cancer cells in some of the patients.[49] Patients in whom circulating tumor cells are seen following surgery have a significantly worse survival when compared with patients in whom carcinocythemia is not found. Similarly, other investigators have used specialized tissue processing and stains to detect microdissemination within regional lymph nodes in patients with T1 lung cancers undergoing curative surgery.[50] Again, some patients with T1 lesions demonstrate microdissemination and have significantly worse outcomes than patients in whom microdissemination has not occurred.

We are still very early in our understanding of tumor biology and the behavior of lung cancer. What we *do* understand is that lung cancers are biologically heterogeneous, and tumor size alone is not adequate to explain their behavior. This has significant implications for lung cancer screening with CT. A major impetus to migrate from chest-x-ray screening to CT screening for lung cancer is the promise of detecting smaller lung cancers. Yet, we do not currently know that outcomes are necessarily better when the cancer is 2 mm as opposed to 20 mm. As purveyors of public policy, we are obliged to avoid the premature endorsement of a screening process before its benefits and liabilities have been reconciled.

2.7 Measuring Screening Effectiveness

2.7.1 *Lung Cancer-Specific Mortality:* As we have seen, although survival from diagnosis is appropriate when measuring the effectiveness of treatment, survival is misleading as a measure of screening effectiveness due to the confounding effects of screening biases. The purpose of lung cancer screening is to prevent or delay lung cancer related death. As such, lung cancer-specific mortality is the most appropriate measure of screening effectiveness. Measurements of mortality are based upon following individuals from the time of the decision to screen, rather than from the time of diagnosis. *(As an aside, case fatality rate measures the number of deaths from the time of diagnosis of cancer but also does not take into account length and overdiagnosis biases).*

Figure 2: RCT Template for Lung Cancer Screening with CT



2.7.2 *The Randomized Controlled Trial (RCT)*: The RCT is particularly appropriate for determining the benefits of screening because it circumvents the limitations imposed by the screening biases of lead-time, length, and overdiagnosis. In the RCT, individuals are randomized to one or more groups in order to equally distribute the known and unknown variables that may influence outcome *(Figure 2)*. The outcome variable, disease-specific mortality, is measured from the time of randomization. As such, any differences seen between the groups may be ascribed to the intervention itself.

2.7.3 *Limitations of the RCT*: Despite the strengths of the RCT in determining screening effectiveness, there are a number of challenges associated with this design. First, the validity of the outcome measurement, lung cancer-specific mortality, depends upon the integrity of the different cohorts with respect to assigned interventions. All study participants must comply with the intervention to which they have been randomized. In practice, a proportion of Experimental participants will drop out of the study for reasons of inconvenience, discomfort associated with the intervention, or simply lack of interest. Similarly, a proportion of Control participants will undergo the Experimental intervention, contaminating the Control group, should the intervention become widely available. Noncompliance by either group may diminish any observed effect of the intervention. With lung cancer screening, this would reduce the potential mortality benefit of screening. Non-compliance must be carefully factored into the parameters of experimental design and accounted for in sample size calculations.

The sample size requirements of a screening RCT and the required duration of surveillance of the separate cohorts are considerable. This is due to the fact that despite targeting individuals at highest risk of lung cancer, few participants will develop lung cancer. Moreover, because of the effects of lead-time and length bias, individuals with early stage diagnoses may have longer survival. Estimates of the sample size that would be required to detect a 30% difference in mortality between cohorts screened for lung cancer with helical CT exceed 20,000 participants. Another limitation of the RCT is misclassification. In the MLP, the Experimental group demonstrated excess lung cancers. Some have ascribed this to overdiagnosis bias in the screened participants. Similarly, underdiagnosis of lung cancer in the Control group *(misclassification of cause of death)* may have been contributory. Such underestimates of lung cancer incidence and mortality in the Control group would lower the observed benefit of screening. Determining the outcomes *(lung cancer incidence, cause of death, diagnosis or treatment complications, etc.)* of all participants in the RCT requires aggressive, long- term surveillance of the cohorts and medical follow-up with chart reviews, physician communication, and review of the National Death Index, processes that are time and labor intensive.

Finally, as with any clinical research design, it is important that the methods can be generalized: they must reflect as much as possible the practices likely to be operative in the community at large, while also ensuring the best opportunity to detect mortality benefit.

2.8 Limitations of Helical CT Screening

The experiences of ELCAP and other CT screening trials also portend the potentially deleterious effects of CT screening due to the detection of large numbers of small, indeterminate nodules that will require additional evaluation. Small nodules in high-risk individuals may require biopsy or, at a minimum, repeated CT scans over 2-3 years to ensure the absence of growth.[44] In the ELCAP prevalence screen, 23% of all screening CT scans were abnormal, meaning that one or more nodules of indeterminate malignant potential were detected. Of these, the majority of nodules were benign. The ELCAP trial followed participants with positive screens with limited high-resolution sequences through abnormal nodules. The images were analyzed using a proprietary program to determine the growth rate over time. Using this method of surveillance, there were no lesions referred for thoracotomy that were not malignant, suggesting that the positive predictive value of follow-up CT is extremely high. Although the proportion of positive *(abnormal)* incidence screening scans in this cohort have been much smaller, the participants have been followed in a controlled fashion using the same scanners and readers over time, a luxury that may not be reproducible across the country.

It is not known whether this degree of success in preventing unnecessary instrumentation for benign disease would be generalized across the country if CT lung cancer screening were to become public policy at this early stage. The indeterminate solitary pulmonary nodule is a vexing problem, particularly in persons at high lung cancer risk. Previous studies have shown that primary lung cancers comprise roughly 30-40% of lung nodules on chest radiographs.[51,52,53] In some reports, half of all surgical

resections for indeterminate nodules yielded benign histologies.[54] The prevalence of indeterminate lung nodules *(e.g., positive screens)* on CT screens will necessarily be higher in regions of the country where certain granulomatous infections *(blastomycosis, coccidioidomycosis, and histoplasmosis)* are common. For example, the Mayo Clinic, where histoplasmosis is endemic, has also reported initial data using low dose helical CT, and observed positive CT screening exams in 51% of prevalence and roughly 15% of incidence scans, respectively.[55] Some investigators recommend that small nodules *(< 5 mm)* be followed with imaging at regular intervals to minimize unnecessary biopsy or surgery.[44]

Additional concerns regarding the utility of screening helical CT include the selection of optimal acquisition parameters, examination costs, and greater time requirements for study interpretation, a limitation for which computer-assisted analysis may be a partial solution.[56]

2.9 Assessing Quality of Life, Psychological Impact, and Economic Costs of Lung Cancer Screening

The traditional measure of cancer screening is a reduction in lung cancer-specific mortality with acceptable financial and medical risks. In recent years, increasing attention has been placed upon screening-related quality of life and psychological impact.[57-63] Such influences begin with the invitation to participate in screening and accrue at each step of the screening process.[57] Throughout the process, participants may experience increased anxiety, intrusive thinking, and depression in the context of screening for a life-threatening disease.

The psychological impact of lung cancer screening with low-dose helical CT merits study for several reasons. First, the baseline screening CT exam is associated with a relatively high false-positive rate, which has ranged from approximately 20% to 50% in two large series performed in the United States.[44,55] Second, the majority of individuals with false-positive studies will require close follow-up CT scans for a minimum of 2 years to confirm the benign nature of a nodule.[44] The unique combination of a high false-positive rate and the long period of observation to confirm a benign diagnosis suggests that lung cancer screening with CT may be associated with a higher psychological impact than traditional screening studies for other cancers.[64]

Positive screening results will trigger additional evaluation that can be expected to produce some degree of physical discomfort and anxiety. These psychological and physical effects will affect participants in whom cancer is established as well as participants with ultimately benign nodules. In both instances, screening may negatively impact quality of life. Although it is expected that the psychological impact of screening will vary among individuals, the psychological cost is likely to be highest in those with false-positive screens and in those determined to have untreatable disease.[57]

Despite these considerations, the earlier detection of lung cancer may be expected to lead to earlier treatment. To the extent that screening is successful, screened participants may realize less suffering from lung cancer. In a previously published cost-effectiveness analysis of mammographic screening, de Haes[65] found that adjustment for quality of life decreased the effectiveness of screening by about 8%, but not enough to eliminate the benefit derived from reduced breast cancer mortality. However, there is currently no data or hypothetical analysis available to indicate how adjustments for quality of life will affect quality associated life years due to lung cancer screening.

This trial provides the opportunity to assess the issues of screening-related quality of life and anxiety. As well, it will enable the benefits of screening to be weighed against the economic costs of a screening program. To our knowledge, no paper has summarized the economic costs for each year of life gained or each quality-adjusted year of life gained as the result of lung-cancer screening with helical CT. Beyond providing information about the psychological consequences of screening, this research may prove useful for influencing screening design, developing strategies to reduce screening-related anxiety, and enhancing compliance with the screening process.

2.10 Lung Cancer Screening with Biomolecular Markers

Lung cancer results from a complex interaction between genetic predisposition and environmental influences. According to the concept of multi-step carcinogenesis, malignant transformation results from the process of initiation, in which exposure of the respiratory epithelium to carcinogens affects mutations

in specific genes, proto-oncogenes, and tumor suppressor genes.[66,67,68] Once epithelial cells undergo initiation, cellular proliferation and monoclonal expansion of the malignant cells depends upon tumor promotion, which is affected by various environmental carcinogens and cellular growth factors such as epidermal growth factor *(EGF)* and gastrin-releasing peptide *(GRP)*. Although lung cancer typically occurs with exposure to carcinogens such as tobacco smoke, radon, etc., there are wide variations in individual susceptibility that relate to these molecular genetic factors. This accounts for the fact that some individuals with heavy tobacco consumption develop lung cancers while others do not.

Table 3: Oncogenes and Markers Associated with Lung Cancer

Oncogene	Mutation	Frequency*	Primary Histology
Dominant Oncogenes or Protooncogenes: Promote Cellular Deregulation			
K-ras	Point mutation	30%	Adenocarcinoma
erb B1 *(or EGFR gene)*	Overexpression	20%	Squamous cell
EGFR *(erb B1 gene product)*	"	90%	Squamous cell
	"	20-75%	Adenocarcinoma
erb-B2 (or *Her-2/neu*)	Overexpression	27-36%	Adenocarcinoma
Recessive Oncogenes or Tumor Suppressor Genes			
p53	Deletion or Point mutation	50-80%	All
3p	Deletion	50%	All
Tumor Associated Antigens Found on Sputum Epithelial Cells			
Hn-RNP *(31 KD glycoprotein)*		90%	NSCLC

* Frequency of occurrence in NSCLC

Several genetic abnormalities have been associated with lung premalignancy or overt lung cancers *(Table 3)*.[69,70,71,72] These gene mutations and their products can be identified in extremely small quantities from sputum and tissue samples using contemporary techniques in molecular biology such as polymerase chain reaction *(PCR)*, single strand conformation polymorphism *(SSCP)* analysis, differential nucleic acid hybridization, and nucleic acid sequencing. The probability of successfully sampling the sputum for epithelial molecular markers of carcinogenesis is enhanced by field carcinogenesis, the concept that exposure of the entire respiratory epithelium to inhaled carcinogens transforms cells throughout the lung. Sputum samples may not contain cells from the most advanced focus undergoing neoplastic transformation but may contain evidence of the proliferative stimuli affecting the epithelium. Moreover, these cells and cancer-associated gene products are shed into the blood stream and may also be found in urine and other body samples.

Tumor-associated antigens expressed on sputum epithelial cells have been identified in sputum samples up to two years prior to the development of non small-cell lung cancer using tumor-associated monoclonal antibodies *(Mab)*. The Mabs detect a 31-Kd glycoprotein cell surface antigen homologous to hnRNP. When the latter was used to examine archived sputum samples from the Johns Hopkins screening trial[23], antigen overexpression was demonstrated in over 90% of lung cancers and predicted NSCLC in individuals with moderate atypical metaplasia who later developed lung cancer with a sensitivity of 91% and a specificity of 88%.[73] Preliminary results of prospective trials by the Lung Cancer Early Detection Working Group *(LCEDWG)* using hnRNP to detect preclinical lung cancer have shown that hnRNP overexpression was predictive of outcome in 32 of 40 participants at risk of a second primary lung cancer within 12 months and was predictive of outcome in 69 of 94 miners at risk of primary lung cancer. Up regulation of hnRNP in sputum correctly predicted cancers in 67% and 69% of patients within these cohorts, respectively.

The classical cancer progression model suggests that cells progress from normal to hyperplasia *(regular metaplasia)*; to slight, moderate, and marked dysplasia; and finally to neoplasia. Overexpression of hnRNP predates morphologic abnormalities in 94% of LCEDWG cases and persists throughout carcinogenesis[74], whereas many of the other markers, such as K-ras and p53 mutations, are seen in half or

more cells with moderately atypical metaplasia.[75,76,77] It may prove that hnRNP expression is the earliest, most sensitive marker of carcinogenesis, while K-ras and p53 mutations and 3p or 9p losses of heterozygosity are late, more specific markers of neoplasia.

These data are optimistic; however, there is no existing panel of markers that will reliably identify pre-malignancy or early lung cancer. Moreover, the collection of sputum samples requires strict quality control mechanisms in order that cellular yields are genuinely representative of the lower respiratory tract rather than the oropharynx, which would be expected to influence epidemiologic results. The cohorts in this study participating in biomarker collection will undergo annual collection of blood (both serum and buffy coat), urine and sputum, which will provide a rich foundation for testing biomarkers found to be promising in preliminary tests conducted outside of the ACRIN trial. Participants will be fully characterized and followed for at least six years. The detection of biomarkers occurring regularly in the setting of pre-malignancy or very early malignancy would have profound implications for more precise selection and stratification of populations at risk for lung cancer and would influence diagnostic strategies to localize lesions using fluorescent bronchoscopy, volumetric CT, or PET. Moreover, the detection of pre-neoplasia would identify cohorts who may benefit from biomarker modulation through aggressive primary prevention with smoking cessation, chemoprevention, or new methods of gene therapy to enhance programmed cell death.

Urine also provides a potentially rich substrate for determining risk of lung cancer, prognosis, and potential methods of treatment. Urine is a rich source of secretory proteins *(natural occurring angiogenesis compounds including Endostatin and Angiostatin were discovered from the urine)*. With continuing rapid advances in proteinomics, urine represents a potentially invaluable source of biomarkers unique to cancer patients. For example, it has become possible to compare protein expression from urine in patients with malignancies to urine from normal individuals in an effort to determine differential expression, and thus create tumor protein profiles. These extremely powerful techniques are unlike genomic array analyses that examine known genes, as the entire spectrum of proteins *(known, unknown, or unsuspected)* could be evaluated. This discovery process could lead to molecular profiles that could then be correlated with clinical data to provide both prognostic and therapeutic information.

2.11 Ethical Considerations of Screening

Also at the heart of screening for lung cancer is the reality of differential health care access across the diverse socioeconomic strata of the United States. Lung cancer cuts across all such boundaries; any multicenter trial must incorporate these diverse strata, ensuring the participation of individuals who may be fully insured, underinsured, and uninsured.

By its very nature, the screening process will convert some ostensibly healthy individuals into patients, who will then be subject to medical interventions at some level of emotional, economic, and medical expense. One challenge of a screening trial is in the execution of a thoughtful, well-designed study with appropriate end-points. Equally important is the challenge of ensuring that outcomes relate to the intervention and are not obscured by differential health care access and treatment due to socioeconomic status.

For example, it is conceivable that a multi-racial screening trial could show mortality advantages for specific ethic groups solely on the basis of differential health care access following a positive screening test. The screening test itself is important only in so far as it advances the diagnosis of cancer such that early intervention is curative, prolongs life (beyond lead time bias), or improves the quality of life. If the evaluation of a positive screening test *(or its speedy treatment)* is delayed in economically disadvantaged persons for lack of financial or medical resources, it is likely that mortality benefit will be realized non-uniformly.

One of the ways in which this trial distinguishes itself is in the clear provision of standardized guidelines for the management of the positive screening test. It is the sincere belief of the study investigators that there is some obligation within the trial to provide medical assistance to the few participants who lack medical resources with which to undergo appropriate evaluation for positive screening tests. It is only

through these provisions that the trial will effectively represent all racial and economic interests as well as ensure that the trial outcomes relate to the screening intervention itself rather than to barriers to the underinsured, the uninsured, and the economically disadvantaged.

2.12 Summary

There is no data yet to show that low-dose helical CT screening will realize a decrease in lung cancer specific mortality. By analogy to the early lung cancer screening trials, a decrease in mortality cannot be inferred by prolonged survival. Moreover, none of the current screening trials has experimental controls, which precludes the determination of the single most valid measure of screening benefit: lung cancer-specific mortality.

The following things are apparent at this time:

- CT screening will detect more cancers, cancers of earlier stage and smaller cancers than are routinely detected by CXR or symptoms;
- Small tumor size, within the size range of early stage *(T1)* cancers, has not been shown to be predictive of the cancer's propensity to spread and cause death;
- Lead-time, length, and overdiagnosis obscure the significance of prolonged survival with screening;
- Prolonged survival does not confer a mortality reduction and does not validate screening effectiveness;
- Prevalence screening CT scans will be abnormal in roughly 20-50% of screened individuals, depending upon the prevalence of granulomatous disease and other respiratory conditions in the screened population. Although fewer incidence-screening tests will be abnormal, the percentage of abnormal incidence screens over time, and their significance, are not known;
- Although the vast majority of abnormal screening studies will be due to benign disease, individuals with abnormal screening CT will effectively become patients, subject to psychological consequences and additional unnecessary, potentially dangerous, procedures such as biopsy or extended follow-up to ensure that the nodules are not cancer.

Given the billions of dollars that would be required to implement annual lung cancer screening for high risk individuals nation-wide, a randomized controlled trial will be critically important to determine whether CT screening confers true societal benefit.

3.0 SPECIFIC AIMS

3.1 Primary Specific Aim

To determine whether lung cancer screening using low-dose helical CT reduces lung cancer-specific mortality relative to screening with chest radiographs in a high-risk cohort.

3.2 Secondary Specific Aims

3.2.1 To compare all cause mortality between screening with CT versus chest radiographs.

3.2.2 To compare differences in stage distribution between the two arms of the study.

3.2.3 To compare lung-cancer related medical resource utilization between the two arms of the study.

3.2.4 To compare issues of quality of life and psychological impact associated with annual screening and with a positive screening test between the two arms of the study.

3.2.5 To assess the economic consequences of screening with CT versus chest radiographs.

3.2.6 To develop a tissue bank from individuals at high risk of lung cancer both with and without pathologically proven lung cancers. This bank will be a rich resource for determining biomolecular markers of high predictive value in stratifying levels of lung cancer risk such as pre-malignancy *(risk of future development of lung cancer)*, subclinical lung cancer, and advanced disease.

3.2.7 To assess the impact of screening on smoking behaviors.

4.0 PATIENT RECRUITMENT AND SELECTION

4.1 Recruitment Strategies

Methods of recruiting high-risk current and former smokers will vary across sites, depending upon the specifics of the participant demographics and resources available.

4.1.1 All sites will base initial recruitment on a national launch coordinated by the NCI Office of Communication. This plan will include a video news release (VNR) for broadcast via satellite, to be promoted in advance to stations in markets of the participating sites. The NCI will also sponsor a teleconference for media outlets allowing for questions and answers with the principal investigators of the NLST or other representatives. The teleconference and VNR will occur on the same afternoon.

In-house resources of the NCI, specifically the Cancer Information Services (CIS), have developed a protocol specific for the NLST. The initial media launch will direct all interested individuals to a toll free number (1-800-4-CANCER) for information about the trial. Trained operators will provide an initial screening to determine eligibility by ascertaining the following data:

- Age 55-74 and 364 days
- Current or former (quit within the last 15 years) smoker
- No history of lung cancer
- No treatment for, or advisement by a physician of evidence of *any* cancer within the past five years, with the exceptions of non-melanoma skin cancer and most in-situ carcinomas. (Treatment for, or evidence of, melanoma or in-situ bladder/transition cell carcinomas within the preceding five years renders the potential participant ineligible.)
- Not enrolled in any other screening or cancer prevention trial
- No chest CT within the prior 18 months

Eligible individuals will be directed to the nearest screening site based on their calling area code. Ineligible individuals will be offered NLST brochures to share with others as well as the availability of referral to Smoking Cessation Call Centers across the country. Former smokers will be given reinforcement for their success at quitting smoking.

Printed materials, including a brochure describing the NLST trial, a question and answer (Q&A) fact sheet, and a web site with downloadable information, as well as pointers to the various NLST sites and other cancer information services, have been developed in conjunction with the joint ACRIN and LSS groups comprising the NLST.

Additional recruitment efforts will involve four primary strategies:

4.1.2 Recruitment by regional public service announcements. Many of the accrual institutions are located in urban areas with large minority populations. With this in mind, local radio and newspaper announcements will be distributed to establish cohorts that include both genders and that accurately represent the racial diversity of the communities. All such media announcements will be approved by the ACRIN Lung Committee and the NCI in advance of their use.

4.1.3 Recruitment through communication with individual physicians, primary physician groups, and lung health programs, and by educational promotion through existing medical clinics and community health programs, free health clinics, women's health centers, hospitals, imaging centers, and cardiovascular clinics.

4.1.4 Targeted mailings within the cities that span the regional ethnic demography. The infrastructure for this method of solicitation is already in place with the Lung Screening Study (LSS) of the PLCO, with which the ACRIN Lung Study has developed a common experimental methodology. The ACRIN and LSS recruitment sites are dissimilar, which will help to ensure that targeted mailings can be successful as a primary means of recruitment for the ACRIN Lung Study without compromising the LSS.

4.1.5 Existing high-risk cigarette smoking cohorts that are already established in conjunction with other trials, or that may be available through organizations that maintain such databases, may be eligible for inclusion pending approval of the respective funding agencies and investigators. For example, participants who satisfy eligibility criteria for this screening trial may be drawn from the following cohorts:

4.1.5.1 Participants screened or enrolled for the Lung Health Study *(LHS) (N = 6000)*. The LHS followed middle-aged cigarette smokers with mild COPD in whom two interventions *(smoking cessation and inhaled anticholinergic bronchodilator)* were compared with smokers receiving *no* intervention.

4.1.5.2 Participants who undergo pre-screening for participation in the National Emphysema Treatment Trial *(NETT)* or the retinoic acid treatment trials. Such individuals must undergo spirometry as part of the determination of eligibility, thus ensuring a means to confirm that they have sufficient pulmonary function to qualify for the ACRIN screening trial.

4.1.6 Potential participants who have been informed of the trial based on targeted mailings, information brochures, or public announcements will indicate interest by returning a reply card *(available with mailing and information brochures)* or by contacting the site by telephone. In the case of written reply cards, the site will contact the potential participant by telephone to administer the E1 Eligibility Form. With telephone reply, the form will be administered at the time that the interested individual calls the site.

4.1.7 Some sites may elect to allow potential participants to complete portions of the E1 Form by mail. The participant-completed questions will be faxed to a dedicated FAX line or mailed to the site upon completion. The site RA will review the form to confirm initial eligibility, contact the potential participant to complete any remaining eligibility questions, and advise individuals of their eligibility status.

4.2 Inclusion Criteria

Based on published relative risk factors for lung cancer development, the following criteria are designed to establish cohorts at highest risk of lung cancer.

4.2.1 Age 55-74 years and 364 days.

4.2.2 Current or previous cumulative cigarette smoking history of $\geq$ 30 pack years *(packs per day multiplied by the number of years smoked).*

4.2.3 Former smokers must have quit smoking within the previous 15 years.

4.2.4 No medical or psychiatric condition precluding informed medical consent.

4.3 Exclusion Criteria

Exclusion criteria are intended to eliminate from consideration individuals unable to give informed consent or who, by virtue of medical disability, would unlikely survive to the end of the trial period. Also excluded are individuals unlikely to complete curative lung cancer surgery *(e.g., thoracotomy with lobectomy or pneumonectomy)*, individuals presenting with symptoms suggestive of lung cancer; individuals who have had recent chest imaging; or those with physical conditions that would preclude high quality screening CT. The exclusion criteria are:

4.3.1 Inability to lie on the back with arms raised above the head. Supine positioning, with or without the support of pillows under the head or extremities, with arms briefly resting above the head, is required for purposes of acquiring helical CT scans.

4.3.2 Metallic implants or metallic devices in the chest or back *(pacemakers or Harrington fixation rods, etc.)* that would cause sufficient beam hardening artifact so as to degrade image quality in the lungs.

4.3.3 Prior history of lung cancer.

4.3.4 Treatment for, or advisement by a physician of evidence of *any* cancer within the past five years, with the exceptions of non-melanoma skin cancer and most in-situ carcinomas. (Treatment for, or evidence of, melanoma or in-situ bladder/transition cell carcinomas within the preceding five years renders the potential participant ineligible.)

4.3.5 Prior removal of any portion of the lung, excluding percutaneous lung biopsy.

4.3.6 Requirement for home oxygen supplementation for respiratory conditions.

4.3.7 Participation in another cancer screening trial (such as the PLCO, ELCAP, or single arm trials such as those of the Mayo Lung Trial, Jewish Heart and Lung Institute, or the Moffitt Lung Trial).

4.3.8 Participation in a cancer prevention trial other than smoking cessation programs.

4.3.9 Present symptoms suggestive of lung cancer, including unexplained weight loss of over 15 lbs within the past 12 months, or unexplained hemoptysis.

4.3.10 No medical condition that poses a significant risk of mortality during the 8-year trial period.

4.4 Criteria for Postponement of Eligibility

Eligibility to participate in the ACRIN Lung Study and randomization should be postponed until the period of time in question under the following conditions:

4.4.1 Individuals within 12 weeks of a pneumonia or acute respiratory infection treated with antibiotics by a physician. *(These individuals would be eligible 12 weeks from the first dose of antibiotics.)*

4.4.2 Individuals within 6 months of receipt of cytotoxic agents for any condition. *(These individuals would be eligible 6 months from the last dose of the agent from the final cycle.)*

4.4.3 Chest CT scan within the preceding 18 months of study enrollment. *(These individuals would be eligible 18 months after chest CT.)*

4.5 Informed Consent

The study specific informed consents must be signed prior to study enrollment.

5.0 CRITERIA FOR SITE PARTICIPATION

5.1 Requirements

5.1.1 Approved as an ACRIN Institution.

5.1.2 Submit a protocol-specific application to ACRIN, including specification of CT scanners and chest radiographic machines to be used, qualifications of participating radiologists, qualifications of participating technologists and medical physicists, and satisfaction of interpretation competence *(see Appendix VII).*

5.1.3 Provide to ACRIN IRB documentation, consisting of a copy of full IRB approval of the protocol and the sample institutional study-specific consent form.

5.1.4 Designate a physician who is willing and committed to participate and oversee the trial at the site.

5.1.5 Have the participation of a Research Associate *(RA).*

5.1.6 Have Internet access for entry and transfer of data.

6.0 STUDY DESCRIPTION AND RANDOMIZATION SYSTEM

6.1 Enrollment Visit and Registration

6.1.1 Participants determined to be eligible based on completion of the E1 Eligibility Form by telephone or live interview will be scheduled for the Enrollment Visit. Since there may be a delay between initial E1-eligibility determination and the enrollment visit, the E1 will be re-administered at the enrollment visit, prior to registration/randomization, to confirm current eligibility. At the Enrollment Visit, the following procedures will be completed:

6.1.1.1 Explanation of the study intention and design.

6.1.1.2 **Informed Consent:** Once eligibility has been established, the potential participant will be consented. The individual will be provided with background information about the study and its goals. The requirements of the study, the implications of randomization, and the necessity for completing the required procedures will be emphasized. Permission will be asked to review medical records (*see Medical Record Release Authorization, or MRRA Form*), store image data, or contact family members to determine medical outcomes. In addition, consent to collect and bank blood, sputum, and urine specimens (*amongst biomarkers participants, Group 1 sites)* and to collect and store tissue specimens that may be obtained subsequent to diagnostic work-up for a positive screen will be obtained *(specimen consent is not mandatory for participation in the ACRIN-NLST trial).*

The following consents will be requested:

[1] General Consent Group 1: Consent to participate in the randomized trial comparing screening CT with chest x-ray. The consent includes review of medical records, contacting participant family or friends to determine participant health or vital status, storage of image data, and completion of various quality of life questionnaires.

[2] General Consent Group 2: Consent to participate in the randomized trial comparing screening CT with chest x-ray. The consent includes review of medical records, contacting participant family or friends to determine participant health or vital status, and storage of image data

[3] Medical Records Release Authorization

[4] Consent to obtain and bank specimens of blood, urine, and sputum at a central specimen repository (Colorado Lung SPORE Tissue Bank)

[5] Consent to bank tissue obtained in the course of diagnostic evaluation of positive screens at a central specimen repository (Colorado Lung SPORE Tissue Bank)

SITES	**CONSENTS TO BE OBTAINED**
Group 1 (10,000 participants)	Consents [1] [3] [4] [5]
Group 2 (15,000 participants)	Consents [2] [3] [5]

Individuals will be advised that their participation is voluntary and that their decision to participate or not to participate will have no effect on their current or future medical care. Efforts will be made to match the ethnicity of the potential participant with that of the interviewer, enlisting the part-time assistance of specifically trained interviewers who can speak Spanish, Farsi, or appropriate Asian languages and dialects. Potential participants for whom English or other appropriate language translation is not available must submit to the NCI documentation of IRB approval to administer an English language ACRIN-NLST Lung Study consent to non-English speaking individuals. All participants will be reimbursed for time and travel at the completion of their screening examinations.

6.1.1.3 Completion of Questionnaires: Following informed consent, all potential participants will complete a detailed Contact Information Form, Sociodemographic/Health Status/Health Habit/Symptom Form (*DP Form*), and Tobacco Assessment Form *(SS Form)* as part of risk profile assessment. The contact information forms are a prerequisite to participation in the trial and are intended to ensure that participants can be reached throughout the course of the trial.

6.1.1.4 Quality of Life Instruments [Group 1 Participants only]: Individuals able to read or understand English or Spanish will complete a baseline quality of life questionnaire that includes both the SF-36v2 and EuroQuol EQ-5D instruments (*QP Form*). As inferred in Section 6.1.1.2 above, participant ethnicity or literacy in English does not influence overall eligibility for the NLST, as informed consent may be administered by translators fluent in the language of the potential participant. However, the quality of life instruments to be administered for the quality of life sub-studies have not been validated in all languages. As such, the NLST will solicit quality of life information only from participants who read or understand English (*American*) or Spanish to preserve the validity of the data collected.

6.1.1.5 Spirometry: Spirometry will be obtained as part of risk profile characterization using standardized procedures. The same hand-held device will be used across all sites. Forced vital capacity *(FVC)*, forced expiratory volume in one second (*FEV_1)*, and the ratio of FEV_1/FVC will be calculated and expressed in absolute terms and as a percentage of predicted values. This information will be recorded on the Pulmonary Function Data

Form *(PA Form)*. Spirometry may be performed before or after enrollment and randomization, according to the specific scheduling constraints of the individual sites.

6.1.1.6 Collection of Specimens for Banking [Group 1 Participants only]: Samples of blood and urine for the specimen banking portion of the study will be collected following randomization. Specimen containers and instructions for the collection of sputum samples at home will also be provided to participants at the time of blood and urine sample collection. Specimen collection kits with unique bar codes are provided to all sites by the Colorado Lung SPORE Tissue Bank. These kits are used at the individual sites to collect all specimens. Bar codes are linked with the NLST participant ID at the ACRIN site; the Colorado Lung SPORE Tissue Bank does not have access to participant identification. Participants may refuse to have samples collected and still participate in the ACRIN trial. Participants who have refused specimen collection at Baseline will *not* be asked to consent to specimen collection in Years 2 or 3. However, efforts *should* be made to obtain consent to procure remnant tissue from participants who undergo a screening–related tissue biopsy or lung resection**.**

6.1.1.7 Registration: The RA will register the participant by logging onto the ACRIN web site *(www.acrin.org)* and selecting the link for Data Center Login. The system triggers a program to verify that all regulatory requirements *(OHRP assurance, IRB approval)* have been met by the institution. The registration screen begins by asking for the date on which the eligibility checklist was completed, identification of the person who completed the checklist, whether the potential participant was found to be eligible on the basis of the checklist, and the date the study-specific informed consent form was signed.

Once the system has verified that the potential participant is eligible and that the institution has met regulatory requirements, it assigns a participant-specific case number. The system then moves to a screen, which confirms that the participant has been successfully enrolled/randomized. This screen can be printed so that the registering site will have a copy of the registration for the participant's record. Two e-mails are generated and sent to the registering site: the Confirmation of Eligibility and the participant-specific calendar. The system creates a case file in the study's database at the Data Management Center *(DMC)* and generates a data submission calendar listing all data forms, images, reports, and the dates on which they are due. To avoid duplicate randomizations, do not re-register or re-randomize a participant; contact the DMC regarding any questions or problems.

Participants will be randomized into Experimental and Control arms in equal proportions using the ACRIN web site. Randomization will be stratified by age, gender, and screening center and blocked, such that at each center each arm will have equal numbers of participants within each gender and age category. Only randomization requests made by personnel designated by the PI of the site and the ACR will be accepted. Randomization requests may be made 24 hours/day using the Internet Services Provider *(ISP)* of each site. Such a configuration employs current, proven Internet infrastructure and is the most economical solution for real-time, reliable access to a centralized computer server.

6.2 Unsuccessful Registrations

6.2.1 If the potential participant is ineligible or the institution has not met regulatory requirements, the system switches to a screen that includes a brief explanation for the failure to register the potential participant. This screen can be printed.

6.2.2 In the unlikely event that the ACR web registration site is not accessible, participating sites may still register a participant by faxing the completed eligibility checklist to the DMC at the ACR *(215-574-0300, ATTN: PARTICIPANT REGISTRATION)*. ACR staff will fax a response to the

registering site with the confirmation of registration and participant case number and randomization status as soon as possible.

6.2.3 Any problems or questions regarding registration or randomization of participants should be directed to the DMC. Never re-register or re-randomize a participant as this may lead to duplicate case randomization.

7.0 DATA COLLECTION AND MANAGEMENT

7.1 General

7.1.1 The ACRIN web address is *www.acrin.org*.

7.1.2 Data collection and management will be performed by the Biostatistics and Data Management Center *(BDMC)* of ACRIN under the direction of Dr. Constantine Gatsonis. The Biostatistics Center *(BC)* is located at the Center for Statistical Sciences in Providence, RI, and the Data Management Center *(DMC)* is located at the American College of Radiology's Data Management Department in Philadelphia, PA.

7.1.3 The BDMC uses screens on the ACRIN web site to register participants, collect participant data, and maintain calendars of data submissions for each participant. By using the World Wide Web, ACRIN has made participant registration, data entry, and updated calendar information available to clinical sites 24 hours a day.

7.2 Clinical Data Submission

7.2.1 As soon as a participant has been registered, the RA may download the participant's data submission calendar, which lists all forms and/or designated reports required by the protocol, along with the date that each form is due at the DMC. The form due dates refer to the data submission timeline and may or may not refer directly to the study activity timeline; all study activities should occur as specified by the protocol. These calendars will be updated as the study proceeds to reflect data that has been received, reply deadlines for queries about unclear data, deadlines for follow-up reports of adverse events, or revisions to the protocol which might change the data being collected or its timing. Updated calendars for each participant can be obtained 24 hours a day from the ACRIN web site.

7.2.2 An investigator is obliged to submit data according to protocol as detailed on each participant's calendar as long as the participant is alive and the case status is designated as open or until the study is terminated. The case is closed when all data has been received, reviewed, and no outstanding queries exist for the case.

7.2.3 To submit data via the ACRIN web site, the RA or investigator logs onto the web site and supplies the preassigned user name and password. Case report forms will be available on the web site through a series of links. The user selects the link to the appropriate form and enters data directly into the web-based form. As information is entered into the case report form, various logic checks will be performed. These logic checks look for missing data, data that is out of range, and data that is of the wrong type *(e.g. character data in a field requiring numeric responses)*. Such errors will be detected as soon as the user attempts to either submit the form or to move to the next page. Errors must be corrected before the form is transmitted to the DMC. The user will not be able to finalize form transmission to the DMC until all data entered passes these logic checks. Forms that are not completed in one sitting can still be submitted and completed at a later date. The data is transferred to the DMC and held.

7.2.4 Once a form is complete, the investigator presses the SUBMIT button on the participant calendar, and the data is transferred into the clinical database. No further direct revision of the submitted data is allowed after this point. An e-mail is generated and sent to the site listing all of the data just completed and submitted. Should a problem occur during transmission, this automated response supplies an explanation and instructions for resubmitting the data.

7.2.5 If a temporary problem prevents access to the Internet, investigators should wait until access is restored to submit data. Investigators should notify the DMC of the problem, and the DMC will give an estimated time when access is expected to be restored. If access will be unavailable for an extended period, sites must seek another Internet Service Provider *(ISP)*. On a short-term basis, the ACR can serve as an ISP.

7.3 Data Security

The registration system has built-in security features, which encrypt all data for transmission in both directions, preventing unauthorized access to confidential participant information. Access to the system will be controlled by a sequence of identification codes and passwords.

7.4 Electronic Data Management

7.4.1 Data received from the web-based forms is electronically stamped with the date and time of receipt by the ACRIN server. The data is then entered into the database. A validation program is used to perform more extensive data checks for accuracy and completeness, etc. The logic checks performed on the data at this point are more comprehensive than those built into the web-based data entry screens. They include checking that answers are logical and based on data entered earlier in the current form. This validation program produces a log of errors, which is sent to the RA for resolution. This program is frequently updated to incorporate exceptions to rules so that subsequent, correctly entered data pass validity checks, minimizing the time the research associate at the DMC needs to spend resolving problems. Additional data review will take place once the data is transferred to the BC. The BC will run thorough cross-form validations and frequency distributions to look for unexpected patterns in data and other summaries needed for study monitoring. Any errors found at the BC will be reported to the DMC Coordinator for protocol 6654 for resolution.

7.4.2 If the program detects missing or problematic data, the DMC Coordinator will send a Request for Information *(Z1)* to the research associate at the institution specifying the problem and citing the case number, form type and specific elements in need of clarification/revision. The Z1 also provide a means of response from the institution. The DMC Coordinator then updates the participant's data submission calendar with the due date for the institution's response.

7.5 Missing and Delinquent Data Submission

In addition to providing the institution with a data collection calendar for each case, institutions are periodically prompted for timely submission of data through the use of a Forms Due Report. This is distributed at least quarterly via e-mail to both the RA and the PI at each site. The Forms Due Report is not a punitive report, but rather a tool to prompt submission of overdue data and serve as a tool to help reconcile data discrepancies between the DMC's case file and that of the institution.

7.6 Data Quality Monitoring

7.6.1 The BC at Brown University will maintain a study database at its site for monitoring data quality and for performing interim analyses. These data will be drawn directly from the DMC's permanent database using a Power Builder utility that allows BC staff to log onto the DMC computer and select needed data. This analysis database will be maintained in permanent SAS *(Statistical Analysis System software)* format on the BC's ACRIN server and updated on a scheduled basis, usually monthly, once the study is in its steady state. Any discrepancies and other data quality issues will be referred to DMC for resolution, since only the DMC can correct the data file. No changes to the data will be made at the BC.

7.6.2 A major goal of the monitoring of data in the BDMC is to assess compliance with the protocol and to look for unforeseen trends that may be indicative of procedural differences among clinical sites. If patterns are discovered in the data, which appear to arise from causes specific to an institution, the BDMC will apprise the site of the problem and work with the site until the

problem has been resolved. If the BDMC cannot find a solution, the problem will be brought to the Executive Committee for further discussion and resolution.

7.6.3 The BC, in conjunction with the DMC, will prepare frequent summaries of the accrued data to be presented to investigators. These summaries will report accrual rates *(overall and by sub-groups of interest to the investigators)*; assess the completeness and accuracy of the data; and discuss any trends that may impact the outcomes of the trial. These intermittent summaries will not include analyses of the study's endpoints.

8.0 DATA COLLECTION

8.1 Data Collection Forms

These are the various forms to be used for the ACRIN 6654 Lung Screening trial. Although many of the forms are completed by the RA directly, others may be completed on paper by participants, physicians, or other personnel and checked by the RA for completeness and legibility. All data are submitted electronically via the web by the RA. Any missing data elements are to be completed before proceeding to other data forms and/or questionnaires. Unless otherwise stated, the completed forms are kept in each participant's folder at the site and entered electronically into the ACRIN web site. All forms are completed at all sites unless otherwise specified.

1) **A0: Eligibility/Registration Form:** This form is the online registration form accessed via the ACRIN web site (www.acrin.org). The online registration provides the randomization for each participant. It also provides a unique case number for each participant. At the time of registration, informed consent is to be signed and dated. In the event of online registration failure, this form can be faxed to ACRIN headquarters.

2) **BL: Biomarker Collection Form:** [Participants of Group 1 sites only]: This form is completed by the RA at the time that samples are obtained from consenting participants. It documents the collection and labeling of the blood samples. A copy of the BL form accompanies the specimens, a copy is submitted to ACRIN via fax or mail, and a copy is retained at the site.

3) **C2: Screening CT Form:** This form is completed by the radiologist at the Baseline, Year 1, and Year 2 Annual Screening Visits. The form documents the technical quality of the helical CT scans, the radiologist's interpretation, and a final screening result. The form applies only to participants randomized to the Experimental Arm, Arm I. The form is submitted via the ACRIN web modules.

4) **Contact Information Form**: This form is completed at the Enrollment Visit. The form collects information used to maintain contact with the participant over the course of the trial as well as the name of a primary (*or other*) physician to whom results can be communicated. It also provides information about prior chest imaging studies and locations of those studies/reports. This form is retained at the site and is not submitted to the ACRIN master database.

5) **CS: Quality of Life Cover Sheet** [Participants of Group 1 sites only]: This form accompanies the Quality of Life Forms (QP, QL, and PQ Forms). It serves as the first page of those questionnaires, documents the time of completion of questionnaires, and notes whether the questionnaires were completed by the participant or with assistance. The form is completed by the RA and submitted by the site via the ACRIN web modules.

6) **CX: Cancer Progression Form:** This form is completed as part of the chart abstraction process and documents disease progression for participants in whom lung cancer is established during the trial. The form is completed by a medical abstractor using any necessary documents from the medical record(s), from the date of the positive screening test onward.

7) **DE: Diagnostic Evaluation and Staging Form:** This form is completed on participants in both Arms 1 and 2 who undergo any diagnostic procedures (*radiographic, medical, surgical*) in the course of evaluating a positive screening test. The form is completed by a medical abstractor using any necessary

documents from the medical record, from the date of the positive screening test onward. The form includes documentation of the source documents utilized, procedures performed, complications of those procedures, diagnoses (*clinical or pathologic*), and lung cancer stage, if applicable.

8) **DP: Demographic/Health Status/Health Habit/Symptom Form**: This form is completed by the participant (*or with assistance of the RA*) at the Enrollment Visit. The form records information on participant medical history, demographics and economic status, occupational exposures to potential carcinogens, respiratory symptoms, family history, and alcohol history. The form is submitted to ACRIN via the ACRIN web modules.

9) **DR: Screening Chest Radiograph Form:** This form is completed by the radiologist at the Baseline, Year 1, and Year 2 Annual Screening Visits. The form documents the technical quality of the CXR, the radiologist's interpretation, and a final screening result. The form applies only to participants randomized to the Control Arm, Arm II. The form is submitted via the ACRIN web modules.

10) **E1: Pre-Registration Eligibility Form:** The form is completed prior to informed consent and enrollment and determines eligibility for the ACRIN-NLST. The form may be completed by live or telephonic interview of participants, or by having participants complete site-specific web-based systems. For a participant to be eligible, the responses must reflect those indicated on the form as true or acceptable responses. Participants should not be advised what represents a qualifying response in order to minimize fraudulent answers. Since there may be a delay between initial E1 eligibility determination and the enrollment visit, the E1 will be re-administered at the enrollment visit, prior to registration/randomization, to confirm current eligibility. This worksheet is retained at the site and is not submitted to the ACRIN master database.

11) **ES: QF Coversheet** [Participants of Group 1 sites only]: This form accompanies the QF Quality of Life. It serves as the first page of the questionnaire, and is completed by the participant. The participant submits the completed paper form to the ACRIN Biostatistics Center (BC) by mail, along with the QF. The BC then submits the CS and QF forms to ACRIN Data Management Center for data entry (see Section 20).

12) **EX: Economic Assessments Form:** Data necessary to conduct comparative analyses of the costs of the two screening procedures will be collected throughout the study. The principal information will be units of utilization. Healthcare utilization will also be acquired for staging and treatment of disease recurrence in the two-year follow-up. Unit cost estimates will be based on Medicare reimbursement rates.

13) **F1 and F2: Follow-up Forms:** The F1 and its revision, the F2 Form, are completed by the participant at six month intervals to document changes in health status, interval medical encounters, medical interventions, (*with the names of facilities where performed*), changes in smoking behaviors, and changes in participation in other clinical trials. The forms will be used to determine cross-over between trial arms, medical resource utilization, and medical outcomes. All participants complete these forms. The forms are submitted by the site via the ACRIN web modules.

14) **FC: Vital Status Update and F1 Coversheet:** This form is completed by the RA at six month intervals or at the time of death of a participant. The form documents the vital status of participants and the source of information regarding vital status. For deceased participants, the cause of death, location of death, and date of request for death certificate are recorded. The form is submitted by the site via the ACRIN web modules.

15) **FS: Follow-Up Supplement:** This form is completed by the participant at 6-month intervals, as necessary, when participants indicate on F1 forms that they have had more provider visits or health care encounters than can be documented on the F1 form.

16) **I8: Historical Images –CXR Arm Form:** This form is completed by the radiologist at Baseline, Year 1, and Year 2 Screening Visits to record results of screening CXR *after* correlation with historical images.

This form applies only to participants randomized to the Control Arm, Arm 2. The form is submitted via the ACRIN web modules.

17) **I9: Historical Images-CT Arm Form:** This form is completed by the radiologist at Baseline, Year 1, and Year 2 Screening Visits to record results of screening CT *after* correlation with historical images. This form applies only to participants randomized to the Experimental Arm, Arm 1. The form is submitted via the ACRIN web modules.

18) **IM: Screening Results Form**: This form is completed by the RA and documents the dates when participant and health care provider letters are sent describing results of screening examinations as well as any diagnostic recommendations for follow-up.

19) **MRRA: Medical Records Release Authorization:** This form is completed at the Enrollment Visit and updated annually. It authorizes the site to obtain medical records from sites where the participant will be *(or has been)* seen. The form allows ACRIN to maintain image data, cytology, or histologic materials for up to ten years for purposes of research and to contact next of kin to determine cause of death as needed. The form is retained at the study site and not submitted to ACRIN.

20) **PA: Pulmonary Function Test Form:** This form is completed during the enrollment process by the RA based on the results of forced expiratory maneuvers performed on a hand-held spirometry device. Information source: the pulmonary function test results from the SpiroPro device (SensorMedics Corp.; Yorba Linda, CA). The form is completed by the RA and submitted by the site via the ACRIN web modules.

21) **Participant Medical Diaries:** These are optional self-completed work sheets that are provided to participants in order to expedite later completion of the F1 Forms. The diaries allow for the recording of all medical encounters by date, type of visit, and whether or not any medical interventions/procedures were performed. These diaries are not collected by the sites or by ACRIN.

22) **PC: Specimen Packing Form:** [Participants of Group 1 sites only]: This form is used to document shipping and receipt of processed blood and urine specimens to the Colorado Lung SPORE Tissue Bank (CTB) for those individuals participating in biomarker collection. The form is completed by the CTB and submitted via mail/fax to ACRIN headquarters to document receipt of samples.

23) **PQ: Participant Impact Questionnaire** [Participants of Group 1 sites only]: This form is completed by the RA on participants who require follow-up of a positive screening test. The form collects information on the subjective impact of the work-up on a participant resulting from the positive screen. The qualitative information includes time away from home or work and amount of discomfort the procedures may have caused. The form is administered to participants with a positive screening test *(Arms 1 and 2)* at the times specified in the protocol (see Section 20).

24) **PR: Protocol Variation Form:** This form is completed by the RA to document protocol deviations, when they occur.

25) **QC: Image Quality Form**: This form is completed by radiologists when reviewing subsets of screening exams for purposes of evaluating image quality.

26) **QF: Health Status/Anxiety Questionnaire (Screening SF-36v2™, EQ-5D, and STAI Y-1)** [Participants of Group 1 sites only]: This form combines two standardized, validated health status questionnaires (*SF-36v2™ and EQ-5D*) with the Spielberger State-Trait-Anxiety Inventory *(STAI-Form Y-1)*, which is used to measure anxiety. The form is administered to a subset of participants with a positive screening test *(Arm 1 and 2)* at the times specified in the protocol. The participant submits the completed paper form to the ACRIN Biostatistics Center (BC) by mail. The BC then submits the QF form to ACRIN Data Management Center for data entry (see Section 20).

27) **QL: Annual Health Status Questionnaire (SF-36v2™ and EQ-5D)** [Participants of Group 1 sites only]: This form combines two standardized and validated health status questionnaires. The form is completed by a subset of participants who read or understand English or Spanish. The form is completed at each annual screening or follow-up visit, according to the methods of the quality of life sub-study (see Section 20) and is submitted by the site via the ACRIN web modules.

28) **QP: Baseline Health Status Questionnaire (SF-36v2™ and EQ Euroquol EQ-5D)** [Participants of Group 1 sites only]: This form combines two standardized and validated health status questionnaires. The form is completed by participants at the Enrollment Visit who read or understand English or Spanish. This form is submitted by the site via the ACRIN web modules.

29) **SS: Smoking Status Form:** This form is completed by the participant (*or with the assistance of the RA*) at the Enrollment Visit. The form records detailed information on smoking history, cigarette brands smoked, smoking cessation thoughts, and second hand smoke exposures. The form is submitted by the site via the ACRIN web modules.

30) **ST: Sputum Transmittal Form:** [Participants of Group 1 sites only]**:** This form documents shipping/receipt of sputum specimens by the Colorado Lung SPORE Tissue Bank (CTB). The form is enclosed in the sputum collection kits given to participants for home collection; the site telephone number is added to the form by the RA. Participants mail their specimens in a self-addressed envelope to the CTB. Upon arrival at the CTB, the form is submitted via mail/fax to ACRIN Data Management Center. A copy of the ST form accompanies the specimens, a copy is submitted to ACRIN via fax or mail, and a copy is retained at the site.

31) **TF: Treatment Form**: This form is completed as part of the chart abstraction process and documents all treatments received by a trial participant in whom lung cancer is established during the trial. The form is completed by a medical abstractor using any necessary documents from the medical record(s), from the date of the positive screening test onward.

8.2 Data Collection Table

Timetables for submission of annual screening studies will be provided at the time of study enrollment (*participant calendars*). Data forms to be completed for follow-up studies will be determined by the results of screening examinations and regular contacts at six-month intervals.

9.0 IMAGE SUBMISSION

9.1 Wherever possible, all images are requested to be provided in digital format. ACRIN has developed software that allows for electronic transmission to the ACRIN image archive of images that have been scrubbed of all patient identifiers. Individual PC computers with this software installed will be supplied to each participating site. ACRIN will be contacting each site individually to determine their readiness and ability to work with this system. If you have preliminary questions, you may contact either Rex Welsh or Fraser Wilton *(215-574-3215)* for information about this system. Once readiness has been determined, imaging personnel from ACRIN will coordinate the shipment and installation of the PC computers and train all operating staff on use of the system.

9.1.1 Annual Screening CT and CXR images will be collected for this study only. At this point in time, provisions are not available for the archiving of additional diagnostic images.

9.1.2 When direct transfer and electronic media *(CD, disk, tape)* of CXR images is not available, original images on film will be submitted via mail for digitization and subsequent entry to the image archive. For film acquisition, the identity of the participant will be reflected as follows: Institution ID, ACRIN Case #, study #. All media and film will be retained by the ACRIN Headquarters unless otherwise requested and return packaging and postage is provided. Mailed film images or images on CD should be addressed and sent as follows:

ACRIN Image Archive
ACRIN 6654 Images
American College of Radiology
1818 Market Street, Suite 1600
Philadelphia, PA 19103
Attn: Anita Murray

9.1.3 Where required, images stored in the ACRIN Headquarters image archive may then be routed to other sites involved, using either FTP or CDROM where appropriate, for purposes of secondary review.

10.0 EXPERIMENTAL PROCEDURES

Both the Experimental and Control groups will undergo the following procedures at the time intervals specified. These procedures will be described in the following paragraphs.

Procedure	**Experimental *(Arm 1)***	**Control *(Arm 2)***
Spirometry	Baseline	Baseline
Low-dose helical CT chest	Baseline, Yr 1, Yr 2	None
Posteroanterior *(PA)* chest radiograph	None	Baseline, Yr 1, Yr 2
Interval health status and medical interventions (*F1 Form*)	6 month intervals	6 month intervals
Participants in Group 1 only Collect blood, sputum, and urine samples	Baseline, Yrs 1, 2	Baseline, Yrs 1, 2
Participants in Group 1 only QOL instruments: SF-36v2, EuroQol EQ-5D	Baseline and Annual*	Baseline and Annual*

*** Subsets of participants from the Experimental and Control Arms of Group 1 sites will complete QOL instruments according to algorithms. *(See Section 20.0)***

Baseline screening examinations should be performed within four (4) weeks of randomization (ideally within two (2) weeks of randomization).

For all cases exceeding the four (4) week window, participants should be questioned to ensure that they do not have an acute lower respiratory infection under treatment with antibiotics that would warrant rescheduling. Year 1 and Year 2 screening exams should be performed within one (1) month prior to three (3) months post the randomization anniversary dates. In cases where screen exams are performed outside these windows, sites should notify the DMC via the PR form.

11.0 LOW DOSE HELICAL CT TECHNIQUES AND PROCEDURES

Low-dose helical chest CT scans will be performed at baseline and annually at Years 1 and 2 (at times T1 and T2) on participants in the Experimental Arm. The scanners used to acquire the helical studies will be exclusively multi-channel helical CT scanners. The rationale for this is multifactorial. [1] The vast majority of positive screening CT scans will be for subcentimeter nodules in the range of 4-10 mm. Only multidetector CT scans effectively realize the spatial resolution mandatory for accurate and reproducible measures of nodule size and nodule attenuation at the level of subcentimeter micronodule that will dominate the positive screening CT. [2] Only MDCT platforms enable data acquisition within a single breath-hold at detector collimations and slice thicknesses of 0.5-2.5 mm. [3] Published and unpublished data from ongoing observational trials with screening CT indicate moderate degrees of reader variability as well as prospective failure to recognize lung nodules on screening CT. Multidetector scanners allow the retrospective reconstruction of image data into data sets of different spatial quality and image characteristics. Although not mandated by the protocol, these additional data sets and their permanent archive within ACRIN Headquarters will provide a resource for determining truth. Ultimately, the use of MDCT platforms will ensure that the screening CT, the primary test under consideration, is of the highest quality, that the primary endpoint is not compromised by inferior image quality, and that the results will have significance beyond the period of this trial.

11.1 CT Acquisition Parameters

Radiation exposures will be as low as possible in keeping with good image quality. Because there is moderate variation in image quality across scanner platforms, a range of technical parameters will be accepted as follows:

- Primary scout performed in PA *projection* (tube at gantry bottom, patient supine) to minimize breast dose.
- kVp = 120
- mAs = 40-80 *(dependent upon participant body habitus and other factors)*. Lower mAs will be accepted provided that excessive quantum mottle does not compromise image quality.
- Detector collimation= 0.5-2.5 mm *(for one data channel)*
- dFOV = smallest diameter of chest wall that will completely contain the lung parenchyma as measured from widest point of outer rib to outer rib
- Image reconstruction as follows:
  (a) Nominal reconstructed slice width: 2-3.2 mm
  (b) Reconstruction interval: 1.8-2 mm
- Reconstruction algorithm: Soft tissue/smoothing algorithm without high spatial frequency enhancement (e.g., GE Standard algorithm, Siemens B30f algorithm, etc.) for assessment of nodule attenuation
- Scan time (breath-hold duration): < 25 seconds if possible
- Table incrementation per rotation: variable according to scanner and participant
- Participants are imaged supine at suspended maximal inspiration with arms elevated over the head to minimize beam-hardening artifact.

The elements above describe the technical parameters for data sets used for primary interpretation. NLST sites may elect to reconstruct the volumetric data into additional data sets of different spatial quality, using different reconstruction algorithms, or with image processing methods such as maximum intensity projection reconstructions, according to their local practices.

All scan data acquired on trial participants will be archived and retained at the institution for the duration of the trial. Soft copy images will be sent to the ACRIN Image Archive for central storage *(see Section 9.0)*. This will enable permanent storage of image data as well as the ready distribution of images to other sites for purposes of image and interpretation quality control. Only annual screening examinations will be archived.

11.2 Screening CT Interpretation

All CT studies will be evaluated by a study radiologist according to the standard of practice at their institution. All studies will be viewed on soft copy workstations at lung windows *(width 1500-1700 HU, level -500 to -700HU) using a 1-up format*. Measurements will be obtained at view full or with magnification. The C2 Screening Data Form will be used to record the radiologist's interpretation of the screening study. Depending upon individual site policies, a separate formal interpretation may be incorporated into the participant's institutional medical record using reporting methods in accordance with the ACR Standard for Communication.[78]

Studies will be interpreted using a fixed sequential review format as follows:

- Isolated interpretation of screening examination
- Interpretation of screening examination in the context of historical images, as appropriate

The observations and conclusions of both the isolated study, followed by the study in the context of historical images, will be recorded. Although the isolated interpretation is not truly representative of screening test performance, both of these data points will be collected for modeling the benefit of screening under different conditions of time interval, etc.

In the event that an abnormality of potential relationship to lung cancer is detected, attempts will be made to procure historical imaging studies for comparison. If historical images become available at any time within four weeks of the screening CT examination, the I9 Form will be completed. Historical images

submitted later than four weeks may be reviewed, and a revised I9 form with changes in the results and recommendations submitted, as appropriate.

11.3 Classification of Nodules on Helical CT

It is recommended that lung nodules detected on Screening CT will be evaluated based on the following classification:

Benign: Lesions with the following characteristics: calcification of central, rim, uniform, or other benign distribution; fat attenuation; linear morphology; and lesions documented to be stable for two or more years. The presence of micronodules < 4 mm diameter will be documented on screening CT but will not result in a positive screen.

Abnormal: Any new nodules > 10 mm diameter or enlarging nodules ≥ 7 mm diameter not satisfying criteria for benign or related to a clinically documented non-neoplastic process *(e.g., newly positive fungal serology, etc.)*. Nodule characteristics such as longest axial perpendicular diameters, margin *(spiculated, smooth, poorly defined, other)* and attenuation *(soft tissue, ground glass, mixed, fluid, etc.)* will be recorded.

Indeterminate: New solitary or multiple micronodules 4-10 mm diameter or enlarging nodules < 7 mm diameter.

12.0 CATEGORIES OF CT SCREENING RESULT AND RECOMMENDED DIAGNOSTIC PATHWAYS

12.1 There are four *(4)* categories of screening results based upon nodule designations and other findings from screening CT. These screening results will drive subsequent management recommendations of the participant as described below:

Screening Result	**Observation**	**Recommended Management**
Negative	▪ No significant abnormalities ▪ Benign nodule*(s)* ▪ Noncalcified micronodule*(s)* < 4 mm ▪ Minor abnormalities, not suspicious for lung cancer	Continue annual screening CT
Negative	Significant abnormalities **not suggestive of cancer**	▪ Evaluation for condition unrelated to lung cancer *(Recommendations exceed the scope of trial)* ▪ Continue annual screening CT
Positive	▪ Nodule*(s)* 4 -10 mm diameter ▪ Enlarging nodules < 7 mm diameter ▪ Other suspicious change in nodule	▪ Repeat low dose helical CT or limited TSCT at 3, 6, (3 to 6), 12, or 24 months from the date of the [+] screening CT, depending upon lesion size and level of suspicion for lung cancer
Positive	▪ Nodule*(s)* >10 mm diameter ▪ Enlarging nodules ≥ 7 mm diameter ▪ Other suspicious change in nodule ▪ Mass ▪ Nonspecific findings suspicious for lung cancer	Additional diagnostic tests, which may include: ▪ Repeat low dose helical CT or limited thin-section CT of nodule*(s)* at 3, 6, (3 to 6), 12, or 24 months, depending upon lesion size and level of suspicion for lung cancer ▪ Diagnostic chest CT with nodule densitometry pre- and post-contrast administration ▪ FDG-PET or Technetium-99m depreotide scintigraphy ▪ Biopsy (percutaneous, bronchoscopic, thoracoscopic, open, etc.) ▪ Other, specify
Inadequate Study	Not applicable	Reschedule Screening CT as soon as possible *(within one month of original screening CT)*

12.1.1 *Negative Screen, no significant abnormalities, benign nodules, non-calcified micronodules < 4 mm, or minor abnormalities not suggestive of lung cancer:* Participants with these screening results will continue with annual screening.

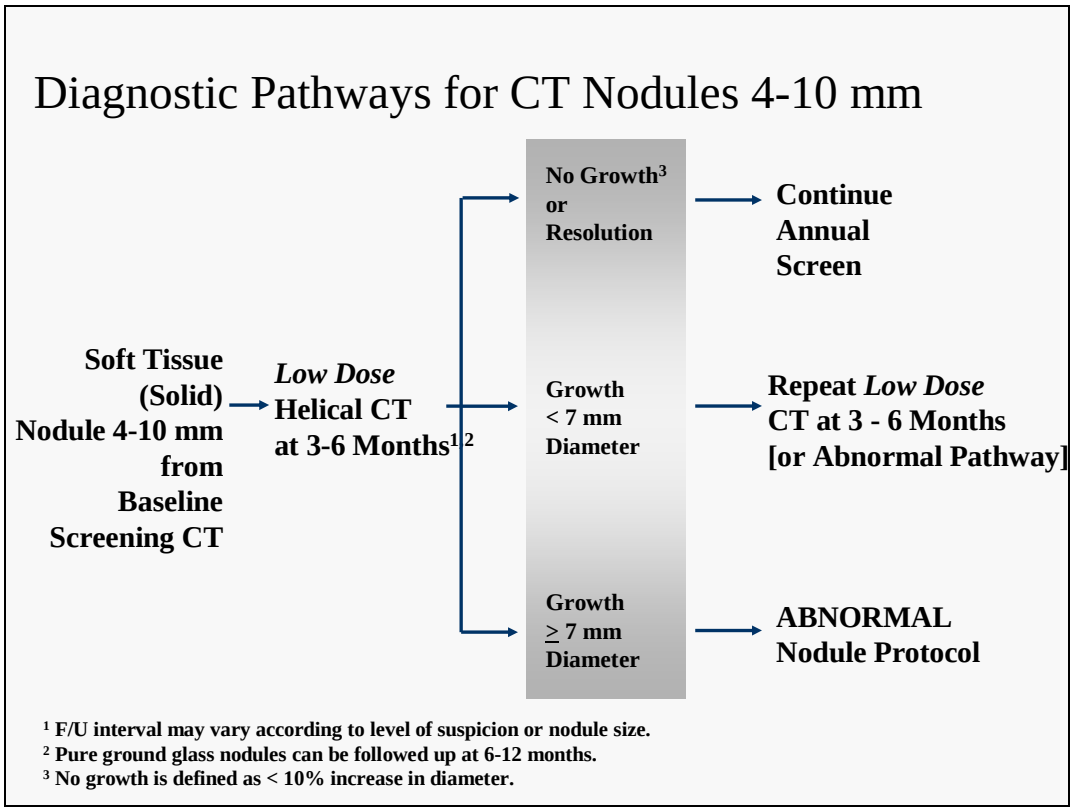
12.1.2 *Negative Screen, Significant Abnormalities Not Suggestive of Malignancy:* Participants found to have abnormalities of clinical significance unrelated to lung cancer will be referred to their physician for follow-up according to standard practices. Sites may or may not provide recommendations for further evaluation depending upon their local practice. The management of these participants is beyond the scope of this trial.

12.1.3 *Positive Screen; Indeterminate Nodules 4-10 mm diameter:* Participants with findings on screening CT suspicious for lung cancer will be advised to undergo additional evaluation designed to confirm a suspicion for lung cancer by documenting growth characteristics, morphology, or radionuclide uptake typical of neoplasm. In some instances, the initial level of suspicion may warrant immediate biopsy or open surgical procedure.

For nodules of 4-10 mm diameter, the standard practice that has been established will be to assess for interval change in size, morphology, or attenuation suggestive of malignancy. The ACRIN protocol will recommend a repeat low dose helical CT scan (or limited thin-section volumetric scan *(0.5-1.25 mm thick sections)* through the nodule at 3, 6, (3-6), 12, or 24 months from the time of the initial positive screening exam. The timing of follow-up is predicated on nodule size and the level of suspicion for lung cancer: smaller nodules or nodules of low suspicion for lung cancer are re-imaged at 4-6 months, while larger nodules or nodules of higher suspicion for lung cancer are usually imaged at 3-4 months. In the absence of change in character of the nodule, further evaluation is generally not required until the Year 1 (T1) screening.

Participants with nodules that show interval growth at follow-up of $\geq$ 7 mm will be referred for more definitive diagnostic testing. Opacities showing no growth or other change suggesting malignancy after 24 months on limited high-resolution CT follow-up will be considered benign. Participants being followed on the Repeat Low Dose Helical Protocol should continue to receive annual screening CT scans unless found to have lung cancer or other pathology that would preclude annual screening.

Figure 3: Recommended Pathway for Nodules of 4-10 mm Diameter on Screening CT



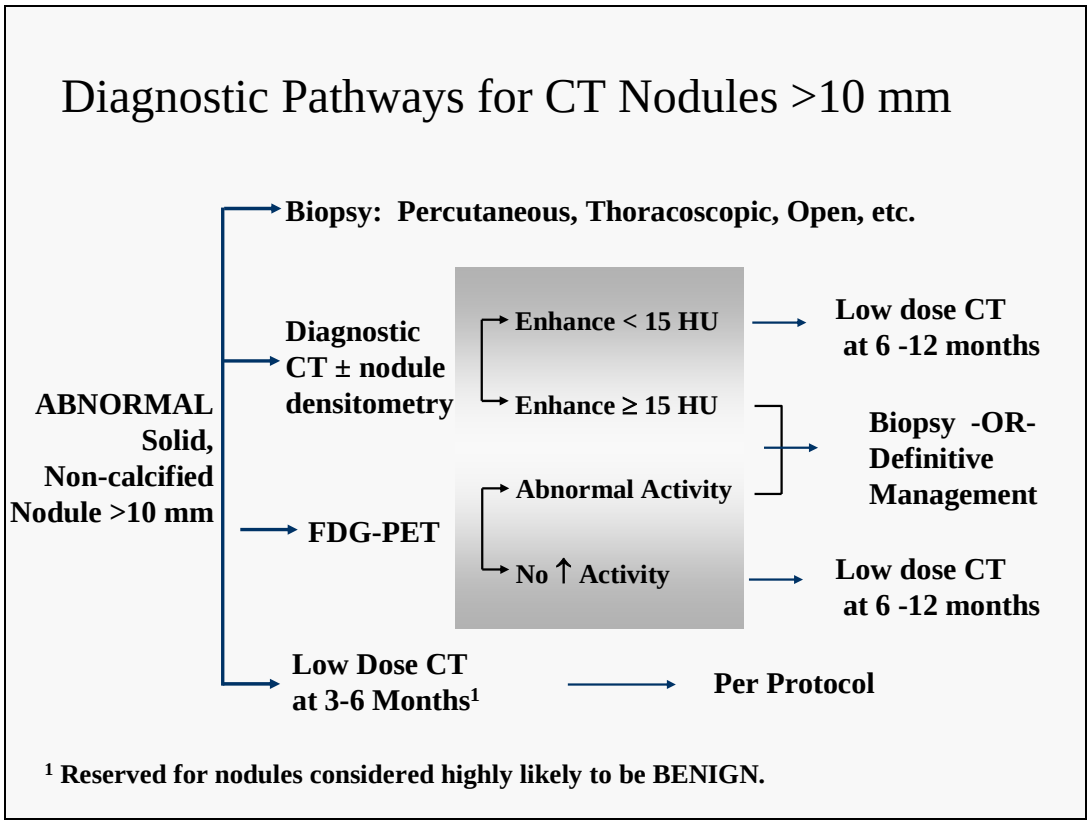
12.1.4 *Positive Screen; Nodule(s) > 10 mm Diameter or Lung Mass:* Participants in whom lung nodules > 10 mm diameter or masses are detected on CT screening will be encouraged to undergo further evaluation with the intent to confirm the presence or absence of malignancy based upon: (a) enhancement characteristics post-intravenous contrast administration, [79,80] (b) increased uptake on radionuclide tests, [81,82,83] or (c) histology, and to provide radiographic staging in preparation for definitive biopsy and treatment. At most sites, diagnostic and staging CT are normally performed as part of this process using relative generic acquisition protocols *(diagnostic CT protocols will not be specified by the ACRIN NLST protocol).*

The results of PET studies or other radionuclide scans will be recorded as part of the diagnostic evaluation of the participant on the DE Form. Excluded from contrast-enhanced nodule densitometry will be thin-walled cavitary or ground glass lesions, as these are known to be inadequately evaluated by this test.

12.1.5 *Positive Screen, Nonspecific Findings Suspicious for Lung Cancer:* Participants found to have nonspecific abnormalities of possible relationship to lung cancer will be considered to have a positive screen even in the absence of a discrete lung nodule or mass. Examples of such radiographic abnormalities are segmental or lobar atelectasis, a hilar or mediastinal mass, or pleural effusion. In such cases, additional evaluation may be advised, whether specifically in the form of diagnostic CT or simply "additional evaluation," depending upon the circumstances and local standard practices.

12.1.6 *Inadequate Study:* Participants with inadequate screening CT exams by virtue of technical limitations *(e.g., motion artifacts, excessive image noise, incomplete study, incorrect acquisition parameters, etc.)* will be rescheduled for a screening CT as soon as possible, but in all instances, within one month of the original screening test.

Figure 4: Recommended Pathway for Abnormal Nodule Seen on Screening CT



13.0 CHEST RADIOGRAPHIC TECHNIQUES AND PROCEDURES

13.1 Chest Radiographic Acquisition Parameters

Posteroanterior *(PA)* projection chest radiographs will be performed at baseline and annually thereafter on participants in the Control Arm *(Arm II)*. The acquisition devices will vary across sites and may include screen/film *(S:F)*, computed radiography *(CR)*, or digital radiography *(DR)* systems, providing that they have a speed of at least 200. The technical parameters vary slightly for the specific devices, with the following parameters applying:

The equipment used will include a rotating anode machine with a tube filtration sufficient to achieve a half value layer *(HVL)* greater than 3 mm of aluminum at 100 kVp. The recommended nominal focal spot size range is 0.6 -1.2 mm but shall not exceed 2.0 mm in any case. The system should provide a beam-limiting device for rectangular collimation. Automatic processing is required for film screen systems.

The technical parameters vary somewhat for the specific devices. The following parameters should serve as guidelines.

PARAMETER	Screen / Film	CR	DR
kV	120-150	100-140	110-150
Maximum* skin entrance exposure *(mGy)*	0.3	0.4	0.3
Maximum exposure time	40 msec	40 msec	40 msec
Source-image distance *(SID)**	≥ 72 inches	≥ 72 inches	≥ 72 inches
Anti-scatter device *(Grid)*	10:1 ratio or greater at 103 lines/inch (stationary), or 80 lines/inch (reciprocating)	Optimal for system	Optimal for system
Minimum collimation	To image receptor	To image receptor	To image receptor

* Skin entrance exposure may exceed these guidelines in large individuals.

Participants will be imaged upright at suspended maximal inspiration *(total lung capacity)* with scapulae positioned outside the lung fields if possible. The image should include both lung apices and both costophrenic angles. There must be adequate definition of the vertebral bodies, the left retrocardiac pulmonary vessels, lateral wall of descending aorta, and left hemidiaphragm. The technical parameters used should result in an image presenting the lung fields at a mid-gray level (i.e., optical density range of 1.4 - 1.8) for S/F systems, or with acceptable degrees of noise without overexposure to the participant in the case of CR or DR.

All screening chest radiographs will be archived and retained at the institution for the duration of the trial. The original images *(or high quality duplicate images where original data cannot leave the institution)* will be mailed to the ACRIN Headquarters for archive. Soft copy images may be sent to the ACRIN Headquarters for central storage at those sites in which CR or DR systems and electronic projectional image transfer is in place. This will enable permanent storage of image data as well as the ready distribution of images to other sites for purposes of image and interpretation quality control. The stored image data will include annual screening chest-x-rays.

13.2 Chest Radiographic Interpretation

All screening chest radiographs will be evaluated by a study radiologist. Because of the transition to digital acquisition devices, there is great diversity in the practice of adult chest radiology. As such, screening chest radiographs will be viewed on film or soft copy workstations, depending upon local resources. Interpretation will use the DR Screening Chest Radiograph Form. Depending upon individual site policies, a separate formal interpretation may be incorporated into the participant's institutional medical record using reporting methods in accordance with the ACR Standard for Communication.[78]

As with the screening CT examinations, screening chest x-rays will be interpreted using a fixed sequential review format as follows:

- Isolated interpretation of screening examination
- Interpretation of screening examination in the context of historical images, as appropriate

The observations and conclusions of both the isolated study, followed by the study in the context of historical images, will be recorded. Although the isolated interpretation is not truly representative of screening test performance, both of these data points will be collected for modeling the benefit of screening under different conditions of time interval, etc.

If historical images become available at any time within four weeks of the screening CT examination, the I8 Form will be completed. Historical images submitted later than four weeks may be reviewed, and a revised I8 form with changes in the results and recommendations submitted, as appropriate.

13.3 Classification of Nodules on Screening Chest Radiographs

Chest radiographs are less sensitive for detecting lung nodules and provide less accuracy when measuring size. As such, the classification of lung nodules detected on screening chest radiographs is broader than that provided for screening CT. Similarly, the diagnostic options are not as well defined. The following definitions for nodules on chest radiographs are provided:

Benign: Focal opacities with the following characteristics: calcification of central, rim, uniform, or other benign distribution and lesions documented to be stable for two or more years.

Abnormal: Any visible new or enlarging nodules not satisfying criteria for benign or not clearly related to a clinically documented non-neoplastic process *(e.g., newly positive fungal serology, etc.)*.

14.0 CATEGORIES OF CHEST RADIOGRAPHIC SCREENING RESULT AND RECOMMENDED DIAGNOSTIC PATHWAYS

14.1 There are four *(4)* categories of screening results based upon nodule designations and other findings from screening chest radiographs. These screening results will drive subsequent management of the participant as described below:

Screening Result	**Observation**	**Recommended Management**
Negative	▪ No abnormalities ▪ Minor abnormality without need for follow-up	Continue annual screening CXR
Negative	Significant abnormalities not suggestive of cancer	▪ Evaluation for condition unrelated to lung cancer *(Recommendations exceed the scope of trial)* ▪ Continue annual screening CXR
Positive	▪ Lung nodule*(s)* ▪ Mass ▪ Other findings suspicious for lung cancer ▪ Abnormalities suspicious for lung cancer, no significant change	Additional diagnostic tests, which may include: ▪ Immediate follow-up CXR with or without additional views (specify: apical/lordotic, shallow obliques, with nipple markers, other views) to better determine whether the finding observed on screening is indeed a lung abnormality and its location *-or-* ▪ Repeat chest x-ray with fluoroscopy to better determine whether the finding observed on screening is indeed a lung abnormality and its location *-or-* ▪ Low kVp chest x-ray to determine whether the screening abnormality is calcified *-or-* ▪ Repeat two-view chest x-ray in three (3) months (may follow antibiotics) *-or-* ▪ Low-dose helical chest CT ▪ Diagnostic chest CT (with or without contrast-enhanced nodule densitometry) *-or-* ▪ Whole body [F-18]-fluorodeoxyglucose positron emission tomography (FDG-PET) scan to determine whether the abnormality observed on screening behaves like a cancer *-or-* ▪ Biopsy of the lesion
Inadequate Study	Not applicable	Reschedule screening chest radiograph as soon as possible *(within one month of original CXR)*

14.1.1 *Negative Screen, no abnormalities or minor abnormalities without need for follow-up:* Participants with no abnormalities or minor abnormalities without need for follow-up will continue with annual screening CXR.

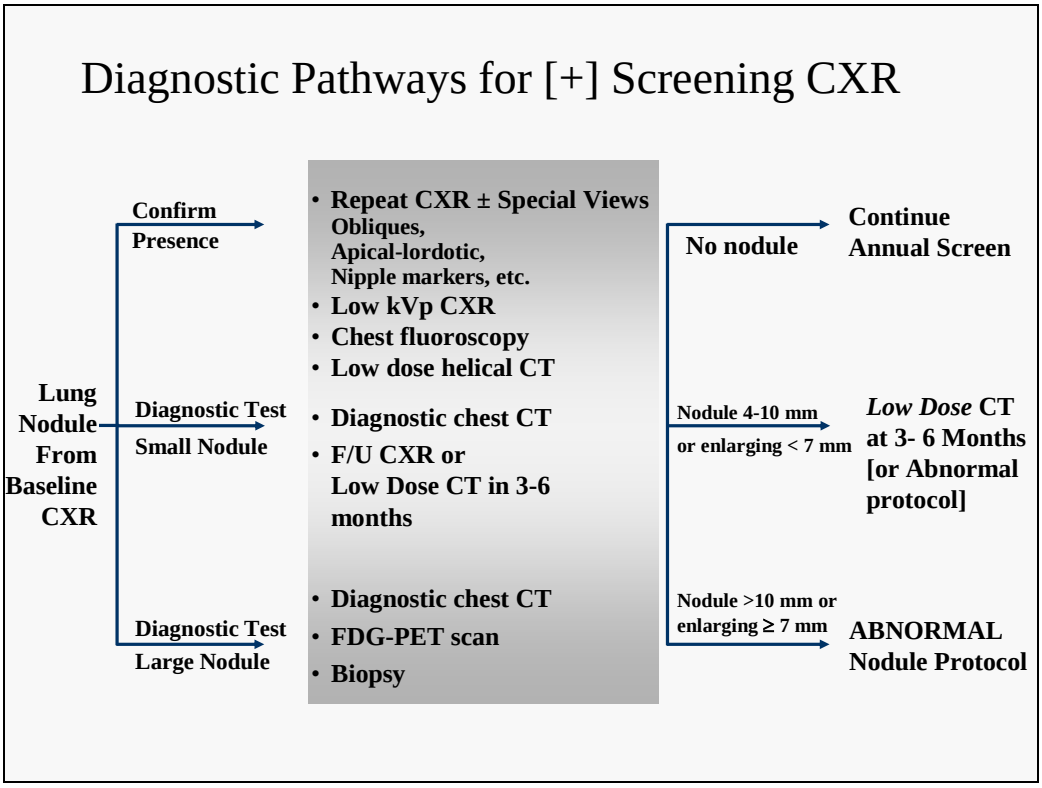
14.1.2 *Negative Screen, Significant Abnormalities Not Suggestive of Malignancy:* Participants found to have abnormalities of clinical significance unrelated to lung cancer will be referred to their physician according to standard practices. Sites may or may not provide recommendations for further evaluation depending upon their local practice. The management of these participants is beyond the scope of this trial.

14.1.3 *Positive Screen; Lung Nodules, Masses, or Other Findings suspicious for Lung Cancer:* Participants with findings on screening CXR suspicious for lung cancer will undergo additional evaluation designed to confirm the presence of the finding and the likelihood of lung cancer by documenting growth characteristics and morphology. In some instances, the initial high level of suspicion may warrant other diagnostic procedures, such as radionuclide imaging, CT, or biopsy procedures.

14.1.4 *Inadequate Study:* Participants with inadequate screening CXR by virtue of technical limitations *(e.g., motion, excessive noise, incorrect acquisition parameters, improper*

positioning, etc.) will be rescheduled for a repeat screening chest radiograph as soon as possible, but in all instances, within one month of the original screening exam.

Figure 5: Diagnostic Pathways for Positive CXR Screen



15.0 DEFINITIVE MANAGEMENT OF PARTICIPANTS WITH SUSPECTED LUNG CANCER

15.1 Given that the ACRIN trial will actively recruit participants across ethnic and economic boundaries, it is anticipated that up to 10% of participants will be under- or uninsured. Among these individuals, some will have positive screening tests and will be converted into patients, effectively ensuring that they will *remain* uninsured. Efforts must therefore be made wherever possible to ensure that diagnostic and therapeutic options are identified and financial assistance is made available to participants who are without other means to pay for the downstream consequences of the screening result. In the absence of this budgetary foresight, the study risks introducing bias in its outcome measures due to barriers imposed by inadequate health care access and financial resources.

The study coordinator will serve as a "case manager" for those participants identified as under- or uninsured with a positive screen. The study coordinator will ensure that each participant is referred to both appropriate financial assistance mechanisms and health care resources.

15.2 Abnormalities of malignant potential will be referred for definitive management under the direction of the primary physician. Local procedures and practice will vary across the accrual sites, but the intention of all subsequent management will be to confirm the presence of malignancy, establish clinical stage, establish surgical stage, and to attempt curative resection or other optimal treatment. These efforts may involve percutaneous lung *(or other organ)* needle aspiration biopsy, bronchoscopic sampling, thoracoscopic-directed or open biopsy, or nodal sampling with transcervical mediastinoscopy or thoracotomy. For invasive or minimally invasive procedures, the process of informed consent, technical standards, and procedures of the respective accrual sites will be observed, but are beyond the scope of this screening protocol. Cytologic or histologic tissue samples obtained from participants may be banked for

future biomolecular research; however, at no time will participants undergo procedures with additional risk solely to procure tissue for banking in this study (see Section below).

15.3 The surgical management of participants found to have lung cancer is not formally addressed by this screening protocol. Yet, the diligence and standardization of treatment is pivotal to ensuring the meaning and validity of collected data such as the outcome measures of mortality and surgical stage. The participating physicians and surgeons at the accrual sites will understand and follow published treatment recommendations, which include the following: [1] Pathologic Stage I lung cancer is early cancer and is best treated surgically; [2] Lobectomy is the procedure of choice; limited resections such as wedge-resection or segmentectomy do not achieve the same long-term survival and should be exclusively limited to patients with respiratory insufficiency or other medical condition that would preclude a safe lobectomy; [3] Pre-operative clinical staging with CT and FDG-PET provides valuable information, but cannot replace surgical staging. The accuracy of mortality data requires that patients undergo surgical staging with mediastinal lymph node evaluation using mediastinoscopy, limited thoracotomy, or lymph node dissection, before or at the time of thoracotomy. This should include a systematic *(usually radical)* dissection of lymph nodes to establish accurate surgical staging. Tissues resected at thoracotomy may include the primary tumor, lymph nodes, bone marrow samples from rib osteotomy, or metastatic lesions. In no instance, will specimen procurement for purposes of banking be associated with additional risk

16.0 SCREENING RESULTS COMMUNICATION AND PROCEDURES FOR PARTICIPANT FOLLOW-UP

16.1 The results of screening exams will be reported in writing to the participant and to their physician of record as indicated on Contact Information Forms completed at the time of participant enrollment. Letters of explanation will be issued within four *(4)* weeks of performance of the screening study. Participants with positive screens with no physician on record will be offered a list of physicians who could receive the results and oversee the management of the participant at the time of study enrollment. Under- or uninsured participants will be offered information on potential sources of financial assistance and access to health care services. Similarly, positive screening results will be reported to the physician of record by mail or fax, and telephone where appropriate. Depending upon individual site practices, formal reports may be issued with the explanatory letters.

Participants with a positive screen will be referred to their physician *(or assigned physician of their choosing)* for further diagnostic work-up and possible treatment according to the study recommendations *(see Sections 12.0 and 14.0)*. Any recommended diagnostic pathways will be described in detail to both the participant and physician of record. All participants, in both Experimental and Control arms, will be followed for the duration of the trial.

Participants may elect NOT to have results of NLST screening examinations sent to their referring physician(s). This must be formally documented in the participant's NLST chart by way of a progress note with participant signature or waiver. A specific waiver has been developed for use by sites that enables the participant to instruct the site NOT to send screening results letters until otherwise instructed by the participant in writing. The waiver provides space for participant signature and date of completion of waiver. Sites are encouraged, but not required, to use this form. The letters of explanation will be kept in the participant's file.

16.2 The participant letter of explanation must include the following information:

- A disclaimer stating that the examination is a screening examination, not a comprehensive examination;
- A statement providing the overall result of the screening examination with reference to any attached supplemental report for further details *(e.g., positive screen, indeterminate or abnormal opacities or masses, positive screen, non-specific finding(s) suspicious for lung cancer, etc.);*
- A statement advising the participant of any diagnostic recommendation(s) based on current practice that may be appropriate for the type of abnormality identified on a positive screening examination, preceded by a qualifier, "Among physicians, it is agreed that this abnormality requires a follow-up evaluation to distinguish between benign and cancerous lesions. The exact follow-up time interval

and method have not been scientifically established, but common methods may include: [list recommendations]."

- A statement that the screening test result as well as these recommendations for follow-up have been sent to the participant's health care provider, who may have alternative methods of evaluation within the range of current practice;
- A statement advising the participant to seek medical attention for a positive screening test result or negative screening test result with significant abnormalities unrelated to lung cancer;
- The site telephone number and the phone numbers of the site RA and PI for any questions or concerns the participant may have.

16.3 The physician letter of explanation must include the following:

- A statement that the ACRIN Lung Cancer Screening Trial is a NCI-sponsored scientific study designed to evaluate screening tests for lung cancer;
- The name of the participant whose results are being reported;
- A disclaimer stating that the examination is a screening examination, not a comprehensive examination;
- A statement providing the overall result of the screening examination with reference to any attached supplemental report for further details *(e.g., positive screen with lung nodules, findings possibly related to cancer, etc.);*
- A statement indicating that the participant has been advised to seek medical attention in the case of positive screening test results (or negative screening test results but with significant abnormal findings not suggestive of lung cancer);
- A statement advising the physician/health care provider of diagnostic recommendation(s) appropriate for the abnormality identified on screening, along with the following qualifier: "Among physicians, it is agreed that this abnormality requires a follow-up evaluation to distinguish between benign and cancerous lesions. The exact follow-up time interval and method have not been scientifically established, but common methods may include [*list recommendations*]."
- A statement that the results of this screening CT examination as well as these recommendations for follow-up have been sent to the participant, with the understanding that the physician/health care provider may have alternative methods of evaluation within the range of current practice;
- A statement encouraging the physician to proceed with diagnostic tests, whether those suggested, or others of his/her choosing, and indicating that all diagnostic follow-up could be performed at the NLST site;
- The site telephone number and the phone numbers of the site RA and PI for any questions or concerns the physician may have;
- A statement that the site RA will assist in scheduling any necessary diagnostic tests;

Sites may elect to follow-up specifically with participants in whom screening results were positive or in whom any recommendations for additional diagnostic testing were made in the screening results letters. The purpose of the follow-up call is to determine whether diagnostic tests were performed and to ensure that under- or uninsured participants are appropriately triaged to health care facilities in order to complete indicated diagnostic tests.

16.4 All Experimental and Control participants will be contacted at six *(6)* month intervals for purposes of determining all interval medical encounters *(hospitalizations, clinic visits, etc.)* over the preceding 6 months and any changes in contact information. The intentions of six-month follow-up are to:

- Maintain regular contact with all participants.
- Determine whether participants have undergone the screening interventions outside of trial.
- Determine interval lung cancers.
- Determine other major morbid medical conditions.
- Determine interval death of participants.
- Determine interval medical encounters (clinician visits, hospitalizations, etc.)

- Determine that under- or uninsured participants with positive screens receive referrals to facilitate access to health care services and financial assistance mechanisms.

The results of these interval follow-up contacts will be recorded on the F1 Follow-up Form and will determine whether additional data from medical facilities must be obtained for purposes of medical chart abstraction. The algorithm to be followed for determining chart abstraction follows *(Figure 5).*

16.4.1 Experimental participants for whom screening studies are positive due to (1) nodule(*s*) > 10 mm or masses, or (2) non-specific finding suspicious for lung cancer will undergo chart abstraction beginning from the time of the positive screening study. Similarly, 100% of CT screens documenting 4-10 mm diameter nodule*(s)* will undergo chart abstraction. All Experimental participants who undergo medical evaluation for significant screening findings unrelated to lung cancer will undergo chart review, given the moderate frequency with which additional evaluation may include thoracic or abdominal imaging procedures.

At six-month interval contact, all participants in whom lung-related encounters are documented *(e.g. imaging procedure, bronchoscopy, PET scan)* and 5% of participants in whom non-lung-related encounters occur will undergo chart abstraction. At the start of Year 2, the algorithms for chart abstraction may be revised depending upon estimated changes in the proportions of participants within each of the above categories and the information gained from chart abstraction.

16.4.2 Control participants with positive screening tests will undergo chart abstraction. At six-month interval contact, all control participants with lung-related encounters and 5% of those with non-lung related encounters will undergo chart abstraction.

16.5 Quality Assurance of Medical Abstraction will be ensured by documentation of the qualifications of the medical abstractors and nosologists as well as the procedures for monitoring the quality of abstraction.

16.5.1 Each abstractor and nosologist will be required to submit qualifications, training, and certification to the BDMC for review. The medical record abstractor should have knowledge of medical record terminology, anatomy, physiology and concepts of disease in addition to basic medical coding instruction. The abstractor should have a minimum of 2 years on-the-job experience abstracting medical records. The nosologist should also possess at least one of the following credentials:

- Certified Coding Specialist *(CSS)*
- Registered Health Information Technician *(RHIT)*
- Registered Health Information Administrator *(RHIA)*

For ICD-O-2 coding and TNM staging, individuals must be CTR or CTR-eligible, as evidenced by one of the following:

- Two years full-time equivalent experience in the cancer registry field
- Successful completion of a college level curriculum in cancer data management /cancer registry, and work experience of 120 hours in a CTR staffed computerized cancer registry or 240 hours in a non-CTR staffed computerized cancer registry.
- One-year full-time equivalent experience in the cancer registry field and successful completion of college level curriculum in medical records, nursing, or other allied health field.
- One year full-time equivalent experience in the cancer registry field and credentialed or licensed status in a recognized allied health field as determined by NBCR.

The BDMC will oversee medical abstraction and will facilitate regular communication with the sites on issues pertaining to medical record abstraction and problem resolution as well as to coordinate training. Depending upon site-specific internal review board policies, medical abstraction may be performed at the site or centrally at the BDMC using medical documents that have been scrubbed to replace all identifiers with trial-specific site and case numbers. The RA

and/or staff assisting with document procurement for medical abstraction and coding at each site will assist the BDMC in monitoring internal quality assurance at their site and providing input to resolve issues of medical abstraction that arise.

16.5.2 A 10% random sample of all participants for whom medical records were abstracted will be re-abstracted using different abstractors who are trained in the study protocol and who fulfill the background qualifications for medical abstraction, coding, and staging required by the ACRIN trial. All participant identifiers will be removed from medical documents and replaced with trial-specific site and case numbers. The results will be compared and reported to ACRIN or to the individual sites where the abstraction was performed.

Figure 5: Probabilities for Chart Abstraction of Participants Based on Study Arm, Screening Result, and Responses on F1 Data Form

Study Arm	Screening Result	Number with Screening Result per 12,500 Screened in Each Arm	Response on F1 Form	Anticipated Number Having Response of Interest on F1 Form (Source of Discovery)	Proportion for Chart Review	Number abstracted/12,500 participants/year
CT Screen Arm (12,500)	Positive Screening CT ▪ Abnormal nodule or mass ▪ Nonspecific findings suspicious of lung cancer	438 (3.5%)	All lung/chest related encounters	438 (Screening CT)	100%	438
	Positive Screen (~90%) ▪ Nodules 4-10 mm diameter (*Indeterminate)*	3937 (31.5%)	All lung/chest related encounters	3937 (Screening CT)	100%	3937
	Negative Screen ▪ No abnormalities ▪ Potentially significant findings not related to lung cancer	125 (1%)	▪ All encounters ▪ Capture non-lung cancer medical interventions prompted by screening CT	125 (Screening CT)	100%	125
	Negative Screen	8000 (64%)	▪ Lung/chest related examination or intervention ▪ Diagnosis of lung cancer	400 (F1 Form[1])	100%	400
			▪ Non-lung/chest related encounters	4000 (F1 Form[2])	5%	200
CXR Screen Arm (12,500)	Positive Screen ▪ Abnormal nodules or mass ▪ Nonspecific findings suspicious of lung cancer	1875 (15%)	All lung/chest related encounters	1875 (Screening CXR)	100%	1875
	Negative Screen ▪ No abnormalities ▪ Potentially significant findings not related to lung cancer	125 (1%)	All encounters	125 (Screening CXR)	100%	125
	Negative Screen	10,500 (84%)	▪ Lung/chest related examination or intervention ▪ Diagnosis of lung cancer	525 (F1 Form[1])	100%	525
			▪ Non-lung/chest related encounters	5250 (F1 Form[2])	5%	263

1: assumes 5% of participants in this category will have interval exams
2: assumes 50% of participants in this category will have interval exams

17.0 QUALIFICATIONS OF PERSONNEL AND QUALITY CONTROL MEASURES FOR IMAGING INSTRUMENTATION, IMAGE QUALITY, AND IMAGE INTERPRETATION

17.1 Qualifications of Personnel

17.1.1 *Qualifications of Radiologists*

Radiologists participating in the trial should meet the following qualifications:

- Certification by the American Board of Radiology, the American Osteopathic Board of Radiology, the Royal College of Physicians and Surgeons of Canada, United Kingdom, or equivalent accrediting board. Must have a valid, active medical license in the state in which screening is performed. Radiologists at federal sites must have an unrestricted license to practice medicine in their clinical specialty issued by one of the States, the District of Columbia, or a possession of the United States.
- Documented training in the physics of diagnostic radiology and radiation safety, as evidenced by completion of an accredited diagnostic radiology residency or 80 hours of documented, relevant classroom instruction. This training should include instruction in radiation monitoring requirements and the hazards of radiation exposure to both patients and radiologic personnel as well as the physical principles of CT and CT artifacts, technical parameters for CT examinations (*e.g. exposure factors, collimation, table speed, field of view, etc.*), screen-film radiography, digital or computed radiography, conventional image processing, and digital image processing.
- Involvement with the supervision and/or performance, review, and interpretation of at least 300 chest CT examinations in the past three (*3*) years -or- completion of an ACGME accredited radiology residency within the preceding 24 months.
- Involvement with the supervision and/or performance, review, and interpretation of at least 200 chest radiographic examinations per year
- Participation in continuing medical education in accordance with the American College of Radiology Standard for Continuing Medical Education (*CME*), which recommends 150 hours of Category 1 (*minimum of 60 hours*) or Category 2 (*maximum of 90 hours*) activities over three (*3*) years. This should include CME credits in chest CT and chest radiology.
- Completion of basic ACRIN certification before the time of site start-up.

In addition to the above, all physicians serving as readers for the screening tests and radiologic technologists will review a training set of images designed to ensure a common knowledge base for the interpretation of both chest radiographic and CT screening examinations. This training set (available on CD) will consist of screening examinations that demonstrate:

- Imaging findings ranging from normal to overtly abnormal, with the inclusion of focal opacities commonly observed in the course of low dose CT screening and chest radiographic screening
- Definitions of what constitutes a lung nodule and the nodule characteristics of attenuation and margin that are being recorded on the NLST data form as well as how to measure a nodule
- Deviations from the technical parameters specified by the protocol
- Suboptimal image quality for reasons of inspiratory volume, motion, beam hardening, etc.

The standard of truth for the training set was determined by consensus between three dedicated thoracic radiologists prior to distribution. The image data was reviewed at training sessions including both ACRIN and LSS physicians and is available for distribution electronically by CD to all readers at all sites. Readers will review the images independently, after which they can review the consensus opinions and explanations for the consensus opinions. Documented completion of this training session will be obtained prior to the reader's certification for the

NLST. Experimental designs to analyze observer variability within and between institutions will be formalized in ancillary projects in the future.

17.1.2 *Qualifications of Radiologic Technologists*

The radiologic technologists involved in the performance of CT scanning or projectional imaging must have the following qualifications:

- Possess an unrestricted license in the appropriate state of practice. This requirement is waived in those states in which state licensure is not required or where there is a specific restricted license that grants privileges for radiologic work (i.e., Minnesota Limited Practice Technologists).
- Be certified by the American Registry of Radiological Technologists *(ARRT)* or by a state regulatory agency (i.e., Minnesota Limited Practice Technologists).
- (CT technologists) Have documented training and experience in CT, including training in the operation of CT equipment and knowledge in radiation physics. They are strongly encouraged to pass the advanced examination for CT certification
- Maintain compliance with ARRT requirement for CME of 24 credits per two (*2*) year period
- Complete a training program and sign a written attestation that they understand the materials describing the acquisition parameters and image quality requirements of the exams for which they will be responsible in the trial.

17.1.3 *Medical Physicists*

A medical physicist(s) will be available at each site to monitor and ensure the quality of equipment used to acquire screening examinations for the NLST. The medical physicist should have the following qualifications:

- Certification by the American Board of Radiology in one of the subfields of Diagnostic Radiological Physics or Radiological Physics.
- Participation in CME in accordance with the ACR Standard, which recommends 150 hours of Category 1 (*minimum of 60 hours*) or Category 2 (*maximum of 90 hours*) activities over three (*3*) years.
- Familiarity with the principles of imaging physics and of radiation protection; the guidelines of the National Council on Radiation Protection and Measurements; laws and regulations pertaining to the performance specifications of the imaging equipment; the function, clinical uses, and performance specifications of the equipment; and calibration processes and limitations of the instruments used for performance testing.
- Availability for questions or concerns regarding radiation dosimetry.

17.2 CT Equipment Certification and Qualifications

Any imaging equipment or scanner device used to acquire screening images for NLST will be certified for use at the time of site qualification.

17.2.1 *CT Equipment Certification*

The following tests and/or documentation will be required of all CT scanners at each site used to acquire screening studies:

- An NLST CT Equipment Certification and Annual Testing form will be submitted to ACRIN for every scanner used in the trial prior to NLST participant scanning.
- CT dosimetry index *(CTDI)* using the technique proposed in the Manual of Operations and using the recommended FDA-specified CTDI phantom
- Water phantom tests for purposes of water calibration, noise, and field uniformity

- Written documentation of the performance testing completed at the time of equipment installation (acceptance testing) is recommended in accordance with ACR standards, and records must be documented by the site, with copies available for review by NLST management.
- Subject dose as measured by an appropriate dosimetry method, such as optical stimulated luminescence *(OSL)* dosimetry or thermolucent dosimetry (TLD) is under consideration in conjunction with a commercial vendor.

Re-certification of the scanner with CTDI measurements and water phantom testing (as above) should be completed after any major changes to the CT instrument, such as a change in the x-ray tube, replacement of a detector, or replacement of the collimator.

The ACR has recently launched a voluntary CT accreditation program. The quality control measures in the NLST trial are based upon this accreditation program. However, formal site accreditation for CT by the ACR will not be required of the NLST sites.

17.2.2 *Ongoing CT Quality Control QC Measures*

A *QC* program will be established for all CT units with the assistance of a qualified medical physicist. The QC program will include at least the following QC measures at the stated frequencies:

- An ACRIN-NLST CT Equipment Certification and Annual Testing form will be submitted to ACRIN for every scanner used in the trial annually as long as scanner is used to scan NLST participants.
- Bimonthly: An ACRIN-NLST CT water data form for determination of water calibration, field uniformity, and noise is submitted to ACRIN bi-monthly for every scanner in the trial.
- Scanner performance surveys including assessment of: (a) alignment light accuracy, (b) slice thickness, (c) spatial resolution, (d) low contrast resolution, (e) image uniformity, (f) noise, (g) artifact evaluation, (h) CT number accuracy, and (i) display devices should be performed annually and documentation maintained on site with copies available for review by NLST management.
- At the regularly scheduled frequencies recommended by vendor: Preventive maintenance by a qualified service engineer with documentation of these maintenance checks.

The site medical physicist should be available to assist in prescribing corrective actions for unresolved problems. All test results, equipment deficiencies, corrective actions, and service records must be documented by the site, with copies available for review by NLST management.

17.3 Chest Radiographic Equipment Certification and Qualifications

Any equipment used to acquire chest radiographic screening images for NLST will be certified for use at the time of site qualification and ongoing quality control monitoring will continue throughout the period during which screening tests are acquired.

The medical physicist should conduct testing of the unit performance at the time of site certification and at least annually thereafter. The following tests are recommended for site certification:

- System assembly evaluation
- Collimation assessment
- Timer accuracy *(if applicable)*
- Linearity of air kerma *(exposure)* with mA and/or mAs *(if applicable)*
- kVp accuracy and reproducibility
- Exposure reproducibility
- Radiographic automatic exposure control *(AEC)* system performance assessment (if applicable)
- Beam quality assessment *(Half-value layer measurement)*
- Artifact evaluation
- Review of technologist QC program and QC tests

- An ACRIN-NLST CXR Equipment Certification and Annual testing form will be submitted to ACRIN for every CXR machine used in the trial prior to imaging NLST participants and annually thereafter as long as CXR unit is used to image NLST participants.

Routine QC procedures should be performed and documented as they apply for a given chest radiographic acquisition technology. Recommended QC procedures include (a) daily processor quality control, (b) weekly darkroom cleanliness, (c) monthly visual checklist, (d) quarterly review of repeat analysis, (e) annual screen cleanliness and screen-film contact, and (f) semi-annual analysis of fixer retention in film. Documentation of these and/or other site-specific quality control tests must be documented by the site, with copies available for review by NLST management.

17.4 CT Image Quality Control

Adherence to protocol technical parameters and maintenance of high image quality will be documented at start-up and ensured in two ways: [1] visual inspection of a continuous sample of at least 10% of screening CT scans from each site throughout the trial, and [2] reviewing of DICOM header information on scan data received at the ACRIN Headquarters.

Visual Inspection: The following elements will be visually reviewed by radiologist(s):

- Display field of view (reconstruction diameter)
- Reconstruction filter
- Appropriate site and anonymous participant ID
- Suspended maximal breath-hold
- Absence of motion
- Full extent of lung fields included on the exam
- Absence of significant beam hardening artifact

Review of DICOM headers at ACRIN Headquarters: Adherence to technical parameters will also be monitored by continuous review of DICOM headers on image data received at the ACRIN Headquarters. DICOM fields to be monitored include:

- No. images total
- kV and mA or mAs
- Slice thickness
- Table speed per rotation (*or pitch*)
- Reconstruction filter
- Participant NLST ID

Instances of protocol discrepancy will be documented and used to monitor trends or patterns of inconsistent use of the prescribed technical parameters that may warrant retraining or other intervention at the site.

17.5 Chest Radiographic Image Quality Control

Adherence to protocol acquisition parameters and image quality will be documented at start-up and throughout the trial, including the following:

- Collimation to include all essential structures
- Proper positioning
- Suspended deep inspiration
- Appropriate contrast and gray scale range
- Acceptable image sharpness and noise
- Absence of artifacts *(dust, lint, roller marks, film fogging, etc.)*
- Appropriate identification markers: site name, participant research ID, exam date, exam time, R/L marker, etc.

Image quality control problems will be logged and used to monitor trends that may warrant retraining or other intervention at the site.

18.0 ADVERSE EVENTS REPORTING

The objective of adverse event (AE) reporting is the documentation of all events occurring that may compromise the welfare and safety of trial participants. Through AE reporting, practice trends at an individual site or trial-wide resulting in unusual morbidity or mortality may be identified *more rapidly* than might be identified through data analyses of secondary outcomes such as medical resource utilization or complication rates. Adverse event reporting is to be distinguished from the collection of data for purposes of analyzing trial endpoints, which is achieved through the recording of specific data elements on case report forms and statistical analysis.

18.1 Definition of Adverse Event

An **Adverse Event (AE)** is any unfavorable and unintended sign, symptom, or disease *temporally* associated with the use of a medical treatment or procedure *regardless* of whether it is considered related to the medical treatment or procedures (attribution of unrelated, unlikely, possible, probable, or definite). (For example, hyperventilation and dizziness following pulmonary function testing)

18.2 Definition of Serious Adverse Event

A **Serious Adverse Event (SAE)** is any adverse event that results in any of the following:

- Death
- In-patient hospitalization (for reasons other than observation) or prolongation of an existing hospitalization
- A persistent or significant disability or incapacity
- Congenital anomaly/birth defects

18.3 Characterizing Adverse Events by Attribution and Severity

Once identified, the site PI should characterize the AE by **attribution** (whether it is related to a trial-related procedure) and **grade** of severity. The following guidelines apply:

The **attribution** of an AE or SAE characterizes its causal relationship to the trial-related procedure as follows:

- Unrelated – clearly **NOT** related to procedure
- Unlikely – doubtfully related to procedure
- Possible – may be related to procedure
- Probably – likely related to procedure
- Definite – clearly related to procedure

Grade denotes the severity of the AE and is graded according to the current version of the Common Terminology Criteria for Adverse Events (CTCAE v3.0), or the following categories (if the term does NOT appear in the CTCAE v3.0):

1 – Mild
2 – Moderate
3 – Severe
4 – Life-threatening or disabling
5 – Fatal

(For terms listed in the CTCAE v3.0, the grade is still recorded as 1, 2, 3, 4, or 5)

18.4 Direct and Indirect AEs in Screening Imaging Trials

- Complications associated with primary interventions are termed ***direct AEs***.
- Screening tests promote downstream, diagnostic interventions; complications associated with these diagnostic interventions are termed ***indirect AEs***.
- The primary interventions in this protocol are the screening helical CT or CXR examinations, phlebotomy for collection of biomarker specimens, and pulmonary function testing.

- In this protocol, **only direct adverse events associated with the primary trial interventions will be reported as adverse events.** Indirect adverse events will be documented as part of trial endpoints on case report forms.

18.5 Potential Expected and Unexpected Adverse Events in the NLST

Adverse events may be *expected* or *unexpected*.

- An ***expected* AE** is one that is described in the protocol, the consent form, or the investigator's manual of operations, such as bruising from phlebotomy.
- An ***unexpected* AE** is one that has not been described.

The adverse events listed below (Table 1) can be found in the Common Terminology Criteria for Adverse Events version 3.0 (CTCAEV3.0) and are relevant to the ACRIN-NLST.

Table 1: Expected Adverse Events within NLST: From Common Terminology Criteria for Adverse Events v3.0 (CTCAE)

Adverse Event	Likely Scenario	Severity Grades of AE				
		Severity 1	**2**	**3**	**4**	**5**
Direct Expected AE						
1. Drinking sputum preservative	Home sputum kit, inadvertent swallowing	1	2	3	___	___
2. Syncope	Phlebotomy, spirometry	___	___	Present	Life threatening consequences	Death
3. Dizziness	Phlebotomy, spirometry	Head movements or nystagmus only, not interfering with function	Interfering with function, but no interfering with ADL	Interfering with ADL	Disabling	Death
4. Hyperventilation	Phlebotomy, Spirometry	Not interfering with function	Interfering with function, but no interfering with ADL	Interfering with ADL	___	___
5. Bruising from needles	Phlebotomy	Localized or in a small, dependent area	Generalized	___	___	___
6. Bronchospasm, Wheezing	Spirometry	Asymptomatic	Symptomatic, not interfering with function	Symptomatic, interfering with function	Life-threatening	Death
7. Vasovagal reaction	Phlebotomy	___	Present without loss of consciousness	Present with loss of consciousness	Life-threatening consequences	Death
8. Cardiopulmonary arrest (non-fatal)	Spirometry	___	___	___	Life-threatening	___
9. Wound infection	Phlebotomy	*See CTAEv3.0*				

18.6 Regulatory and Reporting Requirements

Routine reporting is defined as documentation of adverse events on source documents and the AE CRF, and submission to ACRIN for preparation of a report for Data and Safety Monitoring Committee (DSMC) review, quarterly reports to CDUS, and the final study report.

Expedited reporting will be defined in the ACRIN-NLST as immediate notification of adverse event via telephone report within 24 hours of first knowledge of the AE and/or submission of the AdEERS report form to both the NCI-CIP and ACRIN. The AdEERS report must be submitted within ten (10) working days of first knowledge of the AE. Documentation by routine reporting also applies.

Grade 5 Adverse Events/deaths require (a) a telephone report to both NCI and ACRIN within 24 hours of knowledge of death, (b) expedited reporting as defined above, and (c) routine reporting, as defined above.

18.6.1 Adverse events in the ACRIN-NLST occurring within the timeframe identified below will be reported only during the T_0, T_1, and T_2 periods of time in which participants undergo primary interventions (screening, phlebotomy, pulmonary function tests). The reporting of AEs in this protocol will conform to the following:

1. Grade 3 Expected and Unexpected AEs with attribution of possible, probable, or definite and occurring within two (2) hours of the intervention (exception: 1 week for wound infections) will be reported by **routine reporting procedures** *(see ACRIN Adverse Event Reporting Manual).*

2. All unexpected hospitalizations (or prolongation of existing hospitalization) for adverse events with the severity (intensity) level of CTCAEv3.0 Grade 3, 4, 5 and attribution of possibly, probably, or definitely related to the primary trial intervention will be reported by **Expedited Written Report** within ten (10) working days of first knowledge of the event. Routine reporting procedures also apply.

3. Grade 4 Expected AEs with attribution of possible, probable, or definite and occurring within two (2) hours of the intervention (exception: 1 week for wound infections) will be reported by **routine reporting procedures**.

4. Grade 4 Unexpected AEs with attribution of possible, probable, or definite and occurring within two (2) hours (exception: 1 week for wound infections) will be reported within ten (10) working days of first knowledge of the event by **Expedited Written Report**.

5. Grade 5 AEs or **Deaths** with attribution of possible, probable, or definite relationship and occurring within 48 hours of the primary trial interventions will be reported within 24 hours of first knowledge of the death by Telephonic Report to ACRIN and NCI-CIP and followed by **Expedited Written Report** within ten (10) working days of first knowledge of the event. Documentation by routine reporting procedures also applies. All other deaths will also be reported by routine reporting procedures.

The following table summarizes the reporting requirements for AEs for the NLST:

DIRECT AE GRADE*	EXPECTED AE	UNEXPECTED AE
Grade 3	Routine Report	Routine Report
Grade 4	Routine Report	Routine and Expedited Reports
Hospitalization/Prolongation of hospitalization**	Routine Report	Routine and Expedited Reports
Grade 5***	1. Telephonic Report to NCI-CIP within 24 hours of first knowledge 2. Expedited Report 3. Routine Report	1. Telephonic Report to NCI-CIP within 24 hours of first knowledge 2. Expedited Report 3. Routine Report

* Direct AE considered *possibly, probably,* or *definitely related* and occurring within two (2) hours of the trial intervention (except for wound infection, occurring within one week).

** All unexpected hospitalization/prolongation of hospitalization for adverse events with the severity/intensity level of CTCAEv.3.0 Grade 3, 4, 5 and attribution of *possibly, probably,* or *definitely related* to the primary trial intervention

***Report only Grade 5 AEs (Deaths) considered *possibly, probably,* or *definitely related* that occur within 48 hours of the primary trial intervention.

18.6.1 Assignment of grade and attribution of each AE is the responsibility of the site Principal Investigator.

18.6.2 Events that are clearly reflective of the "main" adverse event (e.g., loss of consciousness, which is known to occur with vasovagal episode) should be noted in the Description of Event in the AdEERS - Single Agent Template report form, and should **not** be reported as separate events. See Section 18.8.2 for URL to obtain the AdEERS Form.

18.6.3 Prompt reporting of adverse events is the responsibility of each investigator, clinical research associate, and nurse engaged in clinical research. Anyone uncertain about whether a particular serious adverse event should be reported need to contact the ACRIN headquarters at 215-574-3150 for assistance. Any adverse event considered NOT directly related to the treatment or procedure should NOT be reported as a serious adverse event in this trial. General guidance can also be found in the ACRIN Adverse Event Reporting Manual.

18.6.4 All unresolved AEs should be followed by the principal site investigator until the AE is resolved, otherwise explained, or the site has documented due diligence in attempting to procure the requisite medical records without success.

18.7 Expedited Adverse Event Reporting Exclusions

For this protocol, the following AEs are specifically excluded from expedited AE reporting:
Complications of the following conditions, hospitalizations, prolonged hospitalizations, or surgeries should NOT be reported as an AE in this trial:

- Complication from diagnostic procedures performed because of the screening intervention
- Elective surgical or minimally invasive procedures for a pre-existing condition
- Hospitalization that is required to determine efficacy for the study
- Therapy for lung cancer
- Death from lung cancer
- Death from other cancer or pre-existing condition

These conditions will be recorded on study case report forms for purpose of endpoint analysis.

18.8 Directions for Reporting Adverse Events

18.8.1 Once the study site becomes aware of a serious adverse event with attribution of possibly, probably, and definitely related to the primary trial intervention, it should be reported using the AdEERS Report within ten (10) working days via fax to NCI and ACRIN, followed by a hard copy to NCI. All fatal (Grade 5) adverse events/deaths with attribution of possibly, probably, and definitely related to the primary trial intervention should also be reported via telephone to both ACRIN and NCI-CIP within 24-hours of first knowledge of the event.

18.8.2 An expedited adverse event written report requires submission of the paper template "Adverse Event Expedited Report—Single Agent" available on the CTEP home page, http://ctep.info.nih.gov. A copy of this form can also be found in the ACRIN Adverse Event Reporting Manual. Specific guidance on how to fill-out this form can be found on the website or obtained by contacting ACRIN at 215-574-3150.

NOTE: Do not send the form via the web site; it will not accept a form without the Course Information and Protocol Agent sections filled in. These sections are not relevant to imaging protocols.

18.8.3 All fatal (Grade 5) adverse events/deaths with attribution of possibly, probably, or definitely related to the primary intervention should be reported by telephone within 24 hours of first knowledge of the event. To make a telephone report, contact NCI-CIP at (301) 496-0737, available 24 hours a day (recorder after hours from 4:30 PM to 8:00 AM Eastern Time).

A copy of all AdEERS reports should be sent to NCI by fax at (301) 480-3507, followed by a hard copy via US Mail within ten (10) working days of first knowledge of the event. Completed expedited reports should be sent to:

Barbara Galen, MSN, CRNP, CNMT, Program Director
Re: Adverse Event Report
Cancer Imaging Program
6130 Executive Blvd., MSC 7412
Room 6050
Bethesda, MD 20892-7412

18.8.4 All fatal (Grade 5) adverse events/deaths with attribution of possibly, probably, or definitely related to the primary intervention should be reported by telephone within 24 hours of first knowledge of the event. To make a telephone report to ACRIN, call (215) 717-2763. This number is available 24 hours a day (recorder after hours from 5 PM to 8:00 AM Eastern Time). During business hours, ACRIN Data Managers for the protocol will be available. A copy of all AdEERS reports should be sent to ACRIN by fax at (215) 717-0936.

18.8.5 All reportable AdEERS reports should be sent to your local Institutional Review Board (IRB). Adverse events *not* requiring expedited reporting are normally reported to the local IRB in an annual report and/or continuing review. Please refer to your local institution's IRB policies regarding adverse events, serious adverse events, and safety reports.

19.0 INSTITUTIONAL AUDITS

19.1 Timing and Composition of Audits: Institutional on-site audits will be completed after the first 100 participants have been accrued or within 12 months of a site's enrolling its first ACRIN participant, whichever comes first. Auditors will follow procedures established by the Cancer Imaging Program (CIP) of the NCI. Instructions for preparing for the audit will be sent to sites in advance of the audit date. With these instructions, the auditors will specify which case records will be reviewed during the audit. Auditors will review 10% of the total number of cases accrued, with a minimum of 30 to a maximum of 40 announced cases per site, plus 6 unannounced cases (full review). The cases will be 2:1 in favor of positive screens. Auditors will review on-site records against the electronically completed case report forms (CRFs), and they will record their findings on specially prepared NLST audit forms. Major discrepancies will be forwarded to the appropriate oversight body within ACRIN. IRB procedures, approvals, and consent forms will also be reviewed at the audit. Subsequent audits will occur at 12 to 18 month intervals or will be scheduled based upon the outcome of the initial audit.

19.2 Site Preparation and Training: To help sites prepare for audits and assure that clinical RAs maintain records appropriately, ACRIN Headquarters and the trial leadership will offer training. This training will include basics of good clinical practice as well as special instructions for finding and filing the kinds of source documentation needed to verify the accuracy of submitted data for this trial.

19.3 Source Documentation: For purposes of the ACRIN-NLST, the screening results C2 or DR Forms will serve as source documents, but must be signed and dated by the interpreting radiologist to be valid. Participant self-completed CRFs will serve as source documents so long as they are signed and dated by the participant. The image interpretation data beyond that documented in the radiology report may be recorded on the CRF and is accepted as source documentation **if signed by the MD.** At the time of audit, the auditor will verify from the medical record the occurrence of the imaging examination, date of examination, the reader, and the date of interpretation. **Any use of an approved CRF as source documentation requires that the CRF be signed and dated and refer to the source of the information (participant questionnaire, CT, MR, etc.).** The medical records that contain data elements required for completion of specific forms (e.g., PA, DE, TF Forms) serve as source documents and should be retained in the participant chart. Section 19.6 includes a listing of study-specific forms, their due dates, and the acceptable source documentation. Any use of CRFs as source documentation when the protocol designates that the information must be audited against the medical record or other documents will be considered a deficiency.

19.4 Institutional Review Board: Sites must have on hand documentation of IRB approval prior to subject registration, including a copy of IRB approval of initial application, copies of IRB approvals of modifications, and copies of annual renewals. Please see Appendix XI for the contents of the NLST Regulatory Binder.

19.5 Conducting the Audit: Site audits for the ACRIN-NLST require the presence of the site principal investigator during the audit and for the exit interview. Whenever possible, the audit team will include a physician member, typically an ACRIN-NLST investigator, for educational purposes and interpretation of the protocol when necessary. The audit is usually conducted over 2-3 days, during which time the audit team must be provided a room with adequate space for the review of participant charts and records in private.

19.6 Audit/Source Documentation

The table below reflects the source documents and signatures required for the ACRN-NLST CRFs. The forms are listed in chronological order. Only forms listed on this table are reviewed at the time of audit.

Form	Data Collection / Timeline	Source Documentation
A0	Participant registration form Completed at registration via ACRIN web site	• A0: – RA signed, dated • E1: – PT signed, dated; RA signed • All Consent Forms: PT signed, dated; other signatures as required by local IRB
MRRA	Medical Records Release Authorization Completed at enrollment and annually with re-screen	• MRRA (Original): - PT signed, dated (copy not acceptable) • Annual MRRA renewal (Original)—PT signed, dated (copy not acceptable)
DP	Demographic/Health Status/Health Habit/Symptom Questionnaire Completed at enrollment	• DP: - PT signed, dated; RA signed to confirm review of data.
BL*	Biomarker Collection Form: Completed by RA to record collection of blood and urine collection. Specimen collection performed at registration or screening visit. Group 1 Biomarker participants sites only. Completed at baseline, Year 1, and Year 2	• Biomarker consent - PT signed, dated; other signature as required by local IRB • BL - RA completed, signed, dated
PA	Pulmonary Function Test Form: Completed by RA to record results of spirometry test, spirometry performed at registration or screening visit. Completed at enrollment	• PA: - RA completed, signed, and dated • Spirometry print-out • PA Questions # 9-13 verified against spirometry print-out
SS	Smoking Status Questionnaire: Completed at enrollment	• SS: - PT completed, signed, and dated; RA signed to confirm review of data.

C2 *Arm 1*	Baseline screen should occur within 4 weeks of randomization; annual re-screens should occur within 1 month prior to 3 months after the anniversary of randomization. Screening CT Form: Completed by radiologist and research associate to document findings and results of the screening CT exam.	• C2: - Reader Physician signed, dated; RA signed, dated to confirm review/completed form • Screening Results Letter: - Reader Physician signed, dated.** **The screening result and any recommendations should be consistent between the C2 Form (or I9 Form) and Screening Results Letter. If discrepant, refer to I9 Form to reconcile.
DR *Arm 2*	Screening Chest Radiograph Form: Completed by radiologist and research associate to document findings and results of the screening CXR exam. Baseline screen should occur within 4 weeks of randomization; annual re-screens should occur within 1 month prior to 3 months after the anniversary of randomization.	• DR: Physician - Reader signed, dated; RA signed and dated to confirm review/completed form. • Screening Results Letter: Physician - Reader signed, dated.** **The screening result and any recommendations should be consistent between the DR Form (or I8 Form) and Screening Results Letter. If discrepant, refer to I8 Form to reconcile.
IM	Screening Results Form: Completed by research associate to document participant and referring physician notification of screening exams. Screening Results letters should be sent within 4 weeks of the screening exam. Data Due: Year 1-within 8 weeks of registration via the ACRIN web site. Year 2, 3-within 4 weeks of screening exam.	• IM: - RA completed, signed, dated • Screening Results Letter: – Reader Physician signed, dated. • Results Withheld Letter or similar chart documentation, as appropriate based on IM. If IM reports that the results letter was not sent to the physician of record because the participant declined to identify a physician or notify his/her physician, either a Results Withheld Letter or other documentation must be in the study chart.
I8 *Arm 2*	Historical Images Form-CXR: Completed by radiologist and research associate to document comparison of screening exam with historical images. Historical images should be reviewed within 4 weeks of screening examination.	• I8: - Reader signed, dated; RA signed, dated; Physician completed, signed, and dated if historical images were reviewed to confirm review/completed form • Screening Results Letter: – Reader Physician signed, dated.

I9 *Arm 1*	Historical Images Form-CT: Completed by radiologist and research associate to document comparison of screening exam with historical images. Historical images should be reviewed within 4 weeks of screening examination.	• I9 - Reader signed, dated; RA signed, dated; Physician completed, signed, and dated if historical images were reviewed. • Screening Results Letter: – Reader Physician signed, dated.
F1/F2	Follow-Up Forms Completed by research associate every 6 months for the duration of the study.	• F1/F2: – PT and/or RA completed; RA signed, dated to confirm review/completed forms.
FS	F1 Form supplement Completed at 6 month intervals as necessary, when participants indicated on F1 forms that they have had more provider visits or health care encounters than can be documented on the F1 Form	• FS: – PT and/or RA completed; RA signed, dated to confirm review/completed form.
FC	Vital Status Form Completed at 6 month intervals or with change in vital status of participant	• RA signed and dated • If medical abstraction required, check for DE and/or TF and associated source medical documents –or– • Documentation of due diligence to obtain source documents for medical abstraction (separate worksheet)
DE	Diagnostic Evaluation Form Completed by Certified Medical Abstractors and Coders (Form is not ACRIN audited)	• If applies, form is in participant case record with abstractor's original signature and date. • Xerox copies of all medical documents that describe the methods, complications, and results of diagnostic tests that are performed as the consequence of an NLST screening result.
TF	Treatment Form Completed by Certified Medical Abstractors (Form is not ACRIN audited)	• If applies, form is in participant case record with abstractor's original signature and date. • Xerox copies of all medical documents that describe the treatments, complications, and responses to therapy for lung cancers diagnosed during the NLST.
CX	Cancer Progression Form Completed by Certified Medical Abstractors (Form is not ACRIN audited)	• If applies, form is in participant case record with abstractor's original signature and date. • Xerox copies of all medical documents that describe the cancer progression from the date of the positive screen forward.
	Medical Resource Guide for Un-insured or Under-insured Participants (Maintain copy of document in Regulatory Binder).	• Referral source for medical care (if A0 Question 15 = 7 or 8, then source documentation of information given to participant will be audited). • Progress note in participant file that the referral resources were provided, signed and dated by RA or PI.
	Smoking Cessation Materials (Maintain copy of document in Regulatory Binder).	• Referral source for smoking cessation for all participants who are current smokers. • Progress note in participant file that the smoking cessation resources were provided, signed and dated by RA or PI.

For participants in whom diagnostic evaluations are performed for suspected lung cancer, negative screens with significant findings not suspicious for lung cancer, symptoms, or other reason during the trial, formal medical abstraction will be performed by certified abstractors based upon source medical records documents procured from hospital or clinic charts. Similarly, all treatment records should be procured for source documentation on treatment evaluations and outcomes. These source documents should be maintained in the NLST participant chart to prevent a discrepancy or inability to document data collected by medical abstraction. Procedures for procuring medical records are detailed in the ACRIN-NLST Manual of Operations.

19.7 After the Audit

See the American College of Radiology Imaging Network AUDIT MANUAL (September 2002 v.8).

20.0 SECONDARY OUTCOMES: QUALITY OF LIFE [GROUP 1 SITES ONLY]

Important secondary end-points in this trial are the differential impact of CT versus CXR screening on quality of life (*QOL*) as well as the impact of a positive screening result on QOL and anxiety. To address these respective endpoints, QOL assessment instruments will be administered to participants according to the schema below *(Figure 6)*.

- **Impact of Screening on QOL *(Study 1)***
  A random sample of 1100 Experimental arm and 1100 Control arm participants will be asked to complete annual QOL questionnaires, from among those study participants who read or understand English or Spanish.
- **Impact of a Positive Screening Result on Quality of Life and Anxiety *(Study 2)***
  Among experimental arm participants, an estimated 30-35% *(approximately 1,500-1,750 participants)* will have positive screening results *(either abnormal or indeterminate nodules)* at the initial prevalence screen. In addition, we anticipate that at least 1% of those participants who screen negative for lung cancer will have potentially significant findings that are not related to lung cancer (approximately 10 participants). We will administer QOL and STAI instruments (*QF Form*) to 825 of the experimental arm participants with a prevalence screening CT positive for lung cancer or other potentially significant findings within one month of the positive screening test and at 6, 12, 18, 24, 30, 36 months following the positive screening test. Similarly, an estimated 10-15% of control arm participants *(500-750 participants)* will have positive screening results at the prevalence screen. As in the CT arm, we expect that at least 1% (approximately 10 participants) will screen negative for lung cancer but have potentially significant findings that are not related to lung cancer. 500 of the control participants with positive radiographic screens positive for lung cancer or other potentially significant findings will complete QOL and STAI instruments at the same time intervals. To serve as controls, equal numbers of participants from the Experimental and Control arms, respectively, with negative screening studies will be matched to the positive screened participants for accrual site, age, and sex. For those patients in the sub-study who are true positives (approximately 75 participants), diagnosed with lung cancer, and their matched controls, we will continue to collect these instruments every six months for the trial duration. In all instances, participants must be able to read or understand English or Spanish, as only these versions if the QOL instruments have been validated. Thus, in this sub-study, we anticipate approximately 2,500 participants. *(See Figure 6.)*

20.1 Tools For Quality of Life Data Collection

The instruments used to assess QOL include the EuroQol EQ-5D and the SF-36v2 instruments.[84-88] Both questionnaires have been demonstrated to be internally consistent, to be acceptable to participants, and to take a total of 12-15 minutes to complete. These questionnaires will be administered at study entry to all study participants who can read or understand English or Spanish. For participants who indicate at the time of enrollment into the study that English is their preferred language, the standard tools will be self-administered. For study participants who indicate that Spanish is their preferred language, translated and validated Spanish versions of the SF-36v2 will be used.[89] Because of the potential for misinterpretation or bias, other translations of these instruments, or translators to administer the instruments, will not be used in the trial. A 5-item Mental Health Index, the MHI-5, will be computed from elements of the SF-36v2 to

augment information about the participants' mental health. This can be computed separately without additional response burden on the individuals.

We will use the Beaver Dam algorithm[90] to convert the SF-36v2 scores into Quality of Well Being *(QWB)* scores, which classifies individuals according to symptoms and functional status. We will use QWB scores to quality-adjust the life years in the cost-effectiveness analysis. Each year of life *(or shorter interval of time)* will be assigned a value between 0 and 1.0 QALYS.

To measure certain effects of screening that may be short-lived, such as anxiety, we will use the Spielberger State-Trait-Anxiety Inventory *(STAI Form Y-1)*. The STAI Form Y-1 is a one-page 20-item questionnaire that can be completed in a few minutes.[91] Translation of the STAI form Y-1 into Spanish has also recently become available.

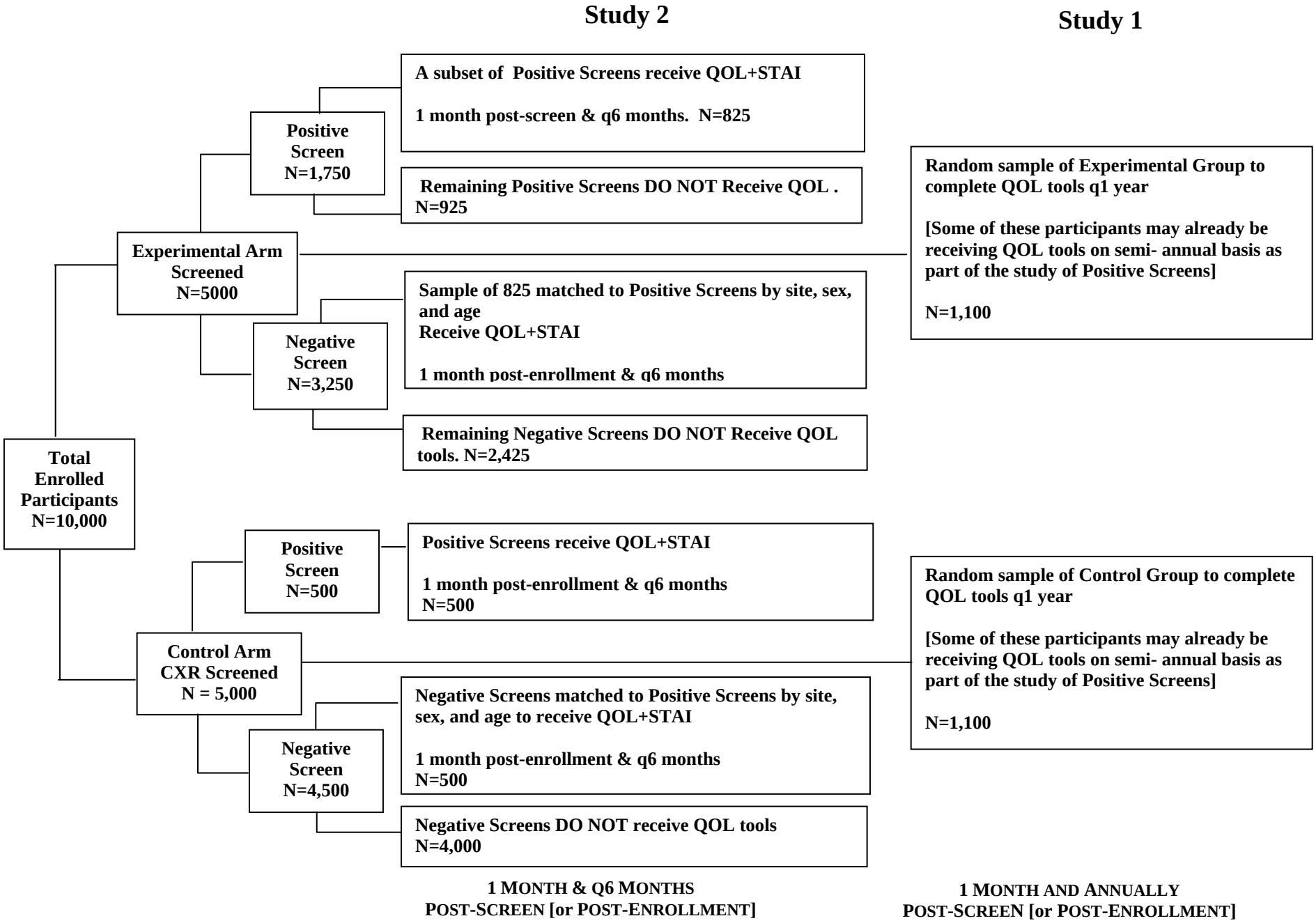


Figure 6: ACRIN NLST: Schema for Administration of the Quality of Life and Anxiety Instruments To be Performed Only at Group 1 ACRIN sites

20.2 Collection of Baseline Information on Quality of Life

To establish a baseline for the quality of life measurements, Experimental and Control arm participants who read or understand English or Spanish will be asked to independently complete the SF-36v2 and EuroQol-EQ5D questionnaires at the Enrollment *(first)* visit prior to randomization.
As necessary, the RA will encourage participants, but will not attempt to interpret the meaning of questions. During the trial-specific training sessions and during routine conference calls devoted to operational aspects of the trial, all RAs will receive training as to the manner in which they may assist participants.

20.3 Overview of General Impact of Screening on Quality of Life *(Study 1)*

A random sample of 1,100 experimental and control arm participants will be asked to complete the QOL instruments. During the portion of the trial in which participants are being screened, QOL instruments may be completed at the time of screening. If participants fail to complete the questionnaire when they return for screening or fail to return for screening, mailing of the quality of life tools will be coordinated from the ACRIN Biostatistics Center *(BC)*, located at the Center for Statistical Sciences, Brown University. BC personnel will mail participants copies of the SF-36v2 and EuroQol-EQ5D instruments (*QL Form*) as well as pre-addressed, stamped envelopes for return mailing to the Biostatistics Center. Participants will be provided with a toll-free number (which is answered by the RA at the BC) should they require assistance with reading questionnaires. If these questionnaires are not returned within 10 working days, the BC RA will telephone the study participants to ensure that the questionnaires were received and to encourage participants to complete and return them. If questionnaires are not returned within 20 working days, the BC RA will attempt to complete the questionnaires in a telephone interview. Telephone interviews will be conducted only as a final measure to avoid any biases introduced by differences in the method of administration of the questionnaires. The RA will make note on the cover sheet that the form was administered orally to the study participant. The RA will not attempt to interpret a question.

20.4 Impact of Positive Screen Result on QOL and Anxiety *(Study 2)*

20.4.1 *CT Screens:* An estimated 30-35% of experimental participants will have positive screening CT studies at baseline. 825 experimental arm participants with screens positive for lung cancer or other potentially significant findings not related to lung cancer will complete QOL and STAI instruments within one month of the positive test result and thereafter at six-month intervals from the time of the screening visit. To provide comparable controls, an equal number of experimental arm participants with negative screening CT exams matched by site of accrual, sex, and age, will complete the QOL and STAI instruments (*QF form*) in the same time intervals.

Chest Radiograph Screens: Based on published reports, we anticipate that only 10-15% of control participants will have positive screening chest radiographs. 500 control participants with screens positive for lung cancer or other potentially significant findings not related to lung cancer will complete QOL and STAI instruments (*QF form*) within one month of the positive test result and thereafter at six-month intervals from the time of the Screening Visit. An equal number of comparable controls will be drawn from control arm participants with negative screening chest radiographs, matched by site of accrual, sex, and age.

20.4.2 After selection into this sub-study, within one month of receiving the positive screening test result, the BC personnel will mail participants SF-36v2, EuroQol-EQ5D, and STAI questionnaires (*QF form*), along with pre-addressed, stamped envelopes for return mailing to the Biostatistics Center.

After the initial set of questionnaires, the four groups of participants will receive the three questionnaires semi-annually for 36 months from the initial date of the index screen. For this substudy, all questionnaires will be mailed from the BC using the approach described in Section 20.3. If these participants are among those already selected to receive annual questionnaires, they will no longer receive questionnaires on the annual schedule, but will be

"upgraded" to receive questionnaires on every six-month anniversary of their intake into the study.

20.5 Administration and Processing of QOL Instruments

A database will be maintained at the BC to monitor selection of study participants for each of the QOL studies and the receipt of mailed questionnaires and telephone contacts. If the questionnaires are not received at the BC within 10 working days of the date of the mailing, a BC RA will telephone the participant to determine whether the questionnaires were received and completed. Participants who did not receive the questionnaires will have additional questionnaires sent by mail after confirming the correct mailing address. If questionnaires were received but never completed, the BC RA will urge the study participant to complete and return the questionnaire. If the questionnaires are not received at BC within 20 working days of receipt of the mailing, the BC RA will telephone the participant and volunteer to assist in questionnaire completion. If necessary, the forms will be administered by telephone; the mode of administration of all such questionnaires will be documented in the trial database.

21.0 DETERMINATION OF SECONDARY OUTCOMES: HEALTH AND MEDICAL RESOURCE UTILIZATION

The impact of lung cancer screening on medical resource utilization will be studied. Among the outcome variables to be measured are:

- Medical resource utilization for positive screening tests resulting from both true positive *(malignant)* and false positive *(benign)* conditions.
- The impact of lung cancer screening on the occurrence of iatrogenic complication/illness requiring medical care.
- The proportion of the Control group that seeks CT screening independently of this clinical trial.

21.1 Methods of Collection of the Health and Health-Care Use Data

To ascertain the frequency and types of medical encounters of potential relationship to lung cancer and lung cancer screening, participants will be contacted at six-month intervals. At this contact, participants will be asked to answer a series of questions regarding interval medical visits, hospitalizations, or interventions that have occurred since the prior contact. Participants in both the Experimental and Control Arms will provide this information via interview (live or telephonic) or self-completed questionnaires. Particular emphasis will be placed on ascertaining whether any lung-related medical visits or hospitalizations have occurred or whether any of a number of specific lung-related diagnostic or therapeutic interventions has been performed.

If participants have had medical contact of potential relationship to lung cancer or lung cancer screening in the past six months, permission to contact the physician/facility of record will be obtained by the site RA for the appropriate facility, as provided for in the informed consent process. Copies of all pertinent medical records will be obtained for purposes of medical abstraction to detail procedures performed, therapies administered, and iatrogenic effects of any procedures or therapies related to lung cancer or lung cancer screening. The source documents from which these data are collected will be retained for purposes of documentation, as allowed by the individual institutions. At those sites in which copies of scrubbed medical documents cannot be released, chart abstraction will occur on site and the necessary data entry completed without retention of source documents.

If a participant cannot be contacted directly, sites will try to establish their vital status and update the contact information for that participant by contacting individuals and personal physicians listed on the Contact Information Sheet completed at enrollment and updated annually.

At the end of the study, the names and social security numbers of any participants reportedly deceased or lost to follow-up will be submitted to the National Death Index to determine whether they have died during the course of the study. For participants that match with the National Death Index, the death certificate will be obtained and the cause of death ascertained. In addition, the participant's

physician and next of kin will be interviewed. In cases for which the cause of death is uncertain, a truth panel consisting of physicians not participating in the trial itself will be used to determine the relationship of the cause of death to lung cancer.

For all participant deaths in the NLST, every effort will be made to procure the death certificate and any available medical record data detailing the terminal events. All lung cancer deaths will be reviewed by an independent Truth Panel of physicians not participating in the NLST to determine the relationships between cause of death, lung cancer, and screening interventions.

All participants will be required at the time of study enrollment to agree to a review of their medical records as well as notification of next of kin or close personal contact in the event of their death. Informed consent for medical record review and notification of next of kin will be renewed annually.

22.0 COST-EFFECTIVENESS ASSESSMENT

22.1 We will collect cost information on those participants to whom we administer the quality of life instruments to assess the impact of positive screening results on QOL and anxiety. In addition, we will obtain billing records from selected sites, such as Dartmouth-Hitchcock Medical Center, to help refine estimates of direct medical costs, direct non-medical costs, and opportunity costs for various alternative screening strategies *(including no screening)*. Direct medical costs will include those related to the screening tests and subsequent diagnostic evaluations, treatment for lung cancer *(and other conditions first detected through the screening process)*, and complications from testing, treatment, and morbidity. Non-medical and opportunity costs will include lost wages, traveling and lodging costs for the original screening tests and all subsequent evaluations and treatment for the screenee *(and caregiver)*. Pain and suffering will not be considered as a cost, but as a disutility measured in QALYS. The cost questionnaires will collect information on non-medical and opportunity costs and help in the collection of direct medical costs. Information to compute direct medical costs will also be abstracted from medical charts. The cost questionnaires will be administered at the same time as the quality of life questionnaires. Cost data will be collected on both Experimental and Control arms to determine whether some of the increased costs of CT screening are offset by lower costs of earlier treatment. We will assess the costs from the societal perspective of Gold.[92] All costs will be adjusted for inflation by using either the most recent general medical care component of the Consumer Price Index-Urban or the Medicare Economic Index as appropriate.[93,94] Future costs beyond the period of the study will be predicted, adjusted for inflation, and annually discounted at different rates in the 0% to 7% range.[92]

22.2 Medical

For many of the procedures and treatments in common use, such as full chest CT, bronchoscopy, and lobectomy, cost estimates will be derived from the existing literature and from Medicare cost data. In choosing among published estimates, estimates of actual costs rather than charges will be used.[92] For some of the procedures whose costs have not been published, Health Care Financing Administration *(HFCA)* cost data will be used to estimate the costs of inpatient hospitalization, physicians' services, and outpatient testing *(http://www.hcfa.gov/stats/pufiles.htm)*.

The costs of some newer procedures, such as screening helical CT and limited helical CT, have neither been published nor estimated by HCFA. For these procedures, we will estimate their costs using the approach of Medicare RBRVS, which divides the costs of radiologic procedures into professional and technical components.[95,96] The professional component is further divided into work, practice cost, and liability RVUs. To estimate the work RVUs, we will collect data on the radiologist's time required for planning and interpreting the examinations. In addition, we may survey a sample of radiologists to estimate a procedure's work RVUs *(by comparing the procedure to one with an established RVU, such as a PA and LAT chest radiograph [RVU of 1.00], or full chest CT exam)*. We will multiply the work RVU by 1.36 to account for the practice and liability RVUs, which together comprise 26.2% of total professional RVUs in radiology (Medicare RBRVS 1995). *(We will also multiply by the radiology conversion factor but not the geographical factor)*. To estimate the technical components, we will collect data regarding resource utilization, including CT examination time, technologist's time, contrast material, film, etc. In addition, we may survey technologists to

estimate the technical RVUs, which do not include a physician work component. We also will look at additional sources to estimate costs based on discharge diagnosis of lung cancer from the Healthcare Cost and Utilization Project.[97]

22.3 Non-medical

We will assess the non-medical costs to the screenee *(and caregiver)* by means of a questionnaire *(PQ Form).* These costs will include out-of-pocket expenses for travel, food, and lodging related to the screening test and subsequent diagnostic tests and treatments related to screening. In addition, we will collect data on the time *(hours)* spent on all the above activities and hours of missed employment and volunteer activities. Similarly, we will collect data on the non-medical costs of lung cancer diagnosis and treatment in the Control arm. No standard questionnaires for this purpose exist to our knowledge. We will develop this questionnaire after examination of other ad hoc questionnaires and after assessment of ACRIN experience with a previously developed questionnaire in use for ACRIN Protocol 6651: Role of Radiology in the Pretreatment Evaluation of Invasive Cervical Cancer.

We will calculate cost-effectiveness with and without the inclusion of some, but not all, future "non-lung cancer" medical costs as recommended by Gold.[92] These issues are currently unresolved. Uncertainty in the analysis will be assessed through sensitivity analysis in which the assumptions about future costs and health states are varied and outcomes are assessed under these different assumptions.

23.0 STATISTICAL CONSIDERATIONS

The primary endpoint of this trial is lung cancer-specific cumulative mortality. Secondary endpoints will be all cause mortality, stage of lung cancer at diagnosis, medical resource utilization, and quality of life and the economic consequences of screening.

23.1 Primary Aim and Secondary Aim 1: *To determine whether lung cancer screening using low-dose helical CT reduces lung cancer-specific mortality relative to screening with chest radiographs in a high-risk cohort. To compare all cause mortality between screening with CT versus chest radiographs.*

The analysis for lung cancer-specific as well as all cause mortality will be carried out from an intent-to-treat perspective. The two study arms will be compared on the basis of the observed cumulative mortality in each arm, measured in deaths per person per years screened.[98] In secondary analyses, regression models will be used to examine mortality differences between subgroups defined by individual participant characteristics. It should be noted that the trial, as designed with 50,000 individuals (combined with the Lung Screening Study of the NLST) is not adequately powered to detect a meaningful difference in all cause mortality.

23.2 Secondary Aim 2: *To assess differences in stage distribution between the two arms of the study.*

Comparisons of TNM stage distributions between CT versus chest radiographic screening will first be carried out by dichotomizing stage according to cancer resectability. Rates of resectable cancers will then be compared using standard methods for binomial proportions. The effect of participant characteristics will be assessed using logistic regression modeling. In an elaboration of the dichotomized stage analysis, the full range of stage categories will be used to define the response variable in an appropriately constructed ordinal regression model. Covariates will include randomization arm and individual participant characteristics.[99] Comparisons of lesion size will be carried out using standard two-group nonparametric comparisons. Parametric comparisons will also be carried out in the form of regression analysis to examine the role of participant characteristics. Size measurements will be appropriately transformed as needed to meet regression model assumptions.

Interim analysis at year 2 of differences in stage distribution between the two arms of the study will be the basis for determining the need for a larger trial.

23.3 Secondary Aim 3: *To compare lung cancer-related medical resource utilization between the two arms of the study.*

Comparisons of medical resource utilization, including the frequency and significance of unnecessary medical interventions for false positive screening results will be made using two-sample techniques appropriate for the type of outcome measure *(binary, discrete, or continuous)*. As before, regression models will be used to carry out secondary analyses, which examine the role of participant characteristics. Comparisons for which repeated measures are available will be made using appropriately constructed models for the analysis of longitudinal data.[100]

23.4 Secondary Aim 4: ***To assess the psychological impact of screening as well as the impact of a positive screening test, and the differential effects on quality of life between the two arms of the study [Participants at Group 1 sites only].***

Longitudinal data models for continuous responses will be used in the analysis of the quality of life assessments.[100] Covariates will include indicators for the groups under comparison *(for example, screen positive vs. screen negative)* and participant characteristics. The extent and nature of missing data will be examined and appropriate procedures for handling missing data and study dropout will be used.[101,102]

23.5 Secondary Aim 5: ***To assess the economic consequences of screening with CT versus chest radiographs.***

Cost-effectiveness analyses as well as data necessary to conduct comparative analyses of the costs of alternative protocols will be collected throughout the study. The principal information will be units of utilization for *(1)* diagnosis and staging, including radiological and clinical procedures, laboratory tests, physician and hospital services; and *(2)* treatment, including surgery, radiation therapy, and hospitalization. Healthcare utilization will also be acquired for staging and treatment of disease recurrence in the two-year follow-up. Unit cost estimates will be based on Medicare reimbursement rates.

This project is designed to determine whether screening with helical CT can decrease lung cancer mortality relative to screening with chest radiographs. In addition, the project will provide some information on the accuracy of several tests, complication rates of testing and treatment, and quality of life. Although all of this information may prove to be very useful, it alone will not directly answer the numerous questions that will likely arise about screening, such as who should be targeted, how often individuals should be screened, and how suspicious findings should be further evaluated.[29] Answers to such questions require a systematic weighing of benefits, harms, and costs, which often entails computations of probabilities and values that are often too complex for the unaided human brain. Therefore, we plan to build a quantitative decision model that can utilize the information generated by our project to help determine if and how lung cancer screening should be implemented.

We intend to analyze numerous screening alternatives, each consisting of some unique combination of screening options pertaining to the selection of the target population and the screening process. The former set of options will include age and smoking history while the latter set will include the screening frequency, interpretation criteria, and method of diagnosis. Understanding that our experimental design specifies only one set of options, we will use the data from the RCT to help build a decision model that includes the natural history of lung cancer, the accuracy of different tests, and the effectiveness of early intervention. Using this model we will simulate the effects of screening alternatives that we have not empirically studied. To some extent, policy formulation always requires some extrapolation from empirical studies *(regarding population, testing, treatment, etc.)*. Each alternative will be linked to a subtree that represents the development and progression of lung cancer, which will be modeled as a Markov process.[103] For the no-screening alternative, the transition probabilities between Markov states during each cycle will be estimated using population-based mortality rates and autopsy data.[104] These transition probabilities cannot be directly validated because disease development and progression are not usually observed without intervention. However, they can be indirectly validated by comparing the age-specific incidence and mortality rates for lung cancer predicted by the model to those observed in SEER. The other screening alternatives will be linked to modifications of the above Markov cycle tree that will include the effects of screening. We will use the results of previously published studies *(prevalence, incidence, stage distribution, false*

positive results, and complications) of screening with helical CT to help us model the intermediate and long-term effects of screening. In our modeling, we will carefully account for known biases related to early detection.[29]

For the analysis of life expectancy, each year of life will be assigned a value of one and death will be assigned a value of zero. For the analysis of quality-adjusted life expectancy, each year *(and some smaller units)* of life will be assigned a value between one and zero to account for morbidities associated with the screening process, lung cancer, and treatment. These values will be estimated using the quality of life instruments in our study. We will assign costs to the screening studies and diagnostic CT, subsequent tests and procedures including percutaneous biopsy, and treatment for cancers detected. We expect to derive many of our cost estimates from existing literature and from Medicare cost data. However, reliable cost estimates for screening CT itself and limited follow-up CT does not currently exist. Therefore, we will be collecting information on these tests in our study to help us estimate their costs.

The health and cost values described above will be accumulated across time to estimate the life expectancy *(LE)*, quality-adjusted life expectancy *(QALE)*, and expected costs for each screening strategy. For the cost-effectiveness evaluation, all strategies will be evaluated in terms of cost and effectiveness *(LE and QALE)*. Dominated strategies, that is, strategies that are less effective and more costly than at least one competing strategy, will be identified and highlighted as strategies that are to be avoided. Such strategies will then be excluded from further baseline analyses, leaving only those alternatives on the "efficient frontier." After these strategies are ordered by increasing cost, the increment in cost and effectiveness will be computed for each. The incremental cost effectiveness ratio, which is the ratio of incremental cost and incremental effectiveness, will be the focus of the economic evaluation. After performing the baseline analyses, we will perform sensitivity analyses on most of the input variables. The sensitivity analyses will help us identify the areas of greatest uncertainty in our analysis of the cost effectiveness of lung cancer screening and the conditions under which the baseline analyses are valid.

23.6 Secondary Aim 6: ***To develop a tissue bank from individuals at high risk of lung cancer both with and without pathologically proven lung cancers*** **[*To be collected from participants at Group 1 sites only*].**

This bank will be a rich resource for determining biomolecular markers of high predictive value in stratifying levels of lung cancer risk such as pre-malignancy *(risk of future development of lung cancer)*, subclinical lung cancer, and advanced disease. Broadly stated, the goals of the analysis for the biomolecular marker data will serve to: *(1)* characterize the pathologic, clinical, genetic, imaging, and epidemiologic data profiles of individuals in the study cohort, both cross-sectionally and longitudinally, and *(2)* assess the potential usefulness of biomolecular profiles as predictors of lung cancer. Multivariate methods for data reduction and regression modeling will be employed in the analysis of both types of profiles. Change point models will be used in the study of the longitudinal course of biomarkers[105] and methods for adjusting for measurement error will be used as needed.

24.0 SAMPLE SIZE CONSIDERATIONS

24.1 Primary Aim

This protocol will be implemented in coordination with the LSS study of the PLCO. The two studies comprise the National Lung Screening Trial (NLST). The projected accrual of NLST is 50,000 participants, with a maximum duration of 8 years. 25, 000 of these participants will be recruited into the ACRIN protocol. Accrual is expected to be completed within 2 years from study opening. NLST participants will be randomized to the two study arms in equal proportions. Each participant will undergo a prevalence screen and two annual incidence screens. Data from the two parts of NLST will be pooled for the analysis of the primary endpoint, which is lung cancer-specific mortality. Sample size and power considerations for the primary endpoint using the data from the full NLST study were presented at the NCI Board of Scientific Advisors (meeting of 14 November 2001). The remainder of this section presents sample size computations for the ACRIN protocol, with the originally projected total study duration of 5 years.

The following table lists estimates of the required sample size per arm for various combinations of the parameters of the design. Lung cancer-specific mortality in the control arm was assumed to be in the range of 0.004 to 0.006 deaths per person years screened. The cumulative mortality reduction refers to a 5-year interval from the beginning of the study. Computations were made using the approach and formulas provided by Gohagan et al.[106]

Power	Cum. Mortality Reduction	Mortality Control	Compliance. Control	Compliance Screen	Sample Size
.9	.5	.006	1.00	1.00	1628
.9	.5	.006	.80	.95	2805
.9	.5	.006	.85	.90	2909
.9	.5	.006	.80	.90	3292
.9	.5	.006	.85	.85	3411
.9	.5	.005	1.00	1.00	1954
.9	.5	.005	.80	.95	3365
.9	.5	.005	.85	.90	3490
.9	.5	.005	.80	.90	3950
.9	.5	.004	1.00	1.00	2442
.9	.5	.004	.80	.95	4206
.9	.5	.004	.85	.90	4362
.9	.3	.006	.85	.85	10,930
.9	.3	.004	.85	.85	16,400
.9	.25	.006	.85	.85	16,240
.9	.25	.005	.85	.90	16,843
.9	.25	.005	.85	.85	19,489
.9	.25	.004	.85	.85	24,361
.9	.20	.006	.85	.85	26,146
.9	.20	.005	.85	.85	31,375

24.2 Quality of Life Data Collection [*Group 1 sites only*]

The sample size for the collection of quality of life data was chosen to provide adequate power for comparing changes in the Quality of Well Being *(QWB)* index within the first year of the study. In particular, such comparisons will be made between participants who screen positive on CT and those who screen negative and between participants who screen positive on chest radiographs and those who screen negative. Based on data from the Beaver Dam study[90] it was assumed that the standard deviation of QWB values will be 0.11 in each group. The computations of sample size were based on the approach described by Diggle et al, assuming equal sample sizes in each of the groups under

comparison.[100] The required power was set at 90% and the Bonferroni correction was used to ensure an overall level of 0.05. The within participant correlation was conservatively assumed to be zero. In the table below, D represents the difference in the 12-month change between the two groups, measured in standard deviation units.

D *(standard deviation units)*	**0.24**	**0.25**	**0.26**	**0.27**	**0.29**	**0.3**
sample size per group	**730**	**673**	**622**	**576**	**500**	**467**

Hence, even allowing for loss to follow-up, the sample sizes for the quality of life data *(about 750 within the positive and negative screen groups, and 500 in the Control group)* will provide adequate power to detect differences in change as low as 0.24 in the screen arm and as low as 0.29 in the control arm.

This study will be monitored by the Clinical Data Update System *(CDUS)*. Cumulative CDUS data will be submitted quarterly to CTEP by electronic means. Reports are due January 31, April 30, July 31, and October 31.

In conformance with the National Institute of Health *(NIH)* Revitalization Act of 1993 with regard to inclusion of women and minority in clinical research, every effort will be made to include participants of all ethnicities and genders.

24.3 Minority Accrual

The recruitment of minorities and women into the protocol is important to ensure that the study findings can be extended to the population of men and women residing in the United States. Any man or woman meeting the eligibility criteria for entrance into the protocol will be asked to participate, regardless of race. Accrual into this study is based on cancer risk status, largely determined by age and smoking history. We expect to recruit minorities and women into our study population in proportion to the prevalence with which members of these minority groups are represented in the United States population and with which they smoke. We anticipate that larger proportions of minority participants will be recruited at the urban institutions, and we plan to focus on recruiting minority populations in areas in which they reside.

According to the 1998 U.S. Surgeon General's Report on Tobacco Use Among U.S. Racial and Ethnic Minority Groups, African American and Southeast Asian men in the U.S. have a high prevalence of cigarette smoking. Asian American and Hispanic women have the lowest prevalence of cigarette smoking. We based our estimates of anticipated minority accrual on smoking prevalence data available from the Centers from Disease Control. This data is based on information obtained from the 1987, 1988, 1990, and 1991 National Health Interview Survey. Because of data availability, our estimates of smoking prevalence are based on current smokers, although we do plan to screen former smokers who have recently quit. For the distribution of minority populations in the United States, we used data from the 2000 census. We applied the expected male to female ratio for residents aged 55-74 from 1990 census data because this information was not easily available from the 2000 data. We assumed that the distribution of minorities was consistent across all age groups. Using these data, we obtained expected proportions of the United States population by gender and race that fell within our inclusion criteria for age *(55-74 years)* and smoking status. We assume that our 25,000 recruited participants will be recruited in proportion to their representation in the general United States population. Minority accrual, by gender, for this study is estimated below:

Planned Minority Inclusion

	American Indian or Alaskan Native	Asian or Pacific Islander	Black, not of Hispanic Origin	Hispanic	White, not of Hispanic Origin	Total
Male	114	363	1,854	1,590	8,613	12,534
Female	136	143	1,561	1,573	9,053	12,466
Total	250	506	3,415	3,163	17,666	25,000

25.0 CORRELATIVE STUDY: BIOMOLECULAR MARKER BANK AND DISCOVERY NETWORK

Our knowledge of the molecular events heralding lung cancer and the specific markers associated with the evolution from initiation to invasion is only partial. This trial represents a tremendous opportunity to collect samples with which to better characterize the molecular events coincident with multi-step carcinogenesis because the participants are a high-risk cohort that will be well characterized and followed longitudinally.

25.1 Specific Aim

To implement a tissue/specimen bank of serum, sputum and urine samples from participants that will be optimally preserved and prepared for future state-of-the-art molecular assays, including but not limited to polymerase chain reaction (*PCR*), proteomics, and oligonucleotide microassays.

25.2 Overview of Blood, Urine, and Sputum Collection [Group 1 Sites Only]

Our hypothesis is that biomolecular markers may be identified in the blood, sputum, or urine that can enhance our understanding of the genetic events proceeding and associated with lung cancer. This can be achieved through an efficient biomarker discovery process. With input from the NCI and appropriate internal review boards of the current lung cancer SPORES *(University of Colorado, Johns Hopkins University, University of Texas, including UT Southwestern and the MD Anderson Cancer Center, and UCLA School of Medicine)*, we propose to develop a specimen bank of blood, sputum, and urine specimens for archiving. Although blood and sputum samples are currently used for most biomarker assays, we believe this trial presents a unique opportunity to also collect urine, which is a rich source of secretory proteins, is "non-invasive" and is easy to obtain. Participants of both the Experimental and Control Arms randomized into the study at sites collecting biomarkers [Group 1 sites only], will undergo collection of these samples at the time of enrollment and at the first and second incidence screens. This will provide a rich foundation for testing biomarkers found to be promising in preliminary tests conducted outside of the ACRIN-NLST trial.

Potential biomarker*(s)* for testing would be identified based upon preliminary data provided by studies performed *outside* of this trial. Request for use of banked specimens for biomarker studies and any associated data collected on NLST participants requires formal application to the ACRIN Biomarker Oversight Committee, comprised of molecular biologists, radiologists, and other scientists. Following approval by this committee, proposals are submitted for final approval to the NCI. The application process involves a description of study hypothesis, specific aims, types of samples requested, types of associated clinical data requested, statistical justification of sample size, assay descriptions, and quality control procedures to be implemented. Importantly, any additional specimens obtained from NLST participants *must also* go through this approval process to ensure that the primary biomarker collection is not compromised.

Biomarker tests could be conducted in one or more laboratories housing the appropriate technology and methods to automate sample preparation as well as documented expertise in the performance of the particular assay. Attention will focus on the development of integrated biomarker sets to analyze multiple markers concurrently. Given considerations of hardware, the requirements of comprehensive database software, and analysis software capable of complex multivariate modeling, these biomolecular assays may be best performed in collaboration with industry. Tests for a particular marker will be conducted at one site for quality control purposes.

25.3 Biomarker Specimen Collection and Banking

Participants at selected sites (Group 1 sites only) who consent to collection of specimens will provide blood, urine, and sputum specimens for banking at the Colorado Lung SPORE Tissue Bank. These Specimens will be collected on both Experimental and Control participants at the Baseline, Year 1, and Year 2 screening examinations. This prospective sequential collection may enable the determination of the sequential genetic changes that precede or herald invasive cancer. To encourage the maximum number of specimens, participants who have refused specimens collection at Baseline, should *not* be asked to consent to specimen collection in Years 2 or 3. However, efforts *should* be made to obtain consent to procure remnant tissue from all participants who undergo a screening–related tissue biopsy or lung resection.

25.4 Tissue Specimen Collection for Banking

At all sites, we propose to collect leftover (remnant) tissue specimens and blood samples from participants who, during this trial, undergo biopsy procedures or surgery to remove tissues based upon a positive screening test or a suspicion of lung cancer. These tissues might include lung tissue, tumor tissue, lymph nodes, muscle, or tissue from organs such as liver or adrenal that are biopsied or removed as part of standard diagnosis or treatment. The tissue specimens may be benign or cancerous. Only tissues that would ordinarily be discarded after analysis for clinical purposes would be used for banking. The sample(s) of tumor taken for research will be taken from the tissue after it has been removed. Therefore, the use of this tissue for research will not result in any additional pain or side effects. No tissues will be removed solely for the purposes of this study. At the time of tissue collection, we would also request a blood sample of approximately 40 ml by routine phlebotomy.

The tissue and blood samples will be processed for banking at the Colorado Lung SPORE Tissue Bank, where the biomarker specimens from participants at the Group 1 sites are also being banked. Those sites that will not permit banking at distant facilities will bank their specimens, given the appropriate storage facilities and Certificate of Confidentiality, at their respective institutions. These specimens will be stored for purposes of future research, which may include genetic tests.

25. 5 Specimen Database

All participant information will be entered into the ACRIN Lung Cancer Screening database. This will include information about participant sociodemographic, health, cigarette smoking, and occupational histories as well as information relevant to cancer diagnosis, cancer therapy, and treatment response. All information will be coded with a study specific identification number and all personal identification information removed in order to maintain confidentiality. Only the tissue and participant study ID number will be retained at the Colorado Lung SPORE Tissue Bank. The Tissue Bank will have no method of associating any specimen with an individual or her/his confidential data.

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Appendix I

AMERICAN COLLEGE OF RADIOLOGY IMAGING NETWORK
ACRIN 6654
NATIONAL LUNG SCREENING TRIAL

SAMPLE CONSENT FOR RESEARCH STUDY
(Includes Biomarker Specimens and QOL)

This is a clinical trial, a type of research study. Clinical trials include only participants who choose to take part. Please take your time to make your decision. You may want to discuss this with your friends, family, or doctor.

The American College of Radiology Imaging Network (ACRIN) and the National Cancer Institute (NCI) sponsor this trial.

You are being asked to take part in this study because you are at increased risk of lung cancer due to your age and smoking history.

WHY IS THIS STUDY BEING DONE?

The purpose of this study is to determine whether screening people at high risk for lung cancer using spiral computed tomography (CT) of the chest will reduce the number of lung cancer deaths in comparison to screening with chest x-ray (CXR). Although it is known that spiral CT can detect smaller lung cancers than can CXR, it is not known whether screening with this new test will prevent lung cancer deaths. In addition, screening with spiral CT is expected to have more side effects than screening with CXR (risks listed below). The only reliable method of determining the benefits of screening with spiral CT versus CXR is a randomized clinical trial, where some participants will be screened with spiral CT and some will be screened with CXR. The value of screening with CXR compared to no screening is currently being assessed in another trial sponsored by the NCI.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

ACRIN is part of a larger trial called the National Lung Screening Trial, NLST, in which a total of 50,000 individuals will be enrolled. About 25,000 people will participate in the ACRIN-sponsored component of the trial. Approximately 1,000 participants will be enrolled at this institution.

WHAT IS INVOLVED IN THE STUDY?

You will be "randomized" into one of the study groups described below. Randomization means that you are put into a group by chance. It is like flipping a coin. You will be assigned to a group by a computer. Neither you nor the study team will choose the group into which you are placed. You will have an equal chance of being placed in either group.

About one-half of the study participants will be screened annually with a low-dose spiral CT; the other half will be screened with CXR.

If you are randomized to the spiral CT group, the exam will require that you lie still on your back on a table that moves slowly through a doughnut-shaped machine. The machine takes a series of

x-rays to create a three-dimensional picture of your lungs. It will be necessary for you to hold your breath for 20-25 seconds while you are being scanned.

If you are randomized to the CXR group, you will receive a single-view chest x-ray. This type of x-ray is commonly used to view the organs inside the chest. It will be necessary that you hold your breath for a few seconds while the x-ray is taken.

As a participant in this study, you will also be asked to give specimens of your blood, urine and sputum (spit). In addition, if you undergo a biopsy or have surgery in which tissue is removed for testing, we would like to keep any leftover tissue that might otherwise be discarded. These specimens and leftover tissues will be kept to help researchers in the future understand what causes cancer, how to prevent it, and how to treat it. The specimens of blood, urine, and sputum will be stored at a central storage facility at the University of Colorado Lung SPORE Tissue Bank. Leftover tissues may also be stored centrally at the Colorado Lung SPORE Tissue Bank or at the facility where you had the procedure(s) to remove the tissue. Participating in the collection of specimens or allowing us to keep any leftover tissues will not benefit you, but may benefit other people with lung cancer. We will ask you to sign separate consents to allow us: [1] to collect specimens of blood, urine and sputum and [2] to store leftover tissue samples. Some of the institutions participating in this trial across the country are not collecting specimens of blood, urine or sputum. However, all institutions will ask to collect leftover tissues for storage. You may decide not to provide blood, urine, and sputum specimens or leftover tissues and still participate in the screening portion of the trial. No matter what you decide to do, it will not affect your care.

<u>If you take part in this study, you will have the following tests and procedures:</u>
All participants will undergo:

- An interview to determine general information about your smoking habits, general health, work history, and personal contact information (address, telephone number, friends and family contacts).
- A simple breathing test through a mouthpiece.
- Every (6) six months you will receive a questionnaire or telephone call to ask about your health status.
- Questionnaires about your quality of life (QOL) at baseline (beginning of the study), at year one (1) and year two (2) follow-up.

<u>Arm 1: Experimental Arm</u>

- A screening spiral CT at the beginning of the study and at the next two annual screening visits.
- You may be asked to complete additional questionnaires about your QOL and anxiety one (1) month after the spiral CT and every six (6) months for up to six (6) to eight (8) years.

<u>Arm 2: Control Arm</u>

- A screening CXR at the beginning of the study and at the next two (2) annual screening visits.
- You may be asked to complete additional questionnaires about your QOL and anxiety (1) one month after the CXR and every six (6) months for up to six (6) to eight (8) years.

You and your physician will be notified of the results of these screening tests. If they show any abnormalities you may be advised to have additional diagnostic tests or procedures. These tests

might include additional CT scans, CXRs, a biopsy or surgery. These procedures are not part of the ACRIN-NLST trial itself. Although it may be in the best interests of your health to have these tests completed, you are not obliged to have them performed as part of this trial.

If you are asked to complete the QOL and anxiety questionnaires, sometimes you will complete them during the annual visit to have the screening test or you may have the questionnaires mailed to you from a central location at ACRIN. Also, you may be contacted on the telephone by an ACRIN representative to help you fill out the questionnaires or to remind you to send it back. Your address, phone number, and contact information for a close friend or family member will be provided to ACRIN for this purpose.

When you have your CXR or spiral CT, it will take approximately 30 minutes to 1 hour of your time. The QOL questionnaires will take approximately 20-30 minutes to complete.

HOW LONG WILL I BE IN THE STUDY?

You are being asked to actively participate in the study for six to eight years, depending on when you were first enrolled in the study. However, the study investigator has the right to take you off this study if you become too ill to have surgery for suspected lung cancer.

You can stop participating at any time. However, if you decide to stop participating in the study, we encourage you to talk to the study investigator or a member of the ACRIN-NLST staff and your regular doctor first.

WHAT ARE THE RISKS OF THE STUDY?

While on the study, you are at risk of the following side effects. You should discuss these with the study investigator and/or your regular doctor. Risks and side effects related to screening for lung cancer include the following:

Very Likely

- Radiation dose from a screening spiral CT (100-300 mrem), which is less than or equal to the average annual dose from natural sources of radiation (300 mrem).
- Radiation dose from screening chest x-ray (8-12 mrem), which is much less than the average annual dose from natural sources of radiation (300 mrem).
- False positive screening spiral CT requiring a limited CT Scan test in 3 months (20-50%). The term "false positive" refers to a screening test in which findings initially of concern for cancer are later found *not* to be cancer.
- False positive screening CXR requiring a non-contrast CT Scan (5-10%).
- Anxiety about evaluation of false positive screening spiral CT or CXR results.
- Detection of abnormalities unrelated to lung cancer that could lead to unnecessary testing or treatment from screening with either spiral CT (10-15%) or CXR (1%).

Less Likely, but Serious

- False positive screening spiral CT requiring a full CT scan with intravenous contrast or other potentially invasive procedures (2-7%).
- False positive screening CXR requiring a full CT scan with intravenous contrast or other potentially invasive procedures (1-5%).
- Earlier diagnosis and treatment of lung cancer that is ineffective or unnecessary (< 2%) from screening with either spiral CT or CXR.
- Failure to detect a lung cancer that is present, and possibly miss an opportunity for cure.
- Death from biopsy (less than 1% of all biopsies); death from surgery (2-4% of all having surgery).

- Death from reaction to contrast material used in diagnostic CT scans (less than 1 in 40,000 of all receiving intravenous contrast).

There also may be other side effects that we cannot predict. Most side effects go away shortly after the screening is completed, but in some cases side effects can be serious or long lasting or permanent. You should also be aware that these screening tests are not a replacement for a physical examination or a substitute for a visit to your doctor.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

If you agree to take part in this study, there may or may not be direct medical benefit to you during the course of the study. The possible benefits of taking part in the study are the same as being screened with a spiral CT of the chest without being in the study. These include:

- Prevention or delay of death from lung cancer.
- Prevention of, or reduction in, symptoms from lung cancer.
- Milder treatment, leading to fewer side effects, from treatment for lung cancer.

We hope the information learned from this study will eventually benefit you and others who are at risk for lung cancer.

WHAT OTHER OPTIONS ARE THERE?

You may choose to not participate in this study. Other screening options that you might consider because of your risk factors may include the following: *(1)* to be screened with a spiral CT of the chest at your own expense, *(2)* to be screened with a CXR at your own expense, or *(3)* not to be screened for lung cancer at all.

Please talk with your regular doctor about these and other options.

WHAT ABOUT CONFIDENTIALITY?

Throughout the course of the study we will collect information from you and your medical records that is relevant to lung cancer screening, including your screening test results, and, if applicable, follow-up tests or treatments related to lung cancer. We will keep this data in a confidential form at this institution and in a computer file at the headquarters of the American College of Radiology Imaging Network (ACRIN and the Center for Statistical Sciences at Brown University). The screening exams performed in this study and any pathological specimens that are obtained will also be retained for at least 10 years, but without any identifying information on them. If you choose to withdraw from the study, you may revoke your approval for the use of your future medical information. To do so, you must contact Principal Investigator in writing. However, to maintain the integrity of the study, we will maintain the information you had already provided for the duration of the study.

Medical abstractors contracted by ACRIN will review your medical records after they have signed a confidentiality agreement. These records would include all lung related visits to a health care provider and all hospitalizations. If you are concerned about the confidentiality of your medical records, the institution's protocol team will de-identify your records before they are sent to the abstractors.

Other individuals or organizations that may inspect and/or copy your research records for quality assurance and data analysis include the NLST protocol team at *institution* (principal investigator, study coordinator, and project assistant[s]), the Institutional Review Board at *institution*, the American College of Radiology Imaging Network (ACRIN), the National Cancer Institute (NCI), and other groups or organizations that have a role in this study.

Information gained from this study may be used in the future for secondary studies and research. No individual names or results that could identify you personally will be used.

Although all efforts will be made to keep your personal information confidential, we cannot guarantee absolute confidentiality. Your personal information may be disclosed if required by law.

WHAT ARE THE COSTS?

The annual screening spiral CT and CXR will be paid for by ACRIN, the study sponsor. You may also be reimbursed for part of your travel expenses necessary for your participation at the time of your screening examinations.

You and your insurance company are responsible for all costs associated with diagnostic tests or treatments that result from screening. If you do not have adequate insurance coverage to pay for these procedures, we will try to find additional resources to help you.

In the case of injury or illness resulting from this study, emergency medical treatment is available but will be provided at the usual charge. No funds have been set aside to compensate you in the event of injury.

You or your insurance company will be charged for continuing medical care and/or hospitalization.

WHAT ARE MY RIGHTS AS A PARTICIPANT?

Taking part in this study is voluntary. You may choose not to take part or may leave the study at any time. Leaving the study will not result in any penalty or loss of benefits to which you are entitled.

A Data Safety and Monitoring Board, an independent group of experts, may be reviewing the data from this research throughout the study. We will tell you about the new information from this or other studies that may affect your health, welfare, or willingness to stay in this study.

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

(This section must be completed)

For information about your screening or participation, and research-related injury, you may contact:

Name_____ Telephone Number_____

For information about this study, you may contact:

Name_____ Telephone Number_____

For information about your rights as a research participant, you may contact:
(OHRP suggests that this person not be the investigator or anyone else directly involved with the research)

Name_____ Telephone Number_____

WHERE CAN I GET MORE INFORMATION?

You may call the NCI's Cancer Information Service at:
1–800–4–CANCER (1–800–422–6237) OR **TTY: 1–800–332–8615**

Visit the NCI's Websites for accurate cancer information at: http://cancer.gov/cancer_information or for comprehensive clinical trials information at: http://www.cancer.gov/clinical_trials. Information about NLST is posted at: http://cancer.gov/NLST. Visit ACRIN's Website for group information at: www.acrin.org.

PERMISSION TO REVIEW MEDICAL RECORDS:

By agreeing to participate, I give permission for my health care providers and hospitals where I have been seen to release my medical records to the study investigators.

SIGNATURE:

I have read all the above, asked questions, and received answers concerning areas I did not understand. I have had the opportunity to take this consent form home for review or discussion.

I willingly give my consent to participate in this program. Upon signing this form, I will receive a copy. I may also request a copy of the protocol *(full study plan)*.

_____ _____

Participant Signature *(or Legal Representative)* Date

Appendix II

AMERICAN COLLEGE OF RADIOLOGY IMAGING NETWORK
ACRIN 6654
National Lung Screening Trial

SAMPLE CONSENT FOR RESEARCH STUDY

(No Biomarker Specimen Collection or QOL)

This is a clinical trial, a type of research study. Clinical trials include only participants who choose to take part. Please take your time to make your decision. You may want to discuss this with your friends, family, or doctor.

The American College of Radiology Imaging Network (ACRIN) and the National Cancer Institute (NCI) sponsor this trial.

You are being asked to take part in this study because you are at increased risk of lung cancer due to your age and smoking history.

WHY IS THIS STUDY BEING DONE?

The purpose of this study is to determine whether screening people at high risk for lung cancer using spiral computed tomography (CT) of the chest will reduce the number of lung cancer deaths in comparison to screening with chest x-ray (CXR). Although it is known that spiral CT can detect smaller lung cancers than can CXR, it is not known whether screening with this new test will prevent lung cancer deaths. In addition, screening with spiral CT is expected to have more side effects than screening with CXR (risks listed below). The only reliable method of determining the benefits of screening with spiral CT versus CXR is a randomized clinical trial, where some participants will be screened with spiral CT and some will be screened with CXR. The value of screening with CXR compared to no screening is currently being assessed in another trial sponsored by the NCI.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

ACRIN is part of a larger trial called the National Lung Screening Trial, NLST, in which a total of 50,000 individuals will be enrolled. About 25,000 people will participate in the ACRIN-sponsored component of the trial. Approximately 1,500 participants will be enrolled at this institution.

WHAT IS INVOLVED IN THE STUDY?

You will be "randomized" into one of the study groups described below. Randomization means that you are put into a group by chance. It is like flipping a coin. You will be assigned to a group by a computer. Neither you nor the study team will choose the group into which you are placed. You will have an equal chance of being placed in either group.

About one-half of the study participants will be screened annually with a low-dose spiral CT; the other half will be screened with CXR.

If you are randomized to the spiral CT group, the exam will require that you lie still on your back on a table that moves slowly through a doughnut-shaped machine. The machine takes a series of

x-rays to create a three-dimensional picture of your lungs. It will be necessary for you to hold your breath for 20-25 seconds while you are being scanned.

If you are randomized to the CXR group, you will receive a single-view chest x-ray. This type of x-ray is commonly used to view the organs inside the chest. It will be necessary that you hold your breath for a few seconds while the x-ray is taken.

As a participant in this study, we will ask to keep and store any leftover tissue(s) obtained from you at the time of biopsy procedures or surgery for possible lung cancer. These tissues are removed for testing to make decisions about your care, after which there may be some leftover (remnant) tissue. Leftover tissues will be kept to help researchers in the future understand what causes cancer, how to prevent it, and how to treat it. The leftover tissues will be stored centrally at the Colorado Lung SPORE Tissue Bank or at the facility where you had the procedure(s) to remove the tissue. Allowing us keep your leftover tissues will not benefit you, but may benefit other people with lung cancer. We will ask you to sign a separate consent to allow us to collect leftover tissues for storage. **No tissues are ever removed from your body solely for purposes of this research**. You may decide not to provide leftover tissues and still participate in the screening portion of the trial. No matter what you decide to do, it will not affect your care.

<u>If you take part in this study, you will have the following tests and procedures:</u>

All participants will undergo:

- An interview to determine general information about your smoking habits, general health, work history, and personal contact information (address, telephone number, friends and family contacts).
- A simple breathing test through a mouthpiece.
- Every (6) six months you will receive a questionnaire or telephone call to ask about your health status.

<u>Arm 1: Experimental Arm</u>

- A screening spiral CT at the beginning of the study and at the next two annual screening visits.

<u>Arm 2: Control Arm</u>

- A screening CXR at the beginning of the study and at the next two (2) annual screening visits.

You and your physician will be notified of the results of these screening tests. If they show any abnormalities you may be advised to have additional diagnostic tests or procedures. These tests might include additional CT scans, CXRs, a biopsy or surgery. These procedures are not part of the ACRIN-NLST trial itself. Although it may be in the best interests of your health to have these tests completed, you are not obliged to have them performed as part of this trial.

When you have your CXR or spiral CT, it will take approximately 30 minutes to 1 hour of your time.

HOW LONG WILL I BE IN THE STUDY?

You are being asked to actively participate in the study for six to eight years, depending on when you were first enrolled in the study. However, the study investigator has the right to take you off this study if you become too ill to have surgery for suspected lung cancer.

You can stop participating at any time. However, if you decide to stop participating in the study, we encourage you to talk to the study investigator or a member of the ACRIN-NLST staff and your regular doctor first.

WHAT ARE THE RISKS OF THE STUDY?

While on the study, you are at risk of the following side effects. You should discuss these with the study investigator and/or your regular doctor.

Very Likely:

- Radiation dose from a screening spiral CT (100-300 mrem), which is less than or equal to the average annual dose from natural sources of radiation (300 mrem).
- Radiation dose from screening chest x-ray (8-12 mrem), which is much less than the average annual dose from natural sources of radiation (300 mrem).
- False positive screening spiral CT requiring a limited CT Scan test in 3 months (20-50%). The term "false positive" refers to a screening test in which findings initially of concern for cancer are later found *not* to be cancer.
- False positive screening CXR requiring a non-contrast CT Scan (5-10%).
- Anxiety about evaluation of false positive screening spiral CT or CXR results.
- Detection of abnormalities unrelated to lung cancer that could lead to unnecessary testing or treatment from screening with either spiral CT (10-15%) or CXR (1%).

Less Likely, but Serious:

- False positive screening spiral CT requiring a full CT scan with intravenous contrast or other potentially invasive procedures (2-7%).
- False positive screening CXR requiring a full CT scan with intravenous contrast or other potentially invasive procedures (1-5%).
- Earlier diagnosis and treatment of lung cancer that is ineffective or unnecessary (< 2%) from screening with either spiral CT or CXR.
- Failure to detect a lung cancer that is present, and possibly miss an opportunity for cure.
- Death from biopsy (less than 1% of all biopsies); death from surgery (2-4% of all having surgery).
- Death from reaction to contrast material used in diagnostic CT scans (less than 1 in 40,000 of all receiving intravenous contrast).

There also may be other side effects that we cannot predict. Most side effects go away shortly after the screening is completed, but in some cases side effects can be serious, long lasting or permanent. You should also be aware that these screening tests are not a replacement for a physical examination or a substitute for a visit to your doctor.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

If you agree to take part in this study, there may or may not be direct medical benefit to you during the course of the study. The possible benefits of taking part in the study are the same as being screened with a spiral CT of the chest or chest x-ray without being in the study. These include:

- Prevention or delay of death from lung cancer.
- Prevention of, or reduction in, symptoms from lung cancer.
- Milder treatment, leading to fewer side effects, from treatment for lung cancer.

We hope the information learned from this study will eventually benefit you and others who are at risk for lung cancer.

WHAT OTHER OPTIONS ARE THERE?

You may choose to not participate in this study. Other screening options that you might consider because of your risk factors may include the following: *(1)* to be screened with a spiral CT of the chest at your own expense, *(2)* to be screened with a CXR at your own expense, or *(3)* not to be screened for lung cancer at all.

Please talk with your regular doctor about these and other options.

WHAT ABOUT CONFIDENTIALITY?

Throughout the course of the study we will collect information from you and your medical records that is relevant to lung cancer screening, including your screening test results, and, if applicable, follow-up tests or treatments related to lung cancer. We will keep this data in a confidential form at this institution and in a computer file at the headquarters of the American College of Radiology Imaging Network (ACRIN and the Center for Statistical Sciences at Brown University). The screening exams performed in this study and any pathological specimens that are obtained will also be retained for at least 10 years, but without any identifying information on them. If you choose to withdraw from the study, you may revoke your approval for the use of your future medical information. To do so, you must contact Principal Investigator in writing. However, to maintain the integrity of the study, we will maintain the information you had already provided for the duration of the study.

Medical abstractors contracted by ACRIN will review your medical records after they have signed a confidentiality agreement. These records would include all lung related visits to a health care provider and all hospitalizations. If you are concerned about the confidentiality of your medical records, the institution's protocol team will de-identify your records before they are sent to the abstractors.

Other individuals or organizations that may inspect and/or copy your research records for quality assurance and data analysis include the NLST protocol team at *institution* (principal investigator, study coordinator, and project assistant[s]), the Institutional Review Board at *institution*, the American College of Radiology Imaging Network (ACRIN), the National Cancer Institute (NCI), and other groups or organizations that have a role in this study.

Information gained from this study may be used in the future for secondary studies and research. No individual names or results that could identify you personally will be used.

Although all efforts will be made to keep your personal information confidential, we cannot guarantee absolute confidentiality. Your personal information may be disclosed if required by law.

WHAT ARE THE COSTS?

The annual screening spiral CT and CXR will be paid for by ACRIN, the study sponsor. You may also be reimbursed for part of your travel expenses necessary for your participation at the time of your screening examinations.

You and your insurance company are responsible for all costs associated with diagnostic tests or treatments that result from screening. If you do not have adequate insurance coverage to pay for these procedures, we will try to find additional resources to help you.

In the case of injury or illness resulting from this study, emergency medical treatment is available but will be provided at the usual charge. No funds have been set aside to compensate you in the event of injury.

You or your insurance company will be charged for continuing medical care and/or hospitalization.

WHAT ARE MY RIGHTS AS A PARTICIPANT?

Taking part in this study is voluntary. You may choose not to take part or may leave the study at any time. Leaving the study will not result in any penalty or loss of benefits to which you are entitled.

A Data Safety and Monitoring Board, an independent group of experts, may be reviewing the data from this research throughout the study. We will tell you about the new information from this or other studies that may affect your health, welfare, or willingness to stay in this study.

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

(This section must be completed)

For information about your screening or participation, and research-related injury, you may contact:

_____ _____

Name Telephone Number

For information about this study, you may contact:

_____ _____

Name Telephone Number

For information about your rights as a research participant, you may contact:

(OHRP suggests that this person not be the investigator or anyone else directly involved with the research)

_____ _____

Name Telephone Number

WHERE CAN I GET MORE INFORMATION?

You may call the NCI's Cancer Information Service at:

1–800–4–CANCER (1–800–422–6237) OR **TTY: 1–800–332–8615**

Visit the NCI's Websites for accurate cancer information at:

http://cancer.gov/cancer_information or for comprehensive clinical trials information at: http://www.cancer.gov/clinical_trials. Information about NLST is posted at: http://cancer.gov/NLST.

Visit ACRIN's Website for group information at: www.acrin.org.

PERMISSION TO REVIEW MEDICAL RECORDS

By agreeing to participate, I give permission for my health care providers and hospitals where I have been seen to release my medical records to the study investigators.

SIGNATURE:

I have read all the above, asked questions, and received answers concerning areas I did not understand. I have had the opportunity to take this consent form home for review or discussion.

I willingly give my consent to participate in this program. Upon signing this form I will receive a copy. I may also request a copy of the protocol *(full study plan).*

_____ _____

Participant Signature *(or Legal Representative)* Date

Appendix III

AMERICAN COLLEGE OF RADIOLOGY IMAGING NETWORK ACRIN 6654

NATIONAL LUNG SCREENING TRIAL

SAMPLE CONSENT FOR RESEARCH STUDY

Blood, Urine, and Sputum Specimens for Banking

WHY IS THIS STUDY BEING DONE?

This portion of the study seeks to collect and store specimens of blood, urine, and sputum that may later be used to look for genetic causes and signs of lung cancer. If you agree, the specimens will be kept and may be used in future research to learn more about cancer and other diseases. The exact studies that will be performed are not all known at this time, but they will likely include biologic factors and inherited traits (genes that can be passed on in families) that may influence whether people develop lung cancer and related conditions. The samples will be given only to researchers approved by the American College or Radiology (ACRIN) and the National Cancer Institute (NCI). Any research using these samples must also be approved by an internal review board (IRB).

Participants in clinical trials include only those who choose to take part. Please take you time making your decisions. We encourage you to discuss your decision with your doctor, family, and friends.

WHAT IS INVOLVED IN THE STUDY?

If you would like to participate in this part of the study, samples of blood, urine, and sputum (spit) will be collected at your initial visit. You will also be asked to provide these same samples when you return for your next (2) two annual screening visits.

We would ask you to do the following:

1. **Blood Collection.** A blood sample will be drawn through a needle from a vein in your arm. The blood sample may amount to about 30 cc (1-2 tablespoons). Blood donation of this type is not mandatory and you may decline to provide blood at any time without jeopardizing your participation in this research or your access to health care.
2. **Urine Collection:** You will provide a urine sample in a urine cup.
3. **Sputum (phlegm) Collection:** You will be given two (2) special containers for collecting sputum samples on six different days (a red-labeled cup and a blue-labeled cup). Upon arising in the morning, you should thoroughly rinse your mouth with water. You must cough deeply into the sputum cup. It is often easier to produce sputum after your morning shower. Cough on three successive mornings into the red-labeled cup, and then three more successive mornings into the blue-labeled cup. **Please indicate the last date of collection for each cup in the space provided on the enclosed Sputum Collection Form. This Sputum Collection Form (SP) should be enclosed with the specimens in the mail.**

   The samples do not need to be refrigerated prior to mailing, but they should be stored at room temperature in a safe place so that they are not inadvertently lost. Once you have provided the sputum, screw the caps tightly and mail the cups directly to the specimen bank using the postage-paid mailing container that has been provided to you.

WHAT ARE THE RISKS OF THE STUDY?

The following are known risks of your participation in this study. The treatments or procedures may involve risks that are currently unforeseen. If you have questions about these risks, the investigators or other designated research staff will answer these questions.

1. Blood Collection: When blood is drawn you may feel a little discomfort as the needle goes through the skin. There may be local bruising or bleeding at the puncture site. Pressing hard on the spot for 1 to 2 minutes after the needle is removed will help prevent a bruise. You may feel queasy around needles. Very rarely, the arm may become infected. The risk is the same as that of having blood drawn at your doctor's office or clinic.

2. Confidentiality: The greatest risk to you is the unintended release of information from your health records. The investigators will protect your records so that your name, address, phone number, and any other identifying information will be kept private. All information about you and your samples will be given a unique code, and your personal identifying information will be removed to protect your confidentiality. Information regarding your assigned identification number will be permanently kept in locked files with access limited to approved study investigators. The chance that this information will be given to someone else is very small. No individual identities will be used in any reports or publications resulting from this study.

ARE THERE BENEFITS TO TAKING PART IN THIS STUDY?

Participation in this part of the study will not provide direct benefit to you. Reports about research done with your specimens will not be given to you or your doctor. These reports will not be put in your health record. The research will not have an effect on your health care. However, your participation in these additional studies, and the analysis of all of the specimens obtained in this study, may help physicians to establish a scientific understanding of what causes lung cancer and other diseases, how to prevent it, and how to treat it.

WHAT ARE THE ALTERNATIVES TO PARTICIPATION?

You may choose not to provide specimens of blood, urine and sputum for banking. You can still participate in the screening part of the trial and yet decline to provide these specimens.

IS THERE PAYMENT FOR PARTICIPATION?

Your samples will be stored and may later be used only for research. Your samples will not be sold. You will not be paid for the use of your samples or for any test or product that is discovered or developed through this research and that may be of commercial value. Neither you nor your insurance company will be billed for your participation in this research.

ARE THERE POTENTIAL COMMERCIAL PRODUCTS?

If a commercial product is developed based on the used of your samples from this study, the commercial product will be owned by the University/Institution or its designee. You will not profit financially from such a product.

WHAT ABOUT CONFIDENTIALITY?

In the future, people who do research may need to know more about your health. While the ACRIN-NLST investigators may given them information about your health, they will not give them your name, address, phone number, or any identifying information that would let other scientists know who you are. Even if your

specimens are used for genetic research (research about diseases that are passed on in families) the results will not be put in your health records or linked to your name.

WHAT ARE MY RIGHTS AS A PARTICIPANT?

Your participation in the collection and storage of biological specimens (blood, urine, and sputum) is voluntary and you may refuse to participate and/or change your mind and withdraw your consent at any time without penalty. Furthermore, you may participate in the screening part of the trial and yet decline to have biologic samples stored for research purposes.

If you initially decide to provide samples of blood, urine, and sputum for future research and you do change your mind, just contact Dr. _____ in writing at (*institution*) and let him/her know that you do not want your samples to be used. We will destroy your samples and they will not be used for research. Otherwise, the samples may be kept until they are used up, or until the study investigators decide that they should be destroyed. No matter what you decide to do, it will not affect your care in this study.

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

(This section must be completed by institution)

For information about your screening or participation, and research-related injury, you may contact:

_____ _____
Name Telephone Number

For information about this study, you may contact:

_____ _____
Name Telephone Number

For information about your rights as a research participant, you may contact:
(OHRP suggests that this person not be the investigator or anyone else directly involved with the research)

_____ _____
Name Telephone Number

YOU CAN PARTICPATE IN THE SCREENING PORTION OF THE STUDY WITHOUT PROVIDING TISSUE, BLOOD AND URINE SPECIMENS.

I have read (or someone has read to me) the information provided above. I have been given an opportunity to ask questions and all of my questions have been answered to my satisfaction. I have been given a copy of this form as well as a copy of the Subject's Bill of Rights. **By signing this form, I willingly agree to participate in the research it describes.**

_____ _____
Signature of Subject Date

_____
Name of Subject

INFORMATION ABOUT MY SPECIMENS

Below, you are asked to let us know if you would like to receive information about the results of this study. Please indicate by checking and initialing the category below what type of information you want to receive. It is your responsibility to let the investigator know if your address and/or telephone number changes. The contact information is in this informed consent form under "Identification of Investigators."

☐ I want to be given general information about what the study found.

☐ **I DO NOT WANT ANY INFORMATION ABOUT WHAT THE STUDY FOUND.**

OTHER RESEARCH QUESTIONS REGARDING MY SPECIMENS

1. My specimens may be kept for use in research to learn about, prevent or treat cancer.
   ☐ **YES** ☐ **NO**

2. My specimens may be kept for use in research to learn about, prevent or treat other health problems (for example: chronic lung disease, Alzheimer's disease or heart disease).
   ☐ **YES** ☐ **NO**

3. Someone from ACRIN or this institution may contact me in the future to ask me to take part in more research.
   ☐ **YES** ☐ **NO**

_____ _____

Signature of Participant **Date**

SIGNATURE OF INVESTIGATOR or RESEARCH ASSOCIATE

I have explained the research to the subject or his/her legal representative and answered all of his/her questions. I believe that he/she understands the information described in this document and freely consents to participate.

_____ _____

Signature of Investigator/ Research Associate Date

_____

Name of Investigator/ Research Associate

Appendix IV

AMERICAN COLLEGE OF RADIOLOGY IMAGING NETWORK

ACRIN 6654

National Lung Screening Trial

(Remnant Tissue Collection)

Lay Title: Contemporary Screening for the Detection of Lung Cancer:
A Study to Collect and Store Leftover Tissue Specimens to Help Establish New Methods for Detecting Lung Cancer Early

Title of Study: Contemporary Screening for the Detection of Lung Cancer
(Remnant Tissue Collection)

WHY IS THIS STUDY BEING DONE?

You are going to have a biopsy (or surgery) to see if you have cancer. Your doctor will remove some body tissue to do tests. The results of these tests will be given to you by your doctor and will be used to plan your care.

We would like to keep some of the tissue that is left over for future research. If you agree, this tissue will be kept and may be used in research to learn more about cancer and other diseases. Please read the information sheet called "How is Tissue Used for Research" to learn more about tissue research. The samples will be given only to researchers approved by the American College or Radiology (ACRIN) and the National Cancer Institute (NCI). Any research using these samples must also be approved by a research or interval review board (IRB).

Your tissue may be helpful for research whether you do or do not have cancer. The research that may be done with your tissue is not designed specifically to help you. It might help people who have cancer and other diseases in the future.

Participants in clinical trials include only those who choose to take part. Please take you time making your decisions. We encourage you to discuss your decision with your doctor, family, and friends.

WHAT ARE THE RISKS OF THE STUDY?

The greatest risk to you is the unintended release of information from your health records. The NLST investigators will protect your records so that your name, address, phone number, and any other identifying information will be kept private. The chance that this information will be given to someone else is very small.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

Participation in this part of the study will not provide direct benefit to you. Reports about research done with your tissue will not be given to you or your doctor. These reports will not be put in your health record. The research will not have an effect on your health care. However, the benefits of research using your tissue and that of others in this trial include learning more about what causes lung cancer and other diseases, how to prevent them, and how to treat them.

WHAT ARE THE ALTERNATIVES TO PARTICIPATION?

You may decide not to have your tissue kept for future research. You can still participate in the screening part of the trial and yet decline to have left over tissue stored.

WHAT ARE MY RIGHTS AS A PARTICIPANT?

The choice to let us keep the left over tissue for future research is up to you. **No matter what you decide to do, it will not affect your care.**

If you decide now that your tissue can be kept for research, you can change your mind at any time. Just contact us and let us know that you do not want us to use your tissue. Then any tissue that remains will no longer be used for research.

WHAT ABOUT CONFIDENTIALITY?

In the future, people who do research may need to know more about your health. While the NLST investigators may give them reports about your health, they will not give them your name, address, phone number, or any other information that will let the researchers know who you are.

Sometimes tissue is used for genetic research (research about diseases that are passed on in families). Even if your tissue is used for this kind of research, the results will not be put in your health records.

Your tissue will be used only for research and will not be sold. The research done with your tissue may help to develop new products in the future.

MAKING YOUR CHOICE

Please read each sentence below and think about your choice. After reading each sentence, circle "Yes" or "No." **No matter what you decide to do, it will not affect your care.** If you have any questions, please talk to your doctor or nurse, or call our research review board at (*IRB's phone number*).

1. My specimens may be kept for use in future research to learn about, prevent or treat cancer.
   ☐ **YES** ☐ **NO**

2. My specimens may be kept for use in research to learn about other health problems (for example: chronic lung disease or heart disease).
   ☐ **YES** ☐ **NO**

3. Someone from ACRIN or this institution may contact me in the future to ask me to take part in more research.
   ☐ **YES** ☐ **NO**

_____ _____

Signature of Participant Date

_____ _____

Signature of Investigator/ Research Associate Date

_____

Name of Investigator/ Research Associate

APPENDIX V

AMERICAN COLLEGE OF RADIOLOGY IMAGING NETWORK

NATIONAL LUNG SCREENING TRIAL

HOW IS TISSUE USED FOR RESEARCH?

Where does the tissue come from?

Whenever a biopsy (or surgery) is performed, the tissue that is removed is examined under the microscope by a trained doctor to determine the nature of the disease and assist with the diagnosis. Your tissue will always be used first to help make decisions about your care. After all tests have been done, there is usually some left-over tissue. Sometimes, this tissue is not kept because it is not needed for the patient's care. Instead, a patient can choose to have the tissue kept for future research. People who are trained to handle tissue and protect the donor's rights make sure that the highest standards are followed by the institution responsible for storing the tissue (Colorado Lung SPORE Tissue Bank). Your doctor usually does not work for the Colorado Lung SPORE Tissue Bank, but has agreed to help collect tissue from many patients. Many doctors across the country are helping in the same way. If you agree, only left-over tissue will be saved for research. Furthermore, at the time of your surgery or biopsy, your doctor will only remove the tissue needed for your care.

The Colorado Lung SPORE Tissue Bank stores your tissue with a special identification number, but the Tissue Bank does not know your name or have access to any information about you. All of your personal information is kept confidentially by the ACRIN investigators.

Why do people do research with tissue?

Research with tissue can help to find out more about what causes cancer, how to prevent it, and how to treat it. Research using tissue can also answer other health questions. Some of these include finding the causes of diabetes and heart disease, or finding genetic links to Alzheimer's disease.

What type of research will be done with my tissue?

Many different kinds of studies use tissue. Some researchers may develop new tests to find diseases. Others may develop new ways to treat or even cure diseases. In the future, some of the research may help to develop new products, such as tests and drugs.

Some research looks at diseases that are passed on in families (called genetic research). Research done with your tissue may look for genetic causes and signs of disease.

How do researchers get the tissue?

Researchers from universities, hospitals, and other health organizations conduct research using tissue. They contact the ACRIN-NLST researchers and the NCI and request samples for their studies. ACRIN and the NLST review the way that these studies will be done, and decide if any of the samples can be used. If the request for tissue is approved, ACRIN will have the Colorado Lung SPORE Tissue Bank send the tissue samples and will also provide some information about you to the researcher. The ACRIN investigators and the Colorado Lung SPORE Tissue Bank will not send your name, address, phone number, social security number, or any other identifying information to the researcher.

Will I find out the results of the research using my tissue?

No, you will not receive the results of research done with your tissue. This is because research can take a long time and must use tissue samples from many people before results are known. Results from research using your tissue may not be ready for many years and will not affect your care right now, but they may be helpful to people like you in the future.

Though research involves the test results of many different people, your biopsy result involves only you. Your doctor will give you the results of your biopsy when results are known. These test results are ready in a short time and will be used to make decisions about your care.

Will I benefit from the research using my tissue?

There will be no direct benefit to you because your tissue may not be used for some time after you donate it and because research can take a long time. However, it is hoped that the results of research on your tissue and tissues from other patients will provide information that will help other patients in the future. Your tissue will be helpful whether you have cancer or not.

Why do you need information from my health records?

In order to do research with your tissue, researchers may need to know some things about you. (For example: Are you male or female? What is your race or ethnic group? How old are you? Have you ever smoked?) This helps researchers answer questions about diseases. The information that will be given to the researcher includes your age, sex, race, diagnosis, treatments, and possibly some family history. This information is collected by your hospital from your health record and sent to the Colorado Lung SPORE Tissue Bank but without your name or other identifying information. If more information is needed, the Colorado Lung SPORE Tissue Bank may send it to the researcher.

Will my name be attached to the records that are given to the researcher?

No. Your name, address, phone number, and anything else that could identify you will be removed before they go to the researcher.

How could the records be used in ways that might be harmful to me?

Sometimes, health records have been used against patients and their families. For example, insurance companies may deny a patient insurance or employers may not hire someone with a certain illness (such as AIDS or cancer). The results of genetic research may not apply only to you, but to your family members. For diseases caused by gene changes, the information in one person's health record could be used against family members.

How am I protected?

The Colorado Lung SPORE Tissue Bank is in charge of making sure that information about you is kept private. The Colorado Lung SPORE Tissue Bank will take careful steps to prevent misuse of records. Your name, address, phone number and other identifying information will be taken off anything associated with your tissue before it is given to the researcher. This would make it very difficult for any research results to be linked to you or your family. Also, people outside the research process will not have access to results about any one person, which will help to protect your privacy.

Appendix VI

Sample Cover Letter

Dear _____,

Thank you for your continued participation in the ACRIN-NLST trial on lung cancer screening. This trial and the information that you provide us as a participant will be very important in determining future health care policy on lung cancer.

When you were first enrolled in the study, we indicated that we would periodically send you brief questionnaires about your overall health and feelings. Two questionnaires are enclosed for you to complete. In addition, we have enclosed a stamped, self-addressed envelope for you to mail back the questionnaires.

It is very important that you complete all of the questions on these questionnaires. We estimate that it may take 10-20 minutes of your time to complete these questions. Please return these forms as soon as possible in the envelope provided.

Please feel free to contact me if you have any questions or if you need help answering the questions. I can be reached at the following telephone number:

_____.

Again, thank you for your time. Your participation in this trial is very important to us, and we appreciate your efforts in answering these important questions.

Sincerely,

_____
RA by name

Institution # _____ **APPENDIX VII**

ACRIN 6654 **ELIGIBILITY CHECK**

Case # _____ ***(page 1 of 2)***

_____(Y) 1. Individual is between the ages of 55-74 years and 364 days.

_____(Y) 2. Individual has a current or previous cumulative cigarette smoking history of ≥ 30 pack years.

_____(NA or Y) 3. If a former smoker, individual has ceased smoking within the previous 15 years.

_____(Y) 4. Individual has no medical or psychiatric condition precluding informed consent.

_____(Y) 5. Individual is able to lie on his/her back with arms raised above his/her head.

_____(Y) 6. Individual has no metallic implants or devices in the chest or back (*pacemakers or Harrington fixation rods, etc.).*

_____(Y) 7. Individual has no prior diagnosis of lung cancer.

_____(Y) 8. Individual has had no treatment for, or advisement by a physician of evidence of *any* cancer within the past five years, with the exceptions of non-melanoma skin cancer and most in-situ carcinomas. (Treatment for, or evidence of, melanoma or in-situ bladder/transition cell carcinomas within the preceding five years renders the potential participant ineligible.)

_____(Y) 9. Individual has no prior removal of any portion of the lung, excluding percutaneous lung biopsy.

_____(Y) 10. Individual does not require home oxygen supplementation.

_____(Y) 11. Individual is not currently enrolled in another cancer screening trial *(PLCO, ELCAP)*.

_____(Y) 12. Individual is not currently enrolled in another cancer prevention trial other than smoking cessation programs.

_____(Y) 13. Individual does not have present symptoms suggestive of lung cancer, including unexplained weight loss of over 15 lbs within the past 12 months, or unexplained hemoptysis.

_____(Y) 14. Individual has no medical conditions that pose a significant risk of mortality during the trial period.

_____(Y) 15. Individual has *not* had a chest CT within the preceding 18 months of study enrollment. *(Individual will be eligible 18 months from the time of the CT)*.

_____(Y) 16. Individual is *not* within 12 weeks of a pneumonia or acute respiratory infection treated with antibiotics by a physician.

_____(Y) 17. Individual is *not* within 6 months of receipt of cytotoxic agents for any condition.

_____(Y) 18. A study-specific informed consent has been signed prior to registration.

The following questions will be asked at Study Registration:

_____ 1. Name of institutional person registering this case?

_____(Y) 2. Has the Eligibility Checklist been completed?

_____(Y) 3. Is the participant eligible for this study?

_____ 4. Date the study-specific Consent Form was signed? *(must be prior to study entry)*

Institution # _____ **APPENDIX VII**

ACRIN 6654 **ELIGIBILITY CHECK**

Case # _____ ***(page 2 of 2)***

_____	5.	Participant's Initials
_____	6.	Verifying Physician (*Site PI*)
_____	7.	Participant's ID Number
_____	8.	Date of Birth (*mm-dd-yyyy*)
_____	9.	Ethnic Category
_____	10.	Race
_____ (M/F)	11.	Gender
_____	12.	Participant's Country of Residence
_____	13.	Zip Code
_____	14.	Participant's Insurance Status
_____ (N/Y)	15.	Will any component of the participant's care be given at a military or VA facility?
_____	16.	Calendar case date (dd-mm-yyyy)
_____	17.	Randomization date (dd-mm-yyyy)
_____	18.	Other Country of Residence
_____	19.	Participant's Age Group (55-59) (60-64) (65-69) (70-74)
_____ (N/Y)	20.	Has the participant signed consent to have his/her tissue kept for use to learn about, prevent or treat cancer?
_____ (N/Y)	21.	Has the participant signed consent to have his/her tissue kept for use to learn about, prevent or treat other health problems?
_____ (N/Y)	22.	Did participant come to the study from the 1-800-4-CANCER hotline?
_____	23.	What recruitment methods prompted the participant to contact the study site?
_____ (Y)	24.	The participant has signed an annual Medical Record Release Authorization?
_____ (N/Y)	25.	Has the participant signed consent to have his/her blood, urine, sputum specimens kept for use to learn about/prevent/treat cancer?
_____ (N/Y)	26.	Has the participant signed consent to have his/her blood, urine, sputum specimens kept for use to learn about/prevent/treat other health problems?
_____ (N/Y)	27.	Has the participant signed consent to allow someone from NLST to contact him/her in the future to ask them to take part in more research?

Appendix VIII: Screening Results Withheld Statement
ACRIN NLST 6654

As a participant in the National Lung Screening Trial (NLST), I am writing to request that my health care provider not be notified of the results of any screening examinations I receive while participating in this study. I realize that I am responsible for contacting my health care provider in the event that I receive an abnormal screening examination and that the [*Insert Site Name*] will not notify my health care provider of such a result. I also realize that the [Insert Site Name] will not function as a primary healthcare provider on my behalf and does not have any responsibility regarding my care beyond providing me with the results of my screening examinations.

If, at any time during the study, I decide that I would like for my health care provider to begin receiving the results of my NLST screening examinations, I realize that I must contact the [*Insert Site Name*] *in writing* to request this change. The contact information for the NLST site is:

Site Name
Site Address
City, State, Zip

If I have any questions regarding my screening examination results or any other aspect of the NLST, I can contact [*Insert Study Coordinator Name*] at [*Insert Site Telephone Number*].

_____

Signature of Participant

_____

Printed Name of Participant

_____

Date

APPENDIX IX

Addendum to the National Lung Screening Trial sponsored by the NCI in cooperation with the PLCO and ACRIN

In an effort to maximize early and sustained accrual to the National Cooperative Trials assessing the early detection of lung cancer, the American Cancer Society (ACS) will initiate a major educational campaign designed to increase study awareness and increase participation. Multimedia informational advertising will be supplemented through telephone contact with health educators delivering eligibility information and offering information regarding local tobacco cessation programs for which the callers might be eligible.

General educational media announcements will address the reason for the study, eligibility requirements, and contact information for those interested in pursuing participation in the study. Individuals calling the National Cancer Information Center (NCIC) of the ACS will be asked to voluntarily supply a minimal amount of information which will be kept confidential and only used for these study purposes as part of the effort to evaluate the impact of various methods of advertising as part of the quality improvement process. The information solicited will include the following:

Name
Current Address
Age
Smoking History
History of previous cancer (non-melanoma skin cancer excluded) within 5 years
Ethnicity
Highest Level of Education Attained
Source of Information Leading to this Phone Inquiry

The callers will be provided with information about the study, their potential eligibility, and contact phone numbers providing access to investigators proximate to the caller. The actual determination of eligibility and the consummation of the consent process will be conducted by the investigators conducting the study.

The primary purpose of this multimedia educational effort will be to accelerate and sustain study accrual in an effort to complete the study in a timely fashion. Data related to demographic information, potential study eligibility and the source of the information leading to the initial call, would be descriptively analyzed using standard techniques. This information will be used to informal subsequent educational advertising efforts.

NLST INTERIM ANALYSIS PLAN

Abstract

The National Lung Screening Trial (NLST), currently underway, has enrolled 53,476 individuals at high risk for lung cancer in order to determine whether screening with spiral CT (SCT) reduces lung cancer mortality relative to screening with chest x-ray (CXR). The purpose of this document is to summarize the efforts made by statisticians working on the NLST in designing an interim analysis plan for the trial. This plan will assist the DSMB in fulfilling the important responsibility of determining whether the trial should continue based on available data at each scheduled interim analysis. It will provide a decision rule based on comparison of a test statistic (computed from observed times on study or until death) to stopping boundaries. The decision rule accounts for multiple analyses of the data and allows early stopping of the trial for reasons of screening efficacy or inefficacy (the respective boundaries are called efficacy and futility boundaries) with a controlled overall level of significance. For the most part, the design of an interim analysis plan involves the choice of a test statistic and a method of stopping boundary construction.

We have chosen to use a weighted log-rank statistic incorporating a "ramp-plateau" weighting function to test efficacy and inefficacy against one-sided boundaries constructed via the Lan-DeMets procedure using the O'Brien-Fleming error probability spending function. The weighting function rises in a linear fashion from no weight at the time of randomization to full weight two years after conclusion of the screening regimen. The efficacy boundary is constructed relative to an overall probability of type I error of 5%, while the futility boundary is constructed relative to an overall probability of type II error of 10% with respect to a relative risk of 0.85. The remainder of this document details the specific meaning of these concepts in addition to the considerations that led to the choice of this interim analysis plan.

The design of an interim analysis plan requires the choice of a series of candidate plans and a set of criteria for their evaluation. Each candidate plan consists of a test statistic and a stopping-boundary construction method. In determining an interim analysis plan for the NLST, candidate plans were assessed on the basis of operating characteristics such as statistical power and the probability of stopping the trial by year 5. As calculation of these required knowledge of the mortality rates for each of the two trial arms, we considered a variety of feasible mortality scenarios. These scenarios encompassed both efficacious and inefficacious outcomes and were inspired by results from other cancer screening trials.

The following cancer screening trials provided input into the mortality scenarios considered: the HIP breast cancer screening trial, the FOBT colorectal cancer screening trial conducted at the University of Minnesota, and the three lung cancer screening trials at Johns Hopkins, Memorial Sloan-Kettering, and the Mayo Clinic. Results are given in Appendix I. For each trial, the cumulative cause-specific and overall mortality ratio patterns over the years of the trial are displayed graphically and in tabular form. The cause-specific ratios exhibit substantial fluctuations in the early years, typically crossing

or approaching a value of 1.0 before stabilizing to a final result. The total mortality ratios, being based on much larger numbers, are much less variable and near 1.0.

Although not statistically significant, these results suggest that crossing hazard functions for the two arms are quite possible, especially in the early years of the NLST. In addition, any death due to lung cancer that is averted by early detection would most likely have not occurred in the absence of screening until after a substantial time lag. Therefore, even under assumed efficacy there will be an observed delay before benefit is observed. Thus, deaths occurring in the early years of the trial assume less importance and should receive less weight than deaths occurring later. This is a scientific rationale for the use of a weighted statistic in tests of efficacy. Therefore, weighted statistics are included among the candidate test statistics considered.

All candidate test statistics considered were variants of the log-rank statistic, which is typically used for screening trials with mortality endpoints. We evaluated the performance of six candidate log-rank statistics – the unweighted and five weighted versions which down-weight earlier events to varying degrees based upon either the order in which they occur or the times they occur. Specifically, we considered three members of the Fleming-Harrington (FH) family of weighted log-rank statistics with increasing weighting function: the FH(0, 0.5), the FH(0, 0.75) and the FH(0, 1) weighting functions. Each of these weighting functions down-weights earlier events based upon the order in which they occur. In addition, we considered two "ramp-plateau" weighting functions, similar to that used in the Beta-Carotene and Retinol Efficacy Trial (Thornquist et al.), assigning weights linearly beginning with zero weight at time on study zero and increasing to unit weight at time on study three years and four years, i.e., one and two years after conclusion of the screening regimen, respectively. These weighting functions are denoted by RP(3) and RP(4), respectively. The weighted log-rank statistic, the Fleming-Harrington family of weighting functions and the ramp-plateau weighting functions are defined in Section 2 of Appendix II.

The choice of candidates for constructing stopping boundaries was made via the following considerations. Since the primary question addressed by this trial is whether screening with spiral CT reduces lung cancer mortality relative to screening with chest x-ray, it is not of primary importance to distinguish between "no effect" and "harm". For this reason, we use a one-sided test of the null hypothesis of identical lung cancer mortality rates at the 5% level of significance, resulting in a one-sided efficacy boundary for stopping in favor of effectiveness of SCT over CXR. In addition, we use a one-sided futility boundary relative to the design power of 90% and a constant relative risk of 0.85 for stopping in favor of a null or harmful effect. The value of 0.85 was chosen based upon the attenuating effect of non-compliance on the relative risk of 0.80 for which the trial is powered. We use the Lan-DeMets procedure to construct both efficacy and futility boundaries because of its generality and flexibility (Jennison and Turnbull). Within the Lan-DeMets framework, we assessed the performance of six candidate spending-function pairs corresponding to construction of efficacy and futility boundaries. All spending functions chosen were either the O'Brien-Fleming (OF) or a member of the power-function family having exponent r (P(r)). These are defined in Section 3 of Appendix II. The OF spending function results in the most conservative boundaries early on (those farthest from the null hypothesis), while the boundaries resulting from the

power spending function with exponent r become less conservative with decreasing r. The P(3) and OF spending functions result in boundaries that are fairly close together, with the OF boundary more conservative at the beginning but the P(3) slightly more conservative later. Candidate spending-function pairs assessed were: OF/OF, P(3)/P(3), P(3)/P(2), P(3)/P(1.5), P(3)/P(1.0), and P(3)/P(0.5), where the efficacy function appears first in each pair.

To summarize the two preceding paragraphs, we assessed thirty-six candidate interim analysis plans arising from the six candidate test statistics in combination with six candidate spending function pairs. As indicated above, the performance of each of these candidate interim analysis plans was assessed by computing operating characteristics under a variety of feasible mortality scenarios (108 in total, summarized in Table 1, about which more will be said later).

Four operating characteristics were considered as criteria for the comparison of the candidate interim analysis plans. Their definitions and the manner in which they are computed are discussed in Section 4 of Appendix II. The first two were the probabilities of crossing the efficacy and futility boundaries. For scenarios leading to relative risks other than unity, the first of these is the power, while the second is the type II error. These were calculated using a recursive formula similar to that in Armitage et al. The last two operating characteristics were summaries of the distribution of the trial duration. Interim analyses were assumed to occur annually starting at the end of the third year of the trial. The two summaries of the distribution of the trial duration considered were its expected value and cumulative probability of stopping at year 5. Year 5 was chosen based on the fact that in our analysis, it was the first year for which the cumulative probabilities of stopping displayed a reasonable amount of variability over the candidate monitoring plans under consideration.

We now describe the feasible mortality scenarios considered. As mentioned above, the construction of these mortality scenarios was based upon the assumption of time-varying lung cancer mortality rates in each of the two screening arms. The list of scenarios encompasses both efficacious and inefficacious trial outcomes. The parameters used to construct these scenarios were drawn from the above-mentioned literature on trials of cancer screening. Table 1 summarizes the range of feasible mortality scenarios considered for the NLST. In all cases the NLST was assumed to have a maximum duration of seven years. The lung cancer mortality rate within an unscreened population, which is used as the basis for all other lung cancer mortality rates, was assumed to be a constant. This constant was assigned two possible values, taken in the neighborhood of that which was observed in the Mayo Clinic lung cancer screening trial – 4 and 4.5 per thousand per year (first column of Table 1). Because the "usual care" arm, screening via CXR, is itself a screened arm, the lung cancer mortality in that arm was assumed to be temporarily higher relative to the unscreened population. A list of feasible CXR-arm lung cancer mortality rate scenarios was constructed, for each of the two choices of lung cancer mortality rates among the unscreened, by specifying a range of time-varying relative cumulative risks for CXR screening versus no screening. These time-varying relative cumulative risks were specified via the first-year relative risks (second column of table 1) and the year at which the maximum benefit of CXR screening relative to no screening is achieved (third column of table 1). Next, a list of feasible lung cancer

mortality rate scenarios corresponding to efficacy in the SCT arm was constructed for each of the CXR mortality rate scenarios by specifying a range of time-varying relative cumulative risks for SCT screening versus CXR screening. These time-varying relative cumulative risks were specified via the first-year relative risks for SCT screening versus no screening (fourth column of table 1) and the year at which the maximum benefit of SCT screening relative to CXR screening is achieved (fifth column of table 1). This results in 72 possible lung cancer mortality scenarios resulting in efficacy of SCT over CXR. For example, the first possible choice in the first three columns of table 1 and the second possible choice in columns four and five result in the following specification of the lung cancer mortality rate among those unscreened and relative cumulative risks by year in the two arms:

4	1.20	1.00	0.95	0.90	0.90	0.90	0.90	1.50	1.00	1.00	0.90	0.80	0.80	0.80

Here, the lung cancer mortality rate among those unscreened is 4 per 1000 per year, the first-year CXR versus no screening relative risk is 1.2, the maximum benefit of CXR over no screening occurs at year 4, the first-year SCT versus no screening relative risk is 1.5, and the maximum benefit of SCT over no screening occurs at year 5. Relative cumulative risks during years intermediate to the first year and year of maximum benefit are set to 1.00 with the exception of the last, which is set to the midpoint of 1.0 and the corresponding maximum benefit. This results in annual lung cancer mortality rates in the CXR arm of 48, 32, 34, 30, 36, 36, and 36 deaths per 10,000 per year, and annual lung cancer mortality rates in the SCT arm of 60, 20, 34, 15.6, 14.4, 28.8 and 28.8 deaths per 10,000 per year.

Next, within each of the twelve scenarios defining lung cancer mortality in the CXR arm, we defined three additional no-benefit scenarios in the SCT arm, yielding 36 scenarios of no benefit. The first of these is referred to as “slight harm” and has SCT versus CXR relative cumulative risks by year of 1.15, 1.15, 1.1, 1.1, 1.1, 1.1, and 1.1. The second of these is referred to as “rebound” and has SCT versus CXR relative cumulative risks by year of 1.3, 1.1, 0.935, 0.87, 0.87, 0.935 and 1.0. It is so named because the relative risk temporarily drops below 1.0 but then attenuates to the null by the conclusion of the trial. The last of the no-benefit scenarios is referred to as the “strong null” and is defined by unit relative risk throughout. In conclusion, Table 1 summarizes 108 mortality scenarios that span the range of mortality scenarios that were considered likely for the NLST.

Since non-compliance is likely to occur, possibly at appreciable levels, in the trial, it is important to take it into consideration when carrying out calculations of operating characteristics of candidate monitoring plans. The effect of non-compliance within the scope of this investigation is that each of the 108 feasible lung cancer mortality scenarios is altered by non-compliance, changing the expected value of the test statistic and the boundary crossing probabilities. Since both arms of the NLST involve screening, there are two types of non-compliance – drop-out and cross-over. Drop-out refers to the case in which a participant decides at some point to stop being screened for lung cancer. Cross-over refers to the case in which a participant in one of the screening arms opts to be screened by the modality of the complementary arm instead of the modality of the arm to which she/he was assigned. We considered each of these phenomena to be irreversible. The specifics of the non-compliance model and its incorporation into the

calculation of operating characteristics are discussed in Sections 1 and 4 of Appendix II.

We now discuss the results of our assessment. As indicated above, this assessment was carried out by computing each of the four above-mentioned operating characteristics under each of the 36 candidate interim analysis plans at each of the 108 mortality scenarios. The performance of each of the 36 candidate interim analysis plans under the variety of scenarios is summarized in the following ways. In Table 2a we list, for each of the 36 candidate plans, its average power and standard error over the 72 beneficial scenarios, where "average" and "standard error" refer to a "prior distribution" assigning equal weight to each of the 72 beneficial scenarios. Next, in Table 2b we list, for each of the 36 candidate plans, its average power and standard error over the 12 rebound scenarios. In Table 2c we list, for each of the 36 candidate plans, its average probability of stopping by year 5 and corresponding standard error over the 12 harmful scenarios. Finally, Table 2d presents the average of the expected value of the trial duration for each of the 36 candidate plans over the 108 mortality scenarios.

We recommend conducting the interim analyses in the NLST using the ramp-plateau weighting function RP(4), which levels off to its maximum value of unit weight at a time on study of 4 years, to test against efficacy and futility boundaries constructed using the O'Brien-Fleming spending function. Crucial in this decision was the desire for balance between the behavior of an interim analysis plan under beneficial mortality scenarios, summarized in Table 2a, and its behavior under those not resulting in benefit, summarized in Tables 2b and 2c. Since scenarios resulting in harm are believed to be much less plausible, more emphasis was placed upon having high power over beneficial scenarios. First, the average powers taken over the 72 beneficial scenarios displayed in Table 2a display more or less the tendency to be increasing from bottom to top and from left to right. This is because a weighted log-rank statistic having weighting function which assigns greater weight to later events has higher power at each of the 72 beneficial scenarios considered, and because the use of more conservative stopping boundaries also results in higher power at each of these scenarios. The same comments apply to the average powers taken over the 12 rebound scenarios displayed in Table 2b for the same reasons. Since we desire high average power over beneficial scenarios, but desire low average power over rebound scenarios, we can see that the candidate plans entail trade-offs between the results displayed in Tables 2a and 2b. Since the probability of stopping by year 5 at each of the twelve harmful scenarios is primarily the probability of crossing the futility boundary, which runs in opposition to the power, the averages of these probabilities over the twelve harmful scenarios, displayed in Table 2c, are more or less decreasing from bottom to top and from left to right. We desire higher values of this quantity, resulting in a trade-off between the results displayed in Tables 2a and 2c. Based upon these considerations, we have chosen to use the RP(4) weighted log-rank statistic and the O'Brien-Fleming boundaries. Table 2d indicates that this combination of test statistic and stopping boundaries has one of the lowest expected trial durations.

References:

Thornquist MD, Omenn GS, Goodman GE, et al. Statistical design and monitoring of the Carotene and Retinol Efficacy Trial (CARET). Controlled Clinical Trials 1993; 14:308–324.

Jennison C, Turnbull BW. Group Sequential Methods with Applications to Clinical Trials. Boca Raton: Chapman & Hall/CRC, 2000.

Armitage P, McPherson CK, Rowe BC. Repeated significance tests on accumulating data. J. Roy. Statist. Soc. A 1969; 132**:** 235–244.

Unscreened Lung Cancer Mortality Rate
Lung Cancer Mortality Rate
Mortality Rate

Unscreened Lung Cancer Mortality Rate	CXR		SCT	
			Efficacious Scenarios	
	Year 1 Elevated Mortality Factor	Year Maximum Benefit Attained	Year 1 Elevated Mortality Factor	Year Maximum Benefit Attained
4.0 per 1000	1.2	Year 4	1.3	Year 4
4.5 per 1000	1.4	Year 5	1.5	Year 5
		Year 6		Year 6
			Inefficacious Scenarios	
			Slight Harm	
			Rebound	
			No Effect	

Table 1 Lung cancer mortality scenarios used to determine interim analysis plan. Entries in columns 1 through 3 represent 12 combinatorial possibilities for lung cancer mortality scenarios among the unscreened and within the CXR arm. The remainder represents 6 efficacious and 3 inefficacious combinatorial possibilities for lung cancer mortality scenarios within the SCT arm. These 9 possibilities in the SCT arm were linked with the 12 possibilities in the CXR arm to yield 108 feasible mortality scenarios.

Table 2a: Average (standard error) of the powers over the 72 beneficial scenarios by candidate statistic according to type of stopping boundary

	FH(0,0)	**FH(0,0.5)**	**FH(0,0.75)**	**FH(0,1)**	**RP(3)**	**RP(4)**
OF – OF	0.348 (0.0056)	0.631 (0.0058)	0.757 (0.0060)	0.850 (0.0048)	0.854 (0.0137)	0.903 (0.00839)
P(3) – P(3)	0.396 (0.0059)	0.692 (0.0055)	0.800 (0.0055)	0.875 (0.0043)	0.872 (0.011)	0.912 (0.0065)
P(3) – P(2)	0.355 (0.0057)	0.607 (0.0060)	0.715 (0.0069)	0.799 (0.0063)	0.835 (0.014)	0.878 (0.010)
P(3) – P(1.5)	0.336 (0.0055)	0.559 (0.0062)	0.661 (0.0077)	0.745 (0.0076)	0.806 (0.016)	0.850 (0.012)
P(3) – P(1)	0.319 (0.0054)	0.508 (0.0065)	0.600 (0.0086)	0.678 (0.0092)	0.767 (0.018)	0.807 (0.015)
P(3) – P(0.5)	0.311 (0.0053)	0.464 (0.0067)	0.539 (0.0096)	0.605 (0.0109)	0.711 (0.018)	0.741 (0.016)

Table 2b: Average (standard error) of the powers over the 12 rebound scenarios by candidate statistic according to type of stopping boundary

	FH(0,0)	**FH(0,0.5)**	**FH(0,0.75)**	**FH(0,1)**	**RP(3)**	**RP(4)**
OF – OF	0.248 (0.0036)	0.523 (0.0107)	0.531 (0.0122)	0.490 (0.0136)	0.74700 (0.010)	0.6570 (0.012)
P(3) – P(3)	0.246 (0.0044)	0.502 (0.0101)	0.527 (0.0110)	0.511 (0.0115)	0.73600 (0.010)	0.6510 (0.011)
P(3) – P(2)	0.221 (0.0033)	0.492 (0.0093)	0.525 (0.0107)	0.511 (0.0114)	0.73600 (0.010)	0.6510 (0.011)
P(3) – P(1.5)	0.202 (0.0028)	0.478 (0.0084)	0.520 (0.0104)	0.511 (0.0113)	0.73300 (0.010)	0.6510 (0.011)
P(3) – P(1)	0.179 (0.0025)	0.452 (0.0070)	0.507 (0.0096)	0.506 (0.0110)	0.72600 (0.010)	0.6470 (0.011)
P(3) – P(0.5)	0.151 (0.0025)	0.403 (0.0050)	0.474 (0.0080)	0.491 (0.0101)	0.70400 (0.010)	0.6320 (0.011)

Table 2c: Average (standard error) of the probabilities of stopping the trial by year 5 over the 12 harmful scenarios by candidate statistic according to type of stopping boundary

	FH(0,0)	**FH(0,0.5)**	**FH(0,0.75)**	**FH(0,1)**	**RP(3)**	**RP(4)**
OF – OF	0.945 (0.0043)	0.802 (0.0126)	0.668 (0.0182)	0.511 (0.0224)	0.686 (0.017)	0.573 (0.021)
P(3) – P(3)	0.925 (0.0056)	0.751 (0.0138)	0.619 (0.0171)	0.483 (0.0186)	0.620 (0.018)	0.518 (0.019)
P(3) – P(2)	0.943 (0.0043)	0.833 (0.0099)	0.741 (0.0130)	0.636 (0.0155)	0.719 (0.014)	0.649 (0.015)
P(3) – P(1.5)	0.950 (0.0037)	0.869 (0.0079)	0.798 (0.0106)	0.714 (0.0130)	0.767 (0.012)	0.717 (0.014)
P(3) – P(1)	0.956 (0.0032)	0.899 (0.0061)	0.849 (0.0081)	0.788 (0.0101)	0.812 (0.0096)	0.781 (0.011)
P(3) – P(0.5)	0.958 (0.0029)	0.921 (0.0047)	0.889 (0.0059)	0.850 (0.0072)	0.847 (0.0075)	0.834 (0.0080)

Table 2d: Average (standard error) of the expected values of the trial duration in years over the 108 mortality scenarios by candidate statistic according to type of stopping boundary

	FH(0,0)	**FH(0,0.5)**	**FH(0,0.75)**	**FH(0,1)**	**RP(3)**	**RP(4)**
OF – OF	5.692 (0.0511)	5.731 (0.0467)	5.512 (0.0506)	5.349 (0.0524)	5.131 (0.0531)	4.838 (0.0512)
P(3) – P(3)	5.626 (0.0515)	5.666 (0.0475)	5.464 (0.0521)	5.317 (0.0546)	5.122 (0.0563)	4.861 (0.0558)
P(3) – P(2)	5.566 (0.0520)	5.610 (0.0486)	5.420 (0.0532)	5.285 (0.0557)	5.108 (0.0576)	4.874 (0.0574)
P(3) – P(1.5)	5.581 (0.0535)	5.612 (0.0492)	5.382 (0.0526)	5.214 (0.0540)	4.992 (0.0542)	4.699 (0.0515)
P(3) – P(1)	5.517 (0.0539)	5.548 (0.0501)	5.338 (0.0544)	5.187 (0.0565)	4.989 (0.0577)	4.728 (0.0565)
P(3) – P(0.5)	5.456 (0.0543)	5.491 (0.0512)	5.295 (0.0555)	5.158 (0.0577)	4.979 (0.0591)	4.746 (0.0583)

National Lung Screening Trial / Lung Screening Study

Manual of Operations and Procedures

Version 8.0
September 14, 2009

A project of the National Cancer Institute

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Not For Distribution Outside of NLST/LSS Sites

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National Lung Screening Trial / Lung Screening Study

MANUAL OF OPERATIONS AND PROCEDURES

Version 8.0

TABLE OF CONTENTS

LIST OF APPENDICES

1. INTRODUCTION

This chapter presents an overview of the Lung Screening Study (LSS) component of the National Lung Screening Trial (NLST), and an introduction to this document, the Manual of Operations and Procedures (MOOP). Although the NLST is comprised of two component studies (ACRIN [the American College of Radiology Imaging Network] and LSS), this MOOP only addresses operations and procedures for the LSS portion of NLST.

1.1 Background of the National Lung Screening Trial and Lung Screening Study

Lung cancer is the leading cause of cancer-related death in the United States among men and women, afflicting about 215,020 and killing about 161,840 each year. Disagreement over spiral computed tomography's (CT) place in lung cancer screening continues. Considering results from the Early Lung Cancer Action Project (ELCAP), some proponents say that the technology could be the single most important advance in decades, claiming that it could increase lung cancer five-year survival to 80 percent. Others say that the exact benefits and risks have yet to be determined and are asking for more research. The argument appears to reflect a much larger divide over what evidence is required and how it should be obtained before an emerging lung cancer early detection technology is adopted. While spiral CT represents one of the most exciting new imaging techniques, it needs to be studied appropriately if the technology is to be translated into an effective screening tool.

Uncertainty regarding the efficacy of spiral CT in reducing lung cancer mortality has resulted in conflicting positions in the medical community. A large randomized trial is required to fully evaluate the efficacy of spiral CT in reducing lung cancer mortality. To assess the usefulness of annual lung cancer screening with spiral CT, the National Cancer Institute (NCI), in collaboration with the American College of Radiology Imaging Network (ACRIN), is conducting the NLST. Two component studies comprise the NLST: (1) the Lung Screening Study (LSS), a special study of the Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial, and (2) a trial conducted under an NCI-funded grant to ACRIN.

The feasibility of the NLST was assessed during the feasibility phase of the LSS. During the two and a half month recruitment period (September 1 – November 15, 2000) and five-month screening

period (September 2000 – January 2001), a total of 3,409 participants were randomized, with 3,188 participants screened. Approximately one year from its start, the feasibility phase of LSS was extended and participants were invited to receive an additional screening examination and to provide follow-up information. This extension of the feasibility phase occurred between October 2001 and April 2002. The feasibility phase is now complete. Participants in this phase will not receive additional screens and will no longer provide follow-up information; however, in the spring of 2007, information from feasibility study participants was submitted to the National Death Index (NDI) for ascertainment of vital status.

Due to the success of the first year of the LSS feasibility phase, the NLST was approved by NCI's Board of Scientific Advisors in November 2001. In the LSS component of the NLST, ten screening centers (SCs) from the PLCO Trial randomized a total of 34,614 men and women at elevated risk of lung cancer. NLST recruitment and randomization lasted approximately one and a half years beginning in September 2002 and ending in April 2004. Participants received a total of three annual screening examinations and are being followed up for at least five years from the date of enrollment. Diagnostic evaluation information was obtained for participants with positive screening examination results and continues to be obtained for participants with reported lung cancers. Treatment information and information on cancer progression is being obtained for participants with a confirmed primary lung cancer diagnosis. Lung cancer mortality rates will be determined and compared between spiral CT and chest x-ray groups. See Figure 1-1 for a timeline of study activities.

LSS Feasibility Phase	**Extension of LSS Feasibility Phase**	**NLST**				
9/00 - 1/01	**10/01 - 4/02**	**9/02 – 8/03**	**9/03 - 4/04**	**5/04 - 1/07**	**2/07 – 8/10**	**9/10 – 9/11**
Enrollment & Screening	Screening & Follow-up	Enrollment & Screening	Enrollment, Screening & Follow-up	Screening & Follow-up	Follow-up & Data cleaning	Follow-up (as necessary), Data cleaning, and final results

Figure 1-1 Timeline of Study Activities

1.2 Objectives of the National Lung Screening Trial

The primary objective of the NLST is to determine whether, in persons at elevated risk of lung cancer, screening with spiral CT is associated with a greater reduction in lung cancer mortality than screening with conventional chest x-ray. The NLST will address the following objectives:

Primary objective:

- To determine whether screening with low-radiation-dose spiral CT, as compared with single-view chest x-ray, reduces lung cancer mortality among high-risk individuals.

Secondary objectives:

- To assess screening parameters, including sensitivity, specificity, and positive predictive value, for both screening modalities.
- To assess incidence, stage, and survival experience of lung cancer cases for both screening modalities.

Additional information regarding the design and objectives of the NLST/LSS is provided in the NLST/LSS Protocol Overview (Appendix 1-1).

1.3 Organizational Structure

The organizational structure of the NLST is shown in Figure 1-2. The groups involved in designing, conducting, and monitoring the NLST/LSS include the NCI, the NLST Data and Safety Monitoring Board (DSMB), the NLST Oversight Committee, the NLST Executive Committee, the Coordinating Center (CC), Screening Centers (SCs), and Information Management Services, Inc. (IMS). The roles and responsibilities of each group are described below. Unless otherwise noted, the remainder of this chapter and manual refer to the NLST/LSS.

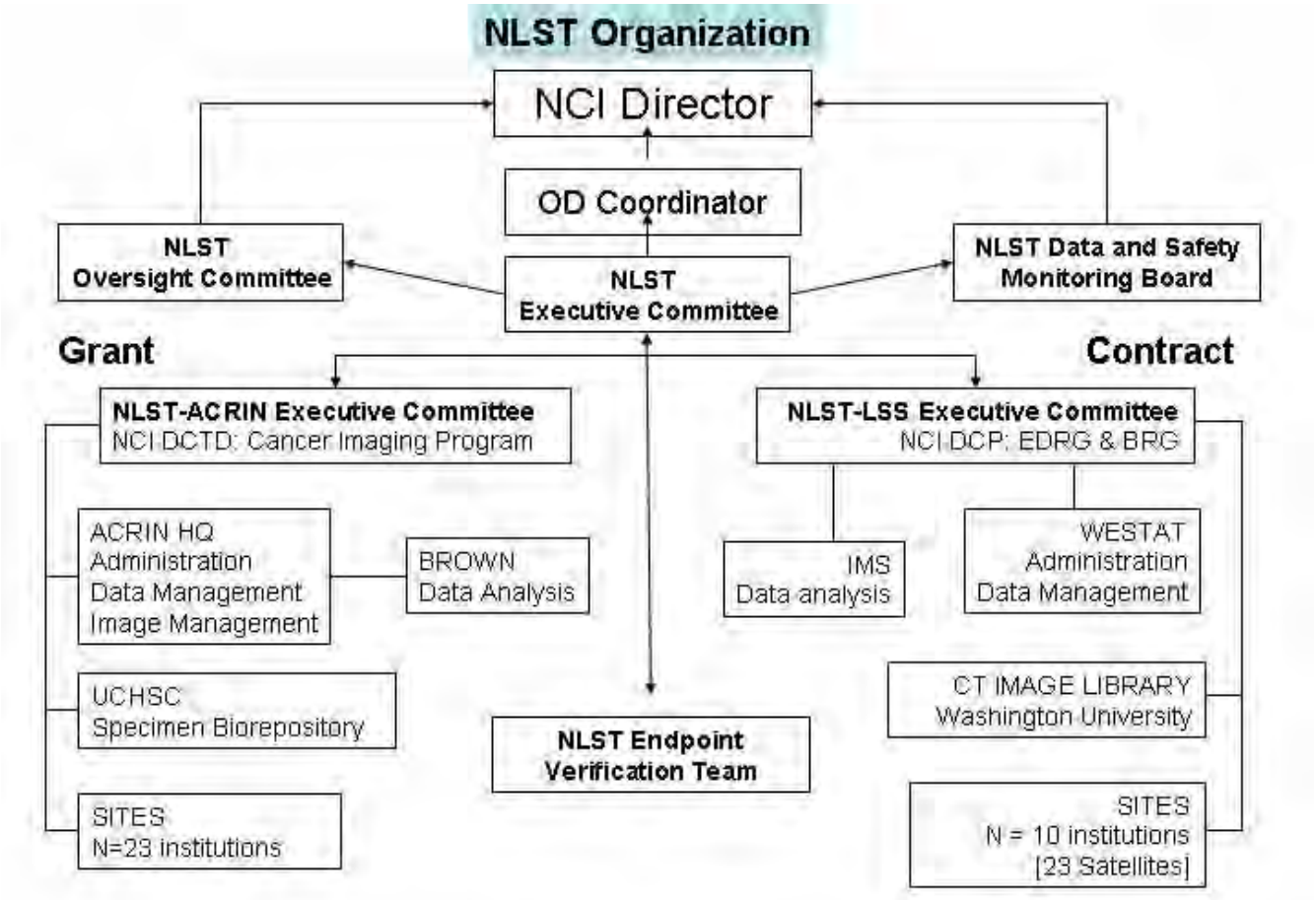
1.3.1 National Cancer Institute

The NLST Project Officer, Dr. Christine Berg, and the Associate Project Officer, Dr. Philip Prorok, are responsible for the oversight of all aspects of the NLST/LSS. The NLST/LSS Assistant Project Officers, Dr. Richard Fagerstrom and Dr. Pamela Marcus are responsible for the day-to-day operations. Dr. Richard Fagerstrom is the Chief Statistician for NLST/LSS. Dorothy Sullivan serves as the Communications Officer for NLST/LSS. The NCI Project Officers work directly with the CC in the development and implementation of the study protocol. They also work with the SCs to ensure that the technical aspects of the study are carried out to meet rigorous scientific standards, and to review and

approve documentation regarding SC plans and procedures. The NCI Project Officers also are responsible for assuring harmonization of the study protocol with ACRIN.

The NCI Contracts Officers are responsible for all contractual matters with the CC and each of the SCs.

Figure 1-2



1.3.2 Data and Safety Monitoring Board (DSMB)

One Data and Safety Monitoring Board (DSMB) is assembled for the NLST; neither LSS nor ACRIN have a separate DSMB. The DSMB is an independent advisory board composed of outside experts in thoracic radiology, pulmonology, surgery, medical ethics, biostatistics, epidemiology, oncology, and other relevant disciplines, as well as a lung cancer patient advocate, who meets semi-annually to review study progress. The DSMB members were chosen by the NLST Executive Committee (see Section 1.3.4) with approval from the Director of the NCI. The DSMB addresses issues of study integrity and participant safety, and reviews results for appropriateness of publication. The DSMB also reviews suggested protocol changes and recommends such changes as needed. As the study progresses, the DSMB reviews the interim data analysis to determine whether significant benefit or harm has been demonstrated for either of the screening modalities. The DSMB also provides advice regarding the possible termination of any aspect of the study should this be deemed necessary. The DSMB also reviews all submissions of publications, presentations, and associated studies (see Section 1.6.2).

1.3.3 Oversight Committee

The Oversight Committee is made up of experts in the fields of oncology, radiology, and biostatistics. The role of the Oversight Committee is to act as an interface between the NLST Executive Committee and the NCI Director.

1.3.4 Executive Committee

The NLST Executive Committee was established to facilitate the decision-making process with regards to the harmonization of protocols and procedures. The Committee addresses issues concerning protocol changes, publications, presentations, and associated studies. The NLST Executive Committee is composed of members from NLST/LSS and NLST/ACRIN. The NLST/LSS members include Christine Berg, Timothy Church, Richard Fagerstrom, Barnett Kramer, David Lynch, Pamela Marcus, Dorothy Sullivan, and Carl Zylak. The NLST/ACRIN members include Denise Aberle, William Black, Barbara Galen, Ilana Gareen, Constantine Gatsonis, Jonathan Goldin, and Mitchell Schnall. The committee conducts monthly conference calls and meets in person annually.

1.3.5 Coordinating Center (CC)

The CC, Westat, works closely with the NCI and the SCs to ensure the success of the NLST/LSS. The CC coordinates activities related to the development of the study protocol, arranges and document meetings, and produces standardized study materials, including this Manual of Operations and Procedures. The CC also is responsible for training the SC Coordinators, Medical Record Abstractors, and Radiologists on study procedures. The CC monitors the work completed at the SCs through receipt of reports and data and establishes regular telephone contact with each of the SC Coordinators. In addition, the CC disseminated monthly reports to the NCI during the screening phase, including the status of recruitment, randomization, screening, and follow-up. The CC disseminates quarterly reports to the NCI during the follow-up phase. The CC will conduct site visits annually, or as necessary.

The CC is responsible for developing and implementing procedures for receipt of data forms, data entry, and editing of data. From September 2002 to February 2004, data processing activities were centralized at the CC. The CC developed a computerized central Study Management System (SMS) to support central data entry, editing, and management. The computer system also supported receipt control of data forms and tracking and monitoring of study participants both at the SCs and at the CC. Data collection forms were shipped to the CC where they were receipted, and the data edited and keyed. The CC reported data retrieval needs to the SCs and monitored data retrieval progress.

During the first quarter of 2004, the CC developed and transitioned SCs to a computerized distributed study management system called the Integrated Data Entry and Administration System (IDEAS). A more detailed discussion of IDEAS is found in Chapter 11, Section 11.2. Training on the use of IDEAS was conducted by CC staff. The CC provided written documentation for IDEAS in the *NLST/LSS IDEAS User's Guide*. With IDEAS, data entry and editing occurs at the SCs rather than at the CC, and electronic data is automatically transmitted to the CC on a nightly basis. The CC performs quality assurance checks on all data and reports results to the NCI, and center-specific results to the SCs. The CC tracks and monitors study participants through monitoring reports created on a monthly basis, or as needed. In April 2007, the CC deployed a Web-based data cleaning system to complement IDEAS. The CC and SCs utilize the system to identify and track data edits and overrides.

During the recruitment and enrollment phase of the trial, the CC provided a mechanism for SCs to randomize participants into the study. The WesTrax™ system was available to the SCs for

randomizing participants using either the Interactive Voice Response (IVR) component by telephone or through submission of electronic files by computer. Instructions on how participants were randomized using the system are included in the *NLST/LSS WesTrax™ User's Guide* (Appendix 2-12).

To support the Endpoint Verification Process (EVP), the CC developed the Web-based Endpoint Verification Internal Computerized Tracking system (EVICT). EVICT is available to the SCs for viewing the status of participants for whom death certificates have been submitted to the CC, and is available to the members of the Endpoint Verification Team (EVT) for completing required forms for cases under review. EVICT is utilized by the CC to monitor the progress of the EVP. See Chapter 9 for more information on the EVP.

1.3.6 Screening Centers

There are ten PLCO SCs that participate in the NLST/LSS. The Screening Centers are as follows:

- University of Colorado
  Health Sciences Center
  Denver, CO

- Georgetown University Medical Center, Lombardi Cancer Research Center
  Washington, D.C.

- Pacific Health Research Institute
  Honolulu, HI

- Henry Ford Health System
  Detroit, MI

- University of Minnesota School of Public Health/Virginia L. Piper Cancer Institute
  Minneapolis, MN

- Washington University School of Medicine
  St. Louis, MO

- University of Pittsburgh Medical Center
  Pittsburgh, PA

- University of Utah Health Sciences Center
  Salt Lake City, UT
  AND

St. Luke's Meridian Medical Center
Meridian, ID

- Marshfield Clinic Research Foundation
  Marshfield, WI

- The University of Alabama at Birmingham
  Birmingham, AL

SCs are responsible for designing procedures necessary to implement the NLST/LSS at their particular institution and for carrying out data collection activities as required by the study protocol and documented in the MOOP. A list of the current SC Principal Investigators is provided in Appendix 1-2. SCs will also be responsible for data entry and editing in IDEAS.

1.3.7 Information Management Services, Inc. (IMS)

Information Management Services, Inc. (IMS), located in Rockville, Maryland, provides support for statistical analysis for the NLST/LSS. IMS staff works closely with the senior statisticians from the NCI to perform analyses and develop data reports using data sets provided by the CC.

1.4 Overview of Data Collection Activities

Figure 1-3 presents a schematic overview of the data collection activities of the NLST/LSS. These activities are briefly outlined below. The remaining chapters of this manual provide detailed information regarding the standardized forms and procedures involved in each of these activities.

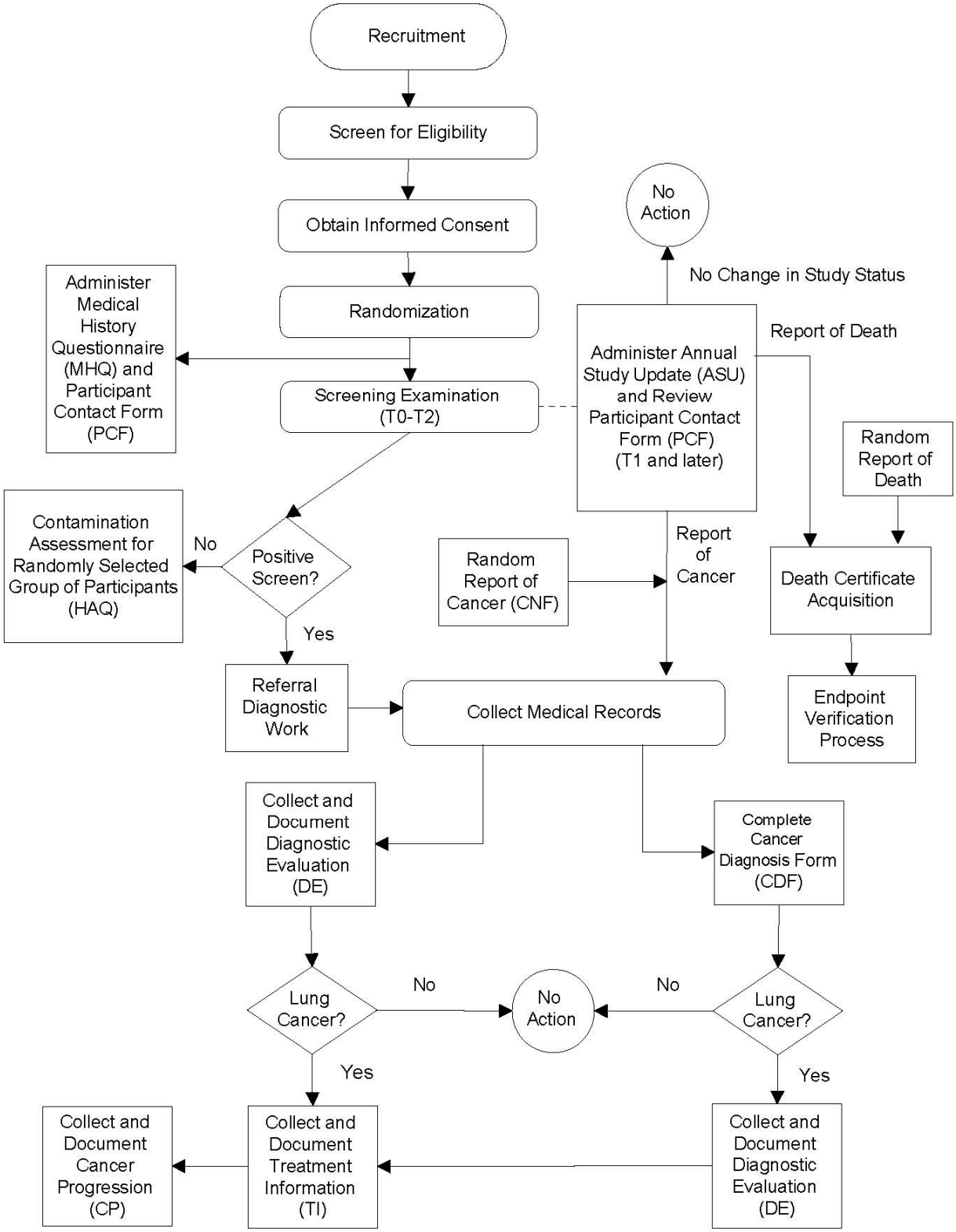
Potential participants (men and women between the ages of 55 and 74) were identified using the recruitment methods outlined in Chapter 2 and screened for eligibility and interest. Those fulfilling the eligibility criteria and interested were recruited into the study and provided written consent. Participants were randomly assigned to one of two study arms: one arm receiving three annual spiral CT screens; the other arm receiving three annual chest x-ray screens. Participants in both arms of the trial completed a questionnaire collecting information on basic demographics, lung cancer risk factors, and other medical conditions. At the screening visits, participants received the screening examination to which they were randomized (spiral CT or chest x-ray) and were asked to provide contact information and information about their health care provider. A questionnaire is administered to all participants annually

to obtain information on cancer diagnosis and smoking habits; additionally, the questionnaire serves to maintain contact with participants and assess vital status. Contamination, defined as receiving lung cancer screening exams outside of the study, is assessed in a randomly selected group of participants each study year.

Participants with positive screening examination results were referred to their health care providers for follow-up. SC radiologists provided common strategies for diagnostic evaluation to these participants. Medical records for these participants were then collected, reviewed, and abstracted for diagnostic evaluation. If lung cancer is diagnosed, medical records are collected and abstracted for information on treatment and cancer progression. Participants diagnosed with lung cancer or other cancers that have metastasized to the lung were not offered screening exams in subsequent years of the study.

Cancer incidence and mortality will be tracked for all participants during the entire course of the study. A death certificate is obtained by the SCs for all participants who are reported to be deceased, both to confirm the death and to establish the cause of death. The Endpoint Verification Process (EVP) will include a thorough review of cause of death information from multiple sources by a central committee, the Endpoint Verification Team (EVT), and will involve collection of supporting documentation by the SCs.

Figure 1-3. NLST/LSS Flow of Data Collection Activities



1.5 Time Schedule of the NLST/LSS

Date	Major Activities
Year 1: September 2002 – August 2003	Randomize and screen about 20,000 new participants (T_0). Follow up all positive screens. Assess positivity rates and lung cancer detection rates. Collect and abstract diagnostic, treatment, and cause of death information.
Year 2: September 2003 – August 2004	Randomize and screen about 20,000 new participants (T_0). Re-contact T_1 participants to identify cancer diagnoses and ascertain vital status. Re-screen up to 20,000 participants (T_1). Follow up all positive screens. Assess positivity rates and lung cancer detection rates. Collect and abstract diagnostic, treatment, cancer progression, and cause of death information. Assess contamination.
Year 3: September 2004 – August 2005	Re-contact all participants to identify cancer diagnoses and ascertain vital status. Re-screen about 40,000 participants. Follow up all positive screens. Assess positivity rates and lung cancer detection rates. Collect and abstract diagnostic, treatment, cancer progression, and cause of death information. Assess contamination.
Year 4: September 2005 – August 2006	Re-contact all participants to identify cancer diagnoses and ascertain vital status. Re-screen about 20,000 participants (T_2). Follow up all positive screens. Assess positivity rates and lung cancer detection rates. Collect and abstract diagnostic, treatment, cancer progression, and cause of death information. Assess contamination. First interim analysis for mortality reduction and risk/benefit comparison.
Year 5: September 2006 – August 2007	Re-contact all participants to identify cancer diagnoses and ascertain vital status. Complete T_2 screening. Collect and abstract diagnostic, treatment, cancer progression, and cause of death information. Assess contamination. Begin data cleaning. Second interim analysis for mortality reduction and risk/benefit comparison.
Year 6: September 2007 – August 2008	Re-contact all participants to identify cancer diagnoses and ascertain vital status. Collect and abstract diagnostic, treatment, cancer progression, and cause of death information. Assess contamination. Continue data cleaning. Third interim analysis for mortality reduction and risk/benefit comparison.
Year 7: September 2008 – August 2009	Re-contact all participants to identify cancer diagnoses and ascertain vital status. Collect and abstract diagnostic, treatment, cancer progression, and cause of death information. Assess contamination. Continue data cleaning. Fourth interim analysis for mortality reduction and risk/benefit comparison.
Year 8: September 2009 – August 2010	Re-contact all participants to identify cancer diagnoses and ascertain vital status. Collect and abstract diagnostic, treatment, cancer progression, and cause of death information. Assess contamination. Continue data cleaning. Fifth interim analysis for mortality reduction and risk/benefit comparison.
Year 9: September 2010 – September 2011	Follow-up (as necessary) through June 2011; data cleaning, analysis, and final results

1.6 Study Policy Guidelines

1.6.1 Guidelines for Describing NLST Sponsorship

Certain guidelines have been established that apply to materials produced for distribution to study participants, health care providers, and others who may be contacted regarding the study. These materials include letters, brochures, and similar items. Guidelines are as follows:

- The sponsorship of the NLST should always be stated in such a way that the NCI is primary; and
- The SCs should use SC stationery for all study materials.

1.6.2 Publications, Presentations, and Associated Studies

All data collected and stored according to the statements of work contained in SC contracts with the NCI for the NLST/LSS are the property of the NCI. However, Principal Investigators and other persons may request to use NLST/LSS data or collect additional data on NLST participants for their research purposes. The NCI has assembled the NLST/LSS Publications, Presentations, and Associated Studies (PPA) Working Group to review the submission of associated study proposals, publications, presentations, and abstracts utilizing LSS data collected as part of the NLST/LSS. This working group is co-chaired by Principal Investigators from two SCs, David Lynch (University of Colorado) and Timothy Church (University of Minnesota), and includes scientists from the Early Detection Research Group and the Biometry Research Group at NCI, with support from the CC. See Appendix 1-3 for the NLST/LSS Publications, Presentations, and Associated Studies Procedures and Authorship Guidelines.

In addition to the PPA Working Group, the NLST Executive Committee has assembled the NLST Publications and Presentations Committee (PPC) as the approving body for data requests, and proposed associated studies, publications, presentations, and abstracts that use NLST (joint ACRIN and LSS) data. This committee is co-chaired by William Black (Dartmouth-Hitchcock Medical Center) and Barnett Kramer (National Institutes of Health), and includes representatives from both ACRIN and LSS. Data requests are evaluated in accordance with the trial-wide NLST Data Release Categories and must be approved by the NLST Chief Statisticians. The PPC Co-Chairs also are involved in the NLST/LSS PPA review process. See Appendix 1-4 for the NLST PPC Policies and Review Procedures.

The CC is responsible for forwarding all submitted materials and monitoring progress through the PPA and PPC review processes, which is accomplished through the use of the NLST Study Tracking and Review Systems (STARS) (See Section 1.6.3.) The review processes, which vary according to the type of application submitted, may involve the PPA Working Group, the NLST Chief Statisticians, the PPC, and the DSMB.

1.6.2.1 Requests to Use NLST/LSS Data

All investigators who request access to NLST/LSS data or images must adhere to the policies and process described in the NLST/LSS Policies and Procedures for Data and Image Access and Use, Appendix 1-5. Data requests must be submitted using the appropriate application in STARS. Data requests that are part of an associated study will be reviewed according to the procedures for reviewing associated studies (see Section 1.6.2.2). Data requests that are not part of an associated study are first reviewed by the CC Data Manager to ensure that the requested data are available and meet the specific aims of the proposal. The NCI NLST/LSS Chief Statistician renders the approval decision according to the categories for data release found in the NLST/LSS Policies and Procedures for Data and Image Access and Use.

1.6.2.2 Associated Study Policy

An associated study is defined as any research that requires either (1) supplemental observations or procedures to be performed on all or a subgroup of NLST/LSS participants according to a set protocol; or (2) additional work to be completed by or information obtained from the CC. To protect the integrity of the trial, such associated studies must be reviewed and approved by the PPA Working Group, the NCI NLST/LSS Chief Statistician, the PPC Co-Chairs, and the DSMB before they can be initiated.

Associated studies must:

- Not interfere with the implementation/operation of NLST/LSS activities;
- Not adversely affect cooperation or compliance of NLST/LSS participants;

- Not divert NLST/LSS funds;
- Not jeopardize the public reputation of the NLST/LSS;
- Not lead to premature publication of any NLST/LSS results;
- Not complicate the interpretation of any NLST/LSS results;
- Not violate the rights of NLST/LSS participants;
- Not present methodological or ethical problems, and
- Not jeopardize the NLST/LSS in any way.

In addition, investigators must:

- Obtain IRB approval from their institution;
- Protect confidentiality of all NLST/LSS data;
- Allow review of manuscripts by the NLST/LSS prior to submission in order to ensure accuracy of statements and data related to the NLST/LSS; and
- Ensure that all NLST/LSS data remain under the direct management of the NLST/LSS principal investigator.

Investigators will be required to provide a brief description of the objectives, methods, and significance of the study. Full details must be provided concerning any procedures to be carried out on participants.

1.6.2.3 Publications, Presentations, and Abstracts

Publications, presentations, and abstracts emanating from approved associated studies must be reviewed by the PPA Working Group. Approval must be granted prior to publication or presentation. A publication or presentation will not be approved if the NCI, PPC, or DSMB judges the release of the data to be inappropriate. The CC maintains an archive of publications and presentations submitted for review, as well as a list of all final publications and presentations.

Presentations and publications must adhere to the terms stated in the NLST/LSS Data Transfer Agreement; that is, they must not contain data that are confidential or include information that

would jeopardize the integrity of NLST/LSS in any way. The Data Transfer Agreement is included as part of the NLST/LSS Policies and Procedures for Data and Image Access and Use.

1.6.3 The Study Tracking and Review System (STARS)

The Study Tracking and Review System (STARS) is a Web-based system that centralizes all of the administrative activities related to proposals that use trial data or images. Applications for data and image requests and proposed associated studies, publications, presentations, and abstracts are completed by investigators and submitted for review using STARS. Registration is required for accessing and submitting applications for data requests, associated study proposals, publications, presentations, or abstracts.

NLST/LSS STARS is located on the Web at https://www.nlststars.com. NLST/LSS STARS is used to facilitate the submission and review of proposals that use LSS data. Background information about the NLST/LSS is available on the public page. Reference materials, including NLST/LSS policies and procedures, details of the PPA review process, and instructions for completing the applications also are available.

The NLST Joint ACRIN/LSS STARS Web site, also located on the Web at https://www.nlststars.com, is available for facilitating the submission and review of proposals that use joint NLST (ACRIN and LSS) data. Background information on NLST, as well as NLST policies and procedures, details of the PPC review process, and instructions for completing the applications also are available.

1.6.4 Research Working Groups

In September 2006, NCI, with input from the SC Principal Investigators and Radiologists, identified five research areas as the focus for the development of working groups in order to promote the generation of associated studies and scientific papers. The five working groups are: Clinical Issues, Electronic Imaging, Epidemiology, Medical Physics, and Methods and Operations. The groups meet at least semi-annually and hold regular teleconferences. The groups maintain a set of active and potential projects, and use meetings to discuss the merit of potential projects, details of project development, and

progress of active studies. While it is not a requirement to have the approval of a working group for a proposed research project, it is expected that a potential project will be discussed with the appropriate working group for feedback prior to submission of a proposal application. Contacting a working group chair or the CC Lead with a proposal concept will enable discussion of the new project on the next call or during the next meeting. See Appendix 1-6 for a list of the working group chairs, NCI Leads, and CC Leads.

1.7 Purpose and Organization of the Manual of Operations and Procedures

1.7.1 Purpose of the Manual

The purpose of this manual is to document the study procedures that will be implemented at all SCs. These procedures will enable each SC to carry out the study requirements as outlined in the protocol. It is expected that the Manual of Operations and Procedures will be reviewed at each SC by the Principal Investigator, the SC Coordinator, Lead Radiologist, and other staff prior to the start of the study activities.

The manual will be updated as necessary throughout the course of the study. Each page will be identified with a version date. Replacement pages will be identified with a new version date. The SC Coordinator will be responsible for ensuring that replacement pages are distributed to each individual at the SC with a copy of this manual.

The NLST/LSS Decision Logs will be used in conjunction with the MOOP. These documents will present the NCI's decisions and resolutions regarding all protocol, procedural, and forms questions; suggestions for changes; and SC administrative and management issues. Each decision log is assigned a number and dated, and will be distributed to all SC Principal Investigators and Coordinators. Study Radiologists will receive an abbreviated version of each decision log containing only the information that pertains to the procedures that involve them.

1.7.2 Organization of the Chapters of the Manual

Recruitment and eligibility determination of study participants, including informed consent, randomization, and enrollment procedures, are covered in Chapter 2. Chapter 3 details the procedures for scheduling and conducting the screening visits and annual activities. Chapters 4 and 5 detail the spiral CT and chest x-ray screening examination protocols. Chapter 6 provides procedures for reporting results of screening examinations to participants and their health care providers. Chapter 7 discusses the procedures for the follow-up of positive results from screening examinations and other reported lung cancers. Chapter 8 discusses the procedures for cancer ascertainment. Chapter 9 details the process of vital status ascertainment and the endpoint verification process. Chapter 10 discusses assessment of contamination in both arms of the study. Chapter 11 describes administrative procedures to be conducted at the SCs, including registration of staff, record keeping, data management, and other management functions. Chapter 12 describes the procedures for collecting pathology specimens from participants with confirmed lung cancer.

Appendices for Chapter 1

NATIONAL LUNG SCREENING TRIAL/LUNG SCREENING STUDY

PROTOCOL OVERVIEW

Study Overview

To assess the usefulness of annual lung cancer screening with spiral CT, the National Cancer Institute (NCI), in collaboration with the American College of Radiology Imaging Network (ACRIN), is conducting the National Lung Screening Trial (NLST), a randomized controlled trial (RCT).

The primary objective of the NLST is:

- To determine whether screening with low-radiation-dose spiral CT, as compared with single-view chest x-ray, reduces lung cancer mortality among high-risk individuals.

Secondary objectives include the following:

- To assess screening parameters, including sensitivity, specificity, and positive predictive value, for both screening modalities.
- To assess incidence, stage, and survival experience of lung cancer cases for both screening modalities.

Two component studies comprise the NLST – an RCT conducted under contract to the NCI as a special study of the Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial (hereafter known as NLST/LSS) and an RCT conducted under an NCI-funded grant to ACRIN. The two component studies will collect the NLST outcome data in the same manner so as to allow for sound data pooling. The remainder of this protocol overview addresses NLST/LSS activities only.

The feasibility of the NLST was assessed during the feasibility phase of the LSS [1]. During the two and a half month recruitment period (September 4 – November 15, 2000) and five-month screening period (September 2000 – January 2001), a total of 3,409 participants were randomized, with 3,188 participants being screened. Approximately one year from its start, the LSS feasibility phase was extended and participants were invited to receive an additional screening examination and to provide follow-up information. This extension of the feasibility phase occurred between October 2001 and April 2002. The feasibility phase is now complete. Participants will not receive additional screens and will no

longer provide follow-up information; however, in the spring of 2007, information from feasibility study participants was submitted to the National Death Index (NDI) for ascertainment of vital status.

Due to the success of the first year of the LSS feasibility phase, the NLST was approved by NCI's Board of Scientific Advisors in November 2001. In the LSS component of the NLST, ten screening centers (SCs) from the PLCO Trial randomized a total of 34,614 men and women at elevated risk of lung cancer, with 34,570 participants eligible to participate. Participants are expected to have received a total of three annual screening examinations as well as follow-up for at least five years from the date of enrollment. Diagnostic evaluation information is obtained for participants with positive screening examination results and participants with reported lung cancers. Treatment information and information on cancer progression is obtained for participants with a confirmed primary lung cancer diagnosis. Lung cancer mortality rates will be determined and compared between spiral CT and chest x-ray groups.

Scientific Background

Lung cancer is the leading cause of cancer-related death in the United States [2]. It is estimated that there will be 161,840 deaths due to lung cancer in 2008 [2]. Although the most straightforward way to reduce lung cancer risk is to stop smoking, smoking cessation programs have had limited success. Furthermore, an elevation in lung cancer risk is believed to remain, at least in the short-term, for former smokers. Because symptoms of lung cancer often do not appear before the disease is advanced, secondary prevention is an appealing option.

Attempts to evaluate lung cancer screening modalities began over 50 years ago. Early studies, including the Philadelphia Pulmonary Neoplasm Research Project [3], the Veterans Administration Study [4], the South London Lung Cancer Study [5], the North London Cancer Study [6], and the Kaiser Foundation Health Plan Multiphasic Screening Trial [7], observed no significant impact of screening. Many of these studies had serious design limitations and consequently, the NCI sponsored, in the 1970s and 1980s, three RCTs to assess lung cancer screening modalities. Two trials, one conducted at Johns Hopkins [8] and the other conducted at Memorial Sloan-Kettering [9], observed no reduction in lung cancer mortality with a regimen of annual chest x-ray and sputum cytology every four months versus annual chest x-ray alone, indicating that sputum cytology as an addition to chest x-ray was not useful. The third trial, the Mayo Lung Project (MLP) [10], observed no reduction in lung cancer mortality with

chest x-ray and sputum cytology every four months versus usual care (with participants in the usual care arm receiving only a recommendation to receive the two tests annually). As no benefit of sputum cytology was observed in the Hopkins and Memorial Sloan-Kettering trials, the results of the MLP were interpreted to indicate that screening chest x-ray does not reduce lung cancer mortality. Over the last 15 years, these findings have played a central role in policy decisions concerning lung cancer screening.

The conclusions of the MLP have been questioned, however, because the trial did not have sufficient statistical power to identify the small but clinically important reduction in lung cancer mortality that may be possible with annual chest x-ray screening. The NCI is currently revisiting this issue in PLCO [11]. The intervention arm in PLCO is receiving an annual chest x-ray while the control arm is receiving nothing. Unlike the MLP, PLCO has ample statistical power to detect a 20 percent reduction in lung cancer mortality. Chest x-ray screening in PLCO is complete.

Since the onset of PLCO, other possible lung cancer screening modalities have been suggested. The most promising modality is a modified version of helical computed tomography. Helical computed tomography, commonly referred to as "spiral CT," is an established lung cancer diagnostic tool that can generate, with excellent resolution, three-dimensional images of lung cancer lesions, including very small lesions. A spiral CT exam that utilizes a lower radiation dose (60 milliamperes as compared with 200 milliamperes received for a diagnostic CT) has been suggested as a lung cancer screening modality, and although the imaging capabilities of a low-radiation-dose spiral CT are inferior to those of a full-dose exam, they are still superior to those of a traditional chest x-ray.

The earliest results regarding the usefulness of low-radiation-dose spiral CT as a lung cancer screening modality come from the Early Lung Cancer Action Project (ELCAP) [12]. ELCAP recruited 1,000 volunteers at elevated risk of lung cancer (at least 10 pack-years of smoking) and screened them with both chest x-ray and low-dose spiral CT. In this study population, spiral CT detected noncalcified nodules in 233 participants (malignant disease confirmed in 27), while chest x-ray detected noncalcified nodules in only 68 participants (malignant disease confirmed in 7). The findings of ELCAP left important questions regarding the usefulness of low-dose spiral CT unanswered. Most importantly, it is uncertain whether every lesion detected by spiral CT in ELCAP would have been diagnosed in the absence of screening.

Although detection of lung cancer lesions at an early stage is intuitively appealing, mass screening of asymptomatic individuals does not necessarily reduce the number of lung cancer deaths that

would have been observed had no screening occurred. Viable treatment options are of course critical to the success of any screening program, but another aspect – that screening can indirectly result in harm and thus negate any potential benefit – also must be considered. In addition to the harm that results from false positive and false negative tests, harm may also result from "over diagnosis," that is, the detection of malignant lesions that would not have been diagnosed in the absence of screening. In this situation, treatment occurs but is actually unnecessary; treatment, however, can result in reduced quality-of-life (due to chemotherapy treatments, for example) as well as morbidity and mortality (including death due to thoracotomy). The existence of a non-lethal lung cancer lesion is challenged by some researchers, but a recent follow-up analysis of MLP participants indicates that such lesions are likely to exist. Such lesions may have been detected in ELCAP, but lack of a randomized control arm and a mortality endpoint precludes further investigation of this possibility. Therefore the identification of more lesions on spiral CT as compared with chest x-ray in ELCAP does not guarantee that screening spiral CT saves lives.

The NCI's Division of Cancer Prevention (DCP) recognizes the need for further study of screening spiral CT prior to establishment of mass screening programs. To this end, plans for a large RCT with statistical power to detect a modest reduction in lung cancer mortality were developed in early 2000. Concerns regarding the acceptability of randomization and extent of spiral CT utilization among the potential study population were raised, however. To assess the feasibility of conducting a large RCT, the LSS, a special study conducted under the auspices of the PLCO Screening Trial, was undertaken in 2000 [1].

The LSS established the feasibility of conducting an RCT of spiral CT versus chest x-ray in the targeted high-risk population. During September, October, and November of 2000, six PLCO Screening Centers enrolled over 3,400 newly-recruited participants to the LSS. Individuals were randomized to a single screening spiral CT or a single screening chest x-ray, with chest x-ray chosen as a control exam to reflect the fact that it may become standard of care if a lung cancer mortality reduction is observed in PLCO. The LSS screening was completed on January 31, 2001 and all medical record abstracting was completed on June 15, 2001. Data regarding detection rates and diagnostic evaluation became available during the summer of 2001.

The feasibility phase was highly successful and assuaged concerns regarding the feasibility of a larger trial. This led to approval of the NLST in November, 2001 by the NCI Board of Scientific Advisors. The NLST will have 90% statistical power to detect a 20% reduction in lung cancer mortality with screening spiral CT, should one exist.

Recruitment

The ten NLST/LSS SCs primarily used mass mailings to enroll participants. Other recruitment methods included posters in medical facilities, recommendations from clinical practitioners, and advertisements in newspapers or magazines. The information package was mass-mailed or supplied to interested persons and contained a cover letter, a fact sheet, a toll-free phone number to call if the potential participant had questions, and a reply card for the participant to return if s/he was interested in participating.

Once a call or a reply card from an interested person was received, the SC determined eligibility by administering the Eligibility Screener (ES), a standard study form. The ES queried the participant as to age, smoking history, and lung cancer history, as well as other eligibility criteria. If the person was eligible, interested, and willing to sign the consent form, an appointment was made either for an orientation session or screening, depending on SC procedures. Eligibility and exclusion criteria were applied as follows:

Eligibility criteria:

- Ages 55-74 on date of randomization;
- Current smoker or former smoker who has quit within 15 years of randomization, and
- Cigarette smoking history of at least 30 pack-years.

Exclusion criteria:

- Spiral CT exam of the lungs, heart, or chest in the 18 months prior to randomization;
- Participation in another cancer screening study, including PLCO;
- Participation in a cancer prevention study other than a study of smoking cessation;
- Previous history of lung cancer;
- Previous removal of any portion of the lungs, except through needle biopsy;
- Evidence of or treatment for cancer (excluding non-melanoma skin cancer and carcinoma in situ other than bladder carcinoma in situ and transitional cell carcinoma in situ) in the past five years;

- Inability to lie flat on his/her back with arms raised over the head;
- Metallic implants in the chest or back (e.g. pacemakers, Harrington fixation rods);
- Requirement for home oxygen supplementation;
- Unexplained weight loss of over 15 pounds in the past 12 months or recent hemoptysis;
- Pneumonia or acute respiratory infection treated with antibiotics by a physician in the past twelve (12) weeks, or
- Unwillingness or inability to sign the consent form.

Informed Consent

Each interested participant was asked to sign a consent form prior to randomization. This was generally in advance of or at the first visit to the SC. The consent form described the study, study procedures, potential benefits and risks, alternatives to participation, the randomization process, the person's rights, potential costs, and procedures to maintain confidentiality. The name of at least one person in the SC to contact and a phone number to call were provided in the consent form. An SC staff member was made available by telephone and in person at the SC to answer questions about the consent form.

Randomization

Randomization occurred via computer or telephone using the WesTrax™ system. The system was available 24 hours a day, seven days a week. Randomization was stratified by gender and age group within each SC. Randomization procedures resulted in roughly equal numbers of participants in the study arms (spiral CT and chest x-ray).

Medical History Questionnaire

A Medical History Questionnaire was administered to all eligible participants enrolled in the study. The purpose of this questionnaire was to collect information on demographics, lung cancer risk factors, and current and past medical conditions.

Screening

Participants randomized to the spiral CT arm received three low-radiation-dose spiral CT scans spaced one year apart; participants randomized to the chest x-ray arm received three postero-anterior (PA) chest x-rays according to the same schedule. The initial screening tests were scheduled to occur within three months of randomization. Most follow up screening tests occurred between one month prior to and three months after the randomization anniversary. Board certified radiologists, who are approved to work on the study, reviewed the chest x-rays and the CT scans. Findings were noted on standardized screening results forms.

Results Reporting

Test results were sent by mail to participants and their physicians within three weeks of exams. If a screening test was suspicious for lung cancer (positive) or negative for lung cancer but had other clinically significant abnormalities, the SC staff also notified the participant by telephone. If the participant was unavailable by telephone, results were sent via certified mail. Positive screening results and negative screening results with clinically significant abnormalities were transmitted to physicians either via telephone, fax, or certified mail. If the fax method was chosen, the physician's office was telephoned and advised of the fax transmittal in advance. The letters to the participant and his/her physician accompanying the screening results report encouraged appropriate diagnostic work-up. If the participant did not have a physician, s/he was offered a list from which to choose a referral physician.

Work-up for Positive Screens

SC Radiologists provided common strategies for diagnostic evaluation to participants with positive screens. Strategies were chosen at the discretion of the reading radiologists and did not represent NLST recommendations. Such strategies were presented in results letters as follows: "*Among physicians, it is agreed that this abnormality requires a follow-up evaluation. The exact follow-up time interval and method have not been scientifically established, but common methods may include*: (list all that apply). *Your physician may have alternative methods of evaluation within the range of current practice.*"

If it was determined that diagnostic work-up was declined by a participant, this fact was recorded and dated, and any supporting information included in the participant's file.

Pathology Tissue Collection

Pathology tissue blocks will be collected for a subset of NLST/LSS participants with resected lung cancer and used for the creation of tissue microarrays (TMAs). The TMAs will be stored and used for additional research related to lung cancer etiology as approved by NCI.

Long-term Follow up

Cancer incidence and mortality will be tracked for all participants through December 2009. For those reported to have lung cancer, medical records are reviewed and abstracted for diagnostic evaluation. For those with confirmed lung cancer, treatment information and information on cancer progression is abstracted.

Death certificates are obtained by the SCs for all participants reported as deceased, both as confirmation of death and to establish cause of death. The Endpoint Verification Process, including the Endpoint Verification Team (EVT), has been implemented in the study. This process will include a thorough review of cause of death information, and will involve, where necessary, collection of supporting documentation and review by the SC and the EVT.

Organizational Structure

NCI Project Officers provide oversight for the NLST/LSS, with input from the NLST Data and Safety Monitoring Board (DSMB). Screening is carried out at ten Screening Centers nationwide. Coordination and data management activities are performed by Westat (Rockville, Maryland), the Coordinating Center.

Screening Center Responsibilities

Screening Center responsibilities will include:

- Recruitment;
- Eligibility assessment;
- Administration of informed consent;
- Randomization;
- Participant retention;
- Administration of Medical History Questionnaire;
- Screening;
- Accurate and timely results reporting to participants and physicians;
- Tracking diagnostic follow-up of positive screens;
- Cancer and vital status ascertainment through administration of Annual Study Update;
- Medical record abstracting;
- Keying and editing of data forms into the Integrated Data Entry and Administration System (IDEAS);
- Data processing and data management;
- Transmitting electronic data to the CC on a monthly basis;
- Shipment of the Medical History Questionnaire (MHQ), Health Assessment Questionnaire (HAQ), Report of Adverse Events (RAE), and copies of the Protocol and HIPAA Violation Form (PHVF) to the CC;

- Collection and shipment of tissue blocks;
- Collection of death certificates and death documentation;
- Maintenance of current, complete, and secure participant files, and
- Assessment of compliance and contamination.

Coordinating Center Responsibilities

Administrative:

- Preparation of OMB exemption package;
- Preparation and approval of IRB package;
- Organization of bi-weekly meetings with NCI;
- Documentation of all meetings;
- Coordination and documentation for all conference calls;
- Support and documentation of all working groups (e.g. Clinical Issues, Electronic Image, Epidemiology, Medical Physicist, Methods and Operations, Screening QA, and Publications, Presentations, and Associated Studies Working Groups);
- Development and maintenance of an NLST/LSS Manual of Operations and Procedures (MOOP), including Decision Logs and annual updates;
- Development and printing of all study forms;
- Training of staff on all procedures and study forms;
- Review and monitoring of experience, credentials, and training for certain NLST/LSS personnel;
- Monitoring progress and protocol adherence at Screening Centers;
- Liaison between Screening Centers and the NCI;
- Preparation of a monthly status report for the NCI;
- QA of all aspects of the study, including screening exams and the MRA process;
- Site visits to Screening Centers;

- Coordination of the Endpoint Verification Process;
- Coordination of the Pathology Tissue Collection effort; and
- Maintenance of a central records file.

Data Management:

- Development and maintenance of a centralized randomization system;
- Development and maintenance of a decentralized Integrated Data Entry and Administration System (IDEAS);
- Development and maintenance of the Web-based Endpoint Verification Internal Computerized Tracking system (EVICT) to support the Endpoint Verification Process;
- Development and maintenance of documentation;
- Receiving, keying, and editing of Medical History Questionnaire (MHQ) and Health Assessment Questionnaire (HAQ) data;
- Centralized data processing, data management, and preparation of reports;
- Data delivery, and
- Data quality assurance.

Data Transmittal

A data extraction module in IDEAS automatically transmits data to the CC server on a nightly basis.

Appendix 1-1 NLST/LSS Protocol Overview

TIMELINE

Date	Major Activities
Year 1: September 2002 – August 2003	Randomize and screen about 20,000 new participants (T_0). Follow up all positive screens. Assess positivity rates and lung cancer detection rates. Collect and abstract diagnostic, treatment, and cause of death information.
Year 2: September 2003 – August 2004	Randomize and screen about 20,000 new participants (T_0). Re-contact T_1 participants to identify cancer diagnoses and ascertain vital status. Re-screen: at least 20,000 participants (T_1). Follow up all positive screens. Assess positivity rates and lung cancer detection rates. Collect and abstract diagnostic, treatment, cancer progression, and cause of death information. Assess contamination.
Year 3: September 2004 – August 2005	Re-contact all participants to identify cancer diagnoses and ascertain vital status. Re-screen about 40,000 participants. Follow up all positive screens. Assess positivity rates and lung cancer detection rates. Collect and abstract diagnostic, treatment, cancer progression, and cause of death information. Assess contamination.
Year 4: September 2005 – August 2006	Re-contact all participants to identify cancer diagnoses and ascertain vital status. Re-screen: about 20,000 participants (T_2). Follow up all positive screens. Assess positivity rates and lung cancer detection rates. Collect and abstract diagnostic, treatment, cancer progression, and cause of death information. Assess contamination. First interim analysis for mortality reduction and risk/benefit comparison.
Year 5: September 2006 – August 2007	Re-contact all participants to identify cancer diagnoses and ascertain vital status. Complete T_2 screening. Collect and abstract diagnostic, treatment, cancer progression, and cause of death information. Assess contamination. Begin data cleaning. Second interim analysis for mortality reduction and risk/benefit comparison.
Year 6: September 2007 – August 2008	Re-contact all participants to identify cancer diagnoses and ascertain vital status. Collect and abstract diagnostic, treatment, cancer progression, and cause of death information. Assess contamination. Continue data cleaning. Third interim analysis for mortality reduction and risk/benefit comparison.
Year 7: September 2008 – August 2009	Re-contact all participants to identify cancer diagnoses and ascertain vital status. Collect and abstract diagnostic, treatment, cancer progression, and cause of death information. Assess contamination. Continue data cleaning. Fourth interim analysis for mortality reduction and risk/benefit comparison.
Year 8: September 2009 – August 2010.	Re-contact all participants to identify cancer diagnoses and ascertain vital status. Collect and abstract diagnostic, treatment, cancer progression, and cause of death information. Assess contamination. Continue data cleaning. Fifth interim analysis for mortality reduction and risk/benefit comparison.
Year 9: September 2010 – September 2011	Follow-up (as necessary) through June 2011; data cleaning, analysis, and final results.

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Appendix 1-2 List of Screening Center Principal Investigators

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NLST/LSS
Publications, Presentations, and Associated Study Working Group Review Procedures and Authorship Guidelines

This document summarizes the procedures for submitting and reviewing proposals using data collected as part of the Lung Screening Study (LSS) of the National Lung Screening Trial (NLST) for: exploratory projects, associated studies, addenda for associated studies, publications, presentations, and abstracts. This document has four sections:

A. Background information on the NLST/LSS Publications, Presentations and Associated Studies Working Group and the NLST/LSS review process;
B. The review procedures;
C. Authorship and reviewer guidelines;
D. Contact information.

The information in this document is complimented by the *Policies and Procedures for NLST/LSS Data Access and Use*, which explains different types of data requests and the proper use of NLST/LSS data; in addition, it contains the NLST Data Release Categories. It may be obtained by contacting Janet Lawler-Heavner at JanetLawler-Heavner@westat.com.

A. Background Information

1.0 The Publications, Presentations, and Associated Studies Working Group

NCI has assembled a subcommittee to review publications, presentations, abstracts, and associated studies proposals for LSS data collected as part of the NLST, to be known as the Publications, Presentations, and Associated Studies (PPA) Working Group. The mission of the PPA Working Group is to ensure that publications, presentations, abstracts, and associated studies will not jeopardize the integrity of the NLST or harm its public reputation, and to ensure a high scientific standard for proposals emanating from the trial. The PPA Working Group:

- Reviews proposals that use NLST/LSS data for publications, presentations, abstracts and associated studies
- Provides oversight and guidance to the LSS research working groups and individual investigators for proposal development
- Monitors and evaluates the progress of approved studies
- Maintains an archive of publications and presentations

The PPA Working Group is co-chaired by two NLST/LSS principal investigators, Timothy Church and David Lynch. Members are NLST/LSS investigators and NCI project officers. Westat, the coordinating center, provides administrative support.

2.0 General Proposal Review Information

Proposal review is a multi-step process involving the PPA Working Group, NCI, the co-chairs of the NLST PPC, and the NLST Data and Safety Monitoring Board (DSMB). The focus of the PPA Working Group review is on the scientific content, methodology, and statistical analysis of the proposal. The role of the NCI Chief Statistician is to evaluate the statistical component of each proposal, and, in the case of data requests, to render a decision on the permissibility of the requested data release. The decision of the Chief Statistician is guided by the NLST Data Release Categories, which are developed in conjunction with the NLST DSMB and updated as the trial progresses.

In compliance with the *NLST Publications and Presentations Committee Policies and Review Procedures*, all research proposals must be reviewed by both the co-chairs of the NLST Publications and Presentations Committee (PPC), whose primary purpose is to ensure that the ACRIN and LSS reviews identified and remedied issues inherent in the project that may negatively affect the integrity of the trial. If the review reveals an issue of concern, the PPC co-chair may request consideration by the full PPC.

Proposals must be approved by the NLST DSMB, whose scope of review is confined to issues related to the integrity of the trial, confidentiality of the data, and protection of trial endpoints. The DSMB may also provide comment on the scientific content and/or the analyses to be performed.

3.0 ACRIN and Combined ACRIN and LSS Data

Investigators may request access to data from the American College of Radiology Imaging Network (ACRIN) component of NLST by following the data request procedures outlined in the *ACRIN NLST Policies on Data Access and Publications* for investigators outside of NLST. This document may be obtained by contacting Irene Mahon at imahon@phila.acr.org. Proposals for projects that use or seek to use data from both ACRIN and the LSS, will be reviewed according to the procedures outlined in the *NLST Publications and Presentations Committee Policies and Review Procedures*, available by contacting Janet Lawler-Heavner at JanetLawler-Heavner@westat.com.

4.0 Responding to Issues of Concern

At each step in the review process, a reviewer may suggest or require changes to a proposal. If changes are suggested, the investigator will be informed, and the proposal can proceed to the next step without a revision. If the reviewer notes an issue of concern, particularly one that might affect the integrity of the trial, he/she may indicate that changes are mandatory. The investigator may address the concern in a response, make appropriate revisions, or withdraw the proposal from further consideration. Proposals that have been rejected may be revised and re-submitted.

5.0 The NLST Study Tracking and Review System (STARS)

Applications for data requests, associated studies, publications, presentations, and abstracts must be completed and submitted using the NLST Study Tracking and Review System (STARS). Access to NLST STARS requires registration on the Program Administrative Resource Web site for the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial (www.parplco.org.)

B. Review Procedures

1.0 Review Procedures for NLST/LSS Data and Image Requests for Exploratory Projects

An investigator may request data for an exploratory project that would be limited in scope and analyzed with the intent to formulate a proposal for an associated study and not for the purposes of presentation or publication. The review of requests for NLST/LSS data and/or images follows these steps:

1. The investigator completes and submits the NLST/LSS Data and Image Request Application form via STARS.

2. The Westat PPA Coordinator reviews the application for completeness, and forwards the application to the Westat Data Manager.

3. The Westat Data Manager reviews the data and image request to ensure that the data requested are available, and to clarify requests for data that do not conform to the variables found on the NSLT/LSS data collection forms, or that do not seem to correspond to the specific aims of the study.

4. After the Westat Data Manager has cleared the data and image request, the Westat PPA Coordinator forwards the Data Manager's comments and the application to the NCI Chief Statistician.

5. The NCI Chief Statistician has two weeks to complete his review of the proposal, and notify the Westat PPA Coordinator of his decision. He may indicate:

   a. approval; the PPA Coordinator sends notification of the approval to the investigator, the Westat Data Manager and the Washington University Computer Tomography Image Library (CTIL) staff when appropriate, or

   b. no approval; the PPA Coordinator notifies the investigator.

2.0 Review Procedures for Associated Studies:

The review of associated study proposals follows these steps:

1. Investigator completes and submits the NLST/LSS Associated Studies application form via STARS.

   a. If the associated study proposal <u>includes</u> a data and/or an image request, the investigator must complete and submit the Associated Studies with Data Request Application form via STARS. The Westat PPA Coordinator will forward the data/image request to the Westat Data Manager, who reviews the data/image request, and then forwards the form and comments to the NCI PPA lead reviewer.

b. If the associated study proposal does not include a data request and/or an image request, upon submission, the Westat PPA Coordinator will forward the application to the NCI PPA lead reviewer.

2. The NCI PPA lead reviewer examines the proposal to determine whether the study will jeopardize the integrity of the trial, or harm its public reputation and to ensure that it contains enough details to allow for adequate review. The NCI PPA lead reviewer may:

a. Assign two reviewers to each proposal, one subject area reviewer and one statistical reviewer, and forward the proposal to the Westat PPA Coordinator for tracking through the approval process, or

b. Return the proposal to the PI, and recommend that the PI clarify or modify the proposal before re-submitting it for formal review.

3. The Westat PPA Coordinator sends the proposal and the NLST/LSS Associated Study Review form to the reviewers who have two weeks to review the proposal and submit the completed review forms to the Westat PPA Coordinator. The reviewers may recommend:

a. Revisions: the Westat PPA Coordinator forwards the information to the investigator. The investigator returns responses and revisions to the Westat PPA Coordinator, who forwards them to the reviewers with an updated review form. Responses from the investigator are sent to both reviewers. Reviewers have one week to respond to the revised proposal. This process continues until the reviewers have no further questions for the investigator.

b. Approval: the Westat PPA Coordinator sends the proposal materials to the PPA Working Group members for discussion on the next scheduled PPA conference call.

4. The proposed study and all review materials are discussed during the PPA Working Group call; reviewers are asked to be present during the call. The PPA Working Group may choose:

a. Approval: the Westat PPA Coordinator sends all proposal materials to the NLST/LSS Chief Statistician for review, or

b. No approval: the Westat PPA Coordinator notifies the investigator of the PPA Working Group decision.

5. The Chief Statistician has two weeks to complete his review of the proposal and notify the Westat PPA Coordinator of the action he chooses:

a. Approval: the Westat PPA Coordinator sends all proposal materials to the co-chairs of the NLST PPC for review, or

b. No approval: the Westat PPA Coordinator notifies the investigator of the Chief Statistician's decision.

6. The co-chairs of the NLST PPC have one week to perform their review and notify Westat of their decisions. They may choose:

a. The NLST/LSS review is sufficient: the NLST PPC co-chairs may accept the review decisions made by the LSS PPA Working Group. The Westat PPA Coordinator sends the proposed associated study to the Chair of the NLST/LSS Data and Safety Monitoring Board (DSMB) for review.

b. Review by the NLST PPC is necessary. The Westat PPA Coordinator notifies the author of the NLST PPC co-chairs decision. It is anticipated that this review may take up to three weeks.

7. The DSMB Chair has two weeks to notify Westat of the action of the DSMB. The Chair may choose:

a. Approval.

b. No approval.

c. Electronic review by all DSMB members.

d. Discussion of the proposal by all DSMB members during the next regularly scheduled meeting of the DSMB. Note that as the DSMB meets every six months, this last option may result in a significant delay in the approval process.

The Westat PPA Coordinator notifies the investigator of the DSMB decision. The NCI NLST Project Officer sends official notification of the approval to the investigator.

It is anticipated that the review process will take at least two months, not including the DSMB review.

3.0 Review Procedures for an Addendum to an Approved Associated Study

Investigators of approved associated studies wishing to request new or additional LSS data or images must complete the PPA Associated Study Addendum application. The application forms for addenda can be obtained from the Westat PPA Coordinator, Janet Lawler-Heavner at JanetLawler-Heaver@westat.com. (The current version of STARS does not process addenda.) The following steps document the abbreviated review of the addendum:

1. Investigator completes and sends the PPA associated study addendum to the Westat PPA Coordinator.

   a. If the addendum includes a data request and/or image request, the Westat PPA Coordinator forwards the data/image request to the Westat Data Manager. The Westat Data Manager reviews the data/image request, and then forwards the form and comments to the NCI PPA lead reviewer.

   b. If the addendum does not include a data request and/or image request, the PPA Coordinator forwards the addendum to the NCI PPA lead reviewer.

2. The NCI PPA lead reviewer has one week to complete the review of the addendum. The NCI PPA lead reviewer may choose to:

   a. Approve the addendum and forward it to the Westat PPA Coordinator for tracking through the review process, or

   b. Return the addendum to the investigator with requests for revisions that must be made in order to obtain approval.

3. The Westat PPA Coordinator forwards the addendum and the initial review to the NLST/LSS Chief Statistician. The Chief Statistician has one week to complete his review of the addendum and notify the Westat PPA Coordinator of the action he chooses:
    a. Approval: the Westat PPA Coordinator sends the addendum and all reviews to the Chair of the NLST Data and Safety Monitoring Board for review, or
    b. No approval: the Westat PPA Coordinator notifies the investigator of the Chief Statistician's decision.
4. The DSMB Chair has two weeks to notify Westat of the action of the DSMB. The Chair may choose:
    a. Approval.
    b. No approval.
    c. Electronic review by all DSMB members.
    d. Discussion of the addendum by all DSMB members during the next regularly scheduled meeting of the DSMB. Note that as the DSMB meets every six months, this last option may result in a significant delay in the approval process.
5. The Westat PPA Coordinator notifies the investigator of the DSMB decision.

4.0 Review Procedures for Publications

Investigators may discuss a proposal for a publication with Timothy Church and David Lynch, or hold discussions with the chair of one of the LSS working groups about the feasibility of such an undertaking. Data requests will not be filled if the NCI Chief Statistician judges release of data to be inappropriate.

Authors are reminded to pay close attention to submission deadlines, so that the PPA Working Group, NCI Chief Statistician, the co-chairs of the NLST PPC, and the DSMB have enough time to complete their reviews.

The review of manuscripts will follow these steps:

1. If the manuscript requires a data request and/or image request, the Westat PPA Coordinator forwards the data/image request to the Westat Data Manager. The Westat Data Manager reviews the data/image request, and then forwards the form and comments to the NCI Chief Statistician. The Chief Statistician may choose:
    a. Approval: the data and/or images are sent to the investigator for preparation of the manuscript.
    b. No approval: the Westat PPA Coordinator notifies the author of the Chief Statistician's decision.
2. The PPA Coordinator will notify the lead reviewer of the manuscript for review. The lead reviewer will assign (at least) two reviewers. Reviewers may be drawn from the PPA Working Group or from outside the Working Group if additional expertise is needed.

3. Manuscripts will also be sent to all members of the PPA Working Group for their critique and also to inform the Working Group of potential publications.

4. Reviewers have two weeks to review the proposal, and return their comments to the PPA Coordinator. The lead reviewer will choose to:

    a. Recommend revisions that need to be made prior to approval: the Westat PPA Coordinator sends the revisions to the author. The author returns responses and revisions to the Westat PPA Coordinator, who forwards them to the reviewers. Responses from the investigator are sent to all reviewers. Reviewers have one week to respond to the revised manuscript. This process continues until the reviewers have no further questions for the author.

    b. Request the discussion of the manuscript during a PPA Working Group conference call (for any manuscript deemed exceptionally controversial or problematic). The Westat PPA Coordinator sends the manuscript and any comments/reviews received to all members of the PPA Working Group in preparation for the call.

    c. Approve: the Westat PPA Coordinator sends the manuscript to the NLST/LSS Chief Statistician for review,

    d. Not approve: the Westat PPA Coordinator notifies the author of the PPA Working Group decision.

5. The Chief Statistician has two weeks to complete his review of the manuscript and notify the Westat PPA Coordinator of the action he chooses:

    a. Approval: the Westat PPA Coordinator sends the manuscript to the co-chairs of the NLST PPC for review, or

    b. No approval: the Westat PPA Coordinator notifies the author of the Chief Statistician's decision.

6. The co-chairs of the NLST PPC have two weeks to perform their review to notify Westat of the action they choose to take. The NLST PPC co-chairs may choose:

    a. The NLST/LSS review is sufficient. The NLST PPC co-chairs may accept the review decisions made by the LSS PPA Working Group. The Westat PPA Coordinator sends the manuscript to the Chair of the NLST/LSS Data and Safety Monitoring Board (DSMB) for review.

    b. Review by the NLST PPC is necessary. The Westat PPA Coordinator notifies the author of the NLST PPC co-chairs decision. It is anticipated that this review may take up to three weeks.

7. The DSMB Chair has four weeks to notify Westat of the action of the DSMB. Manuscripts approved by the PPA Working Group and the NCI Chief Statistician may be submitted while awaiting DSMB approval; any manuscript later denied by the DSMB must be retracted. Manuscripts MUST receive the approval of the DSMB prior to publication. The DSMB Chair may choose:

a. Approval.

b. No approval.

c. Electronic review by all DSMB members.

d. Discussion of the manuscript by all DSMB members during the next regularly scheduled meeting of the DSMB. Note that as the DSMB meets every six months, this last option may result in a significant delay in the approval process.

8. The Westat PPA Coordinator notifies the author of the DSMB decision.

9. It is anticipated that the review process will take at least six weeks, not including the DSMB review.

5.0 Review Procedures for Slide Presentations or Posters

Authors are reminded to pay close attention to submission deadlines, so that the PPA Working Group, NCI Chief Statistician, the co-chairs of the NLST PPC, and the DSMB have enough time to complete their reviews.

The review of presentations/posters will follow these steps:

1. If the presentation/poster requires a data request and/or image request, the Westat PPA Coordinator forwards the data/image request to the Westat Data Manager. The Westat Data Manager reviews the data/image request, and then forwards the form and comments to the NCI Chief Statistician. The Chief Statistician may choose:

    a. Approval: the data and/or images are sent to the investigator for preparation of the presentation/poster.

    b. No approval: the Westat PPA Coordinator notifies the investigator of the Chief Statistician's decision.

2. The Westat PPA Coordinator notifies the lead reviewer of the presentation/poster for review. The lead reviewer will determine if additional PPA Working Group reviewers are needed. Reviewers may be drawn from the PPA Working Group or from outside the Working Group if additional expertise is needed. The lead reviewer or the PPA reviewers may choose to circulate the presentation/poster to the entire Working Group for review if they determine the presentation/poster to be of interest to the entire group or that it needs review by the entire group.

3. The lead reviewer (or the PPA Working Group) has one week to review the presentation/poster and notify Westat of the decision:

    a. Approval: the Westat PPA Coordinator sends the slides or poster to the NLST/LSS Chief Statistician for review, or

    b. No approval: the Westat PPA Coordinator notifies the author of the PPA Working Group decision.

4. The Chief Statistician has one week to complete his review of the presentation/poster and notify the Westat PPA Coordinator of the action he chooses:
    a. Approval: the Westat PPA Coordinator sends the presentation/poster to the co-chairs of the NLST PPC for review, or
    b. No approval: the Westat PPA Coordinator notifies the author of the Chief Statistician's decision.

5. The co-chairs of the NLST PPC have one week to perform their review and notify Westat of the action they choose to take. The NLST PPC Co-chairs may decide that:
    a. The NLST/LSS review is sufficient: the NLST PPC Co-chairs may accept the review decisions made by the LSS PPA Working Group. The Westat PPA Coordinator sends the presentation/poster to the Chair of the NLST/LSS Data and Safety Monitoring Board (DSMB) for review.
    b. Review by the NLST PPC is necessary. The Westat PPA Coordinator notifies the author of the NLST PPC Co-chairs' decision. It is anticipated that this review may take up to three weeks.

6. The DSMB Chair has two weeks to notify Westat of the action of the DSMB. The DSMB Chair may choose:
    a. Approval.
    b. No approval.
    c. Electronic review by all DSMB members.
    d. Discussion of the presentation/poster by all DSMB members during the next regularly scheduled meeting of the DSMB. Note that as the DSMB meets every six months, this last option may result in a significant delay in the approval process.

7. The Westat PPA Coordinator notifies the author of the DSMB decision.

8. It is anticipated that the review process will take at least three weeks, not including the DSMB review.

6.0 Review Procedures for Abstracts

Authors are reminded to pay close attention to submission deadlines, so that the PPA Working Group, NCI Chief Statistician, the Co-chairs of the NLST PPC, and the DSMB have enough time to complete their reviews.

The review of abstracts will follow these steps:

1. If the application for the abstract requires a data request and/or image request, the Westat PPA Coordinator forwards the data/image request to the Westat Data Manager. The Westat Data Manager reviews the data/image request, and then forwards the form and comments to the NCI Chief Statistician. The Chief Statistician may choose:

    a. Approval: the data and/or images are sent to the investigator for preparation of the abstract, or

    b. No approval: the Westat PPA Coordinator notifies the author of the Chief Statistician's decision.

2. If the application for the abstract is complete and does not contain a data or image request, the Westat PPA Coordinator will notify the lead reviewer.

3. The lead reviewer will determine if additional PPA Working Group reviewers are needed for the abstract. Reviewers may be drawn from the PPA Working Group or from outside the Working Group if additional expertise is needed. The lead reviewer or the PPA reviewers may choose to circulate the abstract to the entire Working Group for review, if they determine the abstract to be of interest to the entire group or that it needs review by the entire group.

4. The lead reviewer (or the PPA Working Group) has one week to review the proposal and notify Westat of the decision:

    a. Approval: the Westat PPA Coordinator sends the abstract to the NLST/LSS Chief Statistician for review, or

    b. No approval: the Westat PPA Coordinator notifies the author of the PPA Working Group decision.

5. The Chief Statistician has one week to complete his review of the abstract and notify the Westat PPA Coordinator of the decision:

    a. Approval: the Westat PPA Coordinator sends the abstract to the co-chairs of the NLST PPC for review, or

    b. No approval: the Westat PPA Coordinator notifies the author of the Chief Statistician's decision.

6. The Co-chairs of the NLST PPC have one week to notify Westat of the action they choose to take. Co-chairs may choose:

    a. The NLST/LSS review is sufficient: The NLST PPC co-chairs may accept the review decisions made by the LSS PPA Working Group. The Westat PPA Coordinator sends the abstract to the Chair of the NLST/LSS Data and Safety Monitoring Board (DSMB) for review.

    b. Review by the NLST PPC is necessary. The Westat PPA Coordinator notifies the author of the NLST PPC Co-chairs' decision. It is anticipated that this review may take up to three weeks.

7. The DSMB Chair has two weeks to notify Westat of the action of the DSMB. Abstracts approved by the PPA Working Group and the NCI Chief Statistician may be submitted while awaiting

DSMB approval; any abstract later denied by the DSMB must be retracted. The DSMB Chair may choose:

a. Approval.

b. No approval.

c. Electronic review by all DSMB members.

d. Discussion of the abstract by all DSMB members during the next regularly scheduled meeting of the DSMB. Note that as the DSMB meets every six months, this last option may result in a significant delay in the approval process.

8. The Westat PPA Coordinator notifies the author of the DSMB decision.

9. It is anticipated that the review process will take at least four weeks, not including the DSMB review.

C. Authorship and Reviewer Guidelines

1.0 Authorship Guidelines: It is the responsibility of the PI on any associated study to ensure that all authors have made contributions to any manuscript proposed for publication. The NLST Executive Committee has adopted the following authorship guidelines for the NLST:

Authorship on NLST publications will follow the general guidelines of the International Committee of Medical Journal Editors (ICMJE) (http://www.icmje.org/). Authors should have made substantial contributions to all three categories established by the ICMJE:

- Conception or design, or acquisition of data, or analysis and interpretation of data, and
- Drafting the article or revising it critically for important intellectual content, and
- Final approval of the version to be published.

The following guidelines for publications have been established to satisfy scientific integrity in authorship as well as to enable appropriate recognition of the efforts of individuals and collective groups in the execution, analysis, and publication of content of the NLST. In all instances, additional persons whose contributions warrant authorship may be included with the permission of the Executive Committee.

a. The publication of the primary and secondary endpoints of the NLST will typically be attributed to "The NLST Research Group." The NLST Research Group consists of NLST institutional Principal Investigators and members of the Executive Committee who meet the ICMJE Criteria for authorship. Members of the NLST Research Group will be noted in an appendix, where the names will be grouped by trial role (Principal Investigator or Executive Committee member) and listed alphabetically. The contributions of the institutional Study Coordinators will be noted in an acknowledgement at the end of these manuscripts, with coordinators grouped by institution. The primary endpoint of the NLST is lung cancer mortality. Secondary endpoints are those that relate to screening, influence the primary outcome, and are collected on all NLST participants. Test sensitivity, stage distribution, and all-cause mortality are examples of secondary outcomes.

b. The publication of results from NLST sub-studies (studies that utilize data collected on a subset of NLST participants, such as impact of screening/positive screening tests on quality of life and smoking behaviors, health care utilization, and radiation dosimetry) will be attributed to the appropriate group according to ICMJE guidelines for authorship. In this instance, the decision as to whether individual authors or a specific group will be listed as authors should be a joint decision of the authors, determined prior to initiating the manuscript.

c. The publication of other aspects of the NLST not directly related to study endpoints should be determined by the ICMJE guidelines for authorship. The order of authors should be the joint decision of the authors, and contributors should be prepared to explain the order of the authors.

Individuals who have made substantial contributions to a manuscript, but who do not qualify for authorship should be listed, with their permission, in the Acknowledgments or in an Appendix. For presentations, authorship can be restricted to the presenter, with acknowledgement of the NLST collaborators in the presentation.

2.0 NLST PPA Working Group Reviewer Guidelines and Responsibilities

This section will provide guidance to investigators asked to perform a review for the LSS PPA Working Group. The overall objectives of a PPA review for publications, presentations, abstracts, and associated studies are to ensure that the integrity of the trial is protected, and that the NLST/LSS is accurately described. The requirement for approval is based upon whether the proposal satisfies these two objectives. In addition, reviewers should be guided by the checklist found in the Manual of Operations for NLST/LSS. Proposals should:

- Not interfere with the implementation/operation of NLST/LSS activities;
- Not adversely affect cooperation or compliance of NLST/LSS participants;
- Not divert NLST/LSS funds;
- Not jeopardize the public reputation of the NLST/LSS;
- Not lead to premature publication of any NLST/LSS results;
- Not complicate the interpretation of any NLST/LSS results;
- Not violate the rights of NLST/LSS participants;
- Obtain IRB approval from their institution;
- Not jeopardize the confidentiality of NLST/LSS data;
- Allow review of manuscripts by the NLST/LSS prior to submission in order to ensure accuracy of statements and data related to the NLST/LSS;
- Include the relevant NLST/LSS SC principal investigator as a co-investigator, when appropriate;
- Ensure that all NLST/LSS data remain under the direct management of the NLST/LSS principal investigator;
- Not present methodological or ethical problems, and
- Not jeopardize the NLST/LSS in any way.

In general, ancillary studies, particularly those that require use of NLST/LSS data, require a thorough evaluation of the study methodology and data analysis plan, to ensure a high level of scientific validity. Manuscripts, presentations and abstracts may undergo a more limited review, in anticipation of an extensive review by the journal or society to which they have been submitted.

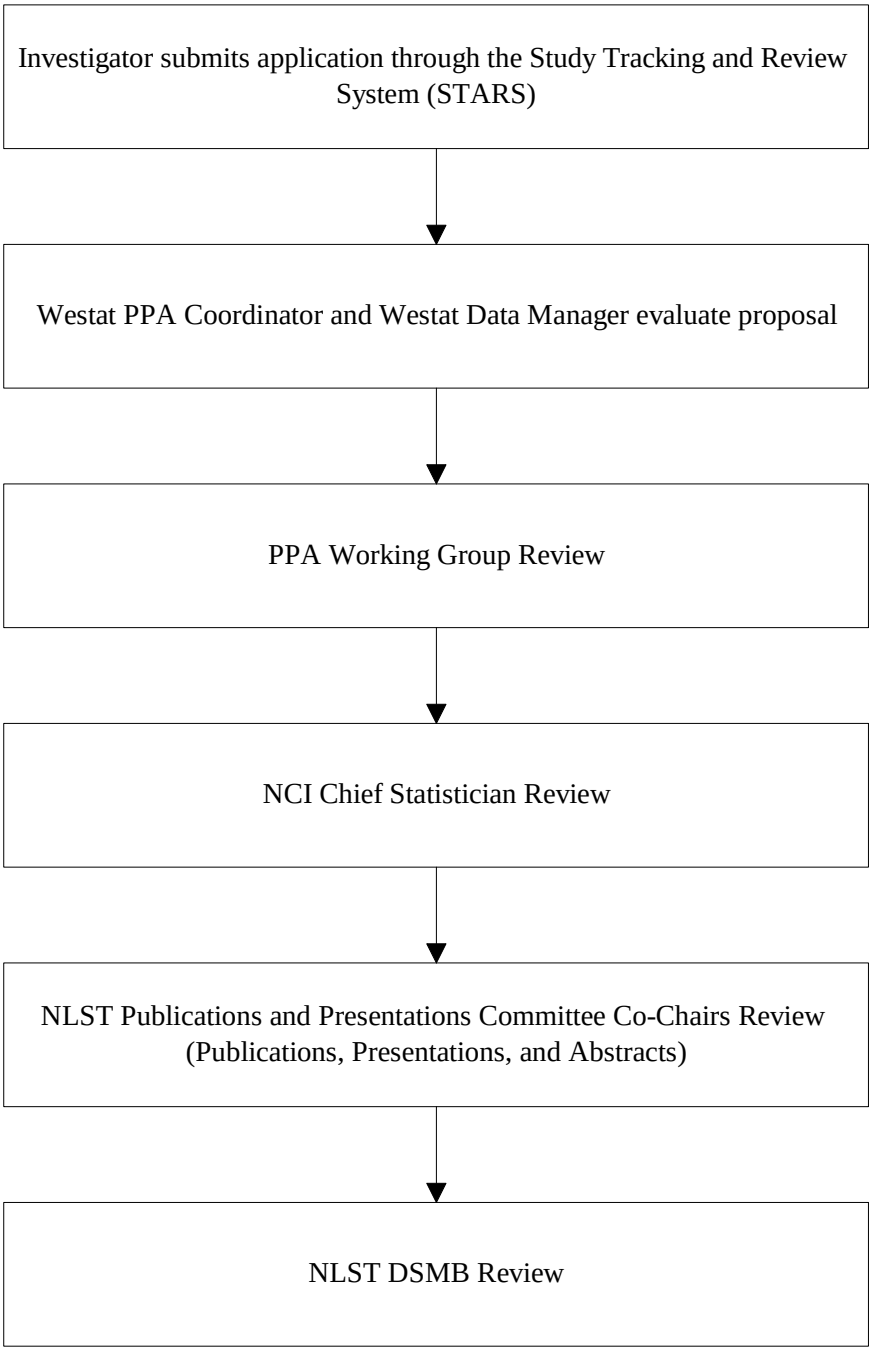
Reviewers are reminded that they must adhere to standards of ethical peer review; the duty of confidentiality in the assessment of presentations and posters must be maintained by all reviewers. The submitted material should not be retained, and must be deleted from reviewer's computer once the review is complete. Any printed copies of the material must be shredded. Reviewers may not make use of any of the data, arguments, or interpretations contained in the presentation or poster without permission from the authors.

D. Contact Information

Title	Name	Phone	Fax	E-mail
NCI PPA Lead Reviewer	Paul Pinsky	301-402-6480	301-402-0816	pinskyp@mail.nih.gov
NLST/LSS Chief Statistician	Richard Fagerstrom	301-496-7458	301-402-0816	fagerstr@mail.nih.gov
PPA Co-Chair	Tim Church	612-625-9091	612-625-4363	trc@cccs.umn.edu
PPA Co-Chair	David Lynch	303-398-1611	303-398-1652	david.lynch@njc.org
Westat PPA Coordinator	Janet Lawler-Heavner	301-315-5938	301-315-5910	janetlawler-heavner@westat.com
Westat PPA Project Administrator	Adam DeBaugh	301-294-4453	301-315-5910	adamdebaugh@westat.com

NLST/LSS PPA Working Group
General Proposal Review Process

This chart outlines the general steps followed by the review procedures for all proposal types except data requests.



NLST Publications and Presentations Committee Policies and Review Procedures

Overview

The NLST leadership has assembled a committee to review all proposed associated studies, publications, presentations, and abstracts that use data from both ACRIN and NLST. This committee will be known as the NLST Publications and Presentations Committee (PPC). The *NLST Publications and Presentations Committee Policies and Review Procedures* document sets forth the policies and procedures for review of proposals that use data collected as part of or derived from the NLST, including images, operations, and methodology, (referred to as "NLST data" in the remainder of this document). All institutional Principal Investigators, NCI Project Officers, American College of Radiology Imaging Network (ACRIN) Project Managers, and NCI Program Directors involved in the Lung Screening Study (LSS) and ACRIN components of the NLST will adhere to these policies and are responsible for ensuring that collaborators and researchers approved to work with NLST data will also adhere to these policies.

1. Membership and Responsibilities of the PPC

a. PPC Responsibilities

The PPC has the following responsibilities:

- To review proposals for joint ACRIN-LSS ancillary studies, publications, presentations, and abstracts to ensure that:
  - the release of NLST data for ancillary studies and related publications and presentations does not jeopardize the primary or secondary endpoints of the trial, and
  - publications and presentations by NLST investigators are of high scientific quality.
- To maintain an archive of completed studies, publications, presentations, and abstracts.

b. Committee Composition and Membership Qualification

The PPC is composed of two co-chairs, eight regular members, and ad hoc members who will be invited as their participation is needed. The co-chairs, one representing each component of the trial, oversee all PPC activities and are also members of the NLST Executive Committee. The eight regular PPC members, represented equally from each component of the trial, are NLST investigators who do not also serve on the NLST Executive Committee. The NLST Executive Committee may modify the composition of the PPC at any time.

c. The NLST PPC members are listed in Attachment I.

2. Central Review Policies

The NLST Executive Committee has set two policies pertaining to the review of proposed associated studies, publications, presentations, and abstracts that use any subset of NLST data.

a. All associated studies, publications, presentations, and abstract proposals that use, or seek to use, NLST data will be reviewed by the appropriate review committee, determined by the source of the data to be used in the project.

i. Research proposals that use ACRIN-only or LSS-only data

This policy recognizes the primacy of the individual ACRIN and LSS review procedures in the review of proposed projects or emanating works using ACRIN-specific and LSS-specific data, and provides a mechanism for reciprocal notification and approval. Review will proceed according to the steps described in the *ACRIN Policies on Data Access and Publications* or the *NLST/LSS Publications, Presentations, and Associated Studies Working Group Review Procedures and Authorship Guidelines.* The individual review procedures must make provision for the participation of both PPC co-chairs, whose primary purpose is to ensure that the ACRIN and LSS reviews identified and remedied issues inherent in the project that may negatively affect the integrity of the trial. The review of the PPC co-chairs should therefore be performed after the initial ACRIN Media and Publications Committee review or LSS Publications, Presentations, and Associated Studies (PPA) Working Group review, but prior to the DSMB review. If the review reveals an issue of concern, the co-chair may request consideration by the full PPC. The co-chairs may also exercise discretionary authority to request review by the full PPC for issues that deserve such attention. Each co-chair will use the attached review form (Attachment II), and inform the other co-chair of his decision.

ii. Research proposals that use both ACRIN and LSS data

The review is conducted according to the PPC review procedures outlined in Section 3.

b. All research proposals must be approved by the NLST Data and Safety Monitoring Board (DSMB), whose scope of review for approval is confined to issues related to the integrity of the trial, confidentiality of the data, and protection of trial endpoints. The DSMB may also provide comment on the scientific content and the analyses performed. See Attachment III for the DSMB Chair Proposed Associated Study, Publications, Presentations, and Abstracts Review Form.

3. **Development of Associated Studies**

The chief purpose of the NLST Research Working Groups is to facilitate collaborative efforts by providing a forum for the exchange and development of research ideas. It is expected that investigators will present a research protocol on a joint working group call or meeting for feedback prior to submission for review to the PPC.

4. **Review Process for Associated Studies, Publications, Presentations, and Abstracts that Use both ACRIN and LSS Data**

The steps in the review process for research proposals that use both ACRIN and LSS data are outlined below; the process is estimated to require at least **eight weeks** for associated studies, and **six weeks**

for publications, presentations, and abstracts. See Attachment IV for a diagram of the PPC review process for associated studies, publications, presentations, and abstracts.

Step 1: The Preliminary Review of a Data Request

When an associated study application has an accompanying request, the investigator will send the application and data request to the PPC Coordinator, who will forward the application materials to the ACRIN and LSS Data Managers for a preliminary review of the data request. The purpose is to ensure that the data are available, and that the requested data items conform to the specific aims of the study.

Step 2: The NLST PPC Review

The PPC coordinator will assign the application to two reviewers: one from ACRIN and one from LSS. One of the two reviewers must be a statistician, epidemiologist, or person with expertise in study design. The other reviewer will be selected to ensure appropriate subject area expertise. (See Attachments V and VI for the subject area and statistical review forms.) The co-chairs or the PPC coordinator may appoint ad hoc reviewers if members of the PPC do not have the necessary scientific expertise for proper review.

Reviewers will have **two weeks** from the receipt of the application to complete their review. The reviewers will provide a brief summary of their review in standardized format, and make an approval recommendation. The reviewers will forward their completed reviews to the PPC coordinator.

In addition to the review step outlined above, each proposed associated study will be required to undergo a review by the entire PPC. A discussion will be held by teleconference to render an approval decision and to use the collective expertise of the group to enhance the scientific value of the proposed research design. It is anticipated that this additional step will add several weeks to the PPC review process.

For publications, presentations, and abstracts, the PPC co-chairs render an approval decision informed by the recommendation of the two preliminary reviewers, as well as a judgment concerning the potential impact on trial endpoints. While a review by the full PPC is normally not conducted for these proposals, the PPC co-chairs may request that a publication, presentation, or abstract with issues of concern be brought to the attention of the entire PPC.

Step 3: The NLST Chief Statistician Review

Following the PPC review, the PPC coordinator will send the proposal to the NLST Chief Statistician who represents the side of the trial not represented by the affiliation of the statistician of the PPC preliminary review. The NLST Chief Statistician will have **two weeks** to complete his review. The purpose of the statistical review is to evaluate the statistical component of the proposal. Approval must be granted to continue to Step 4 in the review process.

When a data request accompanies an associated study application, both Chief Statisticians must review and render an approval decision for the application to proceed.

Step 4: The ACRIN Media and Publications Committee and the LSS Publications, Presentations and Associated Studies (PPA) Working Group Review

Associated Studies:

The PPC coordinator will forward proposals approved by the NLST Publications and Presentations Committee to The ACRIN Media and Publications Committee and the LSS PPA Working Group, for their information. The reviews will be coordinated by the ACRIN Publications Assistant, Irene Mahon and the LSS PPA WG coordinator, Janet Lawler-Heavner, who will forward the proposal to the respective review groups. Comments must be returned to the PPC coordinator within **one week**.

Publications, Presentations, and Abstracts:

The above step will be followed with the exception that the ACRIN Media and Publications Committee must provide approval for the application to continue in review.

Step 5: The NLST Data and Safety Monitoring Board (DSMB)

The PPC coordinator will send the proposal to the Chair of the NLST DSMB for review and final approval. The DSMB Chair has **two weeks** to conduct his review. He may request review by the entire DSMB, a step which will lengthen the time required by an additional two weeks, if performed electronically.

5. **Review Process for Limited Data Requests**

An investigator may request data for an exploratory project, or to determine the feasibility of a project, that would be limited in scope and analyzed with the intent to formulate a proposal for an associated study and not for the purposes of publication. The review of this type of request follows these steps:

Step 1: Application Completion

The investigator completes and submits the NLST Limited Data and Image Request Application form to the PPC Coordinator, who reviews the application for completeness, and forwards the application to the ACRIN and Westat Data Managers.

Step 2: Review by ACRIN and LSS Data Managers

The ACRIN and LSS Data Managers review the data and image request to ensure that the data requested are available, and to clarify requests for data that do not conform to the variables found on the NLST data collection forms, or that do not seem to correspond to the specific aims of the study.

Step 3: Review by the NLST Chief Statisticians

After the Data Managers have cleared the data and image request, the PPC Coordinator forwards the Data Manager's comments and the application to the Chief Statisticians. The Chief Statisticians have two weeks to complete their review of the proposed data request. They must reach an approval consensus for data to be released. The PPC Coordinator will send notification of the decision to the investigator and Data Managers.

6. Review Procedures for an Addendum to an Approved Associated Study

Investigators of approved associated studies wishing to request new or additional NLST data or images, or modify their study protocol, must submit a PPC Associated Study Addendum application. The following steps outline the review process:

Step 1: Preliminary Review of Addenda Applications with Data Requests
Investigator completes and sends the PPC Associated Study Addendum with Data Request application to the PPC Coordinator. The PPC Coordinator forwards the application to the Brown and Westat Data Managers. The purpose of this review is to ensure that the data are available, and that the requested data items conform to the specific aims of the study. The Data Managers review the data and/or image request, and comments are forwarded to the PPC Coordinator, who will share them with the next reviewer.

Step 2: PPC Co-Chair Review *(all addenda applications, with or without data requests)*
Addenda applications without data requests begin review with the PPC Co-chair review. The PPC Coordinator assigns the review to one PPC Co-chair, on an alternating basis. The second PPC Co-chair is informed of the application and may provide optional comments.

The PPC Co-chair has one week to complete the review of the addendum application. He may choose:

a. Approval. The PPC Co-chair may suggest or request revisions. If the changes are required, the investigator must address these to the satisfaction of the PPC Co-chair in order for the addendum to continue through the review process.

b. Rejection.

Step 3: Chief Statistician Review

If the addendum includes a data request, the PPC Coordinator forwards the addendum and the initial review to both NLST Chief Statisticians. The Chief Statisticians have one week to complete their review of the addendum and notify the PPC Coordinator of the action they wish to take:

a. Approval. The Chief Statisticians may suggest or request revisions. If revisions are required, the investigator must address these to the satisfaction of the Chief Statisticians. Following a satisfactory re-review, the PPC Coordinator sends the addendum to the Chair of the NLST Data and Safety Monitoring Board for review.

b. Rejection.

If the addendum does not include a data request, Step 3 will be followed with the PPC Coordinator assigning the review to one Chief Statistician, on an alternating basis. The other Chief Statistician will be informed of the application and may provide optional comments.

Step 4: The NLST DSMB

The DSMB Chair has two weeks to notify the PPC Coordinator of the action of the DSMB. The Chair may choose:

a. Approval. Suggestions or requests for revisions may be made.

b. Rejection.

c. Electronic review by all DSMB members.

d. Discussion of the addendum by all DSMB members during the next regularly scheduled meeting of the DSMB. Note that as the DSMB meets every six months, this last option may result in a significant delay in the approval process.

The PPC Coordinator notifies the investigator of the DSMB decision.

7. **Submission Process for Review by the PPC**

Applications for all proposal types can be obtained from the PPC coordinator, Janet Lawler-Heavner, and submitted to her at JanetLawler-Heavner@westat.com, upon their completion. Publications, presentations, and abstracts submitted to the PPC should be in final form, that is, ready for consideration by a journal or scientific meeting.

8. **Abstract Submissions**

As noted above, approved associated studies, presentations, publications, and abstracts must be submitted to the NLST DSMB, but abstracts need not be submitted to the DSMB prior to their submission to conference organizers. Abstracts submitted without DSMB review must be withdrawn if ultimately they are not approved by the DSMB.

9. **Review Procedures for Trial-wide Data**

In addition to the reviews conducted by the PPC and the NLST Chief Statisticians, the NLST Principal Investigator and Project Officer must also approve these requests.

10. **Archives**

The PPC coordinator will maintain an archive of publications and presentations submitted to the PPC for review.

Attachment I

NLST Publications and Presentations Committee Members

PPC Co-chairs

William C. Black, Dartmouth
Barnett Kramer, NCI

ACRIN members

Fenghai Duan, Brown University
Ella Kazerooni, University of Michigan
James Ravenel, MUSC
Phil Boiselle, Beth Israel

LSS members

Paul Pinsky, NCI
Paul Kvale, Henry Ford Health System
Hrudaya Nath, University of Alabama at Birmingham
David Gierada, Washington University

Ad hoc members

Jon Goldin, UCLA
Caroline Chiles, Wake Forest
Randell Kruger, Marshfield Research Clinic
Tim Church, University of Minnesota
Mona Fouad, University of Alabama at Birmingham

PPC Coordinator

Janet Lawler-Heavner, Westat

Appendix 1-4 NLST Publication and Presentation Committee Policies and Review Procedures

Attachment II

National Lung Screening Trial

NLST Publications and Presentations Committee Co-Chair Review Form for Proposed Associated Studies, Publications, Presentations, and Abstracts

This form serves to document comments or concerns of the NLST Publications and Presentations Committee Co-chairs regarding a proposed release of trial data.

Date sent for review:	Proposal ID:	NLST Data Used in Proposal: ACRIN ☐ LSS ☐
Sponsor/Investigator:		
Institution:		
Target Journal/Conference/date:		
Reviewer:		Date:
Request review to be performed by:		

I. Trial Integrity and Recommendation

- ☐ **Does Not** jeopardize the public reputation of the NLST.
- ☐ **Does Not** lead to premature publication of NLST results.
- ☐ **Does Not** complicate the interpretation of NLST results.
- ☐ **Does Not** violate the rights of NLST participants.
- ☐ **Does Not** jeopardize the confidentiality of NLST data.
- ☐ **Does Not** present ethical problems.
- ☐ **Does Not** jeopardize the NLST in any way.

Approval Decision:

_____Full PPC Working Group Review Required
_____Review by Additional PPC Working Group
_____Approve
_____Approve with Changes Suggested
_____Approve with Changes Required
_____Approve with Changes to Data Request Required
_____Reject

II. Scientific Content and Methodology (optional)

General Comments**:**
Study Strengths**:**
Study Weaknesses**:**
Questions for Investigators:

Attachment III

National Lung Screening Trial
Data and Safety Monitoring Board Review Form for Proposed Associated Studies, Publications, Presentations, and Abstracts

This form serves to document comments or concerns of the NLST DSMB regarding a proposed release of trial data.

Date sent for review:	Proposal ID:	NLST Data Used in Proposal: ACRIN ☐ LSS ☐ Joint ☐
Sponsor/Investigator:		
Institution:		
Title:		
Target Journal/Conference/date:		
Reviewer: E. Sausville		Date:
Request review to be performed by: (DSMB member)		

I. Trial Integrity and Recommendation

☐ **Does Not** jeopardize the public reputation of the NLST.
☐ **Does Not** lead to premature publication of NLST results.
☐ **Does Not** complicate the interpretation of NLST results.
☐ **Does Not** violate the rights of NLST participants.
☐ **Does Not** jeopardize the confidentiality of NLST data.
☐ **Does Not** present ethical problems.
☐ **Does Not** jeopardize the NLST in any way.

Recommendation:

_____Full DSMB Review Required (_____Electronic _____Meeting _____Call)
_____Approve
_____Approve with Changes Suggested
_____Approve with Changes Required
_____Reject

II. Scientific Content and Methodology (optional)

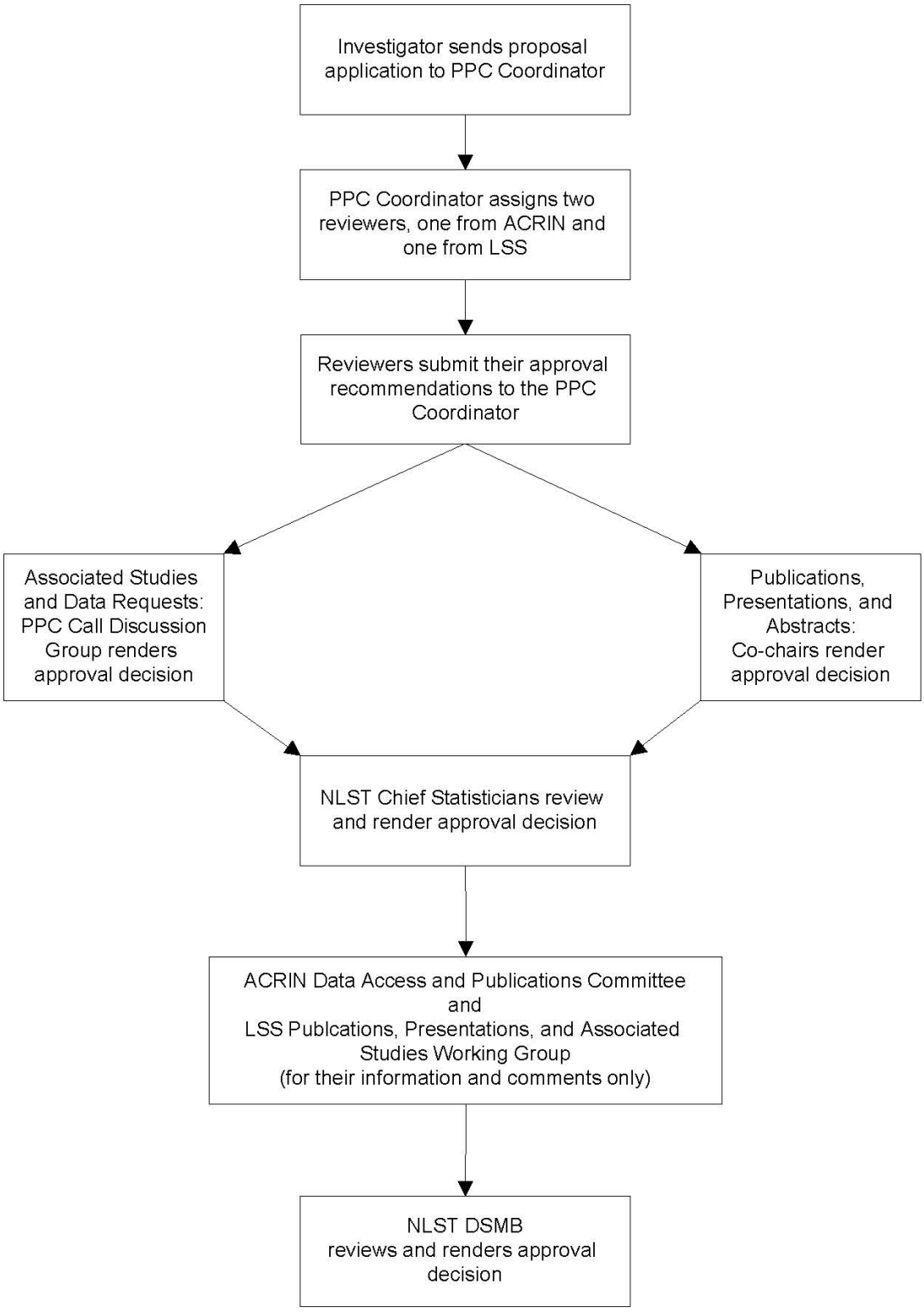
General Comments**:**

Study Strengths**:**

Study Weaknesses**:**

Questions for Investigators:

Attachment IV
NLST Publications and Presentations Committee
Proposed Review Diagram



Attachment V

National Lung Screening Trial
NLST Publications and Presentations Committee
Subject Area Review Form
Proposed Associated Studies, Publications, Presentations, and Abstracts

This form serves to document comments or concerns of the NLST Publications and Presentations Committee Subject Area Reviewers regarding a proposed release of trial data.

Date sent for review:	Proposal ID:	Working Group Affiliation:
Sponsor/Investigator:		
Project Title:		
Institution:		
Target Journal/Conference/date:		
Reviewer:		Date:

I. Trial Integrity

- ☐ **Does Not** jeopardize the public reputation of the NLST.
- ☐ **Does Not** lead to premature publication of NLST results.
- ☐ **Does Not** complicate the interpretation of NLST results.
- ☐ **Does Not** violate the rights of NLST participants.
- ☐ **Does Not** jeopardize the confidentiality of NLST data.
- ☐ **Does Not** present ethical problems.
- ☐ **Does Not** jeopardize the NLST in any way.

II. Evaluation of Scientific Content

Scientific Merit	Specific Aims	Study Design
___ Excellent ___ Good ___ Fair ___ Poor	___ Excellent ___ Good ___ Fair ___ Poor	___ Excellent ___ Good ___ Fair ___ Poor

III. Recommendation

- ____ Approve
- ____ Approve with Changes Suggested
- ____ Approve with Changes Required
- ____ Reject

IV. Additional Comments

Study strengths/ Study weaknesses/Questions for investigators

Attachment VI

National Lung Screening Trial
Publications and Presentations Committee
Statistical Review Form for
Proposed Associated Studies, Publications, Presentations and Abstracts

This form serves to document comments or concerns of the NLST Publications and Presentations Committee Statistical Reviewers regarding a proposed presentation or release of trial data.

Date sent for review:	Proposal ID:	Working Group Affiliation:
Sponsor/Investigator:		
Project Title:		
Institution:		
Target Journal/Conference/date:		
Reviewer:		Date:

I. Trial Integrity

- ☐ **Does Not** jeopardize the public reputation of the NLST.
- ☐ **Does Not** lead to premature publication of NLST results.
- ☐ **Does Not** complicate the interpretation of NLST results.
- ☐ **Does Not** violate the rights of NLST participants.
- ☐ **Does Not** jeopardize the confidentiality of NLST data.
- ☐ **Does Not** present ethical problems.
- ☐ **Does Not** jeopardize the NLST in any way.

II. Evaluation of Study Design and Statistical Plan

Study Design	Sample Size	Data Analysis Plan
___ Excellent ___ Good ___ Fair ___ Poor	___ Adequate ___ Inadequate ___ Insufficient information / Not addressed	___ Adequate ___ Inadequate ___ Insufficient information / Not addressed

III. Recommendation

____ Approve
____ Approve with Changes Suggested
____ Approve with Changes Required
____ Reject

IV. Additional Comments

Proposed project's strengths/Proposed project's weaknesses/Questions for investigators

NLST/LSS

Policies and Procedures for Data and Image Access and Use

1.0 National Lung Screening Trial/Lung Screening Study Data and Images

The NLST is a large randomized trial to determine if screening with low-radiation-dose helical CT, as compared with single view chest x-ray, reduces lung cancer mortality among high-risk individuals. The NLST comprises two research efforts: the ACRIN (American College of Radiology Imaging Network) component and the LSS component, a special study of the Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial.

The NLST/LSS is carried out by the NCI under contract with investigators at ten clinical centers in the United States. Between 2002 and 2004, the ten centers enrolled 34,614 volunteers at elevated risk of lung cancer and randomized the individuals to receive three annual screening exams with either helical CT or postero-anterior chest x-ray. Among other information, NLST/LSS collects and archives:

- Baseline demographic, lung cancer risk factor, and medical history information on all participants;
- Lung screening images (hard copy film and/or digital chest x-ray images and digital helical CT images);
- Diagnostic follow-up data from all positive screening exams;
- Cancer diagnosis, treatment, and cancer progression information for all confirmed lung cancers;
- Cancer diagnosis information for all cancers other than lung, and
- Dates and causes of death for all participants who die regardless of cause.

The purpose of this document is to set forth the policies pertaining to the access and use of Lung Screening Study (LSS) data collected as part of the National Lung Screening Trial (NLST), and the process for requesting NLST/LSS data and/or images. This document is complimented by information in the *Publications, Presentations, and Associated Studies Working Group Review Procedures and Authorship Guidelines,* which explains the process for reviewing proposals.

A. NLST/LSS Data and Image Use Policies

This section of the document outlines the policies, developed by NCI, Division of Cancer Prevention (DCP), regarding NLST/LSS data or image release and the acceptable use of the data or images.

1.0 General Policies

1.1 All studies that request the use of NLST/LSS data and/or images will be reviewed through the PPA review process (see B.2.2) and tracked through the Study Tracking and Review System (STARS), a Web-based system developed and maintained by Westat, Coordinating Center (CC) for the NLST/LSS, as part of the PLCO Program Administrative Resource (PAR) Website (see section B 2.2). N.B. – the NLST/LSS Chief Statistician or designee may have access to any and

all NLST/LSS data for the purpose of monitoring the trial and conducting analyses without regard to this process.

1.2 In certain circumstances, NCI may recommend the involvement in data or image analysis of one or more investigators from NCI DCP, or an investigator from an NLST/LSS Screening Center. The NCI NLST/LSS collaborator may be an NCI investigator from another division. NCI DCP reserves the right to assign a DCP collaborator to any paper or study that is central to the trial or controversial.

1.3 All studies must comply with the policies regarding the use of NLST/LSS data and/or images.

Investigators are required to:

- obtain IRB approval from their institution;
- protect confidentiality of NLST/LSS data and/or images;
- allow NLST/LSS review of publications prior to submission;
- ensure that all NLST/LSS data and images remain under the direct management of the principal investigator, and are kept secure.

Investigators must ensure that their associated studies do not:

- interfere with the implementation/operation of NLST/LSS activities;
- adversely affect cooperation or compliance of NLST/LSS participants;
- divert NLST/LSS funds;
- jeopardize the public reputation of the NLST/LSS;
- lead to premature publication of any NLST/LSS results;
- complicate or obfuscate the interpretation of NLST/LSS results;
- violate the rights or safety of NLST/LSS participants;
- present any other methodological or ethical problems;
- jeopardize the NLST/LSS in any other way.

2.0 Data Release Policies

2.1 Investigators must sign an NLST/LSS Confidentiality Agreement prohibiting the use of NLST/LSS data and/or images for other than the pre-specified uses.

2.2 Release of NLST/LSS data and/or images is time-limited and for approved purpose(s) only.

2.3 Data and/or images cannot be used for additional analyses and/or publications without those additional activities going through the PPA review process.

2.4 The PPA WG may transfer responsibility for studies that are not progressing within a reasonable timeframe, as demonstrated through evaluation of the annual progress reports.

2.5 During development of a proposed research project, data and images will not be released to investigators. Data and image access will be controlled through NCI until final study approval. Only the data and/or images needed for the final approved proposal will be released outside of NCI control if such a release was negotiated during the review process.

2.6 Data and images will be released only as "restricted-use" datasets.

2.7 General identifying information will not appear in any datasets (e.g., participant identification, name, address, social security number, birth date, medical record number, 9-digit zip code, etc.). Data will be given a unique study identification number, distinct from the participant identification number. CTIL images have undergone the process of deidentification as part of routine processing. No identifying information is to be provided in the released data or image sets.

3.0 Data Use Policies

3.1 In order to protect the primary and secondary outcomes of the NLST/LSS, only certain categories of data are permitted for analysis by the NLST Data and Safety Monitoring Board prior to publication of the primary outcomes. The Categories for Data Release (Appendix 1) outlines the data that are currently acceptable for use in associated studies, publications, and presentations. NLST/LSS Project Officers will set this evolving policy in conjunction with the DSMB and the appendix will be updated accordingly.

3.2 Datasets will be released to investigators for use locally (by programmers at the investigator's institution), as determined during the study approval process. Generally, it is preferred that datasets be released as SAS or ASCII files. Additional costs may be incurred for other formats. This will be necessary for anonymized data that would be analyzed by the principal investigator or under grants, as well as analyses supported and funded by NCI.

3.3 Data and images are non-transferable unless prior authorization by NCI has been granted. Data and/or images cannot be used for any purpose other than originally approved and cannot be released outside of the agreed collaborators.

3.4 Investigators may conduct limited analyses on data gathered at their individual screening center for the purpose of feasibility testing. More complex analyses that would lead to the development of a publication or presentation would first need to be approved as an associated study.

3.5 Information about datasets released for approved studies will be available to NLST/LSS collaborators, upon inquiry. This includes data dictionaries corresponding to the datasets (including calculated fields), as well as release dates and other tracking information. Currently, a need has not been identified for releasing these data on PAR.

3.6 NCI may request that analyses be repeated at NCI, if circumstances warrant validation of an investigator's analysis of NLST/LSS data.

B. Requesting NLST/LSS Data and Images

This section of the document provides information on LSS data and images collected as part of the NLST, and the process for requesting access and use of these data.

Appendix 1-5 NLST/LSS Policies and Procedures for Data and Image Access and Use

1.0 Data and Image Requests

Data and images may be requested for an NLST/LSS-associated study, and for use in a publication, presentation or abstract. An investigator may also request data for an exploratory project that would be limited in scope and analyzed with the intent to formulate a proposal for an associated study and not for the purposes of presentation or publication. The process for obtaining NLST/LSS data is described below.

1.1 Requesting Access to NLST/LSS Data or Images

Requests for access to NLST/LSS data or images may originate from a variety of sources. These sources will be one of the following:

- NLST/LSS investigator from an NLST/LSS institution;
- NCI NLST/LSS investigator;
- NCI non-NLST/LSS investigator;
- NLST/ACRIN investigator;
- Investigator from an NLST/LSS institution, but not an NLST/LSS investigator;
- Investigator from a non-NLST/LSS institution.

1.2 Data and Image Requests

Investigators may request data and/or images to determine the feasibility of a project; such requests must be limited in scope and analyzed with the intent to formulate a proposal for an associated study and not for the purposes of presentation or publication. This type of request is made with the "Limited Data Request" application in STARS. Investigators must describe the objectives of the data request, and may identify specific variables from the NLST/LSS data collection forms as part of the application. The review for this type of data request is an abbreviated process that does not require DSMB approval. After the feasibility of a project has been determined, investigators must submit an application for an associated study and receive approval in order to begin the project. A request for additional data can accompany the application in the combined "Associated Study with Data Request" application.

Once an application has been submitted, Westat begins the PPA review process outlined in the *NLST/LSS Publications, Presentations, and Associated Studies Review Procedures and Authorship Guidelines.* The review process is tracked through STARS, which allows applicants to view the status of an application in the system.

1.3 Requesting Additional Data

Requests for updates and significant expansions of previously approved or released data sets must be made through completion of an Addendum Data Request application and submitted for review through the PPA review process.

2.0 Release of Data

2.1 Approval Notification

Upon final approval of a data and/or image request, the PPA coordinator will notify the investigator of the approval via e-mail, with copies to NCI, the Westat Data Manager, and CTIL, when images are included in the request. The notification will inform the investigator that he/she will receive an e-mail from the PPA Coordinator within three business days with an estimate of the time necessary to process the data request, and a determination of its place in the queue. The e-mail will also contain instructions for completing a Data Transfer Agreement (Appendix 2). This legal document between NCI and the investigator makes explicit NCI's retention of title to the NLST data and images, and describes NCI's requirement for confidential use. For example, data and images are not to be transferred out of the immediate supervision of the investigator without written permission, and all results will be reviewed according to the PPA review process and kept confidential until published.

2.2 Processing of the Data or Image Request

2.2.1 The Westat PPA Coordinator will initiate the process for release of the requested data files for approved proposals. Data or images are not available for download by investigators. File content and documentation are individually determined based on the study requirements. The data will be released to the investigator by Westat. The staff of the NLST CT Image Library will provide CT image files following final approval by NCI and DSMB. When both data and images are requested, Westat and the CTIL staff will coordinate the processing of the request.

2.2.2 Data analysis may be performed at the investigator's institution, or may be performed centrally, by IMS. NCI may exercise the discretionary authority to require central analysis of a project.

2.2.3 The time necessary to process a data request depends on several factors:

- The order of the data request relative to other data requests in the queue. In general, data requests will be processed according to the order in which approval notification was received. However, NCI may determine that a particular data request has precedence for processing.
- The involvement of Westat staff in other NLST projects determined by NCI as being of a higher priority or more urgent nature.

2.2.4 Investigators who encounter a problem with images that are problematic or corrupted are instructed to contact the CTIL study manager for replacement.

3.0 Associated Study Analytic Support

NLST/LSS investigators must, as a first course of action, pursue statistical consultants and analytic support through their home institutions for approved associated studies. Westat or IMS, Inc., will provide the investigator with a data file with the approved data items. If there is no satisfactory statistical support available at the time of data analysis, the investigator may petition Dr. Philip Prorok, Chief, Biometry Research Group, at NCI for such support through the existing contract with IMS, Inc. IMS currently provides analytic support for the PLCO main trial endpoint analyses and associated studies. As investigators of this PLCO special study, NLST/LSS investigators may be able to receive analytic support, but should be aware that IMS resources are directed toward the following priorities:

a. Analyses and ad hoc requests for the PLCO and NLST Data and Safety Monitoring Boards;
b. Support for the major trial endpoint analyses for PLCO and NLST;
c. Support for continuing PLCO and NLST associated studies.

4.0 Outside Funding Sources

4.1 Proposals that will involve additional data collection and are endorsed by the NCI NLST/LSS Project Officer are then sent to an outside review group for funding, if appropriate.

4.2 The release of data will be handled as described for general data release.

Appendix 1

Categories for NLST/LSS Data and Image Release (Subject to Revision)

1. The content of this document will be reviewed regularly by the Chief Statistician and will change over time.
2. All data questions not appearing on this list will fall into Category II (May Be Acceptable for Release).
3. Guiding Principles: Analyses of released data should not compromise trial endpoints. Proposals should contain discussion of why the trial will not be harmed and must undergo the review processes established for the LSS and ACRIN components of the NLST as well as the trial as a whole.
4. Requests for all data require formal review by the NCI Chief Statistician, or designee, according to the NLST/LSS PPA review procedures.
5. Data available for release only after all screening and data cleaning activities have concluded.

A. Category I – Data Acceptable for Release

- Enrollment, compliance, retention
- Baseline characteristics

B. Category II – Data That May Be Acceptable for Release

- T_0 screening test results
- T_1 screening test results
- T_2 screening test results
- T_0 diagnostic evaluation procedures
- T_0 lung cancer characteristics (no comparison between arms)
- Limited data sets for specific projects

C. Category III – Data Not Acceptable for Release

- Diagnostic evaluation procedures after T_0
- Lung cancer characteristics after T_0
- Lung cancer treatment data
- Lung cancer incidence
- Lung cancer survival
- Lung cancer mortality
- Other cancer incidence, survival, mortality
- Complications from screening
- Contamination data

D. Category IV – Images

- De-identified images only

Specify data to accompany images, if any. These data are subject to the rules set forth above.

Appendix 2

DRAFT DATA TRANSFER AGREEMENT – Pending Final Revisions

The National Lung Screening Trial (NLST) is a large randomized trial to determine if screening with low-radiation-dose helical CT, as compared with single view chest x-ray, reduces lung cancer mortality among high-risk individuals. The NLST comprises two component studies, ACRIN (the American College of Radiology Imaging Network) and LSS (the Lung Screening Study), a special study of the Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial. Unless otherwise noted, this document addresses policies and procedures for the use of data & images collected as part of the LSS component of NLST (i.e. NLST/LSS).

The NLST/LSS is carried out by the NCI under contract with investigators at ten clinical centers in the United States. Between 2002 and 2004, the ten centers enrolled 34,614 volunteers at elevated risk of lung cancer and randomized these individuals to receive three annual chest screens with either spiral CT or chest x-ray. Furthermore NCI, under a contract with Washington University at St. Louis, has compiled all NLST/LSS images from its screening centers and is able to offer these same data and images as a resource to the academic community.

This Agreement is made by and between the National Cancer Institute, an agency of the United States Government, (hereinafter referred to as "NCI "), and _____ (hereinafter referred to as "Entity"). Collectively or individually, the NCI and Entity shall also be referred to as “Parties” or “Party.”

WHEREAS, NCI desires to share with Entity NLST clinical trial data (“Data”) and CT/x-ray Images (“Images”) from the NLST/LSS study;

WHEREAS, Entity will use the above referenced Data and Images in furtherance of its approved NLST/LSS proposal (hereinafter the “Research Plan”) titled “_____” (NLST/LSS proposal # _____);

NOW, THEREFORE, the Parties agree as follows:

I. Data and/or Images

1. NCI shall provide Data and/or Images to Entity as noted to facilitate the described Research Plan. The Data and/or Images will only be used by Entity for purposes noted in the Research Plan, and for no other purpose.

2. DATA AND IMAGES MAY NOT BE USED IN HUMAN SUBJECTS. Entity agrees to comply with all U.S. Federal rules and regulations applicable to the Research Plan and in accordance with 45 CFR Part 46, “Protection of Human Subjects”. The Data and Images have been collected under an IRB approved protocol in accordance with federal guidelines for the protection of human subjects. No patient identifiable information shall be provided with the Data or Images.

3. The Data and Images represent a significant investment on the part of the NCI, and NCI retains title to the Data and Images in Entity’s possession. Entity's investigator therefore agrees to retain control over the Data and/or Images and further agrees not to transfer them to other people not under her or his direct supervision without advance written

approval of NCI. Entity agrees to share with the NCI all data generated using the Data and/or Images in the course of the Research Plan (Results).

II. Confidential Information

1. For the purposes of this Agreement, "Confidential Information" includes any information in a signed Confidential Disclosure Agreement (CDA) herein incorporated by reference, scientific or business data relating to the Data and Images or the Research Plan and its Results that a Party asserts are confidential and proprietary, except for data that:
   a. have been published or otherwise publicly available at the time of disclosure to the receiving Party; or
   b. were in the possession of or were readily available to the receiving Party from another source prior to the disclosure; or
   c. become publicly known, by publication or otherwise, not due to any unauthorized act by the receiving Party; or
   d. the receiving Party can demonstrate it developed independently, or it acquired without reference to or reliance upon such Confidential Information; or
   e. are required to be disclosed by law.

2. All information to be deemed confidential under this Agreement shall be clearly marked "**CONFIDENTIAL**" by the disclosing Party. Any Confidential Information that is orally disclosed must be reduced to writing and marked "**CONFIDENTIAL**" by the disclosing Party, and such notice must be provided to the receiving Party within thirty (30) days of the oral disclosure.

3. Each Party agrees to accept the Confidential Information and employ all reasonable efforts to maintain the Confidential Information of the other Party secret and confidential, such efforts to be no less than the degree of care employed by each Party to preserve and safeguard its own confidential information. The Confidential Information of the disclosing Party shall not be disclosed, revealed, or given to anyone by the receiving Party, except employees of the receiving Party who have a need for the Confidential Information in connection with the receiving Party's evaluation, and such employees shall be advised by the receiving Party of the confidential nature of the Confidential Information and that the Confidential Information shall be treated accordingly. This obligation shall continue until the earlier of 1) five (5) years after the execution of this Agreement, or 2) publication of the primary outcomes of the NLST/LSS study (so as to prevent fragmentary publication of the results of this clinical study).

4. The Parties agree to work together to make the Results publicly available. Should Entity desire to publish Results, Entity agrees to coordinate their activities with the NCI prior to Entity's submission of a paper or abstract for publication. Such coordination can be accommodated with the Entity's agreement to comply with the review procedures outlined in the *NLST/LSS Publications, Presentations, and Associated Studies Working Group Review Procedures and Authorship Guidelines* and abide by the decisions rendered pertaining to the Entity's proposal. Entity understand that the purpose of this coordination is to ensure the proper pooling of data to reflect the comprehensive nature of the NLST/LSS study, and to likewise ensure that the confidentiality obligations

enumerated above are appropriately addressed in any proposed publication. Results will be kept confidential by the NCI until published or a corresponding patent application has been filed.

III. General Terms

1. This Agreement shall remain in force for two (2) years or until the Research Plan has been completed, whichever occurs first. The term may be extended and the provisions of this Agreement may be modified only by amendment signed by the duly authorized signatory for each Party. The Agreement may be terminated by either Party for any reason by providing written notice at least thirty (30) days prior to the desired termination date.

2. Each Party shall retain title to any intellectual property rights in inventions and works of authorship made by its employees in the course of the Research Project. The parties shall agree to use their best reasonable efforts in cooperation with one other to investigate, evaluate and determine (a) whether and where any joint patent applications are to be prepared and filed and (b) which party shall be responsible for the preparation, filing and prosecution of any such joint applications. Determination of inventorship will be made in accordance with prevailing U.S. patent laws and the contribution of the parties. Apart from patent and copyright, neither Party shall claim property rights over raw data contained within the Results. The Parties understand that nothing herein shall be deemed to constitute, by implication or otherwise, the grant to either Party by the other of any license or other rights under any patent, patent application, or other intellectual property right or interest. In no instance shall Entity make claim to having an ownership right to Data or Images.

3. The exchange of Data, Images, Results, and other related Confidential Information is offered as a service to the research community. THE NCI OFFERS NO WARRANTIES, EXPRESS OR IMPLIED, INCLUDING ANY WARRANTY OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE. NCI makes no representations that the use of Images or Image Data will not infringe any patent or proprietary rights of third parties. Likewise Entity makes no representations that the use of Results will not infringe any patent or proprietary rights of third parties. No indemnification for any loss, claim, or liability is intended or provided by either Party under this Agreement.

4. Entity agrees not to claim, infer, or imply endorsement by the Government of the United States of America, the Department of Health and Human Services, the National Institutes of Health, the NCI, or any employee or subunit, of the research, the Entity, or any of Entity's products or services. Each Party will be given thirty (30) days to review and provide comments on any press releases or abstracts concerning this Agreement or the research described in the Research Plan.

5. This Agreement constitutes the entire understanding between the Parties concerning the subject matter of this collaboration and supersedes any prior understanding or written or oral agreement. The illegality or invalidity of any provision of this Agreement shall not

impair, affect or invalidate the other provisions of this Agreement. Each Party shall maintain sole and exclusive control over its personnel and operations.

6. Each Party expressly certifies and affirms that the contents of any statements made herein are truthful and accurate to the best of knowledge and belief, and each official signing this Agreement on behalf of a Party further certifies and affirms that the official has the authority to do so.

ACCEPTED AND AGREED

FOR THE NATIONAL CANCER INSTITUTE

_____ _____

Kevin Brand Date
Technology Transfer Specialist
Technology Transfer Center
National Cancer Institute, NIH
6120 Executive Blvd., Suite 450
Rockville, MD 20852

FOR THE ENTITY

_____ _____

(Authorized Signatory for Entity) Date

_____

(Printed Name)

_____

(Title of Signatory)

Address:

Acknowledged by Entity Recipient Investigator:

_____ _____

Name Date

Research Plan

Please provide Entity Investigator's proposal for the use of LSS images and/or data.

NLST/LSS Research Working Groups
Chairs, NCI Leads, and CC Leads

Clinical Issues

Co-chairs:	Paul Kvale	pkvale1@hfhs.org	313/874-4840
	David Lynch	lynchd@njc.org	303/398-1611
NCI lead:	C. Berg	bergc@mail.hih.gov	301/496-8544
CC lead:	Nancy Payte	nancypayte@westat.com	512/722-3315

Electronic Imaging

Co-chairs:	David Gierada	gieradad@mir.wustl.edu	314/747-1625
	K. Ty Bae	baek@upmc.edu	412/641-2657
NCI lead:	Guillermo Márquez	marquezg@mail.nih.gov	301/451-3896
CC lead:	Kristen Keating	kristenkeating@westat.com	301/738-3591

Epidemiology

Co-chairs:	Tim Church	trc@cccs.umm.edu	612/625-9091
	Mona Fouad	mfouad@dopm.uab.edu	205/934-2125
NCI lead:	Paul Pinsky	pinskyp@mail.nih.gov	301/402-6480
CC lead:	Jennifer Rosenbaum	jenniferrosenbaum@westat.com	304/876-6243

Medical Physics

Co-chair:	Fred Larke	fred.larke@uchsc.edu	720/848-6604
NCI lead:	Guillermo Márquez	marquezg@mail.nih.gov	301/451-3896
CC lead:	Kristen Keating	kristenkeating@westat.com	301/738-3591

Methods and Operations

Co-chairs:	Julie Varner	Julie.varner@hsc.utah.edu	801/585-7528
	Bonita Wohlers	wohlersb@slrmc.org	208/706-5951
NCI lead:	Pam Marcus	marcusp@mail.nih.gov	301/496-7468
CC lead:	Nancy Payte	nancypayte@westat.com	512/722-3315

2. RECRUITMENT, ELIGIBILITY DETERMINATION, INFORMED CONSENT, AND RANDOMIZATION

2.1 Overview

Each Screening Center (SC) will be responsible for identifying and recruiting participants into the study. Once potential participants are identified, the SC will collect information about them to make a determination of their eligibility for the study. Potential participants who are eligible for and are interested in the study will be asked to sign a consent form and will subsequently be enrolled into the study. The SC will track each potential participant from the time s/he is identified until s/he is enrolled or not enrolled. Each SC will document and report a summary of recruitment and enrollment progress. These activities are discussed in more detail in the sections that follow.

2.2 Recruitment Materials

To aid in the recruitment process, the Coordinating Center (CC) will provide the following recruitment materials to the SCs for distribution to potential participants: an introductory letter, the "Who Can Participate" sheet, a Fact Sheet, and a Reply Card. An NLST brochure developed by the NCI will be distributed to the SCs for use with the CC-provided recruitment materials. The purpose of these materials is to provide potential participants with enough information to allow them to determine if they are eligible for, and interested in, the study.

The introductory letter and the "Who Can Participate" sheet are presented in Appendix 2-1. The introductory letter should be copied onto SC stationery and signed by the SC Principal Investigator. The Fact Sheet, which describes the study and the key eligibility criteria, is presented in Appendix 2-2. The Reply Card allows potential participants to indicate their interest in the study. The card is presented in Appendix 2-3. The brochure contains general information about the purpose of the trial and the eligibility criteria. The brochure can be found in Appendix 2-4.

To provide potential participants with a better understanding of the study, the following topics will be explained in one or more of the introductory materials (letters, fact sheets, etc):

- Purpose of the study;
- Voluntary nature of any response;
- Randomization;
- Extent of confidentiality of information;
- Time period for maintenance of records;
- Disposal of records, and
- Assurances regarding continued care for non-responders.

Appendix 2-5 contains answers to typical questions that potential participants or other persons may ask about the NLST/LSS. These questions and answers are an additional resource to be utilized in recruitment efforts. **These materials are solely for the use of SC staff and should not be distributed to participants.**

The recruitment materials should be used as they are presented in Appendices 2-1 to 2-4. Any modifications to recruitment materials, as well as additional recruitment materials that the SC develops, must be approved by the NCI in advance of their use in the study.

2.3 Identifying Potential Participants

To identify potential participants, the SCs will conduct mass mailings of the recruitment materials. The SC may mail to PLCO ineligible participants but should not rely on these as the sole target of their mailings. Mass mailings may utilize, but are not limited to, the following address lists: Department of Motor Vehicle listings, local hospital and HMO databases, voter registration lists, and the Centers for Medicare and Medicaid Services (CMS) database. It is anticipated that the enrollment yield from a mass mailing will be approximately 0.5 percent.

The eligibility criteria for the NLST/LSS target a retirement age population. In geographic areas where these individuals spend prolonged periods away from their local residences, it may be necessary to increase the mailing size to achieve recruitment goals.

During the recruitment phase, the SC may also concurrently utilize public service announcements with local TV and radio stations. The content of all such public service announcements must be approved by the NCI in advance of their use.

2.4 Eligibility Determination

Potential participants will indicate interest by returning the reply card or contacting the SC by telephone. When potential participants contact the SC by telephone, the Eligibility Screener (ES) will be administered. When potential participants contact the SC by reply card, the SC will call each individual to administer the ES by telephone. A copy of the ES is presented in Appendix 2-6. The ES asks potential participants for information related to all the eligibility criteria listed below.

A potential participant will be considered eligible for the NLST/LSS if s/he meets all of the following eligibility criteria and does not meet any of the following exclusion criteria:

Eligibility Criteria:

- Is at least 55 years of age but no more than 74 years of age on the date of randomization;
- Is a current smoker or former smoker who has quit smoking within the last 15 years, and
- Has smoked at least 30 pack-years (equivalent to an average of at least 20 cigarettes per day for 30 years).

Exclusion Criteria:

- Has had a spiral CT scan of the lungs, or chest within the 18 months prior to randomization;
- Is currently participating in another cancer screening study, including PLCO;
- Is currently participating in a cancer prevention study other than a study of smoking cessation;
- Has been diagnosed with lung cancer;
- Has a history of surgical removal of any portion of either lung (excluding needle biopsy);
- Has undergone treatment for, or had evidence of, any cancer other than non-melanoma skin cancer or carcinoma in situ (except bladder CIS or transitional cell CIS) in the past five years;

- Is unable to lie flat on his/her back with arms raised over the head;
- Has metallic implants in the chest or back (e.g., pacemakers, Harrington fixation rods);
- Has a requirement for home oxygen supplementation;
- Has experienced unexplained weight loss of more than 15 pounds in the past 12 months or recent hemoptysis;
- Has had pneumonia or an acute respiratory infection that was treated with antibiotics by a physician in the past 12 weeks, and
- Is unwilling or unable to sign the consent form.

Once eligibility status is determined and the participant is informed of his or her ineligibility, the responses to the Eligibility Screener can not be changed; the exception being, potential participants who do not meet the eligibility criteria or who meet one or more of the exclusion criteria for reasons that may change over time (such as pneumonia or acute respiratory infection in the past 12 weeks) may be contacted in the future to reassess eligibility.

SCs should encourage participants not to enroll in any other cancer screening or prevention study, except for smoking cessation studies. Enrolling in such studies increases the potential for contamination of NLST data. In addition, the added time and effort of participating in multiple studies could cause "burn-out" among those participants, resulting in greater loss to follow-up and possible attrition bias. However, although enrollment in a cancer screening or prevention study does exclude potential participants from enrolling in NLST, enrolling in such a study after enrolling in NLST does not preclude further participation in NLST. NLST participants who enroll in another cancer screening or prevention study are eligible to continue in NLST.

Specifications for Completion of the ES are given in Appendix 2-7. All apparently eligible participants will be matched against the SC's PLCO roster to verify non-participation in PLCO and matched against the SC's NLST/LSS roster in order to eliminate the potential for duplicate randomization. The roster checks will be performed using a computer pre-processing program provided by the CC. Refer to the *NLST/LSS IDEAS User's Guide* for detailed instructions on using the randomization pre-processing system.

The SC should administer the ES to each individual expressing interest in the trial. If, prior to the formal administration of the ES, a potential participant volunteers information that indicates ineligibility, the SC should record the participant's name and then answer the question on the ES that

addresses the applicable criterion. No other information should be collected. Administration of the ES should be stopped once a potential participant is identified as ineligible. No further questions should be asked.

When the ES is completed, the SC staff should perform the following tasks:

- The ES will be reviewed to determine whether the potential participant meets the eligibility criteria. If an individual does not know whether s/he meets one or more of the eligibility criteria, s/he should be asked to contact his or her health care provider to obtain the information. If the individual refuses or does not have a health care provider, or if after contacting the health care provider, s/he still does not know whether s/he meets the eligibility criteria, s/he is not eligible for the study.
- The potential participant's tracking information will be updated (see Section 2.8 for information on maintaining tracking records).
- If the potential participant is determined to be ineligible based on one or more of the eligibility criteria, the SC staff will record the potential participant's status as "ineligible" on the tracking record.
- ES forms for potential participants who have not been enrolled in the study will be kept on file at the SC until otherwise directed by the NCI. ES forms for enrolled participants should be kept in the participant study file.

If a potential participant has not been randomized within one month of eligibility determination, the SC will make a second determination of eligibility before randomizing the participant. When a potential participant is determined to be eligible, the next step is to obtain a signed consent form.

2.5 General Procedures for Obtaining Participant Consent

Human research subjects are protected through informed consent procedures. The signing of a consent form is required for eligibility to participate in the NLST/LSS. Each SC will obtain written consent for eligible participants before enrollment.

The informed consent process addresses the following important points:

- Each participant must be fully informed of all study procedures and requirements in order to be considered a "knowing" participant; and
- Participation is voluntary and all information provided by participants will be kept confidential.

The SC Coordinator will be fully responsible for obtaining written consent from each participant. Each SC will develop a consent form that must be approved by the NCI.

The Institutional Review Board (IRB) at each SC and the NCI must approve the consent form. SCs recruiting individuals who have very little or no knowledge of the English language must submit documentation of IRB approval to the NCI to administer an English language NLST/LSS consent form to non-English speaking individuals.

In the development of the consent form, each SC will use the template provided by the CC as a guide. The prototype consent form and accompanying cover letter are found in Appendices 2-8 and 2-9, respectively.

All information in the prototype consent form must be included in the SC consent form. Additional information may be added based on individual IRB requirements, but information in the prototype may not be excluded. Any changes made by the IRB will be submitted to the NCI for review. The participant will be given a copy of the consent form after it is signed. The signed original will be kept in the participant's file at the SC.

Administration of the consent form involves providing the participant with background information about the study and its requirements. The implications of randomization and the necessity for completing the required procedures should be emphasized to each potential participant. When the consent form is provided to the potential participant, s/he must be offered sufficient time to carefully read the document and must be given sufficient opportunity to have all questions regarding the study answered before s/he is asked to make a decision regarding participation.

Methods for obtaining informed consent are described below.

2.5.1 Obtaining Informed Consent

The method of administration of the consent form may vary by SC. The SC will obtain a signed consent form by one of the two following methods:

Method A – After completing the ES by telephone, the SC will mail a copy of the consent form with a cover letter to eligible participants. Participant questions regarding the content of this document will be clarified via telephone. Once the potential participant has returned a signed consent form, the SC will complete an Eligibility Verification Form (EVF), (Appendix 2-10) and enroll the participant into the study. See Section 2.6 for more information on completing the EVF. The SC will then contact the participant and schedule the baseline screening visit (T_0).

Method B – After completing the ES by telephone, the SC will invite interested and eligible participants for a clinic visit. The SC will schedule the visits for small groups. At the visit, the SC will provide additional information about the study and the consent form, and will answer questions. The SC will complete an EVF and enroll those individuals who sign a consent form into the study. Depending on his/her individual schedule, the participant will either complete the T_0 screening examination at that time or will schedule a screening visit for a later date.

The Privacy Rule of the Health Insurance Portability and Accountability Act (HIPAA), which says that any health information that would enable someone to identify the patient is protected under federal law, went into effect on April 14, 2001 with a compliance date of April 14, 2003. Some of the SC's were required by their IRB's to ask study participants who had completed a consent form prior to this date to sign an additional form explaining this new legislation.

2.6 Verification of Eligibility

The eligibility of potential participants will be verified using the Eligibility Verification Form **(**EVF), presented in Appendix 2-10. The SC will use information from the ES, the consent form, and the pre-processing program to complete the EVF. The EVF must be completed and retained at the SC for all participants randomized into the study, but need not be completed for individuals who are found to be ineligible for the study.

Parts A and B of the EVF will be completed prior to randomization. In Part A of the form, the SC Coordinator will record the SC and the identifying information of the potential participant. In Part B, the SC Coordinator will confirm eligibility criteria for smoking status and pack-year history, then confirm additional eligibility criteria by checking "Yes" or "No" in response to questions 3 through 14. Refer to Appendix 2-11 for Specifications for Completion of the EVF. In order for a participant to be

successfully randomized, the answers to questions 3 through 14 in Part B of the EVF must be "No." If any "Yes" boxes are marked, the potential participant is not eligible for the study and cannot be randomized. If it is discovered at the time of EVF completion that the potential participant is ineligible, the EVF should be filed with the ES and maintained at the SC until otherwise directed by the NCI.

Prior to randomizing a participant through the Westrax™ system, the SC must perform randomization pre-processing to verify that the potential participant is not a PLCO participant and is not already enrolled in the NLST/LSS. To identify such participants, the pre-processing system provided by the CC will compare potential participant information to a list of PLCO participants and a list of NLST/LSS participants. If the potential participant is not matched to the list of PLCO or NLST/LSS participants, a pre-processing number will be provided and the participant can be randomized.

2.7 Randomizing and Enrolling the Participant

Once the EVF has been completed, the potential participant is ready to be randomized to either the spiral CT or the chest x-ray study arm. Randomization (assignment of the study arm and assignment of a participant identification number) will be completed using the Westrax™ system. For more detailed instructions on using the system for randomization, see Appendix 2-12, *NLST/LSS WesTrax™ User's Guide* and Appendix 2-16, Specifications for Randomization Using the IVRS.

The SC will randomize participants by entering information from the EVF over the telephone or through submission of a batch file by computer. The Westrax™ system will calculate age and smoking pack-years to verify age and smoking eligibility and it will verify that all responses to eligibility criteria on the EVF have been marked as "No." If the system confirms eligibility, the participant will be randomly assigned to one of two study groups (spiral CT or chest x-ray) in a 1:1 ratio, stratifying on gender and age group within SC. A participant identification number (PID) will be assigned.

During the randomization process, if any of the checks indicates that an individual is not eligible, the Westrax™ system will offer the SC an opportunity to correct the data. A randomization confirmation report will be e-mailed to the SC's dedicated e-mail address within two hours following randomization. Each SC is required to set up a separate e-mail account for receiving randomization confirmation reports. The confirmation report will include the PID, study arm assignment, randomization

date, user ID number of the staff member who performed the randomization, pre-processing number, date of birth, smoking history, and gender. The SC should review the report to ensure that no errors in data entry occurred for gender, date of birth, or smoking history. This report should be placed in the participant's study file with the EVF.

The Westrax™ system and User Support hotline (800/509-5559) will be available 24 hours a day, seven days a week. The SC may not be able to access the system because of disruption to telephone service. In such cases, the SC should call the Westrax™ Help Center to ensure that the problem is related to service disruption rather than user error. These steps are detailed in the *NLST/LSS WesTrax™ User's Guide.*

Each participant will be assigned a unique PID. The PID is a unique eight-digit number that will be used throughout the study period to link all data associated with an individual. It is part of a common system for reporting to the CC and will be used by all SCs. No PID, once assigned, will be changed, deleted, or reassigned to another participant. In the event that a participant moves to a location that is in proximity to another SC, s/he will retain the original PID assigned. This policy assures that data associated with a participant will not be lost or inadvertently attributed to another participant. SCs will generate PID labels using IDEAS.

2.7.1 Batch Randomization

The SC can randomize a "batch" of participants by e-mailing an appropriately prepared data file to the designated e-mail address (NCI_Batch@westat.com). If e-mail is unavailable, the batch file may be faxed to (713) 529-4924. The specifications for the data file structure are outlined in the *NLST/LSS WesTrax™ User's Guide*. SCs can prepare their own data file (subject to the file specifications), or they can use IDEAS to prepare the file. The data file will serve as input to the centralized randomization system, where the entire "batch" of participants will be randomized and enrolled into the trial. Individual randomization assignments will be e-mailed to the originating SC. If the system is unable to randomize one or more participants in the "batch" file, a rejection report for that participant will be e-mailed to the SC.

2.7.2 Manual Randomization

During brief periods of planned system maintenance and unplanned system outages, certain components of WesTrax may be unavailable to SC staff for randomization by either the IVRS or "batch" methods of randomization, or both. Manual randomization procedures, described in the *NLST/LSS WesTrax™ User's Guide*, are intended for situations in which a component (IVRS or batch randomization) of the WesTrax™ system is unavailable and immediate randomization is necessary. SCs will be notified of the outage immediately upon detection by WesTrax™ support staff. SCs will then receive an e-mail advising them of the possible options for manual randomization. In the event the WesTrax™ e-mail services are unavailable, the SC should contact the WesTrax™ Help Center for further instruction.

2.7.3 Notifying Participants of Study Arm Assignment

After a participant is randomized, the SC will be notified of his/her study arm assignment by mail, by telephone, or in person. Each participant randomized with the Westrax™ system is confirmed via electronic mail. A randomization confirmation is automatically generated and sent to the SC when a potential participant has been successfully randomized regardless of method.

2.7.4 Changes in Data Used for Randomization

The randomization process carries the potential for errors. These may include randomizing a participant more than once or randomizing a participant who is not eligible for the study. Certain randomization errors result in protocol violations and should be documented appropriately on a Protocol and HIPAA Violation Form (PHVF) (Appendix 11-9) as described in Section 11.5.2. In addition, the CC must be contacted to make corrections in IDEAS.

On occasion study documents such as the MHQ may contain a date of birth that does not match the birth date written on the EVF. If this occurs the participant should be contacted and asked to verify his or her date of birth. The SC should complete a WesTrax™ SC Edit Form including an explanation of the type of error (transcription, keying, transposition) as well as any corrective action taken (e.g., correct birth date verified by participant). The date of birth will not be changed unless it is verified

by the participant. If the participant provides a date of birth that does not match either the EVF or the document on which the discrepancy was discovered (e.g., MHQ) the SC Coordinator should ask for a legal document such as a driver's license or birth certificate to verify the date of birth.

2.7.5 Correcting Randomization Errors Using the WesTrax™ SC Edit Form

The WesTrax™ randomization system has many data quality checks. They are performed in real-time on data submitted through the batch randomization process and entered through the IVRS module. These checks contribute to assuring that erroneous data does not enter and reside within the system. However, it may happen that data has been improperly keyed, transposed, or transcribed, but is still within valid ranges to enter the WesTrax™ system. Erroneous data entering the system can have a magnified, on-going, negative impact on randomization functions if not corrected at the earliest stage possible.

When SC personnel discover that a data entry error has occurred, the WesTrax™ SC Edit Form should be completed. The SC Coordinator or designee will complete the form found in Appendix 2-17 and document the known details of the event. Specifications for Completion of the WesTrax™ SC Edit Form can be found in Appendix 2-18, as well as in the *NLST/LSS WesTrax™ User's Guide*. In addition to completing the form, SC staff must manually correct any corresponding documentation in the participant folder that is impacted by this error (e.g. EVF, ES, etc.). The form should be sent to Ellen Martinusen for appropriate resolution, either electronically, via fax at (301) 963-5455, or hardcopy. If sending via fax or hardcopy, a notification e-mail should be sent in advance. A copy of the form should be placed in the participant folder. Once CC support staff have verified and approved the data change it will be implemented within IDEAS.

It is important to note that requests will be considered on a case-by-case basis and that some change requests may have wide-ranging implications and require NCI approval before implementation. The CC may require additional documentation from the SC Coordinator prior to implementing the change. Not all data change requests through the WesTrax™ SC Edit Form will be honored.

2.8 Tracking Potential Participants and Enrollees

The SCs will track each potential participant from identification through recruitment and randomization to document either his/her entry into the study or his/her reason for non-participation. Tracking of potential participants is critical for the management of the recruitment process and is useful as a tool for the evaluation of the recruitment effort. Each SC should record recruitment data in a manner that allows for easy retrieval for weekly recruitment reports.

Each SC should have a system, manual or automated, for tracking potential participants. This system will include, at a minimum, a tracking record for each potential participant for whom the SC has completed or attempted to complete an ES. Summary totals of potential participants to whom recruitment packets were mailed should be maintained. When an individual responds to the ES, a tracking record should be created for that individual in the SC's active recruitment system. The following information, some of which will be required in reports of recruitment efforts, should be included in the tracking record:

- Full name,
- Address (including ZIP code),
- Telephone numbers,
- Date of birth,
- Gender,
- Date of ES completion, and
- Eligibility status.

Eligibility status should be assigned as follows:

Eligible (E): A potential participant should be classified as "eligible" if s/he meets all of the eligibility criteria but has not yet been randomized.

Ineligible (I): A potential participant should be classified as "ineligible" if s/he fails to meet one or more of the eligibility criteria.

Randomized (R): A potential participant should be classified as "randomized" if a participant meets all the eligibility criteria and has been randomized into the study.

Tracking records must be maintained either individually or as part of a log. A Sample Potential Participant Tracking Log is included as Appendix 2-13. Such a log may be maintained manually or in a computerized tracking system. Summary information regarding potential participants to whom recruitment packages were mailed should also be maintained manually or on a computerized tracking system. The tracking log is for use by each SC to aid its tracking of participants. Completed copies should not be sent to the CC.

2.9 Summarizing, Reporting, and Monitoring Recruitment and Enrollment Efforts

Each SC will summarize and report the status of its recruitment efforts. The purpose of reporting summary recruitment data is to enable the NCI to monitor recruitment. The SC Coordinator also will monitor recruitment, which will enable him/her to identify any problems with recruitment and to redirect recruitment resources, if necessary. The following recruitment data will be summarized on the SC Cumulative Recruitment Summary Form (Appendix 2-14) and entered by the SC into a Web-based form located at **http://www.plcoarp.org/NLST/** on a weekly basis by close of business on Fridays. The Specifications for Completion of the SC Cumulative Recruitment Summary Form can be found in Appendix 2-15.

- **Targets:**

  This represents the recruitment goals established by the SCs in their contracts for the NLST/LSS.

- **Recruitment Packets Mailed:**

  This represents the total number of potential participants mailed recruitment materials to date.

- **Eligible Participants Pending Randomization:**

  This represents the total number of potential participants who have been determined to be eligible for participation in the study, but have not yet been randomized. Once a participant has been randomized s/he is no longer counted in this category.

- **Ineligible Participants:**

  This represents the total number of potential participants who have been determined to be ineligible for participation in the study.

- **Number Randomized:**

  This represents the total number of participants who have been randomized into each arm of the study.

- **Screening Exams Scheduled But Not Yet Complete:**

  This represents the number of screening exams scheduled for randomized participants, but not yet complete, for each arm of the study.

- **Number Screened:**

  This represents the number of screening exams that have been completed for each arm of the study regardless of whether the exam(s) have been read by a radiologist.

- **Percent Screened:**

  This represents the percent of participants in each arm of the study that have been screened. This number is calculated by IDEAS.

- **Screened Plus Scheduled:**

  This represents the number of screening exams the SC has completed in addition to the number of screening exams the SC has scheduled for randomized participants.

- **Percent Screened Plus Scheduled:**

  This represents the percent of screening exams that are complete plus the number of screening exams scheduled for randomized participants divided by the number of randomized participants.

The SC Cumulative Recruitment Summary Report (Appendix 11-16) will be produced by the CC and will be based on the information entered by the SC from the Cumulative Recruitment Summary Form. This report will be posted weekly on Mondays on the designated CC Web site. The report will show the following summary totals for the project through the current week.

- Recruitment Packets Mailed
- Eligible Participants Pending Randomization
- Ineligible Participants
- Number Randomized

  Spiral CT _____

  Chest x-ray _____
- Screening Exams Scheduled but not yet Complete

  Spiral CT _____

  Chest x-ray _____
- Number Screened

  Spiral CT _____

  Chest x-ray _____

- Percent Screened
  - Spiral CT _____
  - Chest x-ray _____
- Screened + Scheduled
- Percent Screened + Scheduled

The SC Cumulative Recruitment Summary Report will enable the SC Coordinator to monitor recruitment and randomization activities. The SC can compare the report posted on the Web site to the previous week's report to monitor and track recruitment data.

Appendices for Chapter 2

2-1 Sample Introductory Letter/"Who Can Participate" Sheet

2-2 Fact Sheet

2-3 Sample Reply Card

2-4 NLST Brochure

2-5 Answers to Potential Participant Questions

2-6 Eligibility Screener (ES)

2-7 Specifications for the Completion of the Eligibility Screener

2-8 Prototype Consent Form

2-9 Sample Consent Form Cover Letter

2-10 Eligibility Verification Form (EVF)

2-11 Specifications for the Completion of the Eligibility Verification Form

2-12 NLST/LSS WesTrax™ User's Guide

2-13 Sample Potential Participant Tracking Log

2-14 SC Cumulative Recruitment Summary Form

2-15 Specifications for Completion of the SC Cumulative Recruitment Summary Form

2-16 Specifications for Randomization Using the IVRS

2-17 WesTrax™ SC Edit Form

2-18 Specifications for Completion of the WesTrax™ SC Edit Form

Appendix 2-1 Sample Introductory Letter/"Who Can Participate" Sheet

National Lung Screening Trial (NLST)

(Participant Name) *(Date)*
(Participant Address)
(City, State, ZIP Code)

Dear *(Participant Name)*:

The National Cancer Institute (NCI) and *Screening Center (Local SC)* are seeking volunteers to participate in the National Lung Screening Trial (NLST), a nationwide study of Americans aged 55 to 74 who have a history of long-time and/or heavy cigarette smoking. The purpose of the NLST is to compare screening with spiral CT (low-radiation-dose computed tomography) and screening with chest x-ray for effectiveness in reducing the number of deaths due to lung cancer. The NLST is seeking to enroll 50,000 participants in the study.

If you have ever smoked, you may be eligible to participate in the NLST. The enclosed page entitled "Who Can Participate" provides more information on who is eligible for this study. We also have included a Fact Sheet that may answer some of your questions.

Your participation in the NLST is voluntary, and if you choose to participate, there are no penalties for withdrawing from the study at any time. Your decision regarding participation will not influence your relationship with *(Local SC)*, its staff, or with any Federal program such as Social Security or Medicare. Furthermore, all information you provide as part of the study will be kept confidential and will not be disclosed to anyone but the researchers conducting this study, except as otherwise required by law. Your name and other information capable of identifying you will not appear in any study documents, as only statistical summaries will be reported. For your information, this study is authorized by the Public Health Service Act, Section 412 [42 USC 285 a-1], and your rights as a study participant are protected by the Privacy Act of 1974.

If you have never smoked, please accept our apologies for contacting you. We do not have personal information about individuals or their smoking habits. Therefore, it was necessary to send this letter to the general public.

If you are interested in participating in the NLST, please return the enclosed reply card. Feel free to contact me or our Coordinator, *(Name of SC Coordinator)* at *(Telephone Number)*, if you have any questions.

We hope you will consider participating in this important study.

Sincerely,

(Name of Principal Investigator)
Principal Investigator
National Lung Screening Trial

WHO CAN PARTICIPATE?

You may be eligible to participate in NLST if you meet all the eligibility criteria below:

- You are between the ages of 55 and 74 years.
- You are a current smoker or have quit smoking within the last 15 years.
- You have a history of long-time and/or heavy cigarette smoking.
- You have NOT had a spiral CT scan of your lungs or chest within the past 18 months.
- You are NOT participating in another cancer screening study, including the PLCO Cancer Screening Trial.
- You are NOT participating in a cancer prevention study, other than a study to help you stop smoking.
- You have NEVER been diagnosed with lung cancer.
- You do NOT have a history of surgical removal of any portion of your lungs (excluding a needle biopsy).
- You have NOT undergone treatment for, or had evidence of, any cancer other than non-melanoma skin cancer and carcinoma in situ (except bladder carcinoma in situ and transitional cell carcinoma in situ) in the past 5 years.
- You ARE able to lie on your back with your arms raised over your head.
- You do NOT have metallic implants in your chest or back (such as a pacemaker or Harrington fixation rods).
- You do NOT have a requirement for home oxygen supplementation.
- You have NOT experienced unexplained weight loss of more than 15 pounds in the past 12 months, and have NOT experienced recent coughing up blood (hemoptysis).
- You have NOT had pneumonia or an acute respiratory infection that required treatment with antibiotics in the past 12 weeks.

If you think you may be eligible to participate in this study, please return the enclosed reply card or contact us at *(SC telephone number)*.

National Lung Screening Trial (NLST)
National Institutes of Health, National Cancer Institute

FACT SHEET

What is the National Lung Screening Trial?

The National Lung Screening Trial (NLST), a cancer screening clinical trial, will compare two ways of detecting lung cancer: spiral computed tomography (CT) and standard chest x-ray. Both chest x-rays and spiral CT scans have been used to find lung cancer early. So far, neither chest x-rays nor spiral CT scans has been shown to reduce a person's chance of dying from lung cancer. This study will aim to show if either test is better at reducing deaths from this disease. The trial also will examine the risks and benefits of spiral CT scans compared to chest x-rays. The NLST will enroll 50,000 current or former smokers and take place at 30 study sites throughout the United States. The study is funded by the National Cancer Institute.

This trial is a randomized, controlled study – the "gold standard" of research studies – and is large enough to determine if there is a 20 percent or greater drop in lung cancer mortality from using spiral CT compared to chest x-ray.

Why is this study needed?

Lung cancer, which is most frequently caused by cigarette smoking, is the leading cause of cancer-related deaths in the United States. It is expected to claim nearly 155,000 lives in 2002. Lung cancer kills more people than cancers of the breast, prostate, colon, and pancreas combined. There are more than 20 million current and former smokers in the United States, all of whom are at high risk for lung cancer.

Currently, when lung cancer is detected, the disease has already spread outside the lung in 15 percent to 30 percent of cases. Spiral CT, a technology introduced in the 1990s, can pick up tumors well under one centimeter (cm) in size, while chest x-rays detect tumors about one to two cm in size. Conventional wisdom suggests that the smaller the tumor, the more likely the chance of survival. But no scientific evidence to date has shown that screening or early detection of lung cancer actually saves lives. The NLST, because of the number of individuals participating and because it is a randomized, controlled trial, will be able to provide the evidence needed to determine whether spiral CT scans are better than chest x-rays at reducing a person's chances of dying from lung cancer.

How does spiral CT work?

Spiral CT, also called helical CT, uses x-rays to scan the entire chest in about 15 to 25 seconds, during a single, large breath-hold. Throughout the procedure, the participant lies still on a table. The table and patient pass through the CT scanner, which is shaped like a donut with a large hole. The scanner rotates around the participant and a computer creates images from the scan, assembling them into a 3-D model of the lungs.

How is spiral CT used in hospitals now?

More than half of the hospitals in the United States own a spiral CT machine. These machines are routinely used for staging lung and other cancers – that is, determining how advanced the cancer is after diagnosis. Recently some hospitals have begun performing spiral CT scans as a new way to find early lung cancer in smokers and former smokers.

What are the possible benefits of participating in this trial?

All participants will receive a free lung cancer screening exam. It is also possible that if lung cancer is detected, it may be caught at an early stage. Early detection of lung cancer may reduce symptoms from cancer, result in milder treatment with fewer side effects, or prolong life, but scientists do not know these things will happen for sure. Data gathered from the NLST will help to clarify some of these uncertainties.

What are some of the possible risks of screening for lung cancer?

Recent studies indicate that 25 percent to 60 percent, or more, of screening CT scans of smokers and former smokers will show abnormalities. Most of these abnormalities are not lung cancer. However, these abnormalities – scars from smoking, areas of inflammation, or other non-cancerous conditions – can mimic lung cancer on scans and may require additional testing. These tests may cause anxiety for the participant or may lead to unnecessary biopsy or surgery.

Lung biopsy, a potentially risky procedure, involves the removal of a small amount of tissue, either through a scope fed down the windpipe (called bronchoscopy) or with a needle through the chest wall (called percutaneous lung biopsy). Though they happen infrequently, possible complications from biopsies include partial collapse of the lung, bleeding, infection, pain, and discomfort.

Depending upon the size and location of the abnormality detected, chest surgery (called thoracotomy or thoracoscopy) to obtain a larger biopsy specimen may be required. Thoracotomy is major surgery that removes substantial amounts of lung tissue. The procedure can damage nerves in the chest, and is more dangerous in people with underlying lung or heart conditions, which tend to be common in current or former smokers.

In addition, studies suggest that screening for lung cancer may detect small tumors that would never become life threatening. This phenomenon, called over-diagnosis, puts some screening recipients at risk from unnecessary biopsies or surgeries as well as unnecessary treatments for cancer, such as chemotherapy or radiation.

How long will the trial last? What will happen during the study?

The study will open for enrollment in fall 2002 and is slated to last eight years. The researchers plan to enroll the 50,000 people needed for the trial study within two years. When people enter the study, they will be randomized – assigned by chance – to receive either a spiral CT scan or a chest x-ray. They will have the same screening procedure again one and two years later. Until 2009, researchers will contact participants at least yearly to monitor their health.

In the future, some NLST centers will collect blood, urine, or sputum (phlegm). These samples will be used for future research to test biomarkers that may someday help doctors better diagnose lung cancer.

During the trial, if participants want to quit smoking, they will be referred to smoking cessation resources. But they do not have to quit to take part in the study.

What is a randomized, controlled study?

A randomized, controlled trial is the most reliable method of determining what medical interventions work best and are safest. Participants are assigned by chance – randomized – to one of two groups, where one group receives one intervention and the other group receives another. One of the groups serves as a comparison group, or "control," for the other.

With a randomized trial, the goal is to determine if there are differences in outcomes between the two groups at the end to the study. The process of randomization aims to evenly distribute between the study groups all factors, such as health histories, that can influence outcome other than the interventions being studied.

If the participants in each group have the same make-up, then any differences seen in outcome between the two groups can be attributed to the intervention. In this screening study, participants will have an equal chance of being assigned to a group that is screened with spiral CT or to a group that is screened with chest x-ray.

Who is eligible to join the NLST?

Current or former smokers, who have smoked heavily or for many years and are between 55 and 74 years of age, may be eligible for this study. The screening tests will be evaluated in current or former smokers who have a high risk of developing lung cancer and who may benefit from early disease detection. All potential participants will be asked a series of questions to ensure that they are eligible to participate.

Potential participants should be in general good health, must not be receiving treatment for any type of cancer other than non-melanoma skin cancer or carcinoma in situ, and must not have a history of lung cancer. Potential participants cannot be enrolled in any other cancer screening or cancer prevention trial and must not have had a CT scan of the chest or lungs within the prior 18 months.

Have current and former smokers participated in studies like this before?

To determine the willingness of participants to join a study like the NLST, NCI launched a small trial, called the Lung Screening Study, to recruit 3,000 current and former smokers in late 2000. Within two months, all the necessary participants agreed to join the study and to be assigned by chance to receive either a spiral CT scan or a chest x-ray. The success of this study's recruitment led NCI to undertake NLST, which will be large enough to answer the important public health question of whether spiral CT reduces lung cancer deaths.

What happens if lung cancer is found during the study?

For participants with positive screening tests, meaning that the screening test reveals an abnormality that might be cancer, the study centers will notify the participants and their primary care physicians and encourage a consultation with a cancer expert. Names of cancer experts will be provided upon request, but decisions regarding further evaluation will be made by participants and their physicians. Any tests performed to follow-up on a positive screening result may be performed at the study center, if participants and their physicians so choose.

Will participating in NLST cost anything?

People participating in the trial will be screened free of charge with either spiral CT or chest x-ray. However, costs for any diagnostic evaluation or treatment for lung cancer or other medical conditions will be charged to the participants in the same way as if they were not part of the trial. A participant's medical insurance will pay for diagnosis and treatment according to the plan's policies. If the participant has no insurance, aid may be available at the local level to pay for biopsies and treatment.

How can a potential participant or a physician get more information about lung cancer or NLST?

People can call the NCI's Cancer Information Service toll-free Monday through Friday, 9 a.m. to 4:30 p.m., at 1-800-4-CANCER (1-800-422-6237) for information about the trial in English or Spanish. The number for callers with TTY equipment is 1-800-332-8615.

Appendix 2-3 Sample Reply Card

NATIONAL LUNG SCREENING TRIAL (NLST)

BUSINESS REPLY MAIL
FIRST CLASS MAIL PERMIT NO 2926
<<CITY, STATE>>
POSTAGE WILL BE PAID BY ADDRESSEE

National Lung Screening Trial (NLST)
SCREENING CENTER
<<Address>>
<<City, State Zip>>

I am interested in learning more about participation in the National Lung Screening Trial (NLST). Please contact me:

Name: _____

Address: _____

City:_____State:_____Zip:_____

Daytime phone:_____

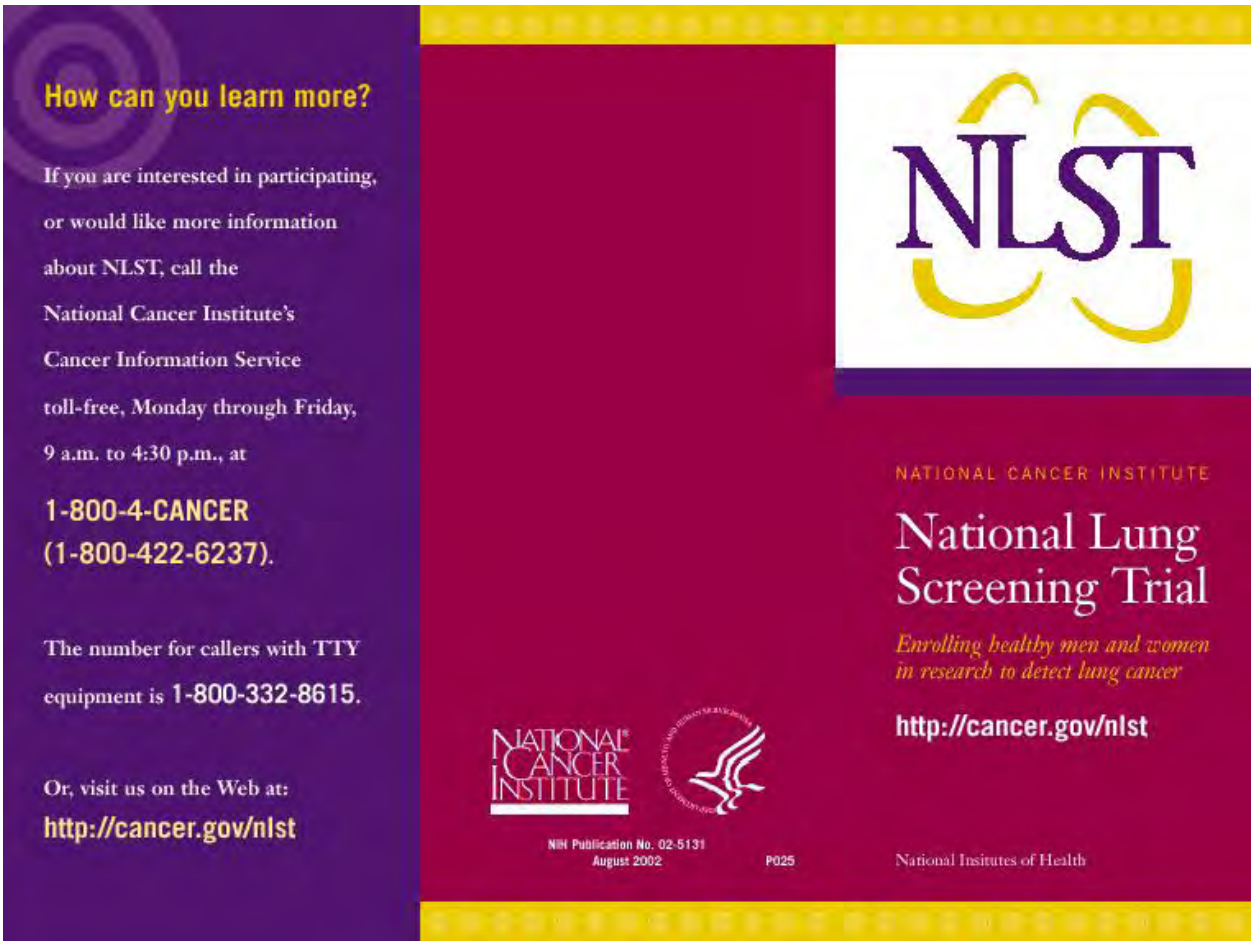
Evening phone:_____

Best time to call: _____

Remember, you must be a current or former smoker between the ages of 55 and 74.

Appendix 2-4 NLST Brochure

National Lung Screening Trial (NLST) Brochure – Front



National Lung Screening Trial (NLST) Brochure – Back

What is NLST?

NLST, the National Lung Screening Trial, is a research study sponsored by the National Cancer Institute for men and women at risk for lung cancer.

Could you be at risk for lung cancer?

If you've smoked heavily or have smoked for many years, the answer is "yes." Smoking puts you at risk even if you no longer smoke or do not have any symptoms.

What's the connection between smoking and cancer?

There's no doubt about it—cigarette smoking can cause lung cancer. In fact, cigarette smoking is the leading cause of lung cancer. Every year, more than 169,000 people in the United States get lung cancer, and nearly 155,000 people die from this disease. Lung cancer is the leading cause of cancer death for both men and women.

Your risk of lung cancer depends on how many cigarettes and how long you've smoked. Quitting reduces the risk, but half of all lung cancers occur in former smokers.

What's the purpose of this study?

NLST is a lung cancer screening trial. *Screening* means testing people to detect a disease before it causes symptoms.

The purpose of NLST is to compare two ways of detecting lung cancer: standard chest x-ray and spiral computed tomography (CT) scan. Both chest x-rays and spiral CT scans are used in an effort to find lung cancer early. So far, neither chest x-rays nor spiral CT scans have been shown to reduce a person's chance of dying from lung cancer. This study aims to show which test is better at reducing deaths from this disease.

Lung cancer research is a high priority for the National Cancer Institute. NCI is supporting NLST at more than 30 locations throughout the United States. NLST is a vital part of the effort to reduce the toll of lung cancer.

Who can join NLST?

You may be eligible to join if:

- You are a healthy man or woman aged 55 to 74, and
- You are a current or former smoker who has smoked heavily, or for many years, and
- You have never had lung cancer, and
- You have not had any cancer (except some skin cancers or in situ cancers) within the last 5 years.

Why should you consider participating?

NLST offers participants:

- The *possibility* of detecting a small lung cancer that may still be curable
- The chance to contribute to medical research and to help others and future generations
- Referrals to smoking cessation resources if you want to quit

What will happen if you join NLST?

If you join this study:

- You will meet with NLST staff to discuss the study, and they will determine your eligibility.
- You will read and sign a consent form that explains NLST in detail.
- You will be assigned by chance (randomized) to have either chest X-rays or spiral CT scans. You will visit the NLST site to have the same test each year for three years.
- Expert radiologists will review your X-ray or spiral CT scan.
- Your test results will be mailed to you and your doctor, who will determine if follow-up tests are needed.
- Periodically, for several years, the study staff will contact you by phone or by mail to update information about your health.
- Some NLST centers may ask to collect your blood, urine, or sputum (phlegm) for future lung cancer studies.

National Lung Screening Trial (NLST)

ANSWERS TO POTENTIAL PARTICIPANT QUESTIONS

Participation:

1. Why should I participate?

You will make an important contribution to lung cancer research. Lung cancer remains the chief cause of cancer death in American men and women.

2. Why should I participate if I don't get the Spiral CT screening test?

Regardless of which exam you receive, you will make an important contribution to lung cancer research. We don't know whether spiral CT screening can reduce lung cancer mortality, relative to chest x-ray screening. To determine whether it does, it is important to compare the participants who receive the spiral CT to a very similar group of study participants who receive chest x-rays. Therefore, persons who receive chest x-rays play a critical role in this study.

3. What does randomly assigned mean?

Random assignment means that a computer will assign the screening test you will receive in an impartial manner. Neither you nor the study staff can choose the type of exam you will receive. You will have an equal chance of being assigned to the spiral CT or chest x-ray exams.

4. What other hospitals are in the study?

Up to 30 Screening Centers from different areas in the country will participate in the study. The NLST/LSS SCs currently involved include the following:

- University of Colorado
  Health Sciences Center
  Denver, CO
- Georgetown University Medical Center/Lombardi Cancer Research Center
  Washington, D.C.
- Pacific Health Research Institute
  Honolulu, HI
- Henry Ford Health System
  Detroit, Michigan
- University of Minnesota School of Public Health/Virginia L. Piper Cancer Institute
  Minneapolis, Minnesota
- Washington University School of Medicine
  St. Louis, Missouri
- University of Pittsburgh Medical Center
  Pittsburgh, PA

- University of Utah Health Sciences Center
  Salt Lake City, UT
  AND
  St. Luke's Meridian Medical Center
  Meridian, ID

- Marshfield Clinic Research Foundation
  Marshfield, Wisconsin

- The University of Alabama at Birmingham
  Birmingham, Alabama

5. I had a bad experience with the hospital/the government lately, why should I help them?

I'm sorry that your experience was not good. However, this is a special research study sponsored by the National Cancer Institute. We are committed to making your participation in this study a positive experience. By participating in the study you are helping us to learn more about the ability of spiral CT to reduce lung cancer mortality.

6. How will I benefit from the study?

We don't know if you will personally benefit but if the study shows that the spiral CT screening exam is effective, then this type of screening for lung cancer may become common practice in the future. If this study shows that spiral CT does not reduce lung cancer mortality, health care providers will know not to use it as a screening test, saving you and others unnecessary inconvenience and expense.

7. Are there any downsides to participating?

There are certain risks that might be associated with the screening procedures. A small amount of radiation, (100-300 mrem) is received as part of the low-dose spiral CT exam. This amount of radiation is less than the recommended limit of radiation received by each person in the United States from natural sources (300 mrem exclusive of medical procedures). A small amount of radiation (3 mrem) is received as part of the NLST chest x-ray exam. This is less than the amount of radiation received from a normal chest x-ray (8-12 mrem). These levels of radiation pose no measurable risk.

Although the actual screening exams pose very little risk, it is possible that the screening spiral CT or chest x-ray will not detect a lung cancer that is present and falsely suggest that you do not have the disease. In this instance, you may miss an opportunity for cure. It also is possible that your screening spiral CT or chest x-ray will suggest that you have lung cancer when in fact you do not. In that case, your health care provider may ask you to undergo additional tests or procedures, such as a biopsy or surgery. These additional tests or procedures may cause pain, anxiety, expense, or medical complications that could have been avoided if you had never undergone the screening test. Additionally, it is possible that the screening spiral CT or chest x-ray will detect a lung cancer, but that the diagnosis and treatment of this cancer may not prolong your life. In this case, you may experience unnecessary pain, anxiety, expense, or medical complications from the diagnosis and treatment of cancer.

Appendix 2-5 Answers to Potential Participant Questions

Eligibility:

1. Am I eligible to participate in this study even though I have _____ (another serious medical problem that is not an exclusion criteria)?

If the medical problem would not interfere with your ability to participate in the screening exam, and if it were acceptable to your health care provider and to *(PI)* here at *(Local SC)* who is directing the study, you would be eligible to participate.

2. If I have _____ (symptom) am I still eligible for the study?

[If a potential participant reports a symptom, s/he should be advised to make an appointment with a health care provider so that the symptom can be evaluated. The potential participant should be asked to contact the SC after the medical evaluation so that eligibility may be determined.]

3. You mentioned that I cannot be in the study because I have _____ (symptom). Should I be worried?

Certain symptoms (unexplained weight loss or hemoptysis) can be signs of a serious health problem. We recommend that you contact your health care provider for a complete evaluation of your symptoms.

4. If I recently had _____ (lung examination), am I still eligible for the study?

[If the screening exam was a spiral CT performed in the last 18 months, then explain to the potential participant that s/he is not eligible for the study. If it was some other test, the SC staff should ask what was the result. If the exam result was normal, s/he may be eligible. If result was abnormal and s/he is currently undergoing diagnostic work-up for lung cancer, s/he should contact the SC when results of the work-up are known.]

5. I'm (younger than 54 years/older than 75 years old). Why can't I be in the study?

We are sorry that you cannot participate. The eligibility criteria are determined by the National Cancer Institute and I cannot change them.

6. I am not a smoker, or have only lightly smoked in my lifetime, why can't I be in the study?

We are sorry that you cannot participate. The eligibility criteria are determined by the National Cancer Institute and I cannot change them. The best way to conduct a study like the NLST is to examine people with an elevated risk of lung cancer. Heavy smokers or long-term smokers have an elevated risk.

Screening:

1. Who will be conducting these screening exams? Are they qualified?

The exams will be conducted by qualified health care providers and x-ray technologists. These individuals have been trained and have experience conducting these tests.

2. Is the spiral CT or chest x-ray painful?

Most people do not find these exams to be painful or uncomfortable. A trained medical professional will tell you exactly what to expect before the exam is given and will work with you to eliminate discomforts.

3. Will you screen my husband/wife/relative/friend?

If your husband/wife/relative/friend is interested in participating in the study, s/he should call the recruitment coordinator *(appropriate person at SC)* to determine if s/he is eligible. Remember that an eligible participant has an equal chance of being assigned to either the spiral CT group or the chest x-ray group. If assigned to the spiral CT group, your husband/wife/relative/friend would only receive the spiral CT exam; if assigned to the chest x-ray group, your husband/wife/relative/friend would only receive the chest x-ray exam.

Screening Exam Results:

1. If my exam results are abnormal, does that mean I have cancer?

Not necessarily. An abnormal screening exam means that further information is needed before a diagnosis can be made. Screening exams do identify cancer, but they also identify other conditions, some of which are harmless. All participants with exam results that are suspicious for cancer will be referred to their health care providers for diagnostic evaluation.

2. I don't have a doctor. Who will get my exam results?

If you do not have a health care provider and you have an abnormal exam result, we will be happy to refer you to a health care provider here at *(SC associated hospital).*

3. Can I have the results of my screening exam?

Yes. Your exam results will be sent to you within three weeks of your screening examination.

4. If something abnormal is found, do I have to go to a doctor here, or can I go to my own doctor?

You may go to the health care provider of your choice. All exam results will be sent to your health care provider. If you would like to be referred to a health care provider here at *(Local SC),* we will be happy to give you a referral list of health care providers.

5. Who will see the results of my screening exam?

You and the health care provider of your choice will be notified by letter of the results of your exam. Your health care provider also will receive a copy of the results. All study personnel conform to the hospital rules and Federal regulations regarding confidentiality. They must keep all information provided by study participants and all exam results confidential. Your results will not be shared with your employer or your insurance company without your signed consent.

Appendix 2-5 Answers to Potential Participant Questions

Diagnostic Evaluation:

1. Will you recommend specific diagnostic examinations if abnormalities are detected on the screening examinations?

If abnormalities are detected on your screening exam, we *(Local SC)* will send a letter notifying you and your health care provider as to the results of the examination. The letter will include common strategies for diagnostic evaluation. These strategies will be recommendations from the radiologist at *(Local SC)* and not from the NLST. The letter will state that we recommend that you make an appointment to discuss these findings with your health care provider. Your health care provider may recommend the same or alternative diagnostic examinations, or refer you to a specialist who can evaluate the abnormality found on the screening exam.

If you do not have a health care provider and would like us *(Local SC)* to provide you with a list of recommended health care providers, we will be happy to do so.

2. If my screening examination detects abnormalities, will you recommend specific doctors, if I ask, to perform a diagnostic work-up?

If the screening exam detects abnormalities and you would like us *(Local SC)* to give you a list of recommended health care providers, we will be happy to do so.

3. Will the *(Local SC)* recommend specific surgeons if I ask?

If you would like us *(Local SC)* to give you a list of recommended surgeons, we will be happy to do so.

Tumor Tissue Slide:

1. When will a tumor tissue slide be collected?

Following a positive screening examination, your health care provider may remove a piece of your lung to determine if you have lung cancer. Likewise, lung tissue may be removed as a part of treatment for lung cancer. If you have a diagnosis of lung cancer, a small piece of what was removed (tumor tissue) will be collected for the NLST.

2. What will be done with my tumor tissue slide?

Your tumor tissue slide will be reviewed to confirm the cancer diagnosis. Your tumor tissue slide may be used by the study investigators for medical research about genetic factors and chemical changes that lead to the development of cancer and other diseases. Your tumor tissue slide will be stored at an NCI-designated location for up to 25 years.

Appendix 2-5 Answers to Potential Participant Questions

General Questions About Cancer:

1. What can I do to lower my risk of lung cancer?

I'll be happy to {make an appointment/give you the telephone number} so you can speak with the Health Education/Risk Reduction clinic here at *(SC associated medical center).* Clinic staff are very knowledgeable in this area, and can answer your questions. Or you can call 1-800-4-CANCER, the Cancer Information Service of the National Cancer Institute and speak with a Cancer Information Specialist who can answer your questions.

2. If I have already been diagnosed with lung cancer, do I have an increased risk of developing other types of cancer?

I'll be happy to [make an appointment/give you the telephone number] so you can speak with the Health Education/Risk Reduction clinic here at *(SC associated medical center).* Clinic staff are very knowledgeable in this area, and can answer your questions. Or you can call 1-800-4-CANCER, the Cancer Information Service of the National Cancer Institute and speak with a Cancer Information Specialist who can answer your questions.

3. Do you have additional information on lung cancer?

I'll be happy to [make an appointment/give you the telephone number] so you can speak with the Health Education/Risk Reduction clinic here at *(SC associated medical center).* Clinic staff are very knowledgeable in this area, and can answer your questions. Or you can call 1-800-4-CANCER, the Cancer Information Service of the National Cancer Institute, and speak with a Cancer Information Specialist who can answer your questions.

4. My relative had lung cancer. Does that mean I'll get it too?

I'll be happy to [make an appointment/give you the telephone number] so you can speak with the Health Education/Risk Reduction clinic here at *(SC associated medical center).* Clinic staff are very knowledgeable in this area, and can answer your questions. Or you can call 1-800-4-CANCER, the Cancer Information Service of the National Cancer Institute, and speak with a Cancer Information Specialist who can answer your questions.

5. There's a lot of cancer in my family, that worries me.

I'll be happy to [make an appointment/give you the telephone number] so you can speak with the Health Education/Risk Reduction clinic here at *(SC associated medical center).* Clinic staff are very knowledgeable in this area, and can answer your questions. Or you can call 1-800-4-CANCER, the Cancer Information Service of the National Cancer Institute, and speak with a Cancer Information Specialist who can answer your questions.

6. My relative was recently diagnosed with lung cancer. I wonder if s/he's getting the right treatment?

I'll be happy to [make an appointment/give you the telephone number] so you can speak with the Health Education/Risk Reduction clinic here at *(SC associated medical center).* Clinic staff are very knowledgeable in this area, and can answer your questions. Or you can call 1-800-4-CANCER, the Cancer Information Service of the National Cancer Institute, and speak with a Cancer Information Specialist who can answer your questions.

7. Do you have a support group for individuals who have lung cancer?

[Yes, I'll be happy to give you the name and telephone number of the contact person] [I'm not sure, so I will give you the telephone number of _____ here at *(SC associated medical center)* who will know what support groups are available/give you the telephone number of Cancer Information Service of the National Cancer Institute, 1-800-4-CANCER. Either one can tell you what support groups are available.]

8. I think I am at high risk for cancer and I should be in the group that receives the spiral CT examination.

Please remember that at this time, it is not known whether screening with spiral CT is beneficial for individuals at high-risk of lung cancer. For scientific reasons, assignments need to be made at random. If you choose to participate, you will have an equal chance of being assigned to either the spiral CT or to the chest-x-ray group.

Appendix 2-6 Eligibility Screener (ES)

National Lung Screening Trial (NLST)

ELIGIBILITY SCREENER (ES)

Administrative Section

Date Completed: |__|__|/|__|__|/|2|0|__|__|

Screening Center ID: |___|___|

Screening Center Staff ID: |__|__|__|__|

Initials Complete: _____

Initials QC: _____

ES

Participant ID Label

NAME: DR./MR./MRS./MISS/MS.	FIRST	MIDDLE	LAST	(JR., SR., etc.)
CURRENT STREET ADDRESS:				APT. NO.
CITY	STATE			ZIP
TELEPHONE NUMBER: HOME: ( )	WORK: ( )		OTHER: ( )	

1. What is your date of birth?

|___|___| / |___|___| / 19 |___|___|
Mo Day Year

CALCULATE AGE: _____

END INTERVIEW IF AGE < = 54 or > = 75.

2. What is your gender?

☐ Male
☐ Female

3. Are you a current or former smoker?

☐ Current smoker
☐ Former smoker
→ How long ago did you quit?
☐ More than 15 years ago (END INTERVIEW)
☐ 15 or fewer years ago
☐ Never smoked (END INTERVIEW)

4. At what age did you begin to smoke?

|___|___|
Age

5. During the times that you've smoked, how many cigarettes did you usually smoke per day?

|___|___|___|
Cigarettes per day

CURRENT SMOKERS GO TO 7

FORMER SMOKERS GO TO 6

6. At what age did you quit smoking for the last time?

|___|___|
Age

7.	In the years you have smoked, was there ever a period of one or more years in which you did not smoke cigarettes?

☐ Yes
☐ No (IF NO, GO TO QUESTION 9.)

8.	a. (Current smokers) Between when you started smoking and now, for how many years in total did you not smoke cigarettes? b. (Former smokers) Between when you started smoking and finally quit smoking, for how many years in total did you not smoke cigarettes?

|__|__|
Years

9.	Have you had a spiral CT scan of your lungs or chest within the past 18 months?

☐ Yes (END INTERVIEW.)
☐ No

10.	Are you currently participating in any other cancer screening study? (This includes the PLCO Cancer Screening Trial.)

☐ Yes (END INTERVIEW.)
☐ No

11.	Are you currently participating in a cancer prevention study other than a study to help you stop smoking?

☐ Yes (END INTERVIEW.)
☐ No

12.	Have you ever been told by a physician that you have lung cancer?

☐ Yes (END INTERVIEW.)
☐ No

13.	Have you ever had any portion of your lungs surgically removed (not including a needle biopsy)?

☐ Yes (END INTERVIEW.)
☐ No

14.	Other than non-melanoma skin cancer and carcinoma in situ (except transitional cell carcinoma in situ, or bladder carcinoma in situ), have you, in the past 5 years, been treated for cancer or been told by a doctor that you have evidence of cancer?

☐ Yes (END INTERVIEW.)
☐ No

15.	Are you able to lie on your back with your arms raised over your head?

☐ Yes
☐ No (END INTERVIEW.)

16.	Do you have any metallic implants in your chest or back (such as a pacemaker or Harrington fixation rods)?

☐ Yes (END INTERVIEW.)
☐ No

17.	Do you have a requirement for home oxygen supplementation?

☐ Yes (END INTERVIEW.)
☐ No

18.	Have you experienced either of the following:

a. Unexplained weight loss of more than 15 pounds in the past 12 months?

☐ Yes (END INTERVIEW.)
☐ No

b. Recent coughing up blood (hemoptysis)?

☐ Yes (END INTERVIEW.)
☐ No

19.	In the past 12 weeks, have you had pneumonia or an acute respiratory infection that was treated with antibiotics by a physician?

☐ Yes (END INTERVIEW.)
☐ No

READ: Thank you. Those are all the questions I have for now. Please give me a few minutes to review your answers and tell you if you are eligible for the study.

- COMPLETE THE **ELIGIBILITY WORKSHEET** (next page).
- IF PERSON IS **INELIGIBLE** READ: I'm afraid you do not meet the eligibility requirements. Thank you very much for your interest in the study.
- IF PERSON IS **ELIGIBLE** READ: You are eligible to participate in this study. If you are interested in participating, I will mail you information about the study as well as a consent form for you to read, sign and return to us. For your convenience, there will be a prepaid and preaddressed envelope for you to return the consent form. Meanwhile, if you have any questions, please feel free to call our study coordinator, [NAME] at [NUMBER]. Once again, thank you very much for your interest in this study.

COMMENTS:

ELIGIBILITY WORKSHEET

A. CALCULATE AGE ELIGIBILITY.

1. IF MONTH AND DAY OF BIRTH (IN Q1) IS **ON OR BEFORE** TODAY'S MONTH AND DAY, CALCULATE AGE:

   a. Current Year ..... | 2 | 0 | | |

   b. MINUS Year of Birth (Q1) ..... | 1 | 9 | | |

   c. EQUALS ..... [ ]

2. IF MONTH AND DAY OF BIRTH (IN Q1) IS **AFTER** TODAY'S MONTH AND DAY, CALCULATE AGE:

   a. Current Year ..... | 2 | 0 | | |

   b. MINUS Year of Birth (Q1) ..... | 1 | 9 | | |

   c. MINUS **1** ..... | | | | 1 |

   d. EQUALS Age [ ]

IF AGE LESS THAN 55 OR GREATER THAN 74, THE PERSON IS **INELIGIBLE** (RETURN TO SCREENER).
IF AGE BETWEEN 55 AND 74, THE PERSON IS **ELIGIBLE** (CONTINUE BELOW)

B. CALCULATE DURATION OF SMOKING HISTORY IN PACK YEARS.

1. ENTER *Age* (Part A Above For Current Smokers) or *Age Quit* (ES-Q6 for Former Smokers) ..... _____
2. MINUS *Age Started Smoking* (ES-Q4) ..... _____
3. EQUALS *Years Since Start Of Smoking* ..... _____
4. MINUS *Years Not Smoked* (ES-Q8) ..... _____
5. EQUALS **TOTAL YEARS SMOKED** ..... [ ]
6. MULTIPLY:

$$\frac{\text{TOTAL YEARS SMOKED [B.5] X CIGARETTES PER DAY (ES-Q5)}}{20} = \text{PACK YEARS}$$

$$\frac{\text{PACK YEARS}}{20} \times 20 = \text{_____}$$

ROUND PACK-YEARS TO ONE DECIMAL PLACE (E.G., 45.7, 29.8).
If the second decimal place is <5, round down. If the second decimal place is = or >5, round up.
IF PACK-YEARS IS LESS THAN 30.0, THE PERSON IS **INELIGIBLE.**
IF PACK-YEARS IS EQUAL TO OR GREATER THAN 30.0, THE PERSON IS **ELIGIBLE**.
(RETURN TO SCREENER)

National Lung Screening Trial (NLST)

Specifications for the Completion of the Eligibility Screener (ES)

The Eligibility Screener will be administered by telephone by an SC staff member. The following are specifications for the administration of the form by telephone with a sample script for introducing the screener. These specifications may also be used as a reference document for answering questions from potential participants.

Administrative Section:

- **Participant ID Label:** The PID is assigned during the randomization process. Therefore, the PID label can only be attached to the form of eligible, randomized participants after the Eligibility Screener is completed.
- **Date Completed:** Record the month, day, and year the Eligibility Screener is completed. Zero-fill month, day, and year, if applicable.
- **Screening Center ID:** Record the two-digit SC ID number.
- **Screening Center Staff ID**: Record the four-digit staff ID number of the staff member completing the Eligibility Screener.
- **Name and Address:** If desired, the SC may affix a mailing label showing the potential participant's name and address in the space provided. Alternatively, the SC may hand write the name and address information.
- **Telephone Number(s):** Record the telephone number(s) that have been provided by the potential participant, including a home number, work number, or other number if provided.

Sample Script for Introduction of Screener:

"Hello, my name is _____ and I'm calling on behalf of (LOCAL SC). Recently, we received a postcard from you requesting information about the National Lung Screening Trial being conducted by the National Cancer Institute. I'd like to tell you more about the study. Is now a good time to talk?"

If no: Find out a good time and make a note of the appropriate time to re-contact the potential participant in the Potential Participant Tracking Log (Appendix 2-13).

If yes: "NLST is an NCI-sponsored nationwide study of Americans aged 55 to 74 who have a history of long-time and/or heavy cigarette smoking. The purpose of NLST is to compare screening with spiral CT (low-radiation-dose computed tomography) and screening with chest x-ray for effectiveness in reducing the number of deaths due to lung cancer. Since health care providers are not sure which screening test is more effective in screening for lung cancer, some of the study participants will receive screening spiral CT examinations, others will receive screening chest x-ray examinations, and the two groups will be compared. Participants will be notified of the results of the screening examination as soon as possible. We will also send the results to participants' health care providers.

"We would like to ask for your participation in the study. The study will provide invaluable information that may help save lives, and we hope you will agree to help. Your participation, however, is voluntary. Are you interested in participating?"

YES.....	(CONTINUE BELOW)
NO	(END INTERVIEW)

"*In order to participate in the trial, you must meet certain eligibility criteria. To determine whether you are eligible to participate in the trial, I would like to ask you a few questions. Before I begin, I must inform you of the following:*

"Collection of this information is authorized by the Public Health Service Act, Section 412 (42 USC 285 a-1). Rights of study participants are protected by the Privacy Act of 1974. Participation is voluntary and there are no penalties for not participating or withdrawing from the study at any time. Participation will not influence a person's relationship with any provider of medical care or any Federal program such as Social Security or Medicare. The information collected in this study will be kept confidential, and will not be disclosed to anyone but the researchers conducting this study, except as otherwise required by law. Names and other identifiers will be separated from information provided and will not appear in any report of the study. Information provided will be combined for all study participants and reported as statistical summaries. Study records will be kept for approximately 10 years past the end of the study, and then destroyed."

(CONTINUE WITH NAME AND ADDRESS VERIFICATION.)

Name and Address:

Complete this section to collect the potential participant's name, address, and telephone number(s). If the reply card containing name and address information is available, the information should be verified and name, address, and phone number(s) should be recorded in the spaces provided on the ES. If there are no changes to the information on the reply card, it may simply be stapled to the ES.

The sample script below may be used in cases where the reply card is available.

"First, I would like to verify your name, address, and telephone number."

NAME *"I have your name listed as (FULL NAME FROM REPLY CARD). Is that correct?"*

If there is a correction, record the corrected name in the space provided. Include title and suffix (such as Jr., Sr., etc.), if applicable. Verify all spelling.

ADDRESS *"I have your address listed as (ADDRESS FROM REPLY CARD). Is that correct?"*

If there is a correction, record the corrected address in the space provided. Verify all spelling.

PHONE NUMBER

"I have your evening phone number listed as (EVENING PHONE NUMBER FROM REPLY CARD). Is that your correct home phone number?"

If there is a correction, record the corrected evening phone number, including the area code, in the space provided for home phone number. This should be the number that corresponds to the home address.

"I have your daytime phone number listed as (DAYTIME PHONE NUMBER FROM REPLY CARD). Is that your correct work number?"

If there is a correction, record the corrected daytime phone number, including the area code, in the space provided for the work phone number.

"Do you have another contact phone number such as a beeper or cell phone number?"

Record the number, including the area code, in the space provided.

Eligibility Questions:

Administer the ES for each individual expressing interest in NLST. If, before formal administration of the ES, a potential participant volunteers information indicating that s/he is ineligible, record the participant's name and then answer the question on the ES that addresses the applicable criterion. No other information should be collected in this instance. Administration of the ES should be stopped once a potential participant is identified as ineligible. No further questions should be asked.

Read each question in the order listed. Read each question exactly as it is written to the potential participant and record his/her response. Do not attempt to elicit a "Don't Know" response to any question; however, if the potential participant indicates that s/he does not know the answer, record "DK" in the white space next to the question.

Specifications for each question are given below.

Q1. What is your date of birth? This question asks about the individual's birthdate. Record the month, day, and year of the participant's birthdate. Zero-fill the month and day, if applicable.

Age may be calculated using the eligibility worksheet. Record the age in the space provided. Age may be calculated at the point of asking the question or at the end of administering the ES.

Final age eligibility for a potential participant is based on the date of randomization. However, when filling out the ES, age will be calculated based on the date of administration. This will not be a problem unless the participant is not quite 55 or is nearing his/her 75th birthday. If the participant is nearly 55, the SC can opt to delay randomization to a date when the participant will be 55 as long as this delay is no longer than one month. If the participant is nearly 75, the SC may expedite randomization so that the participant is 74 on the date randomization is done.

Q2. What is your gender? This question asks whether the respondent is male or female. Record a response to this question without asking the respondent, unless you are unable to determine the gender.

Q3. Are you a current or former smoker? This question asks whether the potential participant is a current or former smoker. Note that this question refers to tobacco cigarette smoking, not pipe or cigar smoking. If a potential participant asks for clarification on who is a current smoker, answer that a current smoker is someone who smokes cigarettes on a regular basis.

If the potential participant is a current smoker, mark the "current smoker" box.

If the potential participant is a former smoker, mark the "former smoker" box. The follow-up question must be asked as indicated by the arrow.

If the potential participant was a smoker in the past, but no longer smokes and quit more than 15 years ago, mark "former smoker—more than 15 years ago" box. The individual is ineligible for the study and the interview should be ended.

If the potential participant was a smoker in the past, but no longer smokes and quit 15 or fewer years ago, mark "former smoker—15 or fewer years ago" box.

If the potential participant has never smoked in his/her life, mark "Never smoked" box. The individual is ineligible for the study and the interview should be ended.

Q4. At what age did you begin to smoke? This question asks the age at which the potential participant began to smoke. If the potential participant is unsure of the age, probe to obtain an estimated age.

Q5. During the times that you've smoked, how many cigarettes did you usually smoke per day? This question asks the potential participant how many cigarettes did/does s/he smoke per day during the times s/he has smoked. Remind the potential participant to provide this information as an average for the entire period of time s/he smoked.

NOTE: CURRENT SMOKERS (Q3) should skip Question #6 and continue with Question #7. Question #6 should only be answered for potential participants identified as former smokers.

Q6. At what age did you quit smoking for the last time? To be answered by former smokers (Q3) only. This question asks the potential participant the age at which s/he quit smoking <u>for the last time</u>. If the participant quit smoking at one time, but started again and quit again, probe for the most recent age at which s/he stopped smoking. If, contrary to Q3, the response to Q6 suggests that the potential participant quit more than 15 years ago, query the participant about this discrepancy. If the answer to Q3 was inaccurate, correct it and end interview.

Q7. In the years you have smoked, was there ever a period of one or more years in which you did not smoke cigarettes? This question asks the potential participant whether there was a period of one year or more in which s/he did not smoke cigarettes. If the participant answers "No," skip to Question 9.

Q8. a. (Current smokers) Between when you started smoking and now, for how many years in total did you not smoke cigarettes?

b. (Former smokers) Between when you started smoking and finally quit smoking, for how many years in total did you not smoke cigarettes?

This question is specific to whether the person is a current smoker or a former smoker. If the person is a current smoker, read the question as stated in 8a. If the person is a former smoker, read the question as stated in 8b.

This question asks the potential participant for the number of years in total in which s/he did not smoke cigarettes between the time when s/he started smoking and when s/he quit smoking or now. If a fraction of a year is given, ask the participant to estimate it to the nearest year. Let the participant determine whether to round up or down to the nearest year.

Q9. Have you had a spiral CT scan of your lungs or chest within the past 18 months? This question asks whether the potential participant has had a spiral CT scan of the lungs or chest within the past 18 months (1.5 years). As part of asking the question, the potential participant should be told that a CT scan of the heart, also called a cardiac CT or coronary calcium scan, is considered a CT scan of the chest. Potential participants who have had a CT scan of the lungs or chest within the past 18 months are ineligible for this study. CT scans of other portions of the body, such as the neck or abdomen, do not exclude an individual from participation in the study.

If the potential participant does not know whether or not s/he has had a CT scan of the lungs or chest within the last 18 months, record "DK" (Don't Know) in the white space next to the question. S/he should be asked to contact his/her health care provider to obtain the information. The ES should be placed in a pending file and the potential participant should be recontacted at a later date to complete eligibility determination. If, after contacting the health care provider, s/he still does not know, s/he is not eligible for the trial.

Q10. Are you currently participating in any other cancer screening study? (This includes the PLCO Cancer Screening Trial.) If the potential participant is currently enrolled in a cancer screening study,***** including PLCO, then s/he is ineligible. Verification that a potential participant is not a PLCO participant will be done using the CC-provided randomization pre-processing program. If the potential participant is unsure of the nature of the study, probe for the name of the study or any other information the potential participant can provide about the study, such as the name of the health care provider associated with the study, the location where screening exams take place, etc. Record this information in the space near the "Yes" response category and continue the interview.

After the interview is completed, the SC should investigate the nature of the study to determine whether or not the potential participant is eligible for NLST. If no further information can be obtained, the individual is ineligible.

****** *A cancer screening study/trial is a study that enrolls persons who are asymptomatic for a specific disease and then administers a test to determine whether they are likely to have that disease. The test can either involve machinery (e.g., spiral CT scan) or collection of a biologic sample (e.g., PSA blood test). If you are unsure of whether a study is a cancer screening study/trial, contact the CC or the NCI.*

Q11. Are you currently participating in a cancer prevention study other than a study to help you stop smoking? This question asks about whether the potential participant is currently participating in a cancer prevention study*, other than a smoking cessation study. If the potential participant is unsure of the nature of the study, probe for the name of the study or any other information the potential participant can provide about the study, such as the name of the health care provider associated with the study, the location where study activities take place, etc. Record this information in the space near the "Yes" response category and continue the interview. If the potential participant is currently enrolled in a cancer prevention study other than a study of smoking cessation, then s/he is ineligible for the study.

After the interview is completed, the SC should investigate the nature of the study to determine whether or not the potential participant is eligible for NLST. If no further information can be obtained, the individual is ineligible.

*A cancer prevention study involves individuals who have never had the cancer of interest but are at elevated risk of developing that disease. The purpose of the study is to examine whether cancer risk can be reduced. A cancer prevention trial may administer a chemopreventive agent (e.g., a drug or a vitamin) or may require participants to behave in a specific manner (e.g., reducing their fat intake). Large ongoing cancer prevention studies include STAR (Study of Tamoxifen and Raloxifine), SELECT (Selenium and Vitamin E Clinical Trial – for prostate cancer), and PCPT (Prostate Cancer Prevention Trial). Women participating in the Women's Health Initiative (WHI) are eligible for NLST. If you are unsure of whether a study is a cancer prevention study, please call the CC.

Q12. Have you ever been told by a physician that you have lung cancer? This question asks about a history of lung cancer. Potential participants who have been diagnosed with lung cancer are ineligible for this study.

- If the potential participant has been told by a physician that s/he has/had lung cancer, mark "Yes." Include both metastatic and primary lung cancer, and lung cancers that are in remission.
- If the potential participant says s/he had lung "tumor," probe to find out whether it was "malignant" or "cancerous." If so, mark "Yes."
- If the potential participant says s/he has a pre-cancerous lesion, mark "No." This includes conditions described as carcinoma in situ and atypical adenomatous hyperplasia.
- If the potential participant does not know whether or not s/he has been diagnosed with lung cancer, s/he should be asked to contact his/her physician to obtain the information. The ES should be placed in a pending file and the potential participant should be recontacted at a later date to complete eligibility determination. If, after contacting the physician, the potential participant still does not know whether or not lung cancer was diagnosed, s/he is not eligible for the trial.

Q13. Have you ever had any portion of your lungs surgically removed (not including a needle biopsy)? This question asks about surgery to remove any portion of the lungs or an entire lung. Other terms for removal of a lung are "pneumonectomy" or "lobectomy." If the potential participant had an <u>entire</u> lung removed, mark "Yes." If the potential participant had a <u>partial</u> lobectomy, that is only part of a lung removed, also mark "Yes." If the potential participant reports a history of having any portion of

the lung(s) removed, other than for a needle biopsy, then s/he is ineligible for this study.

Q14. Other than non-melanoma skin cancer and carcinoma in situ (except transitional cell carcinoma in situ, and bladder carcinoma in situ), have you, in the past 5 years, been treated for any cancer or been told by a doctor that you have evidence of cancer? This question asks whether the potential participant has undergone treatment, or has been told by a doctor that s/he has had evidence of any cancer, other than non-melanoma skin cancer and carcinoma in situ, in the past five years. If the potential participant has undergone treatment for, or has had evidence of, any cancer other than non-melanoma skin cancer and carcinoma in situ in the past five years, then s/he is ineligible for this study. Basal cell or squamous cell skin cancers are considered non-melanoma skin cancers. Carcinoma in situ (CIS) is a precancerous condition and is not considered to be cancer. Therefore, persons who have undergone treatment for, or have had evidence of pre-cancerous lesions or carcinoma in situ, are eligible. However, two exceptions should be noted. If a potential participant has undergone treatment for, or has had evidence of transitional cell carcinoma in situ or bladder carcinoma in situ in the past five years, then s/he is ineligible for this study.

If the potential participant does not know whether s/he has undergone treatment for cancer in the past five years, or does not know whether s/he has had evidence of cancer in the past five years, s/he should be asked to contact his/her physician to obtain the information. The ES should be placed in a pending file and the potential participant should be recontacted at a later date to complete eligibility determination. If, after contacting the physician, the potential participant still does not know, s/he is not eligible for the trial.

Q15. Are you able to lie on your back with your arms raised over your head? This question asks the potential participant if s/he believes that s/he would be able to lie on his/her back with arms raised over his or her head. If the potential participant asks how long s/he must be able to hold this position, tell him/her three minutes. If the potential participant feels that s/he would be physically able to do so, mark the box for "Yes." If a potential participant feels that s/he would be physically unable to do so, mark the box for "No." If "No" is marked, the potential participant is not eligible for participation in the study.

Q16. Do you have any metallic implants in your chest or back (such as a pacemaker or Harrington fixation rods)? This question asks if the potential participant has metallic implants in his/her chest or back. If the potential participant answers "Yes," mark the appropriate box. If the potential participant answers "No," mark the box for "No." This question concerns metallic implants that would obscure a scan of the lungs. Metallic implants or metal objects that do not make the participant ineligible would include: coronary artery bypass markers, sternotomy sutures, metallic heart valves, vascular stents, angioplasty stents, or small amounts of shrapnel or bullet fragments. If the potential participant reports any of these items, mark the box for "No." If "Yes" is marked, the potential participant is not eligible for participation.

Q17. Do you have a requirement for home oxygen supplementation? This question asks if the potential participant has a requirement for home oxygen supplementation. Mark the appropriate box to record the potential participant's response. If "Yes" is marked, the potential participant is not eligible for participation.

Q18. Have you experienced either of the following:

a. Unexplained weight loss of more than 15 pounds in the past 12 months? This question asks the potential participant if s/he has had unexplained weight loss of more than 15 pounds in the past year. Mark the box that corresponds to the potential participant's response. If "Yes" is marked, the potential participant is not eligible.

b. Recent coughing up blood (hemoptysis)? This question asks the potential participant if s/he has recently experienced hemoptysis, or coughing up blood. Blood-tinted sputum is not considered hemoptysis. Mark the box that corresponds to the potential participant's response. If the potential participant reports experiencing recent hemoptysis, mark the "Yes" box; if the potential participant has experienced hemoptysis in the past, mark the "No" box. If "Yes" is marked, the potential participant is not eligible. Please note hemoptysis, or coughing up blood, is not the same as bloody emesis (vomiting blood).

If the potential participant asks for clarification of the word "recent," tell him or her that recent hemoptysis refers to hemoptysis occurring in the past month.

If the potential participant has experienced either of these symptoms and expresses concern, the SC staff member should advise the potential participant that one or both of these symptoms could be a sign of a serious health problem. The participant should be encouraged to contact his/her health care provider for a complete evaluation.

Q19. In the past 12 weeks, have you had pneumonia or an acute respiratory infection that was treated with antibiotics by a physician? This question asks the potential participant if s/he has had pneumonia or an acute respiratory infection that was treated with antibiotics by a physician in the past 12 weeks. If the participant has had pneumonia or an acute respiratory infection that was treated with antibiotics in the past 12 weeks, mark the box for "Yes." If the participant has not had pneumonia or an acute respiratory infection in the past 12 weeks, or has had such an infection but it was not treated with antibiotics, mark the box for "No." If "Yes" is marked, the potential participant is not eligible. If "Yes" is marked, the SC may contact the potential participant in the future to reassess eligibility.

READ: *"Thank you. Those are all the questions I have for now. Please give me a few minutes to review your answers and tell you if you are eligible for the study."*

(Note: If participant is eligible, randomized and then develops pneumonia or an acute respiratory infection between randomization and screening, then inform the participant that the screening exam will be scheduled 12 weeks after he/she completes treatment with antibiotics. The SC should document this situation in the participant's study record. The SC should contact the participant approximately two months following his/her treatment with antibiotics, to schedule a screening examination.)

National Lung Screening Trial (NLST)

PROTOTYPE CONSENT FORM

(Name of Local SC)

DESCRIPTION OF STUDY

I have been invited to take part in the National Lung Screening Trial (NLST), sponsored by the National Cancer Institute, *(Local SC)*, and other centers across the country. The purpose of NLST is to compare screening with spiral CT (low-radiation-dose computed tomography) and screening with chest x-ray for effectiveness in reducing the number of deaths due to lung cancer. There is disagreement among medical experts over the effectiveness of these screening methods for lung cancer. NLST is carefully designed to resolve this controversy.

NLST will enroll approximately 50,000 men and women between the ages of 55 and 74 who are former or current heavy smokers, recruited from centers across the nation. Half of the participants will receive three annual spiral CT exams. The other half will receive three annual chest x-ray exams.

SCREENING EXAM PROCEDURES

By agreeing to receive these exams, I agree to be assigned by a random process to either the spiral CT exam group or the x-ray exam group. I understand that I have an equal chance of being assigned to either group. I will receive the exam once a year for a total of three exams. I agree to have the screening exams performed as recommended.

If I am assigned to the spiral CT exam group, I will receive the spiral CT exam at *(Local SC)*. I will lie very still on a table that moves through the middle of a doughnut-shaped machine. The machine will take a series of x-rays and create a three-dimensional ("3-D") picture of my lungs. It will be necessary for me to hold my breath for about 20 seconds while the x-rays are being taken.

If I am assigned to the x-ray exam group, I will receive a single-view chest x-ray at *(Local SC)*. This type of x-ray is commonly used to view the organs inside the chest. It will be necessary for me to hold my breath for a few seconds while the x-ray is taken.

Both spiral CT and chest x-ray are radiologic exams that doctors use to help diagnose lung cancer and other lung conditions in people with symptoms. I understand that I can receive a chest x-ray exam outside of NLST, and that I may be able to receive a spiral CT exam outside of NLST, depending on where I live. Neither exam, however, has been scientifically established as standard of care for early detection of lung cancer in people without symptoms. The value of chest x-ray as a screening exam for lung cancer is being assessed in another study sponsored by the National Cancer Institute. The value of spiral CT as a screening exam, compared to chest x-ray, will be assessed by NLST.

If NLST shows that screening with low-dose spiral CT is more effective than chest x-ray in reducing the chance of dying from lung cancer, then this exam may become common practice in the future. If NLST shows that screening with low-dose spiral CT is not more effective than chest x-ray in reducing the chance of dying from lung cancer, doctors will know to avoid this procedure as a screening test, thus preventing unnecessary inconvenience and expense.

QUESTIONNAIRES

I agree to complete a questionnaire that asks for information about my medical history, factors related to my health, and my family's history of lung cancer. I also agree to complete a questionnaire regarding my recent health annually for at least four years. I understand that I may be randomly selected to complete an additional health questionnaire after I receive my screening exam each year.

NOTIFICATION OF RESULTS

I understand that results of my screening exam will be sent to me as soon as they become available. If I have provided the name of a doctor or other health care provider, he or she will receive the results also.

If the results indicate a potential medical problem, *(Local SC)* will provide me, if I so choose, with the names of physician specialists from whom I can receive further medical evaluation.

If I am diagnosed with cancer, *(Local SC)* will provide me, if I so choose, with the names of cancer specialists from whom I can receive further medical evaluation.

COLLECTION OF TISSUE

If I am diagnosed with lung cancer, it is possible that my physician will perform surgery to diagnose or treat the lung cancer. During this surgery, I may have some of my tissue removed for the hospital's pathology department to test. After that process is complete, the remaining tissue will be stored in the hospital's pathology department. I agree to have a small amount of that tissue specimen, if available, sent to the National Cancer Institute for review. I understand that since the tissue is removed at the time of surgery or biopsy, this will not lead to any additional procedures or expense.

I understand that part of the tissue specimen may be used by the study investigators for medical research about genetic (both acquired and inherited) factors and chemical changes that lead to the development of cancer and other diseases that occur in my age group. The tissue specimen will be stored at a National Cancer Institute research storage facility for up to 25 years and used to help scientists learn what causes cancer and how to prevent its progression. It is believed that cancer may be caused by both environmental and genetic factors. Therefore, the samples that I contribute may be used in biochemical and genetic studies to identify these causes. The samples collected for these additional studies are for medical research only and the research results are not suitable for use as clinical tests for my medical care. Therefore, the results of these <u>additional studies</u> will not be available to me.

BENEFITS

I understand that I will receive free lung cancer screening exams. I further understand that if I have lung cancer, it is possible that the cancer may be detected at an early stage. Early detection of lung cancer may prolong my life; however, this has not been demonstrated scientifically.

RISKS

I understand that there are certain risks that might be associated with the screening procedures. A small amount of radiation (100-300 mrem) is received as part of the low-dose spiral CT exam. This amount of radiation is less than the recommended limit of radiation received by each person in the United States from natural sources each year (300 mrem exclusive of medical procedures). A small amount of radiation (3 mrem) is received as part of the NLST chest x-ray exam. This is less than the amount of radiation received from a normal chest x-ray (8-12 mrem). These levels of radiation pose no measurable risk.

Although the actual screening exams pose very little risk, it is possible that the screening spiral CT or chest x-ray will not detect a lung cancer that is present and falsely suggest that I do not have the disease. In this case, I may miss an opportunity for cure. It also is possible that my screening spiral CT or chest x-ray will suggest that I have lung cancer when in fact I do not. In this case, I may be asked by my health care provider to undergo additional tests or procedures, such as a biopsy or surgery. These additional tests or procedures may cause pain, anxiety, expense, or medical complications that could have been avoided if I had never undergone the screening test.

Additionally, it is possible that the screening spiral CT or chest x-ray will detect a lung cancer, but that the diagnosis and treatment of this cancer may not actually prolong my life. In this case, I may experience unnecessary pain, anxiety, expense, or medical complications from the diagnosis and treatment of the cancer.

COSTS

All study screening exams are free. No other costs will be covered by NLST.

The costs of diagnostic tests beyond screening will not be covered by the study and must come from insurance or other sources.

The costs of cancer treatment will not be covered by this study.

COMPENSATION FOR RESEARCH-RELATED INJURIES

In the unlikely event of physical injury resulting from my participation in this study, I will be provided with immediate medical treatment. I understand, however, that NLST will not cover the costs of immediate medical treatment and will not cover the costs of any additional treatment that is necessary.

EXCLUDED PROCEDURES

This study includes only the screening exams listed above. Other medical procedures are not part of this study. The exams received in this study are screening exams for lung cancer only and are not intended to be a substitute for routine medical care.

Appendix 2-8 Prototype Consent Form

STORAGE OF STUDY MATERIALS

I understand that all materials relating to my study participation, including questionnaires and images from screening examinations, will be stored at *(Local SC)* for at least ten years after the end of the trial and then destroyed.

INFORMATION ON NEW FINDINGS

I understand that any significant new findings about screening for lung cancer discovered during the term of the study will be given to me if that information will make a difference in my willingness to continue in the study.

CONFIDENTIALITY

All information I provide as part of the study will be kept confidential and will be used only for scientific purposes, in accordance with applicable state and Federal laws. Only groups or organizations that have a role in NLST will have access to this information. My name and other information capable of identifying me will not appear in any study documents. Only group summaries, not individual data, will be reported. Personal identifying information such as name, address, and Social Security Number may be used to locate me in future years or may be used to determine, through state cancer registries, if I have been diagnosed with cancer. According to the Health Insurance Portability and Accountability Act (HIPAA) any health information that would allow you to be identified is protected under federal law.

RIGHT TO WITHDRAW

I understand that my participation in NLST is voluntary. I may refuse to participate at any time without penalty or loss of benefits to which I am otherwise entitled. My decision regarding participation will not influence my relationship with *(Local SC)* or its staff, or with any Federal program such as Social Security or Medicare.

PERMISSION TO REVIEW MEDICAL RECORDS

By agreeing to participate, I give permission for my health care providers and hospitals where I have been seen to release my medical records to the study investigators.

CERTIFICATION

I have read this form or it has been read to me and I understand its contents. Any questions concerning the research or the rights of the participants involved have been and will be answered by *(Names, Titles, Phone Numbers)*.

Appendix 2-8 Prototype Consent Form

A copy of this consent form has been given to me. My signature below means that I freely agree to participate in NLST.

_____

PARTICIPANT'S NAME (PRINT)

_____

PARTICIPANT'S SIGNATURE DATE

_____

WITNESS SIGNATURE

Appendix 2-9 Sample Consent Form Cover Letter

National Lung Screening Trial (NLST)

(Date)

(Participant Name)
(Participant Address)
(City, State, ZIP Code)

Dear *(Participant Name)*:

Thank you for answering questions regarding your eligibility for the National Lung Screening Trial (NLST). Your response is very valuable to us and your effort is greatly appreciated.

As explained to you on the telephone, by signing the enclosed consent form and returning it in the postage-paid envelope, you will be giving us your permission to enroll you in the NLST. The purpose of this study is to compare screening with spiral CT (low-radiation-dose computed tomography) and screening with chest x-ray for effectiveness in reducing the number of deaths due to lung cancer. Your participation is important to the success of the study.

Please be assured that all information you give will be kept confidential and will not be disclosed to anyone but the researchers conducting this study, except as otherwise required by law. No identifying information will be released.

Thank you again for your support of this important research effort. If you have any questions regarding this study, please contact me or my colleague, *(Name of SC Coordinator)* at *(Telephone Number)*.

Sincerely,

(Name of Principal Investigator)
Principal Investigator
National Lung Screening Trial

ELIGIBILITY VERIFICATION FORM (EVF)

PART A: ADMINISTRATIVE SECTION

Name:

Last First Middle

EVF

Date of Birth: .....|___|___| - |___|___| -19 |___|___|
MO DAY YR

Gender (M = 1 / F = 3) |___|

Screening Center ID: |___|___|

Screening Center Staff ID: ..... |___|___|___|___|

Pre-processing # .....|___|___|___|___|___| - |___|

Participant ID Label

PART B: ELIGIBILITY VERIFICATION

SMOKING ELIGIBILITY CRITERIA

1. Smoking status (ES-Q3)

- ☐ **1 = Current smoker**
- ☐ **3 = Former smoker** → How long ago did s/he quit?
  - ☐ **1 = More than 15 years ago**
  - ☐ **3 = 15 or fewer years ago**
- ☐ **4 = Never smoked**

2. Pack-year tobacco exposure

At what age did this individual begin to smoke? (ES-Q4)

|___|___| **YEARS OLD**

During the times that this individual smoked, how many cigarettes did s/he usually smoke per day? (ES-Q5)

|___|___|___| **# PER DAY**

At what age did this individual quit smoking for the last time? (ES-Q6)

|___|___| **YEARS OLD**

In the years this individual smoked, was there ever a period of one year or more years in which s/he did not smoke cigarettes? (ES-Q7)

- ☐ 1 = **YES** →
- ☐ 3 = **NO**

If Yes, for how many years in total did s/he not smoke cigarettes? (ES-Q8)

|___|___| **YEARS**

Total pack-year tobacco exposure

|___|___|___| . |___| YEARS

ELIGIBILITY CRITERIA - CONTINUED	CHECK YES OR NO. IF YES IS CHECKED, STOP. IF NO IS CHECKED, CONTINUE.
3. Has this individual had a spiral CT scan of the lungs or chest in the past 18 months? (ES-Q9)	☐ YES ☐ NO
4. Is this individual currently participating in another cancer screening study, including the PLCO Cancer Screening Trial? (ES-Q10)	☐ YES ☐ NO
5. Is this individual currently participating in a cancer prevention study other than a study to help him/her stop smoking? (ES-Q11)	☐ YES ☐ NO
6. Has this individual ever been diagnosed with lung cancer? (ES-Q12)	☐ YES ☐ NO
7. Has this individual ever had any portion of the lungs surgically removed (not including a needle biopsy)? (ES-Q13)	☐ YES ☐ NO
8. Has this individual undergone treatment for, or had evidence of, any cancer other than non-melanoma skin cancer and carcinoma in situ (except bladder carcinoma in situ and transitional cell carcinoma in situ) in the past 5 years? (ES-Q14)	☐ YES ☐ NO
9. Is this individual **unable** to lie on the back with arms raised over the head? (ES-Q15)	☐ YES ☐ NO
10. Does this individual have metallic implants in the chest or back? (ES-Q16)	☐ YES ☐ NO
11. Does this individual have a requirement for home oxygen supplementation? (ES-Q17)	☐ YES ☐ NO
12. Has this individual had either unexplained weight loss of more than 15 pounds in the past 12 months or recent hemoptysis? (ES-Q18)	☐ YES ☐ NO
13. Has this individual had pneumonia or an acute respiratory infection that was treated with antibiotics by a physician in the past 12 weeks? (ES-Q19)	☐ YES ☐ NO
14. Is this individual unwilling or unable to sign the study consent form?	☐ YES ☐ NO
15. Is YES marked for any of the questions above (Q3 to Q14)?	MARK 1 FOR YES, 3 FOR NO ☐ 1=YES ☐ 3=NO

PART C: RANDOMIZATION AND ENROLLMENT

This individual can **only** be randomized and enrolled into the National Lung Screening Trial if s/he meets the age, smoking status and pack-year requirements AND "No" is marked for each of the questions above.

After randomization is complete, the Participant ID number and randomization group will be specified by the telephone randomization system. Please write the information in the space below. When the e-mail confirmation report is received, please verify the information against what is written below, then file the confirmation in the participant's study file.

Date of Randomization/Enrollment: |___|___| - |___|___| - | 2 | 0 |___|___|
MO DAY YR

Participant ID: |___|___| - |___|___|___|___|___|___| - |___|

Randomization Group (MARK ONE): ☐ Spiral CT
☐ Chest x-ray

Specifications for the Completion of the Eligibility Verification Form (EVF)

This form is to be completed after completing the ES and prior to randomization by the SC Coordinator or a staff member who has been approved to perform the eligibility verification procedures and to use the Interactive Voice Response System (IVRS). Use the ES and the Consent Form as sources of information when completing the EVF. Each of the eligibility criteria listed must be satisfied if the potential participant is to be randomized and enrolled in the NLST.

Part A: Administrative Section:

Name: Record the last and first names, and middle name or initials of the potential participant on the line provided. If the potential participant does not have a middle name, record the second letter of his/her first name in the space provided for the middle initial and record "no middle name" in the margin of the form.

Date of Birth: Record two digits each for the month and day and two digits for the year of the potential participant's date of birth. Zero-fill month and day of birth, if applicable.

Gender: Record a "1" if the potential participant is male or "3" if female.

Screening Center ID: Record the two-digit SC ID.

Screening Center Staff ID: Record the four-digit staff ID number of the staff member completing the form.

Pre-processing #: SCs must verify that the potential participant is neither enrolled in PLCO nor already enrolled in the NLST/LSS. Check each potential participant's name against a list of PLCO and NLST/LSS participants using the pre-processing program in IDEAS. See the IDEAS User's Guide for a detailed description of how to use the pre-processing program. Once the pre-processing is complete for each participant, IDEAS will provide a unique six-digit pre-processing number. Record this number on the EVF. If the potential participant is part of PLCO or is a duplicate, stop; s/he is not eligible for randomization.

Participant ID Label: After randomizing the participant, affix the assigned PID label to the front of the form in the space provided.

Part B: Eligibility Verification:

SMOKING ELIGIBILITY CRITERIA

1. **Smoking status.** This question asks about the smoking history of the potential participant. Check the box that corresponds to the smoking history of this individual (i.e. "Current smoker," "Former smoker," or "Never smoked") as reported on the ES, Question 3. NOTE: the numbers after each response are for your reference when completing the telephone randomization.

If this individual is a former smoker, please check the box that corresponds to how long ago the individual stopped smoking. In order to be eligible, an individual must have a history of smoking, and that smoking habit must have continued to within 15 years of the date the ES was completed.

2. **Pack-year tobacco exposure.** This section asks about total tobacco exposure, as measured in pack-years. Pack-years is the product of duration of exposure (measured in years), and intensity of exposure (measured in packs of cigarettes per day). The formula for calculating pack-years is on the Eligibility Worksheet (Part B.6) that is part of the ES. Enter the components of the formula as follows.

   - **At what age did this individual begin to smoke?** Enter the age exactly as it appears on the ES, Question 4.
   - **During the times that this individual smoked, how many cigarettes did s/he usually smoke per day?** Enter the number of cigarettes exactly as it appears on the ES, Question 5.
   - **At what age did this individual quit smoking for the last time?** Enter the age exactly as it appears on the ES, Question 6.
   - **In the years this individual smoked, was there ever a period of one year or more years in which s/he did not smoke cigarettes?** Check the box for "Yes" or "No," as specified on the ES, Question 7.
   - **If yes, for how many years in total did s/he <u>not</u> smoke cigarettes?** Enter the number of years exactly as it appears on the ES, Question 8.
   - **Total pack-year tobacco exposure.** Enter the total pack-year tobacco exposure for this individual. This number should be copied from the ES Worksheet and will be verified by the telephone randomization system. In order to be eligible, a potential participant must have no less than 30.0 pack-years of tobacco exposure.

ELIGIBILITY CRITERIA - CONTINUED

For each of the remaining eligibility verification questions, check the box for a yes or no answer. Copy the responses as they appear on the ES. The corresponding question from the ES is indicated in the specifications below. If "Yes" is marked, the potential participant is <u>not</u> eligible to be enrolled in the NLST.

3. **Has this individual had a spiral CT scan of the lungs or chest in the past 18 months?** (ES-Q9)

4. **Is this individual currently participating in another cancer screening study, including the PLCO Cancer Screening Trial?** (ES-Q10)

5. **Is this individual currently participating in a cancer prevention study other than a study to help him/her stop smoking?** (ES-Q11)

6. **Has this individual ever been diagnosed with lung cancer?** (ES-Q12)

7. **Has this individual ever had any portion of the lungs surgically removed (not including a biopsy)?** (ES-Q13)

8. **Has this individual undergone treatment for, or had evidence of, any cancer other than non-melanoma skin cancer and carcinoma in situ (except transitional cell carcinoma in situ or bladder carcinoma in situ) in the past 5 years?** (ES-Q14)

9. **Is this individual unable to lie on the back with arms raised over the head?** Please note that this question is worded differently from the ES. If the participant answered "Yes" to being able to lie on his/her back with arms raised over the head on the ES, then this question on the EVF should be marked "No." (ES-Q15)

10. **Does this individual have metallic implants in the chest or back?** This question asks whether the individual has metallic implants in the chest or back (such as a pacemaker or Harrington fixation rod). (ES-Q16)

11. **Does this individual have a requirement for home oxygen supplementation?** (ES-Q17)

12. **Has this individual had either unexplained weight loss of more than 15 pounds in the past 12 months, or recent hemoptysis?** (ES-Q18)

13. **Has this individual had pneumonia or an acute respiratory infection that was treated with antibiotics by a physician in the past 12 weeks?** (ES-Q19)

14. **Is this individual unwilling or unable to sign the study consent form?** This question asks about the potential participant's willingness/ability to sign the consent form for the study. This information should be obtained through in-person or mail contact with the potential participant. If the individual does not sign the consent form for any reason, s/he is not eligible to participate in the study. The SC must have a signed consent form on file in order to mark "No" for this question.

After completing Parts A and B of the EVF, the SC staff member must review the questions to confirm participant eligibility. If the potential participant is a current smoker, or former smoker that quit smoking less than 15 years ago, has a pack-year history of at least 30 years, and Questions 3 through 14 are marked "No," s/he is eligible for randomization. The SC staff member must access the Interactive Voice Response System (IVRS) to randomize the participant. See Appendix 2-12 for the NLST/LSS WesTrax IVRS User's Guide.

<u>After Completing Randomization:</u>

- Complete the Date of Randomization in Part C of the EVF. Record two digits each for the month, day, and year. Zero-fill month and day, if applicable.
- Fill in the assigned Participant ID number and randomization group in Part C of the EVF, using the information received from the IVRS.
- Attach the e-mail confirmation report to the corresponding completed EVF.
- File the original EVF and the confirmation report in the participant's study file.

SC-WesTrax™ Interaction

WesTrax™ provides Interactive Voice Response (IVR) services to randomize study participants and collect data from authorized study personnel. In addition, it allows you to send and receive information from a touch-tone telephone anywhere in the world. WesTrax™ also provides a non-interactive means for participant randomization known as **Batch Randomization**. WesTrax™ randomization services are available 24 hours a day, 7 days a week.

Flow of Distributed Randomization Activities

The NLST distributed randomization process incorporates the following steps.

1. The potential participant fills out the Eligibility Screening form (ES).

2. After verifying that the potential participant is not also enrolled in the NLST or PLCO study (see the section on **Error! Reference source not found.**), the SC fills out the Eligibility Verification Form (EVF) as described in the section on **Error! Reference source not found.**. If no record of the participant is found in these studies, you are asked if you wish to continue with the on-screen EVF or automated telephone randomization.

3. If you use the phone randomization process, WesTrax will place the participant into an arm of the study and will create a comma delimited file of the randomized participants. This comma delimited file will then be mailed back to the originating SC.

4. If you continue with the on-screen EVF data entry, the system will generate a comma delimited file to be sent to WesTrax. The SC will e-mail this file to WesTrax in Houston, Texas. WesTrax will place the participant into an arm of the study and will process the SC-generated comma delimited file, adding three new columns: **StudyArm**, **PID**, and **RandDate** (see the section on E-Mail Data File). This WesTrax comma delimited file will then be mailed back to the originating SC.

5. All WesTrax comma delimited files (extension **.csv**) are e-mailed back to the originating SC. The SC staff will then copy these files and place them into the SC server directory **\\nlstsrvr\NLST\RandomizeImports**.

6. On a regularly scheduled basis IDEAS will search this directory for files with the **.csv** extension by a DTS procedure developed to process the files into the NLST IDEAS database. The DTS program will perform the following actions:

    - Read the **NLST\RandomizeImports** directory for files with the **.csv** extension.
    - Insert the new record(s) into table **qry_Person** if no record exist, or, if a record exist, update the information.
    - Update records in table **qry_Part_EVF** with PID and participant information.

- Update record(s) in table **qry_Part_ContactRand** with PID information.
- Copy the processed file and logs to server directory **\nlst\RandomizeImport\Archive**.
- If an error occurred, copy the processed file and logs to server directory **\nlst\RandomizeImport\Error** and bring up an error log on the screen.

IVRS WesTrax™ Instructions

Setting Up An E-Mail Account

Before you can randomize a participant you must first set up a designated e-mail address ***only to be used for the NLST.*** The majority of documents sent from WesTrax ™ will be e-mailed to the Screening Centers dedicated WesTrax™ e-mail account. The only exception to this is the WesTrax™ User Credentials document that is provided to individual users of the system.

Site Activation

As a result of site activation, your site and dedicated e-mail address are authorized and become operative in WesTrax™. You will receive all randomization confirmations at this address. In addition, the WesTrax™ system only accepts batch randomization files from your SC's dedicated e-mail account.

Setting Up a New User Account

Each Screening Center (SC) staff member approved by the SC coordinator to use the randomization system must be registered with WesTrax Help Center. In order to set up a new user account in the WesTrax system the SC coordinator must contact the WesTrax Help Center at **1-800-509-5555** or e-mail helpcenter@westat.com and provide the following user information:

- Screening Center Name
- Staff Identification Number
- Last Name
- First Name
- Direct Daytime Telephone Number
- Personal E-mail Address
- Fax Number

A cover letter, WesTrax™ Instructions, and user credentials are e-mailed to each new user. Each registered person will receive a unique user identification number (2- digit site number + 4-digit staff ID) and a 4-digit personal identification number (PIN) to use when accessing the system. The user ID and PIN should not be shared and must be stored in a safe place. Figure on the following page is an example of a WesTrax User Credentials document that will be e-mailed to each new user at his/her personal e-mail address.

National Lung Screening Trial (NLST)
WesTrax™ User Credentials Document

Please use the following assigned user ID and PIN when accessing WesTrax™

Caller Name:
Site Number:
Site Name:

User ID:
User PIN:

Additional Instructions:

WesTrax™ Toll-Free Number: 800-955-2342
WesTrax™ Help Desk Number: 800-509-5559

If you have any questions call the WesTrax ™ help desk at 800-509-5559. If you require immediate after hours support call 800-509-5559 and leave a message with the answering service. A Project Coordinator will be paged and will return your call within 15 minutes. For after hours non-urgent assistance please e-mail the help center at helpcenter@westat.com and your request will be handled the next business morning.

Date and Time

WesTrax
Westat Help Center - 800.509.5559 dd/mmm/yyy
FAX - 713.529.4924 00:00:00 CT

Figure 246: *WesTrax User Credentials document*

Automated Telephone Randomization

Users can randomize a participant by calling the toll-free number (**800.955.2342**), 24-hours-a-day, 7-days-a-week, regardless of location. Using your telephone's touch-tone pad, respond to each of the pre-recorded questions asked by WesTrax™. You will receive an e-mail confirmation within 2 hours.

Specifications for Automated IVRS Randomization

Once a potential participant's EVF is completed and the participant is eligible, s/he is ready to be randomized. Randomization can be completed by telephone using the automated telephone IVRS. Each SC staff member approved to use the randomization system must register via the Coordinating Center (CC) in advance to be allowed access to the system. Each registered person will have a unique user ID number (the 2-digit site number + 4-digit staff ID) and personal identification number (PIN) to use when accessing the system. The IVRS can be accessed by dialing **1-800-955-2342** and is available 24 hours a day, 7 days a week. Following is a script of what will be heard on the telephone randomization system and instructions for

completing each step of the randomization. If you have problems, contact the WesTrax™ Help Center at **1-800-509-5559**.

Instructions for Automated Telephone Randomization

Logon/Set Up

For English, press 01.

- Press the numbers 01 on your telephone.

Please enter your assigned user identification number followed by the pound or hash key.

- Enter your user ID number (2-digit site code + 4-digit staff ID), then press the pound key (#).

Please enter your personal identification number or PIN followed by the pound or hash key.

- Enter your PIN, then press the pound key (#).

"*Welcome to the WesTrax Interactive Voice Response System for the Lung Screening Study. Before continuing, please verify that every question on the EVF has been completed. At any time, you can press the pound key to return to the main menu or the star key to return to the previous question."*

"Main menu: To randomize a new participant, press 1. To listen to the randomization group of a previously randomized participant, press 2. To hear these options again, press 3. To exit, press 0."

- If you wish to randomize a new participant, press **1**. If you wish to hear the randomization group assignment of a previously randomized participant, press **2**. If you wish to hear the main menu again, press **3**. To exit the sys-tem, press **0**.

Participant Data (EVF Part A: Administrative Section)

If you press **1** on the main menu to randomize a new participant, the call will continue as follows.

Please enter the individual's date of birth. Enter 2 digits for the month, 2 digits for the day, and 4 digits for the year.

- Enter the individual's date of birth (DOB) as recorded on the EVF.

You entered (MO/DAY/YEAR). If this is correct, press 1. If incorrect, press 3.

- If the DOB was entered correctly, press **1**. If it was entered incorrectly, press **3**. If you press **1**, the call will continue with the next instruction. If you press **3**, the previous instruction will be repeated.

The system will calculate the individual's age. If the individual is not between the ages of 55 and 74, the randomization will be ended as follows.

This participant is not eligible for randomization.

You will automatically be returned to the main menu.

If the individual is between 55 and 74, you will be given the next instruction.

Please enter the gender of the individual. Enter 1 for male or 3 for female.

- If the individual is male, press **1**. If she is female, press **3**.

You entered (male/female). If this is correct, press 1. If incorrect, press 3.

- If the individual's gender was entered correctly, press **1**. If it was entered incorrectly, press **3**. If you press **1**, the call will continue with the next instruction. If you press **3**, the previous instruction will be repeated.

Please enter the preprocessing number followed by the pound key.

- Enter the preprocessing number followed by the pound key (#).

The preprocessing number is (PREPROCESSING #). If this is correct press 1. If incorrect, press 3."

- If the preprocessing number was entered correctly, press **1**. If not, press **3**. If you press **1**, the call will continue with the next instruction. If you press **3**, the previous instruction will be repeated.

Smoking Information (EVF Part B: Eligibility Verification, Q1–2)

Please enter the individual's smoking status. For current smoker, press 1, for former smoker, press 3. If he or she never smoked, press 4.

- If the individual is a current smoker, press **1**. For a former smoker, press **3**.
  If the individual never smoked, press **4**.

You entered that this individual (is a current smoker / is a former smoker / never smoked). If this is correct, press 1. If incorrect, press 3.

- If the individual's smoking status was entered correctly, press **1**. If it was entered incorrectly, press **3**. If you press **1**, the call will continue with the next instruction. If you press **3**, the previous instruction will be repeated.

If the individual never smoked, the randomization will be ended as follows.

This participant is not eligible for randomization.

You will automatically be returned to the main menu.

If the individual is a former smoker, you will be asked to enter whether the individual quit smoking more than 15 years ago, 15 years ago, or fewer years ago.

How long ago did the individual quit smoking? If he or she quit smoking more than 15 years ago, press 1. If he or she quit smoking 15 or fewer years ago, press 3.

- If the individual quit smoking more than 15 years ago, press **1**. If the s/he quit smoking 15 or fewer years ago, press **3**.

You entered that he or she quit smoking (more than 15 years ago / 15 or fewer years ago). If this is correct, press 1. If incorrect, press 3.

- If the number of years was entered correctly, press **1**. If not, press **3**. If you press **1**, the call will continue with the next instruction. If you press **3**, the previous instruction will be repeated.

If the individual quit smoking more than 15 years ago, the randomization will be ended as follows.

This individual is not eligible for randomization.

You will automatically be returned to the main menu.

If the individual is a former smoker and quit smoking 15 or fewer years ago, or if the individual is a current smoker, you will be given the next instruction.

The following questions are needed to calculate the individual's pack-year tobacco exposure. Using 2 digits, please enter the age at which the individual began smoking.

- Using 2 digits, enter the age the individual began smoking, as recorded on the EVF. Zero fill if necessary.

You entered (AGE STARTED) years of age. If this is correct, press 1. If incorrect, press 3.

- If the age was entered correctly, press **1**. If it was entered incorrectly, press **3**. If you press 1, the call will continue with the next instruction. If you press **3**, the previous instruction will be repeated.

Using 3 digits, enter the number of cigarettes the individual usually smoked per day.

- Using 3 digits, enter the number of cigarettes smoked per day, as recorded on the EVF. If the number of cigarettes smoked per day is smaller than **100**, the number entered must be zero filled. For example, **20** cigarettes would be entered by pressing **020**.

You entered (# CIGARETTES) cigarettes per day. If this is correct, press 1. If incorrect, press 3.

- If the number of cigarettes was entered correctly, press **1**. If not, press **3**. If you press **1**, the call will continue with the next instruction. If you press **3**, the previous instruction will be repeated.

If the individual is a former smoker, you will be asked to enter the age at which the individual quit smoking for the last time.

Using 2 digits, enter the age at which this individual quit smoking for the last time.

- Using 2 digits, enter the age this individual quit smoking for the last time, as recorded on the EVF.

You entered (AGE QUIT) years of age. If this is correct, press 1. If incorrect, press 3.

- If the age was entered correctly, press **1**. If it was entered incorrectly, press **3**. If you press **1**, the call will continue with the next instruction. If you press **3**, the previous instruction will be repeated.

Did this individual ever quit smoking for a period of 1 or more years? Press 1 for Yes or 3 for No.

- If this individual ever quit smoking for a period of one or more years, press **1**. If not, press **3**.

You entered (YES/NO). If this is correct, press 1. If incorrect, press 3.

- If the response was entered correctly, press **1**. If not, press **3**. If you press **1**, the call will continue with the next instruction. If you press **3**, the previous instruction will be repeated.

If you pressed **1** for **Yes**, you will be given the following instruction.

Using 2 digits, enter the number of years in total that he or she did not smoke.

- Using 2 digits, enter the number of years the individual did not smoke, as recorded on the EVF. If the number of years not smoking is smaller than **10**, the number entered must be zero filled. For example, **5** years would be entered by pressing **05**.

You entered (# OF YEARS) years. If this is correct, press 1. If incorrect, press 3.

- If the number of years was entered correctly, press **1**. If it was entered incorrectly, press **3**. If you press **1**, the call will continue with the next instruction. If you press **3**, the previous instruction will be repeated.

When all the information is entered correctly, the system will calculate the pack-years of tobacco exposure.

This individual has a total pack-year history of (XX.X).

- Record the number of pack-years in the space provided on the EVF.

If the number of pack-years is smaller than **30.0**, the randomization will be ended as follows.

This participant is not eligible for randomization.

You will automatically be returned to the main menu.

If the number of pack-years is **30.0** or more, the call will continue as follows.

Eligibility Criteria - Continued (EVF Part A: Eligibility Verification, Q15)

Looking at question 15 on the EVF, are any of the questions number 3 through 14 marked Yes? If Yes, press 1. If No, press 3.

- Refer to questions 3 through 14 on the EVF. If any questions are marked **Yes**, press **1**. If **all questions** are marked **No**, press **3**.

You entered that (one or more/none) of the questions 3 to 14 are marked Yes. If this is correct, press 1. If incorrect, press 3.

- If the response was entered correctly, press **1**. If the response was entered incorrectly, press **3**. If you press **1**, the call will continue with the next instruction. If you press **3**, the previous instruction will be repeated.

If you pressed **1** for **Yes**, the randomization will be ended as follows.

This participant is not eligible for randomization.

You will automatically be returned to the main menu.

Randomization Information (EVF Part C: Randomization And Enrollment)

After answering all of the questions, the individual will be randomized and the PID number and randomization group will be assigned.

This participant has been assigned participant ID number (##-#####-#). This participant has been assigned to the (spiral CT/chest x-ray) randomization group.

- Record the date of randomization/enrollment, the Participant ID (PID) number, and the randomization group assignment on Part C of the EVF.

To hear this information again, press 1. To continue, press 3.

- If you wish to hear the PID and assigned randomization group again, press **1**. If you want to perform another activity, press **3**. If not, you may disconnect.

This randomization was successful. Thank you.

You will automatically be returned to the main menu.

After randomization is complete, you will receive an e-mail confirmation report within 2 hours. The confirmation report will include the unique pre-processing number, so that you can match it to the appropriate EVF and participant. Review the information recorded on the EVF for accuracy and file the confirmation report and the EVF in the participant's study file (see the section on Randomization Confirmation below).

Verifying Previously Randomized Participants' Data (Optional)

If you press **2** on the main menu to listen to the randomization group assignment of a previously randomized participant, the call will continue as follows.

Please enter the 8-digit participant identification number followed by the pound key for the participant for whom you would like to hear randomization information.

- Enter the PID for the participant in question followed by pound key (#).

You entered (PID number). If this is correct, press 1. If incorrect, press 3.

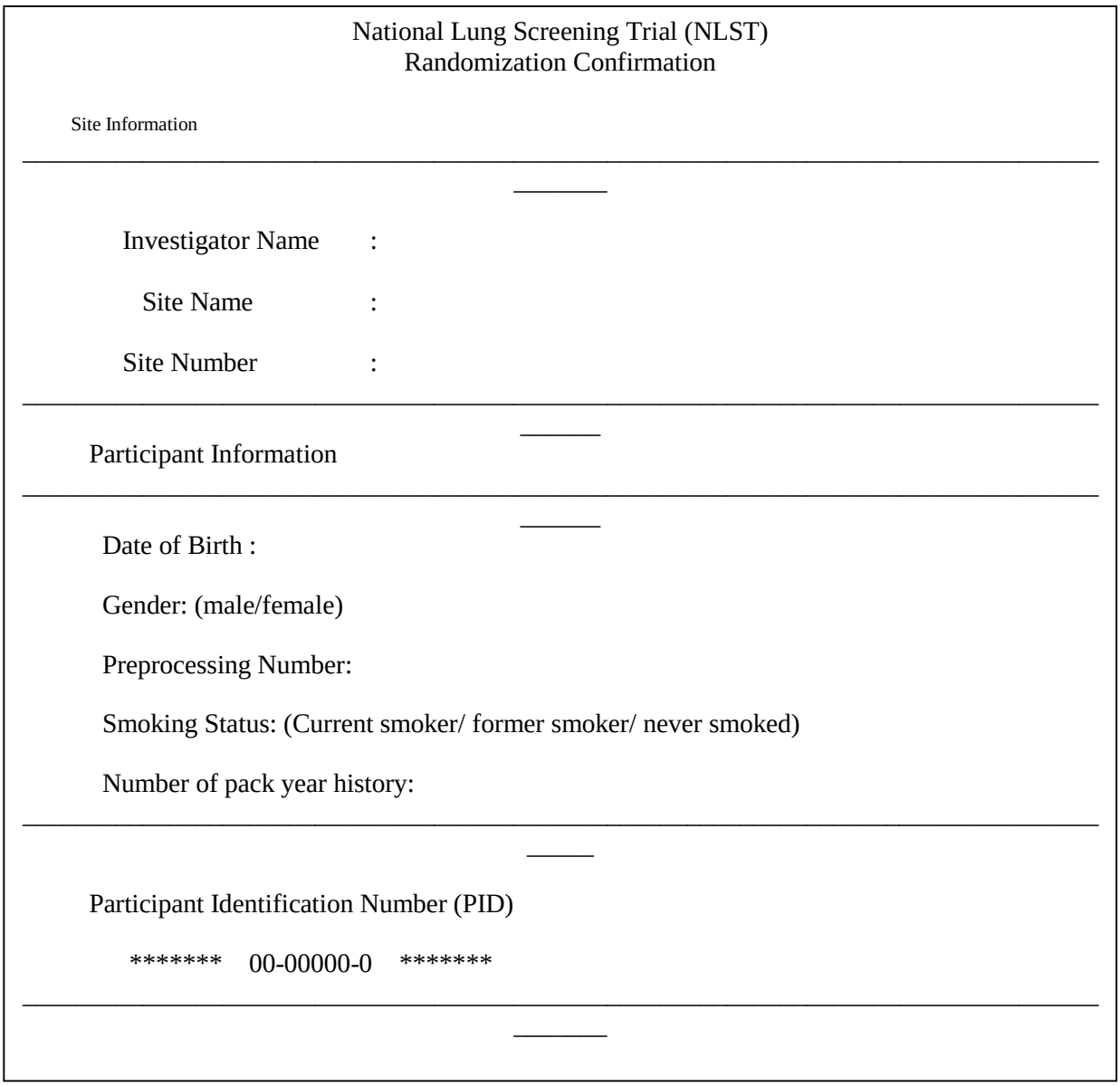
- If the PID number was entered correctly, press **1**. If not, press **3**. If you press **1**, the call will continue with the information requested. If you press **3**, the previous instruction will be repeated.

This participant was randomized on (date) to the (spiral CT/chest x-ray) randomization group. If you need a confirmation e-mail of this information, please contact the Help Center at 1-800-509-5559.

You will automatically be returned to the main menu.

Randomization Confirmation

A randomization that is successfully completed by using the IVRS will generate a confirmation (Figure 247) to be delivered from the WesTrax™ system to your SCs dedicated e-mail account within two hours of the phone call. Upon receiving a confirmation from the WesTrax™ system, please review it for any errors. If you have inadvertently entered into the WesTrax™ system data that is within valid ranges, but incorrect, then please refer to the WesTrax™ SC Edit Form Instructions section of this document. If the confirmation does not contain any errors it should be filed in the participant's study folder.



National Lung Screening Trial (NLST)
Randomization Confirmation

Site Information

Investigator Name :

Site Name :

Site Number :

Participant Information

Date of Birth :

Gender: (male/female)

Preprocessing Number:

Smoking Status: (Current smoker/ former smoker/ never smoked)

Number of pack year history:

Participant Identification Number (PID)

******* 00-00000-0 *******

Figure 247: *Randomization confirmation*

Batch Randomization Instructions

Data File Completion

Before you enter the EVF data into the data file you must obtain a pre-processing number (see the Pre-Processing User's Guide). Each time you start the preprocessor, a "session" will be created and will allow you to obtain a pre-processing number. During the session, users can enter the EVF data for each participant and a record will be appended to the file containing all the data fields. You may create your own data file (Figure) that contains each of the following data fields: **PreProcessID**, **CurrSite**, **RndSite**, **ScreenerID**, **DOB**, **Gender**, **Smoker- Type**, **Age**, **AgeBeganSmoking**, **CigsPerDay**, **AgeQuitSmoking**, **OneOrMoreYearsNS**, **TotalYearsNS**, **PackYears**, **Q15** (see also Duplicate Check in the section on Randomization Operations).

E-Mail Data File

E-mail the **Batch Randomization** spreadsheet to NCI_Batch@westat.com. You will receive an e-mail randomization confirmation within 24 hours from receipt of an e-mail request. (This turnaround time is per data file).

NOTE: All e-mails are sent to and received only from the site's dedicated e-mail address. Check your site's dedicated e-mail address periodically to obtain confirmations and new information pertaining to the WesTrax™ system.

See also the section on file generation and file naming convention and Figure 248 for a view of the **Batch Randomization** spreadsheet.

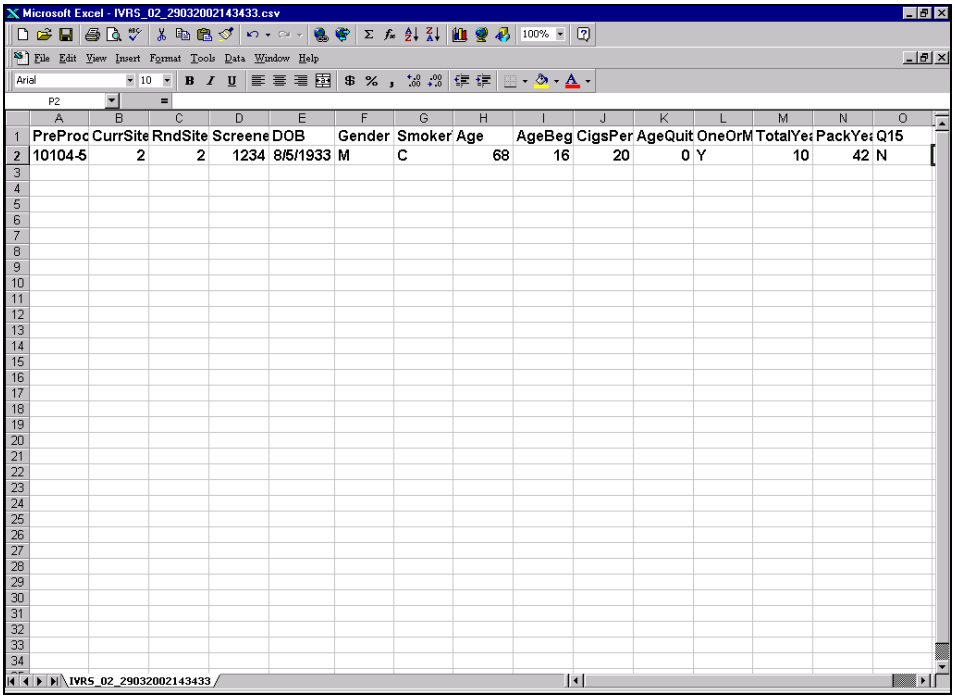


Figure 248: *Batch randomization spreadsheet*

After a batch file has been successfully processed by the WesTrax™ system, you will be e-mailed within 24 hours a copy of your original file with three (3) extra columns. The three added columns are **StudyArm** – indicating the participant's assignment to the SCT or X-Ray group, **PID** – the participant's unique ID number, and **RandDate** – the date the participant was randomized (see the appended fields in Figure 249).

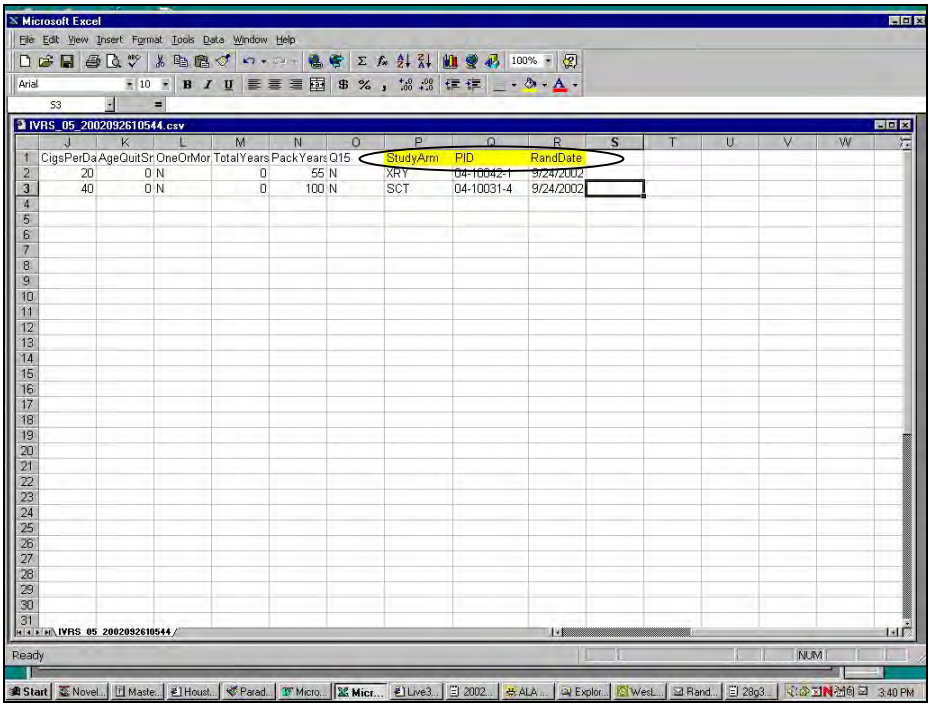


Figure 249: *The three additional WesTrax-appended columns*

Batch Randomization Exception Report

If, in the submitted data file, WesTrax™ finds invalid data, you will receive a **Batch Randomization Exception Report**, and that participant will not be randomized from the data file that contains invalid data.

The following are reasons for rejection:

- You have submitted a spreadsheet that does not include all of the requested data fields.
- The data under each data field is invalid.

If you receive a **Batch Randomization Exception Report** e-mail, save the corresponding file **XXXXXX.001** as **XXXXXX.CSV**, make the necessary corrections per **Batch Randomization Exception Report**, save the corrections as **xxxxxx.CSV**, and resubmit the saved correction file to NCI_Batch@westat.com.

NOTE: Be sure to open the file with the Notepad or Wordpad application, as opening it in Excel and subsequently saving the file in Excel can alter the formatting.

You can submit a new data file with the corrected data, and you will receive a confirmation within 24 hours from receipt of the e-mail.

National Lung Screening Trial (NLST)
Batch Randomization Exception Report
for File xxxxxxxxxxxxxxx.CSV

Site Information

_____

Investigator Name: John Doe, MD

Site Name: National Cancer Institute

Site Number: 2

_____

Instructions:

_____

Save corresponding file xxxxxx.001 as xxxxxx.CSV
Open spreadsheet xxxxxx.CSV
Make corrections per errors below
Save corrections
Resubmit xxxxxx.CSV to NCI_Batch@westat.com

_____

Errors:

_____

Line 1:
PRE_PROC_ID:Data Field not provided.

Line 2:
PRE_PROC_ID:Invalid Preprocess ID.
Gender: Invalid gender
Age: too old

_____ Date and Time

Figure 250: *Batch Randomization Exception Report*

Randomization Confirmation of Batch Submissions

A randomization that is successfully completed by using the batch randomization method will generate a confirmation to be delivered from the WesTrax™ system to your SC's dedicated e-mail account within 24 hours of submission. Upon receiving the confirmation, please review it for any errors. If you have inadvertently submitted data that is within valid ranges, but incorrect, then please refer to the WesTrax™ SC Edit Form Instructions section of this document. If the confirmation does not contain any errors it should be filed in the participant's study folder.

WesTrax™ Help Center

If you have questions about using WesTrax™ or participant randomization, call the WesTrax™ Help Desk at **1-800-509-5559**. The Help Desk is available 24 hours a

day, 7 days a week. All overflow or after-hours calls will be handled by our answering service. All pages are considered top priority and will be returned within 15 minutes from receipt of the page. When leaving a message with the answering service, please provide your name, study name, and your telephone number.

Manual Randomization In System Outages

The following procedures are intended for use by personnel at the SCs (site coordinators or systems support staff) responsible for randomizing potential study participants for the NLST. During normal operation the WesTrax™ system supports randomization through two different methods. (1) The first method is by **batch** submission of EVF information from a file that is created by the system (see the sections on Duplicate Check and EVF Data Entry). Participants randomized under this method will have confirmations delivered to the SC's dedicated e-mail approximately 24 hours after the data submission to WesTrax™. (2) The second method **automated telephone IVRS**. The IVRS allows for the randomization of potential participants after completion of an interactive telephone script confirming the eligibility of the participant. Participants randomized under this approach will have their confirmations delivered to the SC's dedicated e-mail address approximately 2 hours after the data submission to WesTrax™.

During brief periods of planned system maintenance or unplanned system outages, certain WesTrax™ components may be unavailable to SC staff for randomization. Planned maintenance will be preceded by an e-mail notice from WesTrax™ one week prior to the service activities and again 24 hours before the maintenance. Generally the planned service outages will be scheduled at a time that is least disruptive to the SC's workflow (e.g., early morning). In addition, the majority of the planned system maintenance operations will be executed in less than 2 hours. When planned service outages are scheduled, it is recommended that the SCs temporarily organize their workflow around this loss of service. When WesTrax™ experiences an unplanned outage, or the workflow cannot be temporarily reorganized to limit the SC's randomization needs, the following manual randomization procedures should be utilized.

Note: Manual randomization procedures are intended for situations in which a WesTrax™ component (IVRS or Batch Randomization) is unavailable, and immediate randomization is necessary. The SCs will be notified of the outage immediately upon its detection by WesTrax™. The SCs will receive an e-mail advising them of the possible options for manual randomization. There may be instances where problems are detected and resolved by WesTrax™ before the SCs receive the service disruption e-mail message. If this occurs, the SCs will be advised to verify the receipt of confirmations for participants randomized during the period of time that the WesTrax™ system experienced difficulties. After the problem has been resolved, the SCs will receive a final e-mail message informing them that the WesTrax™ system is operational.

Example Scenarios

Scenario 1 – IVRS Phone Service Unavailable

- E-mail batch randomization would remain unaffected in this situation. If you normally use the batch process, you may continue to send in randomization batches as usual.
- If you use the phone system and urgently need to randomize a participant, use **Option 1** or **Option 2** under Options for Manual Randomization.

Scenario 2 – Phone, Batch Randomization Services Unavailable

- Use **Option 1** or **Option 2** under Options for Manual Randomization.

Scenario 3 – Phone, Batch, And E-Mail Services Unavailable

- Use **Option 3** under Options for Manual Randomization.

Options for Manual Randomization

Option 1 – Fax the Eligibility Verification Form (EVF)

1. Make a copy of the EVF for the participant that you wish to randomize.

2. **Blacken** out the participant's name on the front page of the EVF copy.

3. Attach the PID label to the front page of the EVF in the upper right corner of the box in Part A of the form. (If a label is unavailable, write the PID number **clearly** in Part A of the form.)

4. Fax the EVF (attention: Help Center) to WesTrax™ at **713-529-4924**.

5. Immediately call the WesTrax™ Help Center at **800-509-5559**. Inform the Help Center how many EVFs are being faxed and provide your **phone number** and valid **Screener ID**.

6. The Help Center will call you back as soon as possible with the screening arm designation for each participant. ***Note**: This method requires approximately 5 minutes for each potential participant randomized.*

7. Randomization confirmations will be e-mailed to the SC's dedicated WesTrax™ e-mail account within 24 hours.

Option 2 – E-Mail the Batch Randomization File

1. Create a batch randomization file by using as shown in the Randomization Operations section of this document. This file should be created in exactly the same manner as a normal batch randomization file. From your SC's dedicated e-mail address e-mail the batch file as an attachment to NCI_Batch@westat.com just as you would normally send a batch.

2. Following this, call the WesTrax™ Help Center at **800-509-5559**. Inform the Help Center that you have sent a batch randomization file and need immediate manual randomizations. You will be asked to provide your **name**, **Screener ID**, and **phone number**.

3. The WesTrax™ Help Center will ask you to verbally verify the **PID number** for each participant you wish to manually randomize.

4. After concluding the phone call, the WesTrax™ Help Center will manually randomize the participants and call you back with the screening arm designation. ***Note**: This method requires approximately 5 minutes for each participant randomized.*

5. Randomization confirmations will be e-mailed to the SC's dedicated WesTrax™ e-mail account within 24 hours.

Option 3 – Call Help Center to Randomize Potential Participants

***Note**: This option is the most labor intensive due to the requirement that the WesTrax™ Help Center verify each data point verbally.*

1. Collect the EVF for each potential participant you wish to randomize.
2. Call the WesTrax™ Help Center at **800-509-5559**. Provide the Help Center with your **Screener ID** and **PIN**.
3. Provide the Help Center with the following information about the first potential participant: **Date of Birth**, **Gender**, **Screening Center**, **Preprocessing number**, **PID number**, and answers to questions **1**, **2**, and **15** of the EVF.
4. Wait for the Help Center to manually randomize and provide the screening arm designation for this participant. ***Note**: This method requires approximately 8 minutes for each participant randomized.*
5. After the WesTrax™ Help Center has provided the screening arm designation for the first participant, verbally verify the screening arm and restate the participant's **PID number** and **Preprocessing number**.
6. Proceed to the next potential participant and repeat steps **3** through **5** for each potential participant that you are attempting to randomize.
7. Randomization confirmations will be e-mailed to the SC's dedicated WesTrax™ e-mail account within 24 hours.

WesTrax™ SC Edit Form Instructions

Introduction

The WesTrax™ randomization system has many data quality checks. They are performed in real-time on data submitted through the batch randomization process or entered through the IVRS module. These checks contribute to assuring that erroneous data does not enter and reside in the system. However, there are opportunities in the field for data that is within valid ranges but has been improperly keyed, transposed, or transcribed to enter the WesTrax™ system. Erroneous data entering the system can have a magnified, on-going, negative impact on randomization functions if not corrected at the earliest stage possible.

When SC personnel discover that randomization information has been improperly keyed or incorrectly submitted, the WesTrax™ SC Edit Form should be utilized. The SC coordinator or designee will complete the form and document the known details of the event. In addition to completing the document, the SC must manually correct any corresponding documentation in the participant folder that is impacted by the error, e.g., EVF, ES, etc.. The form should be faxed to the WesTrax™ Help Center at **713-529-4924** for appropriate resolution. A copy of the edit form should be placed in the participant folder and the original document should be forwarded with the weekly shipment of data collection forms to the CC. Once WesTrax™ has verified and approved the data change, it will be implemented within the WesTrax™ system.

Requests will be considered on a case-by-case basis, and some change requests may have wide ranging implications and may require NCI approval before implementation. The CC may require additional documentation from the SC coordinator prior to implementing the change. Not all data change requests through the WesTrax Edit Form will be honored. A full view of the WesTrax™ SC Edit Form is shown below.

WESTRAX™ SC EDIT FORM

ADMINISTRATIVE SECTION

Completion Date: |__|__|-|__|__|-|2|0|__|__| (Month / Day / Year)

Screening Center ID: |__|__|

Screening Center Staff ID: |__|__|__|__|

SC staff member telephone number (____) _____

SC staff member fax number (____)_____

WSC

Participant ID Label

Date of Randomization: |_|_|-|_|_|-|2|0|_|_| (Month / Day / Year)

PART A. DATA UPDATE SECTION

INSTRUCTIONS: Circle EVF Item, complete incorrect data, corrected data and a description of the error in Part B below for each item to be updated. *Note: Upon correction of asterisked items it may be necessary to submit a Protocol Violation Form (PVF) if it is determined that the participant is a randomized ineligible

EVF Item	Variable Name (WesTrax™ Use Only)	Incorrect Data	Corrected Data
1. Date of Birth*	*DOB** (Age at DOR < 55 or Age at DOR > 74 = ineligible)		
2. Gender	*Gender*		
3. SC Staff ID	*ScreenerID*		
4. Smoking Status	*SmokerType*		
5. Former-Quit*	*FormerQuit** (>15 = ineligible)		
6. Age started smoking	*AgeBeganSmoking*		
7. Cigarettes per day	*CigsPerDay*		
8. Age stopped smoking	*AgeQuitSmoking*		
9. One + years stopped smoking	*OneOrMoreYearsNS*		
10. Years did not smoke	*TotalYearsNS*		
11. Total Pack Years*	*PackYears** (29.95 = ineligible)		
12. Any 'Yes' to Q3-Q14*	*Q15** (Yes = ineligible)		

PART B. COMMENTS

EVF Item #	Description of the Error

Fax the completed WesTrax™ SC Edit Form to the WesTrax Help center at (713) 529-4924.
Include the original document in the weekly shipment of forms to the CC.

Figure 251: *WesTrax™ SC Edit Form*

Specifications for Completing the SC Edit Form

This form is to be completed by an SC staff member to document changes to data after a study participant has been successfully randomized and the SC has received a confirmation. Specifications for completing each item of the form are given below.

Administrative Section

Participant ID Label: Affix a PID label to the space provided in the upper right corner of the form.

Randomization Date: Record the date when the participant was randomized. Month and day should be zero filled, and the last two digits of the year should be recorded (**02**/**07**/20**02**).

Completion Date: Record the date the WesTrax SC Edit Form was completed. Month and day should be zero-filled, and the last two digits of the year should be recorded (**02**/**07**/20**02**).

Screening Center ID: Record the two-digit SC ID number.

Screening Center Staff ID: Record the four-digit SC staff ID number of the person completing the form.

SC staff member telephone number: Record the telephone number of the person completing the form.

SC staff member fax number: Record the fax number of the person completing the form.

Part A. Data Update Section

One WesTrax™ SC Edit Form should be completed for each participant with erroneous data. For each EVF item requiring a data correction, circle the item number requiring the change, enter the incorrect data value and the corrected data value along with a description of the error. Multiple changes to one EVF form can be listed. However, once the form has been submitted to the CC, subsequent edits should be noted on another WesTrax™ SC Edit Form.

EVF Item: Circle the item from the Eligibility Verification Form that requires correction. In some cases multiple items will need to be corrected as a result of one error, e.g., date of birth errors would affect both the age of the participant at the time of randomization and the total pack years that the participant smoked.

Variable Name: ****For Administrative Use Only****

Incorrect Data: Enter the incorrect data value in this field on the form. Be sure to consider other values that may have been affected by this error and make corrections appropriately.

Corrected Data: Enter the correct value corresponding to the incorrect data value in this form field.

Part B. Comments

EVF Item #: Record the EVF Item # from the above section that corresponds with the comment. For example, if providing a comment about an error to the Date of Birth, record "1" as the EVF Item #. Only record the EVF Item # once per comment, even if the Description of the Error continues for more than one line.

Description of the Error: Provide a brief, but detailed description of each error. Details should include the date of discovery, the type of error (transcription, keying, transposing) as well as any corrective actions taken to reduce the potential for the error to occur in the future.

As an example of completing the WesTrax™ SC Edit Form, suppose there is a change to the date of birth due to a transposing error by a staff member keying information into the IVRS during a randomization phone call. It might be recorded as follows:

Table 1: Example of completing the WesTrax™ SC Edit Form

EVF Item	Variable Name	Incorrect Data	Corrected Data
1. Date of Birth*	*DOB** (Age at DOR < 55 or Age at DOR > 74 = ineligible)	03/21/1942	03/12/1942

PART B. COMMENTS	
EVF Item #	Description of the Error
1	Transposing error was discovered after receipt of randomization confirmation on 3/31/03. Discussed the error with data entry
	personnel to reduce potential for future occurrences. The following error does affect pack year calculation; see correction below.

After Completing the Form

- The form should be checked to make sure it is accurate, legible, and complete.
- The SC staff member should review the form and make certain that no additional variables will be affected by the requested data change; if additional variables will be affected then this should be appropriately indicated on the form.
- Fax the completed form to the WesTrax™ Help Center and include the original WesTrax™ SC Edit form in the weekly shipment to the CC.
- File a copy of the form in the participant's study file.

Appendix 2-13 Sample Potential Participant Tracking Log

National Lung Screening Trial (NLST)

SAMPLE POTENTIAL PARTICIPANT TRACKING LOG

SC _____ SC Coordinator _____

Full Name	Address (incl. ZIP code)	Home Telephone	Work Telephone	Other Telephone	Date of Birth	Sex (M or F)	Date ES Completed	Eligibility Status (E, I, or R)
					/ /		/ /	
					/ /		/ /	
					/ /		/ /	
					/ /		/ /	
					/ /		/ /	
					/ /		/ /	
					/ /		/ /	
					/ /		/ /	
					/ /		/ /	

CODES

Sex:
M = Male
F = Female

Eligibility Status:
E = Eligible
I = Ineligible
R = Randomized

Appendix 2-14 SC Cumulative Recruitment Summary Form

National Lung Screening Trial (NLST)

SC CUMULATIVE RECRUITMENT SUMMARY FORM

Recruitment Activity	SC										TOTAL
	01	02	03	04	05	06	08	09	10	11	
Recruitment packets mailed											
Eligible participants pending randomization											
Ineligible participants											
Number randomized											
Spiral CT											
Chest x-ray											
Screening exams scheduled, but not yet complete											
Spiral CT											
Chest x-ray											
Number screened*											
Spiral CT											
Chest x-ray											
Percent screened**											
Spiral CT											
Chest x-ray											
Screened+Scheduled											
Percent Screened+Scheduled											
Week ending											

*Number screened = Number of screening exams completed regardless of whether or not radiologist has read

**Percent screened = Number screened /number randomized

National Lung Screening Trial (NLST)

Specifications for Completion of the SC Cumulative Recruitment Summary Form

This web-based form is to be completed by the SC by the close of business every Friday or by close of business on the proceeding business day, if Friday is a holiday. The form can be accessed at **http://www.plcoarp.org/NLST/**. The purpose of the form is to provide an overview of recruitment efforts to the NCI on behalf of the screening centers.

Specifications for completing each item of the form are given below.

Completing the Recruitment Activity Table:

Enter all information in the column, which represents your screening center.

Recruitment packets mailed: Enter the cumulative number of recruitment packets mailed to date. New packets mailed this week should be added to the total mailed from previous weeks, therefore the number entered will increase each week.

Eligible participants pending randomization: Enter the total number of eligible participants pending randomization. This includes all those who were pending randomization last week that have not been randomized to date. The number of those pending randomization will change weekly since some participants pending randomization from last week will be removed from the total once randomized and new participants who are pending randomization will be added.

Ineligible participants: Enter the cumulative number of ineligible participants to date. This number will increase weekly as more ineligible participants are identified.

Number randomized: Enter the cumulative number of participants randomized to date. This number will increase weekly as the number of randomized participants increases.

Spiral CT: Enter the cumulative number of participants randomized to the spiral CT study arm. This number will increase weekly as the number of participants randomized to spiral CT increases.

Chest x-ray: Enter the cumulative number of participants randomized to the chest x-ray study arm. This number will increase weekly as the number of participants randomized to chest x-ray increases.

Screening exams scheduled, but not yet complete: Enter the cumulative number of screening exams scheduled for those participants already randomized, but not yet completed. This number will change weekly since some screening exams from the previous week will still be pending, and new screening exam appointments will be added.

Spiral CT: Enter the cumulative number of spiral CT screening exams scheduled for randomized participants, but not yet completed. This number will change weekly since some screening exams from the previous week will still be pending, and new screening exam appointments will be added.

Chest x-ray: Enter the cumulative number of chest x-ray screening exams scheduled for randomized participants, but not yet completed. This number will change weekly since some screening exams from the previous week will still be pending, and new screening exam appointments will be added.

Number screened: Enter the cumulative number of screening exams completed regardless of whether the radiologist has read the exam.

Spiral CT: Enter the cumulative total of participants screened by spiral CT. This number will increase each week as more participants are screened.

Chest x-ray: Enter the cumulative total of participants screened by chest x-ray. This number will increase each week as more participants are screened.

Percent screened: The percent screened represents the number of randomized participants that also have been screened. This is calculated by the number screened divided by the number randomized. This field will be calculated automatically.

Spiral CT: This is the percent of participants randomized to spiral CT that have been screened (the number screened with spiral CT divided by the number randomized to spiral CT). This field will be calculated automatically.

Chest x-ray: This is the percent of participants randomized to chest x-ray that have been screened (the number screened with chest x-ray divided by the number randomized to chest x-ray). This field will be calculated automatically.

Screened plus scheduled: This represents the number of screening exams the SC has completed in addition to the number of screening exams the SC has scheduled for randomized participants. This field will be calculated automatically.

Percent Screened Plus Scheduled: This represents the percent of screening exams that are complete plus the number of screening exams scheduled for randomized participants divided by the number of randomized participants. This field will be calculated automatically.

Week ending: Enter this week's end date (usually a Friday unless there is a holiday).

Totals will be calculated for all screening centers. Please only enter information in your screening center column.

National Lung Screening Trial (NLST)

Specifications for Randomization Using the IVRS

Once the potential participant is eligible and the EVF is completed and the SC is in receipt of a signed informed consent, s/he is ready to be randomized. Randomization is completed by telephone using the Interactive Voice Response System (IVRS). Each SC staff member approved to use the randomization system must register via the CC in advance to be allowed access to the system. Each registered person will have a unique user identification number (his/her two-digit site number + four-digit staff ID) and personal identification number (PIN) to use when accessing the system. The IVRS can be accessed by dialing 1-800/880-5962 and is available 24 hours a day, seven days a week. Following is a script of what will be heard on the telephone randomization system and instructions for completing each step of the randomization.

Instructions:

LOGON/SET UP

"For English, press 01."
- Press the numbers 01 on your telephone.

"Please enter your assigned user identification number followed by the pound or hash key."
- Please enter your user ID number (two-digit site code + four-digit staff ID), then press the # key.

"Please enter your personal identification number or PIN followed by the pound or hash key."
- Please enter your PIN, then press the # key.

"Welcome to the Westrax Interactive Voice Response System for the Lung Screening Study. Before continuing, please verify that every question on the EVF has been completed. At any time, you can press the pound key to return to the main menu or the star key to return to the previous question."

"Main menu. To randomize a new participant, press 1." "To listen to the randomization group of a previously randomized participant, press 2." "To hear these options again, press 3." "To exit, press 0."
- If you would like to randomize a new participant, press 1. If you would like to hear the randomization group assignment of a previously randomized participant, press 2. If you would like to hear the main menu options again, press 3. If you would like to exit the system, press 0.

PARTICIPANT DATA (EVF PART A: ADMINISTRATIVE SECTION):

If you press 1 on the main menu to randomize a new participant, the call will continue as follows.

"Please enter the individual's date of birth. Enter two digits for the month, two digits for the day, and four digits for the year."
- Enter the individual's date of birth as recorded on the EVF.

"You entered (MO/DAY/YEAR). If this is correct, press 1. If incorrect, press 3."

- If the individual's date of birth was entered correctly, press 1. If the individual's date of birth was entered incorrectly, press 3. If you press 1, the call will continue with the next instruction. If you press 3, the previous instruction will be repeated.

The system will calculate the individual's age. If the individual is not between the ages of 55 and 74, the randomization will be ended as follows.

"This participant is not eligible for randomization."
You will automatically be returned to the main menu.

If the individual is between the ages of 55 and 74, you will be given the next instruction.

"Please enter the gender of the individual. Enter 1 for male or 3 for female."
- If the individual is male, press 1. If the individual is female, press 3.

"You entered (male / female). If this is correct, press 1. If incorrect, press 3."
- If the individual's gender was entered correctly, press 1. If the individual's gender was entered incorrectly, press 3. If you press 1, the call will continue with the next instruction. If you press 3, the previous instruction will be repeated.

"Please enter the pre-processing number followed by the pound key."
- Enter the pre-processing number followed by the # key.

"The pre-processing number is (PRE-PROCESSING #). If this is correct, press 1. If incorrect, press 3."
- If the pre-processing number was entered correctly, press 1. If not, press 3. If you press 1 the call will continue with the next instruction. If you press 3, the previous instruction will be repeated.

SMOKING INFORMATION (EVF PART B: ELIGIBILITY VERIFICATION, Q1 - 2)

"Please enter the individual's smoking status. For current smoker, press 1, for former smoker, press 3, if he or she never smoked, press 4."
- If the individual is a current smoker, press 1. If the individual is a former smoker, press 3. If the individual never smoked, press 4.

"You entered that this individual (is a current smoker/is a former smoker/never smoked). If this is correct, press 1. If incorrect, press 3."
- If the individual's smoking status was entered correctly, press 1. If the individual's smoking status was entered incorrectly, press 3. If you press 1, the call will continue with the next instruction. If you press 3, the previous instruction will be repeated.

If the individual never smoked, the randomization will be ended as follows.

"This participant is not eligible for randomization."
You will automatically be returned to the main menu.

If the individual is a former smoker, you will be asked to enter whether the individual quit smoking more than 15 years ago, or 15 years or fewer years ago.

"How long ago did the individual quit smoking? If he or she quit smoking more than 15 years ago, press 1. If he or she quit smoking 15 or fewer years ago, press 3."

- If the individual quit smoking more than 15 years ago, press 1. If the individual quit smoking 15 or less years ago, press 3.

"You entered that he or she quit smoking (more than 15 years ago /15 or fewer years ago). If this is correct, press 1. If incorrect, press 3."

- If the number of years was entered correctly, press 1. If the number of years was entered incorrectly, press 3. If you press 1, the call will continue with the next instruction. If you press 3, the previous instruction will be repeated.

If the individual quit smoking more than 15 years ago, the randomization will be ended as follows.

"This individual is not eligible for randomization."
You will automatically be returned to the main menu.

If the individual is a former smoker and quit smoking 15 or less years ago, or if the individual is a current smoker, you will be given the next instruction.

"The following questions are needed to calculate the individual's pack-year tobacco exposure. Using two digits, please enter the age at which the individual began smoking."

- Enter the age this individual began smoking, using two digits, as recorded on the EVF. Zero fill if necessary.

"You entered (AGE STARTED) years of age. If this is correct, press 1. If incorrect, press 3."

- If the age was entered correctly, press 1. If the age was entered incorrectly, press 3. If you press 1, the call will continue with the next instruction. If you press 3, the previous instruction will be repeated.

"Using three digits, enter the number of cigarettes the individual usually smoked per day."

- Enter the number of cigarettes smoked per day, using three digits, as recorded on the EVF. If the number of cigarettes smoked per day is less than 100, the number entered must be zero filled. For example, 20 cigarettes would be entered by pressing 020.

"You entered (# CIGARETTES) cigarettes per day. If this is correct, press 1. If incorrect, press 3."

- If the number of cigarettes was entered correctly, press 1. If the number of cigarettes was entered incorrectly, press 3. If you press 1, the call will continue with the next instruction. If you press 3, the previous instruction will be repeated.

If the individual is a former smoker, you will be asked to enter the age at which the individual quit smoking for the last time.

"Using two digits, enter the age at which this individual quit smoking for the last time."

- Enter the age this individual quit smoking for the last time, using two digits, as recorded on the EVF.

"You entered (AGE QUIT) years of age. If this is correct, press 1. If incorrect, press 3."

- If the age was entered correctly, press 1. If the age was entered incorrectly, press 3. If you press 1, the call will continue with the next instruction. If you press 3, the previous instruction will be repeated.

"Did this individual ever quit smoking for a period of one or more years? Press 1 for Yes or 3 for No."

- If this individual ever quit smoking for a period of one or more years, press 1. If not, press 3.

"You entered (yes/no). If this is correct, press 1. If incorrect, press 3."

- If the response was entered correctly, press 1. If the response was entered incorrectly, press 3. If you press 1, the call will continue with the next instruction. If you press 3, the previous instruction will be repeated.

If you pressed 1 for Yes, you will be given the following instruction.

"Using two digits, enter the number of years in total that he or she did not smoke."

- Enter the number of years the individual did not smoke, using two digits, as recorded on the EVF. If the number of years not smoking is less than 10, the number entered must be zero filled. For example, 5 years would be entered by pressing 05.

"You entered (# OF YEARS) years. If this is correct, press 1. If incorrect, press 3."

- If the number of years was entered correctly, press 1. If the number of years was entered incorrectly, press 3. If you press 1, the call will continue with the next instruction. If you press 3, the previous instruction will be repeated.

When all of the information is entered correctly, the system will calculate the pack-years of tobacco exposure.

"This individual has a total pack-year history of (XX.X)."

- Record the number of pack-years in the space provided on the EVF.

If the number of pack-years is less than 30.0, the randomization will be ended as follows.

"This participant is not eligible for randomization."
You will automatically be returned to the main menu.

If the number of pack-years is 30.0 or more, the call will continue as follows.

ELIGIBILITY CRITERIA - CONTINUED (EVF PART A: ELIGIBILITY VERIFICATION, Q15)

"Looking at question 15 on the EVF, are any of the questions number 3 through 14 marked Yes? If Yes, press 1. If No, press 3."

- Refer to questions 3 through 14 on the EVF. If any questions are marked Yes, press 1. If all questions are marked No, press 3.

"You entered that (one or more/none) of the questions 3 to 14 are marked Yes. If this is correct, press 1. If incorrect, press 3."

- If the response was entered correctly, press 1. If the response was entered incorrectly, press 3. If you press 1, the call will continue with the next instruction. If you press 3, the previous instruction will be repeated.

If you pressed 1 for Yes, the randomization will be ended as follows.

"This participant is not eligible for randomization."

You will automatically be returned to the main menu.

RANDOMIZATION INFORMATION (EVF PART C: RANDOMIZATION AND ENROLLMENT)

After answering all of the questions, the individual will be randomized and the PID number and randomization group will be assigned.

"This participant has been assigned participant ID number (##-#####-#). This participant has been assigned to the (spiral CT/chest x-ray) randomization group."

- Record the date of randomization/enrollment, the Participant ID, and the randomization group assignment on Part C of the EVF.

"To hear this information again press 1. To continue, press 3."

- If you would like to hear the PID and assigned randomization group again press 1. If you would like to perform another activity, press 3. If not, you may disconnect.

"This randomization was successful. Thank you."
You will automatically be returned to the main menu.

After randomization is complete you will receive an email confirmation report within 2 hours. The confirmation report will include the unique pre-processing number so that you can match it to the appropriate EVF and participant. Review the information recorded on the EVF for accuracy and file the confirmation report and the EVF in the participant's study file.

VERIFYING INFORMATION ON PREVIOUSLY RANDOMIZED PARTICIPANTS (OPTIONAL):

If you press 2 on the main menu to listen to the randomization group assignment of a previously randomized participant, the call will continue as follows.

"Please enter the eight digit participant identification number followed by the pound key for the participant for whom you would like to hear randomization information."

- Enter the PID for the participant in question followed by the # key.

"You entered (PID number). If this is correct, press 1. If incorrect, press 3."

- If the PID number was entered correctly, press 1. If the PID was entered incorrectly, press 3. If you press 1, the call will continue with the information requested. If you press 3, the previous instruction will be repeated.

"This participant was randomized on (date) to the (spiral CT/chest x-ray) randomization group. If you need a confirmation e-mail of this information, please contact the Help Center at 1-800/509-5559."

You will automatically be returned to the main menu.

Appendix 2-17 WesTrax™ SC Edit Form

National Lung Screening Trial / Lung Screening Study (NLST/LSS)

WESTRAX™ SC EDIT FORM

ADMINISTRATIVE SECTION

Completion Date: |___|___|-|___|___|-|_2_|_0_|___|___|
Month Day Year

Screening Center ID: |___|___|

Screening Center Staff ID: |___|___|___|___|

SC staff member telephone number (____) _____

SC staff member fax number (____)_____

Participant ID Label

Date of Randomization: |_|_|-|_|_|-|2_|0_|_|_|
Month Day Year

PART A. DATA UPDATE SECTION

INSTRUCTIONS: Circle EVF Item, complete incorrect data, corrected data and a description of the error in Part B below for each item to be updated. *Note: Upon correction of asterisked items it may be necessary to submit a Protocol Violation Form (PVF) if it is determined that the participant is a randomized ineligible

EVF Item	Variable Name (WesTrax™ Use Only)	Incorrect Data	Corrected Data
1. Date of Birth*	*DOB** (Age at DOR < 55 or Age at DOR > 74 = ineligible)		
2. Gender	*Gender*		
3. SC Staff ID	*ScreenerID*		
4. Smoking Status	*SmokerType*		
5. Former-Quit*	*FormerQuit** (>15 = ineligible)		
6. Age started smoking	*AgeBeganSmoking*		
7. Cigarettes per day	*CigsPerDay*		
8. Age stopped smoking	*AgeQuitSmoking*		
9. One + years stopped smoking	*OneOrMoreYearsNS*		
10. Years did not smoke	*TotalYearsNS*		
11. Total Pack Years*	*PackYears** (≤29.95 = ineligible)		
12. Any 'Yes' to Q3-Q14*	*Q15** (Yes = ineligible)		

PART B. COMMENTS

EVF Item #	Description of the Error

Fax the completed WesTrax™ SC Edit Form to Ellen Martinusen at (301) 963-5455.
Include the original document in the weekly shipment of forms to the CC.

National Lung Screening Trial / Lung Screening Study (NLST/LSS)

Specifications for Completion of the Westrax™ SC Edit Form

This form is to be completed by an SC staff member to document changes to data after a study participant has been successfully randomized and the SC has received a confirmation.

Specifications for completing each item of the form are given below:

Administrative Section:

Participant ID Label: Affix a PID label to the space provided in the upper right corner of the form. **Do NOT** write the participant ID in this space.

Completion Date: Record the date the Westrax™ SC Edit Form was completed. Month and day should be zero-filled, and the last two digits of the year should be recorded (02/07/2002).

Screening Center ID: Record the two-digit SC ID number.

Screening Center Staff ID: Record the four-digit SC staff ID number of the person completing the form.

SC staff member telephone number: Record the telephone number of the person completing the form.

SC staff member fax number: Record the fax number of the person completing the form.

Part A. Data Update Section:

One WesTrax™ SC Edit Form should be completed for each participant. For each EVF item requiring a data correction, circle the item number requiring the change, enter the incorrect data value and the corrected data value along with a description of the error. Multiple changes to one EVF form can be listed. However, once the form has been submitted to the CC, subsequent edits should be noted on another WesTrax™ SC Edit Form.

On occasion study documents such as the MHQ may contain a date of birth (DOB) that does not match the DOB written on the EVF. If this occurs the participant should be contacted and asked to verify his or her DOB. The DOB will not be changed unless it is verified by the participant. The SC should complete a WesTrax™ SC Edit Form including an explanation of the type of error as well as any corrective measures taken. If the participant provides a date of birth that does not match either the EVF or the document on which the discrepancy was discovered (e.g., MHQ), the SC Coordinator should ask for a legal document such as a driver's license or birth certificate to verify the DOB.

EVF Item: Circle the item from the Eligibility Verification Form that requires correction. In some cases multiple items will need to be corrected as a result of one error e.g. (Date of birth errors would affect both the age of the participant at the time of randomization and the total pack years that the participant smoked).

Variable Name: ****For Administrative Use Only****

Incorrect Data: Enter the incorrect data value in this field on the form. Be sure to consider other values that may have been affected by this error and make corrections appropriately.

Corrected Data: Enter the correct value corresponding to the incorrect data value in this form field.

Part B. Comments:

EVF Item #: Record the EVF Item # from the above section that corresponds with the comment. For example, if providing a comment about an error to the Date of Birth, record "1" as the EVF Item #. Only record the EVF Item # once per comment, even if the Description of the Error continues for more than one line.

Description of the Error: Provide a brief, but detailed description of each error. Details should include the date of discovery, the type of error (transcription, keying, transposing) as well as any corrective actions taken to reduce the potential for the error to occur in the future.

As an example of completing the Westrax™ SC Edit Form, suppose there is a change to the date of birth due to a transposing error by a staff member keying information into the IVRS during a randomization phone call. It might be recorded as follows:

EVF Item	Variable Name	Incorrect Data	Corrected Data
1. Date of Birth*	*DOB** (Age at DOR < 55 or Age at DOR > 74 = ineligible)	03/21/1942	03/12/1942

PART B. COMMENTS	
EVF Item #	**Description of the Error**
1	Transposing error was discovered after receipt of randomization confirmation on 3/31/03. Discussed the error with data entry
	personnel to reduce potential for future occurrences. The following error affects pack year calculation; see correction below.

After completing the form:

- The form should be checked to make sure it is accurate, legible, and complete.
- The SC staff member should review the form and make certain that no additional variables will be affected by the requested data change; if additional variables will be affected then this should be appropriately indicated on the form.
- Fax the completed form to Ellen Martinusen at (301) 963-5455 and file the original Westrax SC Edit form in the participant's study file.

3. SCHEDULING, CONDUCTING, AND REPORTING BASELINE SCREENING EXAMINATIONS AND ANNUAL PARTICIPANT FOLLOW-UP ACTIVITIES

3.1 Overview

Over the course of the study, Screening Centers (SCs) will schedule and conduct baseline and annual screening visits, administer annual study questionnaires, and collect necessary participant follow-up information. Lung cancer screening exams will occur at baseline (T_0) and annually for two years (T_1 and T_2). At these screening visits, participants will complete forms that will collect contact information, health status information, and consent to request medical records. Concurrent with annual screening visits and through 2009, SCs will contact the participants by mail or telephone annually to complete the Annual Study Update (ASU) or the Annual Study Update – Post Screening (ASU-PS), the Participant Contact Form (PCF) or the Participant Contact Update Form (PCUF), and the Medical Records Release Authorization Form. An accelerated ASU-PS completion schedule will be employed in 2010. The schedule is described in Section 3.6.1. SCs will also contact a random sample of participants each year to complete the Health Assessment Questionnaire (HAQ) and will administer a satisfaction survey, if the SC chooses to implement this, to selected participants. The HAQ is discussed in Chapter 10. The scheduling, conducting, monitoring, and reporting of the remaining activities are described in detail in the following sections.

3.2 Activities During the Baseline Year

The following section discusses the activities that take place during the participant's first year in the study, the baseline year (T_0). The timeline for these events is based upon the date the participant is randomized into the study. The SC Coordinator is responsible for overseeing the completion of these activities according to the established study timeline.

Prior to a participant completing his/her baseline screening visit (T_0), the SC should ensure that the following study tasks are completed.

- Obtain written consent from participants prior to randomization. See Chapter 2 for detailed procedures for obtaining participant consent.

- Administer the Participant Contact Form (PCF). The PCF should be completed between eligibility assessment and the screening visit or at the screening visit. See Section 3.2.1.3.

- Obtain authorization to collect medical records. Authorization should be obtained during the screening visit. See Section 3.2.1.4.

- Obtain completed Medical History Questionnaire (MHQ). See Section 3.2.1.5.

The T_0 screening visit should take place as soon as possible after the participant's randomization. The screening examinations will be conducted according to the protocols described in Chapters 4 and 5. The SC Coordinator will monitor the completion of all required examinations and study forms. The results of all screening exams will be recorded on the designated form, entered into IDEAS, and reported to the participant and health care provider within three weeks of the examination. The SC Coordinator will also oversee the process of reporting screening exam results to participants and their health care providers.

After the completion of the baseline visit (T_0) but prior to the T_1 screening visit, the SC, if it chooses, may administer a satisfaction survey to a random sample of participants. See Section 3.2.2.

The scheduling, conducting, monitoring, and reporting of the above activities are described in detail in the following sections (3.2.1 to 3.2.2). Figure 3-1 outlines the timing of these events.

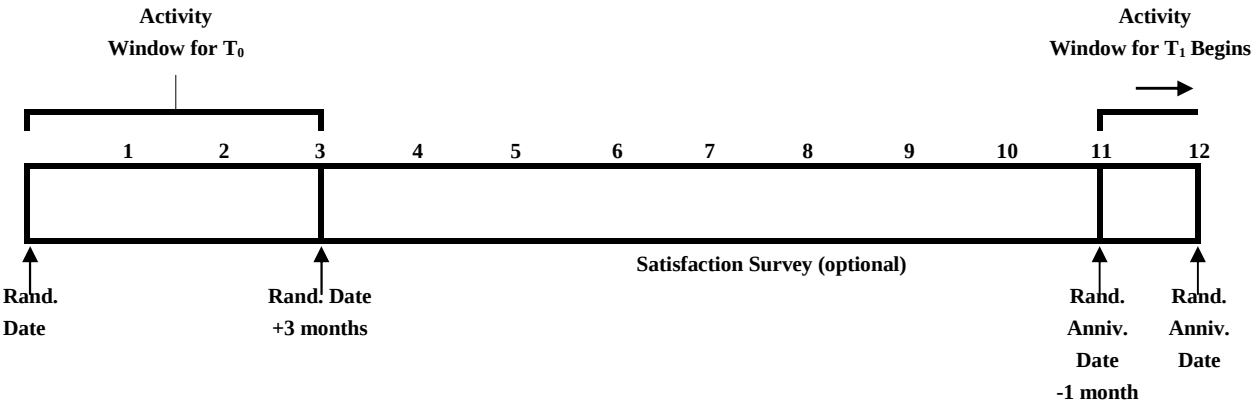


Figure 3-1. Baseline Study Year (T_0)

3.2.1 Scheduling the Baseline Screening Visit

The SC should make every effort to complete the T_0 screening visit at either the time of the participant's randomization or during the activity window, which is within three months of randomization (see Figure 3-1). The SC should attempt to schedule appointments based upon participants' availability. This is especially relevant in areas where older adults may travel for long periods during the winter months. The activity window for follow-up activities in subsequent study years should be built around the randomization anniversary date.

All randomized participants, including randomized ineligibles, should receive a T_0 screen. If scheduling the baseline screening exam does not occur at randomization, the SC should identify and contact participants by mail or telephone to schedule the screening visit. It is recommended that each participant be re-contacted in advance of the appointment date either by telephone or mail and given a reminder of the appointment time and place. Maps and parking instructions, as appropriate, and a written or verbal description of the screening examinations should be provided. To provide this information in a standardized format, the SC may wish to develop participant information sheets. Such information sheets must be approved by the NCI prior to distribution to participants.

Appointments will be recorded in a scheduling system. Each SC will develop its own manual or automated scheduling system for tracking participant contact and appointment times. If a participant does not show up for his/her baseline screening visit, s/he should be re-contacted and rescheduled as soon as possible. Methods for rescheduling screening visits should be outlined by each SC. The SC Coordinator should aggressively attempt to reschedule no-shows and cancellations within the activity window.

If the SC is unable to schedule a participant in the activity window, the SC may schedule a screening exam and/or collect data collection forms until the next activity window begins. Appropriate T_0 data collection forms or Missing Data Forms (MDFs) (Appendix 11-1), if necessary, should be entered into IDEAS before the beginning of the next activity window.

3.2.1.1 Preparing for the T_0 Screening Visit

Before the T_0 screening visit, the SC Coordinator should prepare the following study forms for the visit:

- Participant Contact Form (PCF);
- Medical Record Release Authorization Form;
- Chest X-ray Screening Examination Form (XRY) or Spiral CT Screening Examination Form (SCT), and
- Medical History Questionnaire (MHQ).

The SC staff should prepare the data collection forms in advance of the visit by affixing PID labels and completing the administrative section at the top of each form. Only the administrative section of the data collection forms should be completed in advance of the visit. A folder that contains all forms that need to be completed at the study visit should be prepared for each participant and used in the screening clinic. The other study forms, such as enrollment documents, correspondence, and medical record abstracts should not be sent to the screening clinic.

3.2.1.2 Explaining Procedures for the T_0 Screening Visit

When the participant arrives for the screening examination, s/he should be greeted and given a verbal description of what will happen during the visit. Written materials describing the procedures may also be provided at this time. The participant will be told that the examination is a screening test for lung cancer and is not intended to be a complete physical exam or a substitute for a visit to a health care provider. The participant will be told that s/he will receive written documentation of the results of the screening examination within three weeks and that s/he will be contacted by telephone and/or certified mail if there is a positive result, or a negative result with a clinically significant abnormality. After explaining the procedures and answering participant questions, the SC Coordinator should review the participant's file to determine which forms need to be completed. Once a screening visit begins, forms may be completed in any order.

Questions that participants might ask about the NLST and suggested answers are found in Appendix 2-5. The SC staff should become familiar with these potential questions and answers.

3.2.1.3 Administering the PCF

The SC will ask the participant to complete a Participant Contact Form (PCF) (Appendix 3-1). The PCF is used to collect information that will help the SC contact the participant in the future, including name, Social Security Number (if the participant is willing to provide it), the names of two persons who live in the participant's household, and the names of two persons who will know how to contact the participant. This form will also be used to document the name, address, and telephone number of the participant's health care provider. Appendix 3-2 contains the Specifications for Completion and Review of the PCF. This form may be completed at the time of the visit or may be mailed in advance. If it is sent in advance, the participant should be reminded to bring the PCF to the screening examination appointment. SCs that prefer to mail the PCF to potential participants with the consent form (before randomization) must obtain local IRB approval for this procedure in order to meet OMB requirements.

SC staff should strive to obtain health care provider information on the PCF. If the participant refuses to provide this information, this should be documented on the PCF. If the participant provides this information but requests that the health care provider not receive study information, such as screening exam results, the health care provider information should be recorded on the PCF and the participant should read and sign the Results Withheld Statement (Appendix 3-3). A copy of the signed statement should be given to the participant and the original should be placed in the participant's study file.

The SC Coordinator or staff should review the PCF for legibility and completeness. If completed during a screening visit, the participant should be asked to complete any missing items before proceeding to the screening exam. If completed and returned by mail, the participant should be telephoned to complete any missing items. The completed form will be kept in the participant's study file.

3.2.1.4 Obtaining Authorization to Collect Medical Records

The SC will ask the participant to compete a Medical Record Release Authorization Form. The Medical Record Release Authorization Form is located in Appendix 3-4. This form will serve as

consent from the participant for SCs to request medical records in the event of a positive screen or a report of a cancer diagnosis.

3.2.1.5 Administering the MHQ

The MHQ will be used to collect information on demographics, lung cancer risk factors, and medical conditions. It is recommended that the SC administer the MHQ during the T_0 screening visit, but this information can be collected any time during the activity window. The MHQ will be administered by SC staff as an in-person interview during a screening visit, by SC staff as a telephone interview, or by mail for participant self-administration. The MHQ and Specifications for Completion of the MHQ are located in Appendices 3-5 and 3-6.

SC staff should review all completed MHQs for legibility and consistency. If an MHQ has illegible or inconsistent information, the participant should be queried before the end of the screening visit or should be contacted by telephone to obtain the information. **Critical data items** (race and cancer diagnosis) require data retrieval.

A response rate of 90 percent is expected for the MHQ. To reach this rate, follow-up is required for those participants who have not returned the MHQ within three weeks or who have submitted an incomplete or illegible MHQ (see manual editing guidelines, Section 11.6.1). Each non-respondent should be contacted once by telephone to remind him/her to complete the MHQ and to determine if a second MHQ should be sent. If the participant is willing, the MHQ can be administered by telephone. At a minimum, the follow-up efforts, as described in Section 3.9.1, should be made when following up with non-respondents. If the MHQ has been lost or misplaced, the SC should provide one more complete mailing to the participant. If more than one MHQ is received, the form that was completed first should be used. If a participant refuses to complete the MHQ, the SC will enter a Missing Data Form (MDF) (Appendix 11-1) for the MHQ.

The MHQ should be copied and the original, except the cover page with identifying information, should be sent to the CC. The copy of the MHQ should be placed in the participant's study file.

3.2.1.6 Conducting, Documenting, and Reporting Results of the T_0 Screening Examinations

The procedures for conducting and documenting the screening examinations are described in Chapters 4 and 5. Detailed procedures for reporting the results of screening examinations are provided in Chapter 6.

3.2.1.7 Follow-up for Inadequate Examinations

If it is determined during the visit that a participant's chest x-ray or spiral CT is inadequate, the screening examination should be repeated. If the participant is unable to repeat the screen at the visit or the screen is determined to be inadequate after the conclusion of the visit, a second screen should be scheduled. The second screen should be scheduled as soon as possible after the initial screening examination. A maximum of three exams is allowed per visit and a maximum of two visits is allowed per study year.

3.2.1.8 Concluding the T_0 Screening Visit

At the conclusion of the screening visit, the SC Coordinator will review the participant's study file to make sure that all required forms are complete. If a screening examination needs to be rescheduled, every effort should be made to reschedule the exam within the activity window (i.e., within three months of the randomization date). The rescheduled date will be noted in the SC's appointment scheduling system. The SC Coordinator will remind the participant that results of the screening examination will be sent within three weeks and that s/he will be contacted by telephone or certified mail in the event of a positive result or a negative result with clinically significant abnormalities. SC staff should thank the participant for participating in the study and provide a card containing the name and telephone number of a contact person at the SC who can respond to any study-related questions or problems.

3.2.2 Administering the Satisfaction Survey

In an effort to maximize participant retention, the SC, if it so chooses, may contact a random sample of participants to complete a satisfaction survey. This survey will be developed individually by each SC and should focus on ways to increase participant satisfaction and retention. The survey should be a maximum of two pages in length, and should take no more than three minutes to complete. The survey must be submitted to the CC for NCI approval prior to implementation. Data collected in these surveys will be for the SC use only and will not be transmitted to the CC. Each SC will also develop its own system to track the completion of this survey. Details concerning the administration of such a survey are left to the discretion of the SC.

3.3 Annual Study Activities

Annual study activities will be conducted for each participant through 2009. The purpose of these follow-up activities is to perform screenings on participants in years T_1 and T_2, to obtain information regarding recent health and smoking status by the ASU or ASU Post Screening (ASU-PS), and to update participant contact information utilizing the PCF (Appendix 3-1) or the Participant Contact Update Form (PCUF) (Appendix 3-7). As part of annual study activities, the SC should:

- Conduct screening examinations in study years T_1 and T_2. See Section 3.4.1 and refer to detailed procedures in Chapters 4 and 5.
- Obtain authorization to collect medical records. Authorization should be obtained at the screening visit for T_1 and T_2 study years. The Medical Record Release Authorization Form should be mailed to participants after the T_2 study year, possibly with the ASU, PCF, or PCUF.
- Administer the ASU or ASU-PS to obtain information on participant cancer and recent smoking status. The ASU should be mailed to the participants or completed by telephone in advance of the screening visit or administered in person at the screening visit for the T_1 and T_2 study years. The ASU-PS should be mailed to participants or completed by telephone annually after the T_2 study year. IDEAS allows for a "smart" ASU or ASU-PS which can be pre-printed with the date of the previously completed ASU, ASU-PS, or the randomization date, whichever is most recent, and mailed to the participant or administered by telephone. Instructions for generating a directive in IDEAS for the "smart" ASU or ASU-PS can be found in the *NLST/LSS IDEAS User's Guide*. The "smart" ASU and ASU-PS allow for consistent collection of data from participants for a defined period throughout all study years.

- Request a participant review of the PCF to update contact information. The PCF should be mailed to the participants in advance of the screening visit or reviewed in person at the screening visit for the T_1 and T_2 study years. The PCF should be mailed to participants after the T_2 study year. The PCF also can be reviewed by telephone in all study years. IDEAS allows for a "smart" PCF which can be pre-printed with the previously entered data from the PCF on an IDEAS generated PCUF. Instructions for generating a PCUF can be found in the *NLST/LSS IDEAS User's Guide*. A PCF or PCUF must be receipted into IDEAS each study year, whether or not there are any changes from the previous year.

- Administer a satisfaction survey to a random sample of participants (optional).

- Administer the HAQ to randomly selected participants in April and May (for detailed procedures see Chapter 10).

Participants who have a reported or a confirmed lung cancer or cancer that has metastasized to the lung are not eligible to receive screening examinations. All annual study activities listed above, except for the screening examination, should be performed for these participants. Randomized ineligible participants, however, will continue to receive screening examinations.

The activity window for all annual activities, with the exception of the HAQ and satisfaction survey, is designated as one-month prior through three-months past the participant's randomization anniversary date. The SC should be aggressive about completing annual activities during the activity window. If all of the required data have not been collected by the end of the four-month activity window, data collection efforts, including scheduling of screening examinations, should be continued until the next annual activity window opens, i.e. one-month prior to the next randomization anniversary date (see Figure 3-2).

The SC Coordinator will monitor the completion of all required follow-up activities. The results of all data collection will be transmitted to the CC on a weekly basis. The SC Coordinator will also oversee the process of reporting screening examination results to participants and their health care providers. The following sections (3.4 through 3.7) describe the annual study activities in more detail.

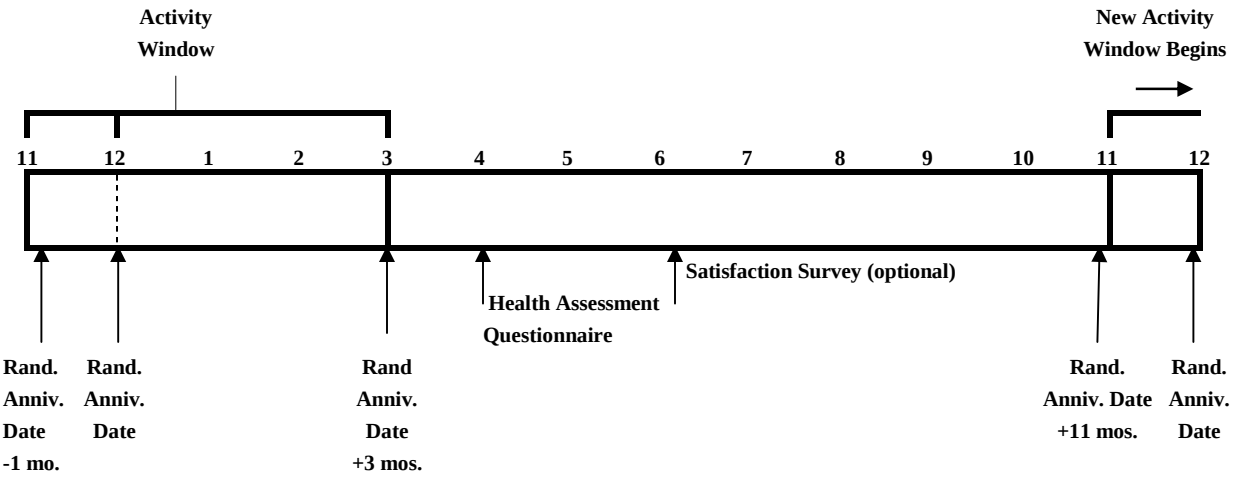


Figure 3-2. Follow-up Study Years (T_1 through T_2)

3.4 Scheduling the Annual Visit

Participants will be scheduled for annual screening examinations in each of the two years following the T_0 visit, the T_1 and T_2 study years. At any point in the study, a report or diagnosis of lung cancer or cancer that has metastasized to the lung will immediately exclude a participant from all further study screening examinations; however, the SC should continue with other study activities. If the report of lung cancer is investigated and is found to be erroneous, the participant again becomes eligible for screening exams.

Appointments will be scheduled for participants who are entering or are currently in their activity window and will be recorded in the SC's scheduling system. The SC Coordinator will contact these participants and make every effort to schedule appointments for annual visits to take place any time within the activity window.

It is critical that participants be screened during their four month activity window. However, situations may occur that make administering the screening examination during the window impossible. Late screening at T_0 and T_1, while preferable to no screening, creates potential difficulties in scheduling future study exams, especially if the next screening window opens soon after the late screen. SCs should refer to the following guidelines for performing screening exams outside the window:

- Ideally, each participant should receive three screens. If a participant has not been screened by the end of his or her screening window, the SC should continue attempts to bring that participant in for the screen. The participant may receive the screen as late as the day before the next screening window opens. No T_2 screening exams may be performed once the T_3 study window opens.

- If a late screening exam has been obtained, the next screening exam should occur no earlier than eight months later than the previous screen. In other words, the SC should aim to space the screens at least eight months apart.

- On the rare occasion that screens cannot be spaced at least eight months apart, the SC should contact the CC prior to scheduling screens. The CC will discuss the issue with NCI, who will then make a decision as to whether it is appropriate to screen using a shorter interval.

In order to maximize retention, it is strongly suggested that reminder phone calls be placed to participants in advance of their appointment date. During this contact, the participant should be given instructions on preparing for the screening visit and directions to the SC. In the event of a no-show or cancellation, the SC Coordinator should aggressively attempt to reschedule the participant within the activity window. Additional retention strategies are described in Appendix 3-9, NLST Retention Strategies.

3.4.1 Conducting the Annual Screening Visit

Prior to the annual visit, the SC Coordinator will pull the study files for all scheduled participants. The SC Coordinator should ensure that a signed consent form is present in the participant's file prior to the beginning of the visit. The forms that will be completed during each annual visit will vary, depending on whether the participant was randomized to the spiral CT or the chest x-ray study arm, and whether the participant completed any form(s) in advance of the visit by mail or telephone. The SC Coordinator will also ensure that all required study forms have PID labels affixed and that the administrative section at the top of each form is complete.

Two forms should be prepared for each screening visit, regardless of the study arm or follow-up year. These are (1) the screening examination form (SCT or XRY), and (2) a Medical Record Release Authorization Form. If the ASU and the PCF or PCUF have not been completed prior to the screening visit, these forms should also be prepared for administration during the visit.

Upon arrival, the participant should be greeted and given a verbal description of what will happen during the visit. Written materials describing the procedures may also be provided at this time. Once a visit begins, follow-up activities can be performed in any order. The Medical Records Release Authorization Form (see Section 3.5), ASU, and PCF, or PCUF if not completed in advance, (see Section 3.6) will be administered during the screening visit.

The procedures for conducting the screening examinations and for reporting results of the screening examinations are described in Chapters 4, 5, and 6. The procedures for concluding an annual screening visit, are identical to those for the T_0 screening visit, and are described in Section 3.2.1.8.

Six months after the completion of the T_2 visit the SC Coordinator should mail to each participant a T_2 Retention letter (Appendix 3-10). This letter explains what is expected of the participant during the remainder of the study.

3.4.2 Follow-up for Inadequate Examinations

If it is determined during the visit that a participant's chest x-ray or spiral CT is inadequate, the screening examination should be repeated. If the participant is unable to repeat the screen at the visit or the screen is determined to be inadequate after the conclusion of the visit, a second screen should be scheduled. The second screen should be scheduled as soon as possible after the initial screening examination. A maximum of three exams is allowed per visit and a maximum of two visits is allowed per study year.

3.4.3 Concluding Screening Operations

SCs should attempt to schedule outstanding T_2 screening exams up until the T_3 activity window opens for each participant. If the SC has made substantial efforts to locate and/or schedule a participant but has not been successful, SC staff may use their discretion when deciding whether to receipt a Missing Data Form (MDF) for the screening exam.

At each SC, when the last randomized participant enters his/her T_3 activity window, all screening must cease. Requests to cease screening prior to that time should be forwarded to the CC and

include a brief written justification for early cessation. The request will be reviewed by the CC and forwarded to the NCI for approval. Once screening operations have officially ended, the SC may not perform any additional screening exams. If a participant requests a screening exam after screening operations have been closed, the SC should inform the participant that screening is no longer provided by the NLST and refer the participant to his/her health care provider to discuss lung cancer screening. SCs must continue to perform equipment QC as specified in Sections 4.9.1 and 5.9.1 until screening operations are closed, at which time equipment QC is no longer required.

3.5 Obtaining Authorization to Collect Medical Records

The Medical Record Release Authorization Form should be administered every year. It can be administered during the screening visit at T_0, T_1, and T_2. In subsequent years, the SC will mail the Medical Record Release Authorization Form to participants, potentially in conjunction with the ASU and the PCF or PCUF.

3.6 Administering the ASU or ASU-PS and the PCF or PCUF

The Annual Study Update (ASU) (Appendix 3-11) and the Annual Study Update – Post Screening (ASU-PS) (Appendix 3-13) are self-administered questionnaires that will be used to collect information about the past year's medical history and recent smoking status from each participant on an annual basis.

The ASU should be administered by mail or telephone in advance of the screening visit during the T_1 and T_2 years, or it can be administered during the screening visit. Mailing or telephone administration of the ASU during this time will be necessary for participants who do not complete annual screens. Administration (including transmission) of the ASU through electronic mail is not permitted. The following information will be collected on the ASU:

- Cancer diagnoses since enrollment or the last annual study activity;
- Type of cancer and date of diagnosis;
- Recent smoking status, and

- Recent pneumonia or respiratory infection treated with antibiotics.

For subsequent years of the study (T_3 and beyond), the ASU-PS should be mailed or completed by telephone. Administration (including transmission) of the ASU-PS through electronic mail is not permitted unless prior approval has been granted by NCI. The ASU-PS collects the same information as the ASU with the exception of recent pneumonia or respiratory infection treated with antibiotics. In addition, the ASU-PS includes information for current smokers on how to access resources to help quit smoking.

The Specifications for Completion of the ASU are given in Appendix 3-12. The Specifications for Completion of the ASU-PS are given in Appendix 3-14. These specifications may be used by the SC Coordinator to answer participant questions regarding the completion of the form.

All participants will also be asked to confirm or update their contact information on the PCF or PCUF annually. The purpose of the PCF or PCUF is to provide the SC with information that can be used to trace the participant if s/he becomes lost to follow-up. During the T_0 study year, a blank PCF should be administered in advance of the screening visit or during the screening visit. During subsequent study years, a blank PCF should be attached to a copy of the previous PCF, or a pre-printed PCUF should be used. The participant should be instructed to review the previous PCF or the pre-printed PCUF and mark any necessary revisions on the form or in the spaces provided. The PCF should not be transmitted by the SC through electronic mail unless prior approval has been granted by NCI. The PCUF should never be transmitted by the SC through electronic mail since it contains personal identifying information. The PCF and Specifications for Completion and Review of the form can be found in Appendices 3-1 and 3-2. The PCUF and Specifications for Completion and Review of the form can be found in Appendices 3-7 and 3-8. These specifications may also be used by the SC Coordinator to answer participant questions about the completion of the forms.

Any mailed ASU, ASU-PS, PCF, or PCUF should be accompanied by a cover letter that introduces the forms and instructs household members to contact the SC if the participant is unable to complete them (due to death, illness, etc.). A sample cover letter for the annual forms is included as Appendix 3-15. This letter may be customized for individual SC use.

A response rate of 90 percent is expected for the ASU and ASU-PS. To reach this rate, follow-up is <u>required</u> for those participants who have not returned an ASU or ASU-PS within three weeks, or who have submitted an incomplete or illegible form. Non-respondents and participants who

submit incomplete forms should be contacted by telephone to be reminded to complete the form or to obtain missing information. Follow-up for non-respondents should be conducted as outlined in Section 3.9.1. If the forms are lost or misplaced by either the participant or the SC, the SC will mail an additional set to the participant or collect the information by telephone.

In special circumstances when the participant cannot be contacted by mail or telephone, the SC may request permission from NCI to administer the ASU-PS or PCF by electronic mail. Such requests must include the PID, an explanation of why electronic administration is necessary, and whether the request applies to the current study year or all future study years. Requests must be submitted in writing to the CC for review by NCI and will be considered on an individual basis. If NCI approval is granted, the SC must obtain from the CC a specially created ASU-PS and/or PCF file that is suitable for electronic transmission. The SC also must inform the participant at the time of transmission that electronic transmission of study forms and data may not comply with NIH security requirements, that the security of the data is not guaranteed, and that s/he is providing the information at his/her own risk. The SC must keep a copy of this notification in the participant's folder.

After the ASU or ASU-PS and PCF or PCUF are completed, they should be manually edited for completeness and legibility. Item 1 on the ASU and ASU-PS (cancer diagnosed since the date of the last ASU or ASU-PS) is considered a **critical data item**. Critical data items require data retrieval if the response is incomplete, unclear, missing, or illegible. Once the ASU or ASU-PS is complete, a qualified medical record abstractor should investigate all cancers reported to be diagnosed on or before December 31, 2009. Cancers reported to be diagnosed after December 31, 2009 will not be investigated. See Chapter 8 for more information on documenting cancers diagnosed after December 31, 2009. If the participant indicates on the ASU or ASU-PS that a cancer was diagnosed, but the date of diagnosis was not within the time period covered by the ASU or ASU-PS and the cancer has previously been reported, the participant's response to Item 1 can be edited. If the participant indicates that a cancer was diagnosed within the time period covered by the ASU or ASU-PS, the response should not be edited, even if the cancer was previously reported or confirmed through another source.

If the participant fails to return the ASU or ASU-PS, or the SC is unable to collect information by telephone before the beginning of the next activity window, the SC Coordinator will complete an MDF to indicate that the data were not collected for that year. Refer to Section 11.5.1 for detailed information on completing an MDF for non-response. If an ASU or ASU-PS form is lost before it has been entered into IDEAS and the form is less than one year old, it should be re-administered to the

participant. If the form is older than one year, the SC should not attempt re-administration. Instead, an MDF should be completed for this missing form. An MDF is not required for the PCF or PCUF.

3.6.1 Administering the Final ASU-PS and PCF or PCUF

From January 1, 2010 through June 30, 2010, final ASU-PSs must be administered such that administration is complete by June 30, 2010. Although ASU-PSs may be receipted during the three-month period from July 1, 2010 through September 29, 2010, it is strongly recommended that as many forms as possible be receipted by June 30, 2010. SCs may prepare mailings in advance, but must not mail or administer any final ASU-PS before January 1, 2010.

In order to meet the goal of receipting all ASU-PSs by June 30, 2010, NCI suggests that SCs consider using the following strategy:

1. Mail or telephone-administer the final ASU-PS forms in order of the participants' randomization month, starting with January.
2. For ASU-PS forms administered through the mail: perform initial mailing of as many ASU-PS forms as possible between January 1, 2010 and March 31, 2010. Between April 1, 2010 and June 30, 2010, mail remaining ASU-PS forms and re-mail any ASU-PS forms to participants with updated addresses.
3. For ASU-PS forms administered over the telephone: make phone calls and complete ASU-PS forms between January 1, 2010 and June 30, 2010.
4. Use the period from July 1, 2010 to September 29, 2010 to receipt "straggler" ASU-PS forms. Do not use this period to perform other tasks such as initial mailings.

In order to facilitate follow-up of cancers or deaths reported on the final ASU-PS, it is suggested that the PCF or PCUF be administered or mailed together with the ASU-PS; however, this decision will be left to the discretion of the SC Coordinator who must ensure that the inclusion of the PCF or PCUF will not compromise the SC's ability to adhere to the accelerated ASU-PS schedule.

Any final ASU-PS that is administered by mail should be accompanied by a cover letter. A sample cover letter for the final ASU-PS and PCF or PCUF is included as Appendix 3-16. This letter may be customized by each SC.

It is important that cancers or deaths reported on the final ASU-PS are documented and, if necessary, followed up promptly. To facilitate timely follow-up, it is recommended that each SC implement procedures to immediately review all returned and completed final ASU-PS forms and prioritize processing for those forms with reported cancers diagnosed on or before December 31, 2009 or reported deaths occurring on or before December 31, 2009.

3.7 Administering the Satisfaction Survey

As discussed in Section 3.2.2, a satisfaction survey may be administered to a random sample of study participants if the SC chooses to implement such a survey. If developed, the survey must be submitted to the CC for NCI approval prior to implementation. Details concerning the administration of such a survey are left to the discretion of the SC.

3.8 Retaining Study Participants

Over the course of the study, the SCs will engage in a variety of activities designed to retain participants in the study. Some activities are required while others are optional. The SC Coordinator should use his/her discretion when deciding which retention strategies to employ.

During the screening phase of the trial, SCs may utilize the NLST Retention Strategies (Appendix 3-9) to respond to participant concerns about screening. SCs also may administer a satisfaction survey as described in sections 3.2.2 and 3.7. To maximize compliance to screening exams, SCs should offer convenient appointment times, such as evenings, weekends, or holidays, if at all possible. Appointment letters and reminder phone calls may also be utilized. Some SCs may offer free parking, gas cards or other transportation, food and/or lodging vouchers, or compensation for time.

Upon completion of screening, SCs are required to mail the T_2 retention letter (Appendix 3-10) as described in section 3.4.1. During the follow-up phase of the trial, it is important that SCs make concerted efforts to maintain participant involvement in the study. Examples of retention methods include mailing token gift items (e.g. calendars, pens, umbrellas, etc.), birthday cards, and/or sympathy cards. In addition, the NCI will provide an NLST study-wide newsletter twice per year, which is required

to be mailed to all participants. SCs may create SC-specific inserts for these newsletters or may mail SC-specific newsletters alternating with the study-wide newsletters.

To assist with SC retention activities, the CC will work with the SCs to draft retention materials and will obtain NCI approval for use of these materials. The CC will monitor participant retention through the use of study data and will communicate regularly with the SCs and NCI to discuss progress and address any concerns.

3.9 Non-Response for Baseline and Annual Study Activities

On occasion, participants may miss scheduled screening visits or may not complete an ASU or ASU-PS, PCF or PCUF, MHQ, or satisfaction survey. As well, some participants, when contacted to schedule an appointment for the T_0, T_1, or T_2 visit, will be unable or unwilling to participate in one or more of the study activities. Additionally, there may also be situations in which the study protocol prohibits completion of a screening examination (e.g., when lung cancer has been reported or confirmed). The following sections describe follow-up procedures for non-respondents and the procedures for documenting non-participation.

3.9.1 Follow-up for Non-Respondents

If a participant does not complete or inadequately completes a required study form, s/he should be contacted by telephone. The telephone call should serve as a reminder to the participant to complete and return the form. It can also serve as an opportunity for the SC to administer the form by telephone. The following efforts, at a minimum, should be used to contact participants:

1. Five attempts should be made to contact a participant by telephone;
2. Each call should be placed on a different day of the week (Monday through Friday);
3. The calls should be made at a different time each day (morning, afternoon, evening), and
4. The first and last calls should be separated by at least one week.

The SC should devise a strategy to ensure a high contact rate. If necessary, this may include having staff available to make calls in the evenings or on weekends. These calls should also be tracked so that they will be made in a systematic way. A Sample Call Record is located in Appendix 11-13. If, after repeated attempts to reach a participant by telephone, the participant cannot be contacted, the SC may contact the participant by electronic mail, if an address was provided. The SC should use electronic mail to re-establish contact with the participant and to obtain a current telephone number and mailing address. The SC should not collect study data by electronic mail and should not transmit study forms as attachments to electronic mail unless prior approval has been granted by NCI.

3.9.2 Documenting Non-Participation

When a participant does not complete one or more study activities, the SC Coordinator will complete a Missing Data Form (MDF) (Appendix 11-1) to indicate that the data form will not be collected for that year.

A participant may not undergo one or more of the annual study activities for one of the following reasons:

- Refusal;
- Mental or physical illness;
- A reported or confirmed primary lung cancer or cancer that has metastasized to the lung;
- Lost to follow-up;
- Out of the area, or
- Death.

The first four reasons listed above (refusal, mental or physical illness, reported or confirmed primary lung cancer or cancer that has metastasized to the lung, and lost to follow-up) are described in the following sections (3.9.2.1, 3.9.2.2, 3.9.2.3, and 3.9.2.4) which also include procedures for resolving and documenting them.

3.9.2.1 Non-Participation Due to Refusal

If a participant refuses screening, the SC should determine the reason for refusal and make an effort to address the participant's concerns. Such efforts should be made at the discretion of the SC Coordinator. If the participant refuses to schedule an appointment for a screening examination, an MDF should be completed with a reason code for the specific reason for refusal (see Appendix 11-2, Specifications for Completion of the MDF). The participant should still be encouraged to complete the ASU and the Medical Record Release Authorization Form, and to review the PCF or PCUF. See Section 11.5.1.1 for more information regarding handling participant refusals.

3.9.2.2 Non-Participation Due to Mental or Physical Illness

If a participant is declared mentally incompetent and a legal guardian is appointed, the SC may request that the guardian complete the ASU or ASU-PS. The participant's legal guardian, in consultation with the SC staff and the participant's health care provider, should decide whether the participant is able to engage in the activities necessary to complete the screening examination. If not, an MDF should be completed with a reason code "10 – Physical illness/cognitive impairment." If a participant is physically unable to complete the screening examination, the SC staff should encourage the participant to complete any other study activities.

3.9.2.3 Non-Participation Due to Lung Cancer

Notification of the diagnosis of lung cancer can occur at any time during the study. Forms that capture this information include the ASU and ASU-PS, completed annually by the participant, and the Cancer Notification Form (CNF, Appendix 8-1), completed by the SC when a cancer is reported by a source other than the ASU or ASU-PS. A participant who reports having, or is reported to have, primary or metastatic lung cancer is considered ineligible for further study screening examinations at the time of the report. It is necessary to follow up with medical record abstraction to confirm and document the diagnosis of the reported lung cancer in a timely manner. If a reported lung cancer is investigated and determined to be erroneous, the participant once again becomes eligible for further screening examinations. If a primary or metastatic lung cancer is confirmed, further screening visits should not be scheduled.

3.9.2.4 Non-Participation Due to Lost to Follow-up

During the course of the study, a participant may become lost to follow-up. For these participants, the SC should attempt tracing (as described in Section 9.2.3). Beginning in 2006, each SC will submit data files of participants who are lost to follow-up to the National Center for Health Statistics for a search of the National Death Index (NDI) database. This submission will be coordinated by the CC and may be conducted annually as determined by the NCI Project Officers. Please refer to Chapter 9 for more information on the procedures for NDI submissions.

3.10 Protocol Violations Associated with Screening Visits

The most frequently encountered protocol violations associated with screening visits are duplication of a screening visit in an activity window, administering the wrong screening examination, using incorrect technical parameters, not performing the comparison read of the screening exams at T_1 or T_2, and failing to maintain original and/or backup screening exam images. These protocol violations require a Protocol and HIPAA Violation Form (PHVF) to be completed. The PHVF and Specifications for Completion of the PHVF can be found in Appendices 11-9 and 11-10. The following is a brief review of procedures that need to be followed when these protocol violations occur.

3.10.1 Protocol Violation Due to Duplicate Screening Visit

If a participant is inadvertently screened more than once in the same study year, the examination form from the first visit should be considered the official study examination for that year. The following steps should be taken to document the situation:

1. The form for the second visit should not be processed;
2. The hardcopy examination form(s) from the second visit should be kept in the participant's study file with a note (initialed and dated) documenting the situation;
3. The participant and his/her health care provider should be informed of the error and given the results of all exams (from both the first and second visit), and

4. A PHVF should be completed and sent to the CC, noting the date of the second screening examination. A copy of the examination form(s) from the second visit should be sent to the CC with the PHVF.

If an erroneous screening exam is performed that results in a positive screen, a Diagnostic Evaluation (DE) form must be completed and kept in the participant's study file. The DE form for an erroneous screening exam should not be entered into IDEAS.

3.10.2 Protocol Violation Due to Incorrect Screening Examination

If a participant receives the screening exam to which s/he was not randomized, s/he should not be re-screened during the activity window. If the error occurred at the T_0 or T_1 screening visit, the participant should undergo the screen s/he was randomized to receive during the subsequent year's activity window. The following steps should be taken to document the situation:

1. The examination form for the visit should not be processed;

2. The hardcopy examination form from the visit should be kept in the participant's study file with a note (initialed and dated) documenting the situation;

3. The participant and his/her health care provider should be informed of the error and given the results of the exam;

4. An MDF should be completed for the expected exam form. Code 88 "Other (SPECIFY)" should be used for the MDF and the reason should be documented as "Incorrect exam performed," and

5. A PHVF should be completed, documenting the error, and noting the date of the incorrect screening examination.

If an erroneous screening exam is performed that results in a positive screen, a Diagnostic Evaluation (DE) form must be completed and kept in the participant's study file. The DE form for an erroneous screening exam should not be entered into IDEAS.

3.10.3 Protocol Violation Due to Incorrect Technical Parameters

If a screening exam is performed using technical parameters that are outside the ranges specified in MOOP section 4.4 and Appendix 4-1 for spiral CT, and MOOP section 5.4 and Appendix 5-1 for chest x-ray, the error must be noted on a PHVF.

For spiral CT exams, the mAs and effective mAs may be below minimum values if an adequate reason is documented on the SCT form (e.g., higher kVp, less filtration, etc.) in the Comments section (Part A.6). The maximum effective mAs may also be exceeded to achieve acceptable image quality for very large patients, as needed, and must be documented in the Comments section (Part A.6). These above exceptions are not considered protocol violations therefore a PHVF does not need to be completed.

3.10.4 Protocol Violation Due to Not Performing Comparison Read

As described in sections 4.7 and 5.7, T_1 screening exams must be compared with T_0 screening exams and T_2 screening exams must be compared with T_0 and T_1 exams. If the screening examinations from all three study years are negative, then the T_2 screening examination may be compared with either the T_0 or T_1. If the T_0 and T_1 exams are lost or are otherwise unavailable and the comparison read cannot be performed, it is considered a protocol violation and the SC must complete a PHVF. If either the T_0 or T_1 screening exam was not completed, then the T_2 exam should be compared to the existing previous exam and no PHVF is required. It is not acceptable to complete a PHVF because it was inconvenient to do a comparison read.

3.10.5 Protocol Violation Due to Failure to Maintain Original and/or Backup Screening Exam Images

As described in sections 4.6.2 and 5.6.2, screening exam images must be stored as photo documentation of the exam and the capability to retrieve images at any time must be maintained. If the original hard copy or digital screening exam can no longer be accessed (due to loss, corruption, or irreversible modification such that the image can no longer be read according to study protocol) and a backup copy does not exist, this is considered a protocol violation and must be documented on a PHVF.

If the image was lost or corrupted before it was read, so that the participant never received results from the exam, s/he should be informed and invited for another screen.

Appendices for Chapter 3

National Lung Screening Trial (NLST)

PARTICIPANT CONTACT FORM (PCF)

For Office Use Only

Screening Center ID: |__|__|

Screening Center Staff ID: |__|__|__|__|

Study Year: T|__|

Initials Complete: _____

Initials QC: _____

PCF

Participant ID Label

Returning participants only: If your contact information has not changed since you last completed this form, mark this box. |__|

1. What is today's date? |___|___| / |___|___| / |2|0|__|__|
MONTH DAY YEAR

2. What is your full name and contact information?

NAME: MR./MRS./MISS/MS./DR.	FIRST	MIDDLE	LAST	(JR., SR., etc.)

STREET ADDRESS 1	STREET ADDRESS 2
CITY	STATE / ZIP
HOME TELEPHONE NUMBER: ( )	WORK TELEPHONE NUMBER: ( )
CELL PHONE NUMBER: ( )	FAX NUMBER: ( )
E-MAIL ADDRESS	

3. What other last names have you had? (Please include your maiden name and any names from previous marriages)

MAIDEN NAME OTHER LAST NAME(S)

4. What is your Social Security Number?

|___|___|___| - |___|___| - |___|___|___|___|

The National Institutes of Health is requesting your Social Security number under Public Health Service Act 42 USC 285a. The primary use of this information is for researchers to locate you in the future if they are unable to locate you at your home address, and to search vital records in a follow-up study conducted in the future. Additional disclosures of information may be: to HHS contractors, grantees, and collaborating researchers and their staff in order to accomplish the research purpose for which the records are collected; to a congressional office from the record of an individual in response to an inquiry from the congressional office made at the request of the individual; and as otherwise required by Law. **Furnishing your Social Security number is voluntary, and you will not be denied any federal right, benefit, or privilege by your refusal to disclose it.**

PCF (over)

5. Do you currently have a physician/health care provider?

☐ No, I currently do not have a physician/health care provider. → Please skip to Question 7.

☐ Yes, I have a physician/health care provider. → Please provide the name, address, and telephone number of your physician/health care provider below:

FULL NAME OF PROVIDER OR CLINIC		
STREET ADDRESS 1	STREET ADDRESS 2	SUITE OR OFFICE NO
CITY	STATE	ZIP
TELEPHONE NUMBER: ( )		

6. **Question Discontinued**

7. Please list the names of two adults who live in your household and their relationship to you. (Include your spouse, partner, children, relatives, and/or roommates.) (IF NOT APPLICABLE, CHECK HERE AND GO TO QUESTION 8. ☐ → Not applicable

NAME: MR./MRS./MISS/MS./DR.	FIRST	MIDDLE	LAST	(JR., SR., ETC.)	RELATIONSHIP TO YOU
NAME: MR./MRS./MISS/MS./DR.	FIRST	MIDDLE	LAST	(JR., SR., ETC.)	RELATIONSHIP TO YOU

8. Will you please provide us with the names and addresses of **two** people who could give us your new address should you move? We would only contact these people if we were unable to reach you at your home address. It would be helpful to get the names of people who do not live with you.

☐ → Yes, please provide the contact information below. ☐ → No, please skip to Question 9.

NAME: MR./MRS./MISS/MS./DR.	FIRST	MIDDLE	LAST	(JR., SR., ETC.)	RELATIONSHIP TO YOU
STREET ADDRESS 1	STREET ADDRESS 2				TELEPHONE NUMBER
CITY			STATE	ZIP	( )
NAME: MR./MRS./MISS/MS./DR.	FIRST	MIDDLE	LAST	(JR., SR., ETC.)	RELATIONSHIP TO YOU
STREET ADDRESS 1	STREET ADDRESS 2				TELEPHONE NUMBER
CITY			STATE	ZIP	( )

9. Do you spend a significant part of the year at another location? ☐ YES ☐ NO

If YES, please provide that information below. If NO, we will assume that you can be reached at the address and telephone numbers that you listed in Question 2 throughout the year.

STREET ADDRESS 1	STREET ADDRESS 2	
CITY STATE	ZIP	
HOME TELEPHONE NUMBER: ( )	WORK TELEPHONE NUMBER: ( )	
CELL PHONE NUMBER: ( )	FAX NUMBER: ( )	
E-MAIL ADDRESS		
DATES AT THIS ADDRESS |___|__|/|___|___| TO |___|___|/|___|___| MO DAY MO DAY		

National Lung Screening Trial (NLST)

Specifications for Completion and Review of the Participant Contact Form (PCF)

This form is self-administered. It is to be completed at the time of randomization and updated, if necessary, each subsequent year of the study by all participants. The SC staff should compare the new PCF with the one completed for the previous study year and confirm any changes with the participant. If the initial PCF is mailed to the participant along with the consent form, the SC must receive approval from its IRB of this process. The PCF may be administered with the final ASU-PS, though it is not required. Specifications for completing each item of the form are given below:

For Office Use Only:

This section should be completed by SC staff prior to the screening visit or prior to mailing:

Participant ID Label: Affix a PID label to the space provided at the top of the form.

Screening Center ID: Enter the two-digit SC ID number.

Screening Center Staff ID: Enter the four-digit SC staff ID number.

Study Year: Enter the current study year for the participant.

Completed by Participant:

Please complete any information that has changed since your last National Lung Screening Trial screening exam. If no information has changed, please mark the box.

1. **What is today's date?** This is the date the form is completed. Instruct the participant to enter the month, day, and year. Month and day should be zero filled, if applicable.

2. **What is your full name and contact information?** Instruct the participant to record his/her title (Dr., Mr., Ms., Mrs., Miss); first, middle, last name, and suffix (Jr., Sr., III, Esq.); street address, city, state, ZIP code; home telephone number, and, if applicable, work telephone number, cell phone number, fax number, and e-mail address.

3. **What other last names have you had? (Please include your maiden name and any names from previous marriages)** Instruct the participant to record any other last names such as a maiden name or any previous married names.

4. **What is your Social Security Number?** Instruct the participant to record his/her Social Security Number in the boxes provided.

   If the participant does not wish to provide his or her Social Security Number, the coordinator should ask if s/he would be willing to provide the last four digits.

   Box explaining request for Social Security Number: If the form is administered by SC staff, this statement should be read to the participant.

5. **Do you currently have a physician/health care provider?** Instruct the participant to record whether s/he has a physician or health care provider. If s/he does not have a

physician or health care provider, s/he should mark "No" and go to Question 7. If s/he has a physician or health care provider, s/he should mark "Yes" and provide the name and contact information for the provider in the designated spaces. If s/he has a physician or health care provider but refuses to provide this information, this should be documented on the PCF.

6. **Question Discontinued.** The question "Do you currently have any type of health insurance, such as group health insurance (either through your employer or another organization such as AARP), Medicaid, Medicare, or some other type of health insurance?" has been discontinued and no longer appears on the form.

7. **Please list the names of two adults who live in your household and their relationship to you. (Include your spouse, partner, children, relatives, and/or roommates.)** Instruct the participant to record the names of two adults living in the same home as the participant and their relationship to the participant. If only one other adult is living with the participant, s/he should record that person's name and their relationship to the participant. If no adults aside from the participant live in the participant's household, instruct the participant to place a check in the box next to "Not applicable."

8. **Will you please provide us with the names and addresses of two people who could give us your new address should you move?** This information will be used by the SCs to trace a participant if s/he cannot be contacted at his/her residential address(es). If "Yes," instruct the participant to provide the names of two people who do not live with the participant and who could provide the new address if the participant were to move. Instruct the participant to record the full name, street address (including apartment number, city, state, ZIP code), and telephone number including area code of each contact in the space provided. Instruct the participant to record the relationship of each contact to him/her in the space provided. If "No," contact information will not be provided by the participant.

9. **Do you spend a significant part of the year at another location?** If "Yes," instruct the participant to record this address, including city, state, and ZIP code, telephone number at this address, and, if applicable, work telephone number, cell phone number, fax number, and e-mail address, as well as the months spent at this address each year. If "No," the SC will assume that the participant can be reached at their primary residence throughout the year.

After completing the form:

- Thank the participant for completing the form.
- The form should be checked to make sure it is accurate, legible, and complete.
- The SC staff member who completed the form should write his/her initials in the space labeled "Initials Complete" in the box at the top of the first page.
- The SC staff member who checked the form for completion should write his/her initials in the space labels "Initials QC" in the box at the top of the first page. This should not be the same SC staff member who completed the form.
- Compare the form to the previous year's form (if applicable).
- Confirm any changes in information with the participant.

- File the form in the participant's folder.

For the follow-up years, each participant will be asked to update the PCF. The SCs can choose to utilize the Participant Contact Update Form (PCUF) or administer the original PCF, although the PCUF does have the advantage of allowing a participant to verify existing information on the pre-printed PCUF form. Instructions for generating a directive in IDEAS that will pre-print previously entered data from the PCF onto an IDEAS generated PCUF can be found in the *NLST/LSS IDEAS User's Guide*. The participant should be instructed to review the previously completed PCF or the information provided on the PCUF and mark any changes on either the blank PCF or the right side of the PCUF. SC staff should compare information from the new PCF or PCUF with the PCF or PCUF completed for the previous study year and confirm any changes with the participant. All copies of PCFs and PCUFs should be kept in the participant's file.

National Lung Screening Trial (NLST)

As a participant in the National Lung Screening Trial (NLST), I am writing to request that my health care provider NOT be notified of the results of any screening examinations I receive while participating in the study. I realize that I will be responsible for contacting my health care provider in the event that I receive an abnormal screening examination and that the *Screening Center* will not notify my health care provider of such a result.

If, at any time during the study, I decide that I would like for my health care provider to begin receiving the results of my NLST screening examinations, I realize that I must contact the *Screening Center* in writing to request this change. The address for contacting the *Screening Center* is:

Screening Center
SC Address
City, State, Zip Code

If I have any questions regarding my screening examination results, or any other aspect of the National Lung Screening Trial, I can contact the study coordinator, *SC Coordinator*, at *SC phone number*.

Signature of Participant

Print Name

Date

For Office Use Only

Study Year: T|___|

Participant ID Label

Appendix 3-4 Medical Record Release Authorization Form

National Lung Screening Trial (NLST)

(Letterhead of Screening Center)

ASSURANCE OF CONFIDENTIALITY - All information which would provide identification of the individual will be held in confidence, will be used only for study purposes, and will not be disclosed or released to anyone other than the study team, unless required by law.

AUTHORIZATION TO OBTAIN INFORMATION

FROM MEDICAL RECORDS

I, _____, hereby authorize the release of information from medical records and staff of a health care facility where I have been seen. This information will be used for the National Lung Screening Trial being conducted by (*Name of Screening Center)* and the National Cancer Institute. I understand that I may revoke this consent at any time except to the extent that action has already been taken. I also understand that this authorization expires one year from the date of signature. I further understand that all information obtained will be held confidential, and will not be disclosed to anyone but the researchers conducting this study, except as otherwise required by law.

_____
Signature of Participant

_____
Print Name

_____
Date

For Office Use Only
Study Year: T|___|
Participant ID Label

National Lung Screening Trial (NLST)

MEDICAL HISTORY QUESTIONNAIRE FOR PARTICIPANTS (MHQ)

Participant ID Label

Thank you for participating in the National Lung Screening Trial (NLST). Your participation is helping to answer some very important questions about the effects of lung cancer screening on overall health. As a part of the study, we would like to obtain some baseline information about your personal medical history. Please take a few minutes to answer the following questions and then return this questionnaire to the Screening Center.

General Instructions:

Print your answers in the spaces provided, or place a "✓" or "X" in the boxes where appropriate.

Please provide the following information and then proceed to page 2. beginning with "Today's Date." to complete the remainder of the questionnaire:

Your Name: _____
First Middle Initial Last

Your Date of Birth: |__|__| |__|__| |1|9|__|__|
MO DAY YEAR

Your Telephone Number: (_____)-_____
Area Code

Appendix 3-5 Medical History Questionnaire (MHQ)

MEDICAL HISTORY QUESTIONNAIRE (MHQ)

For Office Use Only

Screening Center ID: |___|___|

Screening Center Staff ID: |___|___|___|___|

Study Year: T|__|

Initials Complete: _____

Initials QC: _____

MHQ

Participant ID Label

Today's Date: |___|___| |___|___| |2|0|___|___|
MO DAY YEAR

Who is completing this questionnaire?

- ☐ Study participant
- ☐ Someone else (Specify relationship to study participant)

_____

Appendix 3-5 Medical History Questionnaire (MHQ)

General Information about You

1. Are you of Hispanic or Latino origin?

   ☐ Yes ☐ No

2. Which of these groups describe you? (Check all that apply.)

   ☐ White
   ☐ Black or African-American
   ☐ Asian
   ☐ American Indian or Alaska Native
   ☐ Native Hawaiian or Other Pacific Islander

3. What is the highest grade or level of schooling you completed?

   ☐ 8th grade or less
   ☐ 9th-11th grade
   ☐ High school graduate/GED
   ☐ Post high school training, other than college (for example, vocational or technical school)
   ☐ Associate degree/some college
   ☐ Bachelor's degree
   ☐ Graduate school
   ☐ Other, specify:_____

4. What is your current marital status?

   ☐ Married or living as married
   ☐ Widowed
   ☐ Divorced
   ☐ Separated
   ☐ Never married

5. What is your current weight?

   Pounds: _____

6. How tall are you?

   Feet: _____ Inches: _____

Your Work Experience

7. Did you ever work for 12 months or more in any of the following industries or occupations?

Asbestos work	Cotton or jute processing	Hard rock mining
Baking	Farming	Painting
Butchering or meat packing	Fire fighting	Sandblasting
Chemicals or plastics manufacturing	Flour, feed, or grain milling	Welding
Coal mining	Foundry or steel milling	

☐ Yes ☐ No ***(If No, check box for "No" and please skip to question 9.)***

8. Please fill in the appropriate information for **each** industry or occupation.

Industry or Occupation	Do you or did you work in this industry or occupation for 12 months or more? Please check the appropriate box for each industry or occupation listed. If you mark Yes for any industry or occupation, answer → → →	Write the total number of years you worked in this industry or occupation in the space provided, answer → → →	Do you or did you usually wear a facemask or other equipment to protect your lungs while working?
Asbestos work	☐Yes ☐No	No. of years _____	☐ Yes ☐ No
Baking	☐Yes ☐No	No. of years _____	☐ Yes ☐ No
Butchering or meat packing	☐Yes ☐No	No. of years _____	☐ Yes ☐ No
Chemicals or plastics manufacturing	☐Yes ☐No	No. of years _____	☐ Yes ☐ No
Coal mining	☐Yes ☐No	No. of years _____	☐ Yes ☐ No
Cotton or jute processing	☐Yes ☐No	No. of years _____	☐ Yes ☐ No
Farming	☐Yes ☐No	No. of years _____	☐ Yes ☐ No
Fire fighting	☐Yes ☐No	No. of years _____	☐ Yes ☐ No
Flour, feed, or grain milling	☐Yes ☐No	No. of years _____	☐ Yes ☐ No
Foundry or steel milling	☐Yes ☐No	No. of years _____	☐ Yes ☐ No
Hard rock mining	☐Yes ☐No	No. of years _____	☐ Yes ☐ No
Painting	☐Yes ☐No	No. of years _____	☐ Yes ☐ No
Sandblasting	☐Yes ☐No	No. of years _____	☐ Yes ☐ No
Welding	☐Yes ☐No	No. of years _____	☐ Yes ☐ No

Your Smoking Habits (Other than Cigarettes)

9. Has there ever been a time in your life when you regularly smoked at least one cigar a month?

☐ Yes ☐ No ***(If No, check box for "No" and please skip to question 12.)***

10. For how many years did you regularly smoke at least one cigar a month?

___ # of years (If less than 1 year, please enter 0.)

11. During these years, how many cigars did you smoke in a typical month?

___Number of cigars smoked in a typical month

12. Has there ever been a time in your life when you regularly smoked at least one pipeful of tobacco a month?

☐ Yes ☐ No ***(If No, check box for "No" and please skip to question 15.)***

13. For how many years did you regularly smoke at least one pipeful of tobacco a month?

___ # of years (If less than 1 year, please enter 0.)

14. During these years, how many pipesful of tobacco did you smoke in a typical month?

___ Number of pipesful of tobacco smoked in a typical month

Your Passive Smoke Exposure

15. Have you ever lived with a smoker?

☐ Yes
☐ No

16. Have you ever worked in a room or closed space where people were often smoking?

☐ Yes
☐ No

Your Alcohol Habits (Questions 17-18 refer to your recent drinking behavior.)

17. How often do you have a drink containing alcohol?

☐ Never ***(If Never, check box for "Never" and please skip to question 19.)***
☐ Monthly or less often
☐ Two to four times a month
☐ Two to three times a week
☐ Four or more times a week

18. How many drinks containing alcohol do you have on a typical day when you are drinking? *(One drink is defined as a 12-ounce beer, a 5-ounce glass of wine, or a 1.5-ounce shot of liquor, either alone or in mixed drinks)*

☐ 1
☐ 2-3
☐ 4
☐ 5-7
☐ 8 or more

Your Medical History

19. Has a doctor ever told you that you had or have any of the conditions or illnesses listed below? Please mark all that apply and indicate the age at which you were diagnosed. If you have had the same illness or condition more than once, please record your age the first time you were diagnosed.

☐ Yes ☐ No ***(If No, check box for "No" and skip to question 20.)***

☐ Asbestosis	|__|__| Age at diagnosis
☐ Asthma - first diagnosed as a *child*	|__|__| Age at diagnosis
☐ Asthma - first diagnosed as an *adult*	|__|__| Age at diagnosis
☐ Bronchiectasis	|__|__| Age at diagnosis
☐ Chronic Bronchitis	|__|__| Age at diagnosis
☐ Chronic Obstructive Pulmonary Disease (COPD)	|__|__| Age at diagnosis
☐ Diabetes	|__|__| Age at diagnosis
☐ Emphysema	|__|__| Age at diagnosis
☐ Fibrosis of the lung	|__|__| Age at diagnosis
☐ Heart Disease or Heart Attack	|__|__| Age at diagnosis
☐ Pneumonia	|__|__| Age at diagnosis
☐ Sarcoidosis	|__|__| Age at diagnosis
☐ Silicosis	|__|__| Age at diagnosis
☐ Tuberculosis (TB)	|__|__| Age at diagnosis
☐ High Blood Pressure (Hypertension)	|__|__| Age at diagnosis
☐ Stroke	|__|__| Age at diagnosis

20. Have you ever had a chest x-ray? (Not including a chest x-ray for NLST.)

☐ Yes ☐ No ***(If No, check box for "No" and please skip to question 23.)***

21. What was the year of your last chest x-ray?

\|__\|__\|__\|__\|__\|
Year

22. What was the reason for your last chest x-ray? (***Please mark only one.)***

☐ Because of a specific health problem
☐ Follow-up to a previous health problem
☐ Part of a routine physical exam or as a screening exam *(A screening exam is a medical test used to detect disease before symptoms have occurred.)*

23. Have you ever had a "whole body" CT exam or a CT exam of your chest or lungs? (Not including a CT exam for NLST.)

☐ Yes ☐ No **(*If No, check box for "No" and please skip to question 26.*)**

24. In what year did you have your last "whole body" CT exam, or CT exam of your chest or lungs?

\|__\|__\|__\|__\|__\|
Year

25. What was the reason for your last "whole body" CT exam, or CT exam of your chest or lungs? (***Please mark only one.***)

- ☐ Because of a specific health problem
- ☐ Follow-up to a previous health problem
- ☐ Part of a routine physical exam or as a screening exam *(A screening exam is a medical test used to detect disease before symptoms have occurred.)*

26. Have you ever been diagnosed as having any of the cancers listed below?

☐ Yes ☐ No ***(If No, check box for "No" and then skip to question 27.)***

↓

Please mark all that apply and indicate the age at which you were diagnosed. If you have had the same type of cancer more than once, please record your age the first time you were diagnosed.

☐ Bladder cancer	|__|__| Age at diagnosis
☐ Breast cancer	|__|__| Age at diagnosis
☐ Cervical cancer	|__|__| Age at diagnosis
☐ Colorectal cancer	|__|__| Age at diagnosis
☐ Cancer of the esophagus	|__|__| Age at diagnosis
☐ Kidney cancer	|__|__| Age at diagnosis
☐ Cancer of the larynx	|__|__| Age at diagnosis
☐ Lung cancer	|__|__| Age at diagnosis
☐ Mouth (oral) cancer	|__|__| Age at diagnosis
☐ Nasal cancer	|__|__| Age at diagnosis
☐ Pancreatic cancer	|__|__| Age at diagnosis
☐ Cancer of the pharynx	|__|__| Age at diagnosis
☐ Stomach cancer	|__|__| Age at diagnosis
☐ Thyroid cancer	|__|__| Age at diagnosis
☐ Transitional cell cancer	|__|__| Age at diagnosis

27. Have any of the following blood relatives ever had lung cancer? ***(Please write the appropriate response code in the space provided next to each relative.)***

01 No
02 Yes
98 Does not apply
99 Unknown / I prefer not to answer

- \|__\|__\| Father
- \|__\|__\| Mother
- \|__\|__\| Brother(s), including half-brothers
- \|__\|__\| Sister(s), including half-sisters
- \|__\|__\| Child (biological)

Thank you for taking the time to fill out this questionnaire.

National Lung Screening Trial (NLST)

Specifications for Completion of the Medical History Questionnaire (MHQ)

This form is to be completed by all participants. If the participant has difficulty in the completion of the form, an SC staff member may either assist the participant in its completion or administer the questionnaire as an interview (in-person or by telephone).

The specifications provide guidelines for the completion of each question on the form. The specifications also include specific guidelines for the SC staff on editing or data retrieval, as appropriate. The "For Office Use Only" sections must always be completed by the SC staff according to the guidelines provided for those specific question. Personal identifying information (page 1) should be removed from the MHQ prior to submitting it to the CC.

An asterisk (*) in these specifications indicates a critical data item. These are race (Item # 2), and whether the participant has ever been diagnosed with cancer (Item # 26). The SC should perform data retrieval on all critical data items.

General instructions for editing and data retrieval:

An attempt should be made to collect any outstanding information and correct all errors or discrepant data on the questionnaire before the participant leaves the SC. Once the participant has left the SC, an attempt should be made to collect any outstanding information and correct all errors or discrepant data on the questionnaire without contacting the participant. Any data items that are incomplete or unclear may be clarified with the participant through data retrieval at the discretion of the SC Coordinator. If a data item cannot be completed either with or without data retrieval, it should remain as it was recorded by the participant and not changed. All original responses, editing, and recording must be clearly documented on the form.

Specifications for completing the form are given below:

Cover Page:

- **Participant ID Label:** Affix a PID label in the space provided.
- **Participant Name:** Enter the full name (first, middle initial, and last) of the participant. Include any titles or suffixes.
- **Participant Date of Birth:** Enter the month, day, and year of the participant's date of birth. Month and day should be zero filled, and the last two digits should be recorded for the year (e.g., 03/01/1930).
- **Participant Telephone Number:** Enter the participant's telephone number, including area code. This should be the number at which the participant would like to be contacted.

NOTE: This page should be removed prior to sending the MHQ to the CC.

Appendix 3-6 Specifications for Completion of the Medical History Questionnaire (MHQ)

For Office Use Only:

This section should be completed by the SC staff **prior to giving the MHQ to the participant.**

Participant ID Label: Affix a PID label in the space provided.

Screening Center ID: Record the two-digit SC ID number.

Screening Center Staff ID: Record the four-digit SC staff ID number.

Study Year: Enter the current study year for the participant.

Preliminary Information:

This section is to be completed by the participant.

- **Today's date:** Enter the date the questionnaire (MHQ) is being completed using the month, day, and year format. Month and day should be zero filled, and the last two digits should be recorded for the year (e.g., 03/01/2002).

- **Who is completing this questionnaire?** Check the box that corresponds to the person who is completing the questionnaire, which will be either the study participant or another individual. If someone other than the participant is completing the questionnaire, then that information should be recorded in the space provided, noting the relationship to the participant.

General Information about You:

This section of the questionnaire is concerned with the participant's general background.

1. Are you of Hispanic or Latino origin?

The following definitions are to be used for determining ethnic background.

- **Hispanic or Latino:** A person of Cuban, Mexican, Puerto Rican, South or Central American, or other Spanish culture or origin, regardless of race.

2.* Which of these groups describe you?

The following definitions are to be used for determining race or ethnic background. The participant is asked to check all the groups that apply.

- **White:** A person having origins in any of the original peoples of Europe, the Middle East, or North Africa.

- **Black or African-American:** A person having origins in any of the black racial groups of Africa.

- **Asian:** A person having origins in any of the original peoples of the Far East, Southeast Asia, or the Indian subcontinent including, for example, Cambodia, China, India, Japan, Korea, Malaysia, Pakistan, the Philippine Islands, Thailand, and Vietnam.

- **American Indian or Alaska Native:** A person having origins in any of the original peoples of North and South America (including Central America), and who maintains tribal affiliation or community attachment.

- **Native Hawaiian or Other Pacific Islander:** A person having origins in any of the original peoples of Hawaii, Guam, Samoa, or other Pacific Islands.

SC Instructions: This question is a critical data item. If it is incomplete or not answered, data retrieval must be attempted. If data retrieval is successful, make any changes in a different color ink, and record your initials and the date of data retrieval in the white space next to the question. If data retrieval is unsuccessful, write "D.R. attempted," your initials, and the date of the data retrieval attempt in the white space next to the question.

3. What is the highest grade or level of schooling you completed?

Record the highest grade completed, regardless of skipped or repeated grades. If the participant attended school in a foreign country, in an ungraded school, under a tutor, or under special circumstances, ask the participant to give the nearest equivalent of years in a regular U.S. school. The following guidelines should be used for determining the highest grade completed.

- **8th grade or less:** The participant completed 1 to 8 years of school (elementary and junior high/middle school).

- **9th through 11th grade:** The participant completed 9 to 11 years of school (some high school).

- **High school graduate/GED:** The participant completed 12 years of school or completed high school. If the participant received a Graduate Equivalency Degree (GED), s/he would also check this box.

- **Post high school training, other than college (for example, vocational or technical school):** The participant completed training other than college following high school. This includes secretarial school, mechanical or computer training, nursing school where only a diploma is offered, other vocational trades, and business schools outside the regular school system and attended by the participant after completion of high school.

- **Associate degree/some college:** The participant completed some college but did not attain a four-year college degree. An Associate of Arts (AA) degree from a community college or a junior college is included in this category.

- **Bachelor's degree:** The participant obtained a bachelor's degree from a college, university, nursing school, or seminary.

- **Graduate school:** The participant has had some graduate training or completed graduate work. Receiving a degree is not a necessary criterion for this category. This category includes Masters and Doctoral programs, as well as professional schooling (e.g. medical, dental, law, or veterinary school).

- **Other (specify):** Schooling cannot be classified by the categories above.

SC Instructions: If the participant has marked more than one response, the highest level of education should be kept; the remaining responses should be deleted.

4. What is your current marital status?

"Current" is at the time the participant completes the questionnaire (i.e., a woman or man who was widowed but has remarried is considered married). Separated refers to living apart because of marital discord, not circumstantial separation (such as a spouse living in a nursing home).

5. What is your current weight?

Current weight is the participant's weight, in pounds, at the time when the questionnaire is being completed.

6. How tall are you?

This question asks for current height of the participant. Height should be recorded in feet and inches. If the participant reports his/her height to the half-inch, round up to the nearest inch.

Your Work Experience:

This section of the questionnaire is concerned with the participant's work history. "Working" is working for pay (wages, salary, commission, or pay-in-kind), or working without pay in a business or farm operated by a household member. Volunteer or other unpaid work for a church, charity, or similar organization is not included. Individuals who have "retired" from their usual occupation but are currently working either full or part-time for pay are considered working unless they work less than 20 hours per week.

7. Did you ever work for 12 months or more in any of the following industries or occupations?

This question asks about experience working in specific industries or occupations. If the participant has no previous work experience in these types of jobs, s/he should mark "No" and skip to Question 9.

8. Please fill in the appropriate information for each industry or occupation.

This table asks for more specific information about work experience in the industries or occupations listed in Question 7. The participant should mark a response in the second column for each industry or occupation listed. If "Yes" is marked for any industry or occupation, additional information should be recorded in the third and fourth columns.

- **Write the total number of years you worked in this industry or occupation:** This information should be provided in years, if possible. If periods of time have elapsed during which the participant did not or could not work in this occupation, record the total number of years excluding the time not spent in the industry or occupation.

- **Do you or did you usually wear a facemask or other equipment to protect your lungs while working?** The participant should mark "Yes" if s/he used any protective equipment for his/her lungs while working in these industries or occupations.

Your Smoking Habits (Other than Cigarettes):

This section of the questionnaire is concerned with the participant's history of smoking cigars or pipes. Current smokers of cigars or pipes are to reply in regard to their current habits. Ex-smokers are to reply in regard to their usual habits when they smoked cigars or pipes.

9. Has there ever been a time in your life when you regularly smoked at least one cigar a month?

This question asks about the participant's habits regarding cigar smoking. If no, skip to Question 12.

10. For how many years did you regularly smoke at least one cigar a month?

This question asks the length of time in which the participant had a cigar-smoking habit of one cigar or more per month. If less than a year, enter 0.

11. During these years, how many cigars did you smoke in a typical month?

This question asks the number of cigars typically smoked in a month by the participant during the time in which the participant had a cigar-smoking habit of one cigar or more per month.

12. Has there ever been a time in your life when you regularly smoked at least one pipeful of tobacco a month?

This question asks about the participant's habits regarding pipe smoking. If no, skip to Question 15.

13. For how many years did you regularly smoke at least one pipeful of tobacco a month?

This question asks the length of time in which the participant had a pipe-smoking habit of one pipeful of tobacco or more per month. If less than a year, enter 0.

14. During these years, how many pipesful of tobacco did you smoke in a typical month?

This question asks the number of pipesful of tobacco typically smoked in a month by the participant during the time in which the participant had a pipe-smoking habit of one pipeful of tobacco or more per month.

Your Passive Smoke Exposure:

This section of the questionnaire is concerned with the participant's exposure to tobacco smoke of others.

15. Have you ever lived with a smoker?

This question asks whether the participant has ever lived in the same household as a regular smoker.

16. Have you ever worked in a room or closed space where people were often smoking?

This question asks whether the participant has ever worked in close proximity to persons who often smoked.

Your Alcohol Habits:

This section of the questionnaire is concerned with the participant's recent drinking behavior.

17. How often do you have a drink containing alcohol?

This question asks the frequency that the participant consumes any beverage containing alcohol. If never, skip to Question 19.

18. How many drinks containing alcohol do you have on a typical day when you are drinking?

This question asks the number of alcoholic drinks that the participant consumes in a typical drinking day. *(One drink is defined as a 12-ounce beer, a 5-ounce glass of wine, or a 1.5-ounce shot of liquor, either alone or in mixed drinks)*

Your Medical History:

This section of the questionnaire is concerned with the participant's personal medical history.

19. Has a doctor ever told you that you had or have any of the conditions or illnesses listed below?

The condition must be diagnosed by a doctor; we are not interested in self-diagnosed conditions. Place a mark next to any condition that the participant has been told that s/he has or had. The participant should mark all conditions or illnesses that apply and indicate at which age s/he was diagnosed with that illness or condition. In the instance of multiple diagnoses of the same illness or condition, the participant should report the age at which the first diagnosis of an illness or condition was made.

If no is marked for all conditions listed, then skip to Question 20.

SC Instructions: Definitions should not be provided for any of the conditions. Allow the participant to record his/her response based on her understanding of the condition.

20. Have you ever had a chest x-ray?

If "Yes," Questions 21 and 22 must be completed. If "No," go to Question 23.

21. What was the year of your last chest x-ray?

This question records the date of the participant's most recent chest x-ray. Enter the year of the participant's most recent x-ray. Four digits should be recorded for the year (e.g., 2001).

22. What was the reason for your last chest x-ray?

This question asks for the reason that the chest x-ray was performed. Please make sure to mark only one response.

23. Have you ever had a "whole body" CT exam, or a CT exam of your chest or lungs?

If "Yes," Questions 24 and 25 must be completed. If "No," go to Question 26.

24. In what year did you have your last "whole body" CT exam, or CT exam of your chest or lungs?

This question records the date of the participant's most recent "whole body" CT exam, or CT exam of the chest or lungs. Enter the year of the participant's most recent "whole body" CT exam, or CT exam of the chest or lungs. Four digits should be recorded for the year (e.g., 2001).

25. What was the reason for your last "whole body" CT exam, or CT exam or your chest or lungs?

This question asks for the reason that the "whole body" CT exam, or CT exam of the chest or lungs was performed. Please make sure to mark only one response.

26.* Have you ever been diagnosed as having any of the cancers listed below?

This question records previous cancer diagnoses for specific types of cancer, and the participant's age at the time of diagnosis. A doctor must diagnose the cancer. We are interested in only the cancers listed. The participant should mark all cancer diagnoses that apply and indicate at which age s/he was diagnosed with that cancer. In the instance of multiple diagnoses of the same cancer, the participant should report the age at which the first diagnosis was made.

SC Instructions: This question is a <u>critical data item</u>. If it is incomplete or not answered, data retrieval must be attempted. If data retrieval is successful, make any changes in a different color ink, and record your initials and the date of data retrieval in the white space next to the question. If data retrieval is unsuccessful, write "D.R. attempted," your initials, and the date of the data retrieval attempt in the white space next to the question.

27. Have any of the following blood relatives ever had lung cancer?

Lung cancer in non-blood relatives, such as spouse, adopted, or step-children, should not be recorded. The cancer must be diagnosed by a doctor; we are not interested in a self-diagnosed cancer.

<u>After completing the form</u>:

- The form should be checked to make sure it is accurate, legible, and complete.
- The SC staff member who completed the form should write his/her initials in the space labeled "Initials Complete" in the box at the top of the first page.

- The SC staff member who checked the form for completion should write his/her initials in the space labeled "Initials QC" in the box at the top of the first page. This should not be the same SC staff member who completed the form.
- Receipt the form into the IDEAS.
- Remove the cover page (page 1).
- Copy the form.
- Send the original form to the CC in the weekly shipment.
- File a copy of the form in the participant's study file.

National Lung Screening Trial (NLST)

PARTICIPANT CONTACT UPDATE FORM (PCUF)

For Office Use Only		
Screening Center ID: |__|__| Screening Center Staff ID: |__|__|__|__| Study Year: T|__|	Initials Complete: _____ Initials QC: _____	Participant ID Label

1. What is today's date? |___|___| / |___|___| / |2|0|_|_|
MONTH DAY YEAR

Please review the information printed in the left column of each section below. If the information in that section is correct, place a check mark in the box labeled **No Changes Needed**. If the information in the left column is not correct, leave the check box blank and record the correct information in the column on the right **only** for the information that has changed.

2. Please verify your full name and contact information and indicate any changes in the right column of the form. ☐ **No Changes Needed**

Full Name:	**Full Name:**
Current Home Address:	**Current Home Address:**
Home Telephone: **Work Telephone:**	**Home Telephone:** (_____) _____-_____ **Work Telephone:** (_____) _____-_____
Cell Phone: **Fax Number:** **E-mail address:**	**Cell Phone:** (_____) _____-_____ **Fax Number:** (_____) _____-_____ **E-mail address:** _____

3. Please verify other last names you provided in the past and indicate any changes in the right hand column of the form. ☐ **No Changes Needed**

Other Names **Maiden Name:** **Other Last Name(s):**	**Other Names** **Maiden Name:** _____ **Other Last Name(s):** _____

4.	Social Security Number:	☐ **No Changes Needed**
	|_X_|_X_|_X_| - |_X_|_X_| - |___|___|___|___|	|___|___|___| - |___|___| - |___|___|___|___|

The National Institutes of Health is requesting your Social Security Number under Public Health Service Act 42 USC 285a. The primary use of this information is for researchers to locate you in the future if they are unable to locate you at your home address, and to search vital records in a follow-up study conducted in the future. Additional disclosures of information may be: to HHS contractors, grantees, and collaborating researchers and their staff in order to accomplish the research purpose for which the records are collected; to a Congressional office from the record of an individual in response to an inquiry from the Congressional office made at the request of the individual; and as otherwise required by Law. **Furnishing your Social Security Number is voluntary, and you will not be denied any federal right, benefit, or privilege by your refusal to disclose it.**

5.	Please verify the contact information for your physician/health care provider(s). ☐ **No Changes Needed**	
	Full Name of Provider or Clinic # 1:	**Full Name of Provider or Clinic # 1:**
	Address:	**Address:**
	Telephone 1: **Telephone 2:**	**Telephone 1:** (_____) _____-_____ **Telephone 2:** (_____) _____-_____
	Fax Number:	**Fax Number:** (_____) _____-_____
	Full Name of Provider or Clinic # 2:	**Full Name of Provider or Clinic # 2:**
	Address:	**Address:**
	Telephone 1: **Telephone 2:**	**Telephone 1:** (_____) _____-_____ **Telephone 2:** (_____) _____-_____
	Fax Number:	**Fax Number:** (_____) _____-_____

6.	**Question Discontinued**

7.	Please verify the name and relationship of the adult(s) listed as living in the same household as you. ☐ **No Changes Needed**		
Full Name:	**Relationship:**	**Full Name:**	**Relationship:**

8.	In the past you provided us with the names and addresses of the following people who could give us your new address should you move. Please confirm that the people listed are still the best contacts for you. ☐ **No Changes Needed**		
Full Name:	**Relationship:**	**Full Name:**	**Relationship:**
Address:		**Address:**	
Telephone:		**Telephone:** (_____) _____-_____	
Full Name:	**Relationship:**	**Full Name:**	**Relationship:**
Address:		**Address:**	
Telephone:		**Telephone:** (_____) _____-_____	

9.	In the past you may have indicated that you spend a part of the year at another location. Please verify this information and make any necessary changes. ☐ **No Changes Needed**
Other Location Address:	**Other Location Address:**
Home Telephone: **Work Telephone:**	**Home Telephone:** (_____) _____-_____ **Work Telephone:** (_____) _____-_____
Cell Phone: **Fax Number:** **E-mail address:**	**Cell Phone:** (_____) _____-_____ **Fax Number:** (_____) _____-_____ **E-mail address:** _____
Dates at this Address:	**Dates at this Address:** |___|___|/|___|___| TO |___|___|/|___|___| MONTH DAY MONTH DAY

National Lung Screening Trial (NLST)

Specifications for Completion and Review of the Participant Contact Update Form (PCUF)

This form is to be completed annually and can be administered one month prior to the opening of, or during the participant's study window. The PCUF may also be administered with the final ASU-PS, though it is not required. The SCs will be able to generate a directive in IDEAS that will pre-print previously entered data from the PCF on an IDEAS generated PCUF. The pre-filled data will include information for each item from the previously entered PCF or PCUF with the exception of Social Security Number. The PCUF will only show the last four digits of the Social Security Number when they are available. This will ensure participant privacy while allowing for the possibility of capturing previously unrecorded Social Security Numbers.

The SCs can choose to utilize the PCUF or administer the original PCF, although the PCUF does have the advantage of allowing a participant to verify existing information on the pre-printed PCUF form. The PCF or the PCUF should be mailed to the participants in advance of the screening visit or completed in-person at the screening visit for the T_1 and T_2 study years. Either form should be mailed to participants after the T_2 study year. The PCF or PCUF can also be completed by telephone in all study years. The PCUF can be administered electronically, whereby the information is directly entered into IDEAS during a participant interview, or the information can be entered onto a hard copy of the PCUF by the SC or the participant, and then later entered into IDEAS. Instructions for generating a directive in IDEAS for the PCUF and additional information on data entry of the PCUF can be found in the *NLST/LSS IDEAS User's Guide*. The SC staff should compare information from the new PCUF with the PCF or PCUF completed for the previous study year and confirm any changes with the participant. Specifications for completing each item of the form are given below:

For Office Use Only:

This section should be completed by SC staff or pre-printed from an IDEAS directive for the PCUF prior to the screening visit or prior to mailing:

Participant ID Label: Pre-printed from IDEAS

Screening Center ID: Pre-printed from IDEAS

Screening Center Staff ID: Enter the four-digit SC staff ID number.

Study Year: Enter the current study year for the participant.

Completed by Participant:

1. **What is today's date?** This is the date the form is completed. Instruct the participant to enter the month, day, and year. Month and day should be zero filled, if applicable.

The following sections will be pre-printed from IDEAS. The participant should be instructed to review the information displayed on the left hand side of the PCUF. For each section, if the information is correct, then instruct the participant to place a check mark in the box labeled "No Changes Needed." If the information has changed or is incorrect, instruct the participant to complete the corresponding section

on the right hand side of the PCUF. Instruct the participant that it is only necessary to complete the items where the information has changed or is incorrect.

2. **Please verify your full name and contact information.** Instruct the participant to verify his/her title (Dr., Mr., Ms., Mrs., Miss), first, middle, last name, and suffix (Jr., Sr., III, Esq.), street address, city, state, ZIP code, home telephone number, and, if applicable, work telephone number, cell phone number, fax number, and e-mail address. If no changes are needed, then the participant should check the box "No Changes Needed." If the information has changed or is incorrect, instruct the participant to complete the corresponding sections on the right hand side of the form only for those items where the information has changed or is incorrect.

3. **Please verify other last names you provided in the past.** Instruct the participant to verify other last names such as a maiden name or any previous married names he/she provided in the past. If no changes are needed, then the participant should check the box "No Changes Needed." If the information has changed or is incorrect, instruct the participant to complete the corresponding sections on the right hand side of the form only for those items where the information has changed or is incorrect.

4. **Social Security Number.** For privacy reasons, IDEAS will only pre-print the last four digits of the participant's Social Security Number when available. If the information is unavailable (i.e., the participant chose not to complete the information previously), this section will be blank. Instruct the participant to verify the last four digits of his/her Social Security Number. If no changes are needed, then the participant should check the box "No Changes Needed." If the information is incorrect, or if the participant decides to list his/her Social Security Number, instruct the participant to complete the corresponding sections on the right hand side of the form.

   Box explaining request for Social Security Number: If the form is administered by SC staff, this statement should be read to the participant.

5. **Please verify the contact information for your physician/health care provider(s).** Instruct the participant to verify the information regarding his/her primary care physician or health care provider. If the information is unavailable (i.e., the participant does not have a primary care physician or health care provider previously listed), this section will be blank. If no changes are needed, then the participant should check the box "No Changes needed." If the information has changed or is incorrect, instruct the participant to complete the corresponding sections on the right hand side of the form only for those items where the information has changed or is incorrect. If s/he has a physician or health care provider but refuses to provide this information, this should be documented on the PCF.

6. **Question Discontinued.** The question "Do you currently have any type of health insurance, such as group health insurance (either through your employer or another organization such as AARP), Medicaid, Medicare, or some other type of health insurance?" has been discontinued and no longer appears on the form.

7. **Please verify the name and relationship of the adult(s) listed as living in the same household as you.** Instruct the participant to verify the names of two adults living in the same home as the participant and their relationship to the participant. If no changes are needed, then the participant should check the box "No Changes Needed." If the information has changed or is incorrect, instruct the participant to complete the corresponding sections

on the right hand side of the form only for those items where the information has changed or is incorrect.

8. **In the past you have provided us with the names and addresses of the following people who could give us your new address should you move. Please confirm that the people listed are still the best contacts for you.** This information will be used by the SCs to trace a participant if s/he cannot be contacted at his/her residential address(es). If the information is unavailable (i.e., the participant did not previously list any names), this section will be blank. Instruct the participant to verify the names of the people listed who do not live with the participant and who could provide the new address if the participant were to move. Instruct the participant to verify the full name, street address (including apartment number, city, state, ZIP code), and telephone number including area code of each contact. If no changes are needed, then the participant should check the box "No Changes Needed." If the information has changed or is incorrect, instruct the participant to complete the corresponding sections on the right hand side of the form only for those items where the information has changed or is incorrect.

9. **In the past you may have indicated that you spend a significant part of the year at another location. Please verify this information.** If this information is unavailable (i.e., the participant did not previously indicate that s/he spent a significant part of the year at another location), this section will be blank. Instruct the participant to verify this address, including city, state, and ZIP code, telephone number at this address, and, if applicable, work telephone number, cell phone number, fax number, and email address, as well as the months spent at this address each year. If no changes are needed, then the participant should check the box "No Changes Needed." If the information has changed or is incorrect, instruct the participant to complete the corresponding sections on the right hand side of the form only for those items where the information has changed or is incorrect. If the information is left blank, the SC will assume that the participant can be reached at their primary residence throughout the year.

After completing the form:

- Thank the participant for completing the form.
- The form should be checked to make sure it is accurate, legible, and complete.
- The SC staff member who completed the form should write his/her initials in the space labeled, "Initials Complete" in the box at the top of the first page.
- The SC staff member who checked the form for completion should write his/her initials in the space labels "Initials QC" in the box at the top of the first page. This should not be the same SC staff member who completed the form.
- File the form in the participant's folder.

All copies of previous and current PCUFs should be kept in the participant's file.

National Lung Screening Trial / Lung Screening Study (NLST/LSS)

NLST Retention Strategies

Issues:

1. **Participant does not want to come in because he or she feels it is inconvenient or a waste of time:**

   Strategy: Focus on the fact that the success of NLST depends on persons receiving their three screens. Query the participant to see if there is anything that can be done (money, transportation, etc.) to facilitate attendance.

   Sample response to participant: It is crucial for the success of NLST for study participants to receive their three screening exams. If people do not come in for their study exams, NLST may not be able to answer important questions about lung cancer screening. We hope you will reconsider and come in for your exam. If there is anything I can do to make it easier for you to come in, please tell me and I'll see what I can do.

2. **Participant does not want to come in because he or she had a negative screen last year:**

   Strategy: Focus on the fact that a negative screen one year does not guarantee that future screens will be negative or that participant is free of lung cancer.

   Sample response to participant: We understand that you may no longer be very concerned about lung cancer because your first screening exam did not show abnormalities. Please be aware, however, that a negative result on your first screening exam does not guarantee that you are free of lung cancer a year later. Very small abnormalities that were not visible a year ago may have grown and may now be detectable through screening. We hope that you will reconsider and come in for your screening exam.

3. **Participant does not want to come in because he or she is disappointed that his or her screening assignment was chest x-ray:**

   Strategy: Focus on the fact that it is unknown if spiral CT is better than chest x-ray at reducing lung cancer death, and that participants in the chest x-ray arm are an important part of NLST

   Sample response to participant: At this point in time, we do not know that spiral CT is a better lung cancer screening exam than chest x-ray. We are conducting NLST to determine which screening exam, if either, is better. Although spiral CT is better than chest x-ray at detecting very small abnormalities, it is not known if this means it will be able to save more lives. NLST participants who are assigned to chest x-ray are of equal importance as those assigned to spiral CT. We hope that you will reconsider and come in for your screening exam.

4. Participant had extensive work-up following a positive NLST and is concerned that he or she will need to undergo the same work-up if his or her second screen is positive:

Strategy: Tell the participant that it is unlikely that he or she will need to undergo extensive work-up if the abnormality has not changed. Also, mention that their second screening exam will be compared to the first screening exam by NLST radiologists, which in some instances will suffice for follow-up of a second positive screen.

Sample response to participant: If the abnormality observed on your first exam is observed on your second screening exam but has not changed, it is unlikely that you will need to undergo the same follow-up. As part of the NLST, a radiologist will compare your two (three) screening exams and will make a recommendation based on both (all) exams. If nothing has changed, it is very likely that he or she will recommend no additional follow-up.

5. Participant has undergone extensive work-up following a positive NLST and feels that he or she has been fully evaluated and therefore does not need a screening exam:

Strategy: Focus on the fact that the success of NLST depends on persons receiving their three screens. Acknowledge that having a screening exam soon after extensive diagnostic work-up may appear to be unnecessary, but that we need the participant's help to make NLST a success.

Sample response to participant: We recognize that having a screening exam soon after extensive diagnostic work-up may appear to be unnecessary. However, it is crucial for the success of NLST for study participants to receive their three screening exams, regardless of the exams or medical procedures they have in between NLST exams. If people do not come in for their study exams, NLST may not be able to answer important question about lung cancer screening. We hope you will reconsider and come in for your exam.

6. Participant is concerned about radiation exposure:

Strategy: Focus on the fact that radiation exposure is minimal.

Sample response to participant: Minimizing radiation exposure is of particular interest in NLST, and measures have been taken that assure that study images are taken at the lowest radiation dose possible. It's a good idea to minimize radiation exposure, but in the instance of screening exams, it is generally believed that the small amount of radiation exposure does not outweigh the possible benefits of screening. The radiation exposure with screening exams is small, in fact, the dose with CT is similar to that of a mammogram, and the dose with chest x-ray is significantly less than that of a mammogram.

Appendix 3-10 T_2 Retention Letter

National Lung Screening Trial (NLST)

(Participant Name) *(Date)*
(Participant Address)
(City, State, ZIP Code)

The National Cancer Institute (NCI) and *(Local SC)* would like to thank you for participating in the initial phase of the National Lung Screening Trial (NLST). Your valuable participation in this study is an important contribution to winning the battle against lung cancer and is greatly appreciated.

Now that you have passed the screening phase of the trial, you have entered the second and equally important phase. During this follow-up phase, which is expected to last at least through 2009, you will receive periodic questionnaires that assess changes in your health. The questionnaires will take just a few minutes of your time, but will provide valuable information for NLST. Additionally, please continue to keep us aware of your contact information by completing and returning the Participant Contact Form that is mailed to you annually. Should you relocate or have any changes to your personal contact information, call or write *(Local SC)*.

As a result of your smoking history, you continue to be at an increased risk for lung cancer. Therefore, during the remainder of NLST and beyond, we encourage you to continue with your usual health care. If you currently smoke, we would encourage you to consider quitting. If you wish, you may contact *(SC Coordinator)* at *(Local SC)*, who can assist you in getting information or support to help you stop smoking.

If you have any questions regarding the follow-up phase of the trial, please call your local NLST Coordinator *(Name of SC Coordinator)* at *(telephone)*. Again, the National Cancer Institute and *(Local SC)* thank you for your time and effort in helping us complete this landmark study.

Sincerely,

(Signature NCI Project Officer)
NCI Project Officer
National Lung Screening Trial

(Signature SC Principal Investigator)
SC Principal Investigator
National Lung Screening Trial

National Lung Screening Trial (NLST)

ANNUAL STUDY UPDATE (ASU)

For Office Use Only	
Screening Center ID: |___|___| Screening Center Staff ID: |__|__|__|__| Study Year: T|__|	Initials Complete: _____ Initials QC: _____ ASU Participant ID Label

We need to find out about all health care visits you have had in the period from (_____/_____/_____) to the present. Please answer the following questions as best you can. ***If you cannot remember an exact date, please provide an approximate date.***
Date

1. In the period from (_____/_____/_____) to the present, have you been diagnosed with cancer by a health care provider?
Date
(Do not include basal-cell or squamous-cell skin cancers.)

☐ Yes
☐ No (If no, go to Item 4)

2. What type of cancer was diagnosed? (Please record all cancers diagnosed during this period except basal-cell and squamous-cell skin cancers.)

Type/Site of Cancer (breast, lung, etc)	Date of Diagnosis	Hospital or Clinic Where the Cancer was Diagnosed
A. _____	_____/_____/_____	_____
B. _____	_____/_____/_____	_____
C. _____	_____/_____/_____	_____

3. What is the name, phone number and address of the health care provider who diagnosed the most recent cancer?

FULL NAME OF PROVIDER OR CLINIC

STREET ADDRESS 1	STREET ADDRESS 2	SUITE OR OFFICE NO
CITY	STATE	ZIP
TELEPHONE 1 ( )	TELEPHONE 2 ( )	FAX NUMBER: ( )

4. Have you smoked any cigarettes, even a puff, in the last seven days?

☐ Yes
☐ No

5. In the past 12 weeks, have you had pneumonia or an acute respiratory infection that was treated with antibiotics by a physician?

☐ Yes
☐ No

6. Who completed this questionnaire? (Please mark one)

☐ Study Participant ☐ Spouse ☐ If someone else provided this information, please specify their name and relationship:

Name and Relationship: _____

7. What is today's date? |___|___| |___|___| |_2_|_0_|___|___|
MO DAY YEAR

8. Comments: _____

_____

_____

_____

_____

_____

_____

_____

Thank you for completing this questionnaire. Please return this form in the enclosed envelope.

(SC Name)
(Address)

National Lung Screening Trial (NLST)

Specifications for Completion of the Annual Study Update (ASU)

The ASU is to be completed annually by all participants for each year of follow-up, starting with T_1. In situations where the participant is unable to complete the form, the form may be completed by someone else such as a spouse, other family member, or friend. The form may also be administered by an SC staff member.

IDEAS allows for a "smart" ASU which can be pre-printed with the date of the previously completed ASU and mailed to the participant or administered via the telephone. Instructions for generating a directive in IDEAS for the "smart" ASU can be found in the *NLST/LSS IDEAS User's Guide*. If the SC chooses not to use the "smart" ASU then the date when the ASU was previously completed or the anniversary date of randomization, whichever is most recent, must be manually entered in the space provided.

The ASU can be administered as part of the screening visit during the T_1 and T_2 years. It can also be administered by mail or by telephone in advance of the screening visit. For subsequent years of the study, the ASU should be mailed or completed by telephone during the participant's activity window. Only one ASU should be receipted for each participant per study year.

For Office Use Only:

This section should be completed by the SC Coordinator prior to the screening visit.

Participant ID Label: Affix a PID label in the space provided.

Participant's Name: Write the participant's name in the designated space in the upper right corner of the sheet. (This is also the space where the PID label will be placed once the ASU is completed and returned.)

Screening Center ID: Record the two-digit SC ID number.

Screening Center Staff ID: Enter the four-digit SC staff ID number.

Study Year: Enter the current study year for the participant.

Specifications for completion of the form are given below. This section may be completed by the participant or administered by an SC staff member.

1.* In the period from (date) to the present, have you been diagnosed with cancer by a health care provider? (Do not include basal-cell or squamous-cell skin cancers.)

Instruct the participant to mark "Yes" or "No" depending on whether or not s/he was diagnosed with cancer during this time period. This does not include self-diagnosed cancer. The participant must have been told by a health care provider (health care provider, nurse, etc.) that s/he has cancer. The date on this question will either be pre-filled by an IDEAS directive or must be manually filled in by the SC. The date should be the date the last ASU was completed or the randomization anniversary date, whichever is most recent.

**This question is a critical data item. If it is incomplete or not answered, data retrieval must be attempted. If data retrieval is successful, make any changes in a different color ink,*

and record your initials and the date of data retrieval in the white space next to the question. If data retrieval is unsuccessful, write "D.R. attempted," your initials, and the date of the data retrieval attempt in the white space next to the question.

2. What type of cancer was diagnosed? (Please record all cancers diagnosed during this period except basal-cell and squamous-cell skin cancers):

Instruct the participant to list each cancer that was diagnosed during the period of time outlined in Question 1 (i.e., "from your last screening examination to the present"). As noted in the question, basal-cell and squamous-cell skin cancers should not be recorded on the form. Also instruct the participant to complete the month, day, and year of the diagnosis and the hospital or clinic where the cancer was diagnosed. If the exact day is unknown, the participant should record the correct month or year and record "99" for the day.

The following instructions apply to the ASU:

A. If Q.1 = Yes and no cancer is listed in Q.2 or if Q.1 = No or is blank and cancer is listed in Q.2, data retrieval needs to be performed.

B. If Q.1 = Yes and cancer is listed in Q.2, regardless of the type of cancer, a Cancer Diagnosis Form (CDF) must be completed. If the reported cancer is lung cancer, the CDF will trigger the expectation of a Diagnostic Evaluation Form (DE).

C. If Q.1 = Yes but the date in Q.2 is not within the time period covered by the ASU and the cancer has been previously reported, data retrieval can be performed by editing the participant's response (i.e. Q.1 = No). If the cancer has not previously been reported (regardless of the diagnosis date) or if it was diagnosed within the time period covered by the ASU, even if it has been reported or confirmed by another source, the participant's response to Q.1 cannot be edited and a CDF must be completed.

3. What is the name, phone number, and address of the health care provider who diagnosed the most recent cancer?

Instruct the participant to list the health care provider's name, phone number, and address.

4. Have you smoked any cigarettes, even a puff, in the last seven days?

Instruct the participant to mark yes or no to indicate if s/he has smoked any cigarettes in the past seven days.

5. In the past 12 weeks, have you had pneumonia or an acute respiratory infection that was treated with antibiotics by a physician?

Instruct the participant to mark yes or no to indicate if s/he has had pneumonia or an acute respiratory infection that was treated by antibiotics by a physician in the past 12 weeks.

If the participant has had pneumonia or an acute respiratory infection that was treated with antibiotics in the past 12 weeks, the box for "Yes" should be marked. If "Yes" is marked then the SC should inform the participant that the screening exam will be scheduled 12 weeks after he/she has completed treatment with antibiotics. The SC should document this

situation in the participant's study record and ensure that the screening exam is scheduled in the appropriate timeframe.

If the participant has not had pneumonia or an acute respiratory infection in the past 12 weeks, or has had such an infection but it was not treated with antibiotics, the box for "No" should be marked.

6. Who completed this questionnaire?

If the participant completed the form himself/herself, s/he should mark the box next to "Study Participant."

If the participant's spouse completed the form for the participant, s/he should mark the box next to "Spouse."

If the person who completed this form is not the participant or his/her spouse (e.g., brother, friend, neighbor, SC staff member), the respondent mark the box next to "Someone else" and specify the relationship to the participant on the line provided.

7. What is today's date?

The participant should write the month, day and year s/he completed this questionnaire in the space provided.

- If the participant left all parts of the date blank (month, day, and year), replace the blanks with the full receipt date (month, day, and year). Record this date in another color ink in the space provided.

- If the participant wrote a partial date (e.g., month, day only) or a partially incorrect date (e.g., month and day fall prior to date questionnaire was completed), replace what the participant wrote with the full receipt date (month, day, and year). Record this date in another color ink in the space provided. Do not replace part(s) of the completion date with part(s) of the receipt date.

- In the white space next to the question, record the fact that the date is the receipt date and your initials.

8. Comments:

The participant may use this space to record any other information or comments that s/he would like to communicate to the SC staff.

Upon receiving the form at the SC:

- If this form was administered by SC staff, thank the participant for answering the questions.
- If completed by the participant at the SC, instruct him/her to return it to the designated SC staff member or location. Thank the participant for completing the form.

- If the form is to be completed by the participant at home, instruct him/her to mail the form to the SC address at the bottom of the form. The SC should provide a self-addressed envelope for this purpose.
- Black out the participant's name in the PID label spot in the upper right corner of the form. Black out the name on both sides of the form. Affix a PID label in this space. Place it over the participant's name. **DO NOT** write the PID in.
- The form should be checked to make sure it is accurate, legible, and complete.
- The SC staff member who completed the form should write his/her initials in the space labeled "Initials Complete" in the box at the top of the first page.
- The SC staff member who checked the form for completion should write his/her initials in the space labeled "Initials QC" in the box at the top of the first page. This should not be the same SC staff member who completed the form.
- Enter the form into IDEAS.
- File the form in the participant's study file.
- If cancers were reported, complete a CDF for each cancer.

National Lung Screening Trial (NLST)

ANNUAL STUDY UPDATE – POST SCREENING (ASU-PS)

For Office Use Only	
Screening Center ID: |___|___| Screening Center Staff ID: |__|__|__|__| Study Year: T|__|	Initials Complete: _____ Initials QC: _____ ASU-PS Participant ID Label

Please answer the following questions as best you can. ***If you cannot remember an exact date, please provide an approximate date.***

1. **In the period from (_____/_____/_____) to the present, have you been diagnosed with cancer by a health care provider?** (Do not include basal-cell or squamous-cell skin cancers.)
   Date
   ☐ Yes
   ☐ No (If no, go to Item 4)

2. **What type of cancer was diagnosed?** (Please record all cancers diagnosed during this period except basal-cell and squamous-cell skin cancers.)

Type/Site of Cancer (breast, lung, etc)	Date of Diagnosis	Hospital or Clinic Where the Cancer was Diagnosed
A.	____/____/____	
B.	____/____/____	
C.	____/____/____	

3. **What is the name, phone number and address of the health care provider who diagnosed the most recent cancer?**

FULL NAME OF PROVIDER OR CLINIC

STREET ADDRESS 1 | STREET ADDRESS 2 | SUITE OR OFFICE NO

CITY | STATE | ZIP

TELEPHONE 1 ( ) | TELEPHONE 2 ( ) | FAX NUMBER ( )

(OVER)

4. Have you smoked any cigarettes, even a puff, in the last seven days?

☐ Yes*

☐ No

***If you are a smoker and would like to quit smoking, we would like you to know that FREE information about quitting is available by calling 1-800/QUIT-NOW (1-800/784-8669) or by accessing www.smokefree.gov. They can provide information to you by mail or by telephone. They have helped many smokers, and, again, their services are free.**

5. Who completed this questionnaire? (Please mark one)

☐ Study Participant ☐ Spouse ☐ If someone else provided this information, please specify their name and relationship:

Name and Relationship: _____

6. What is today's date? |___|___| |___|___| |_2_|_0_|___|___|
MONTH DAY YEAR

7. Comments: _____

_____

_____

_____

_____

_____

_____

_____

Thank you for completing this questionnaire. Please return this form in the enclosed envelope.

(SC Name)
(Address)

National Lung Screening Trial (NLST)

Specifications for Completion of the Annual Study Update – Post Screening Form (ASU-PS)

The ASU-PS is to be completed annually through 2009 by all participants in the T_3 study year and beyond. In situations where the participant is unable to complete the form, the form may be completed by someone else such as a spouse, other family member, or friend. The form may also be administered by an SC staff member.

IDEAS allows for a "smart" ASU-PS which can be pre-printed with the date of the previously completed ASU or ASU-PS and mailed to the participant or administered via the telephone. Instructions for generating a directive in IDEAS for the "smart" ASU-PS can be found in the IDEAS Users Guide. If the SC chooses not to use the "smart" ASU-PS then the date when the ASU or ASU-PS was previously completed or the anniversary date of randomization, whichever is most recent, must be manually entered in the space provided.

The ASU-PS can be administered by mail or completed by telephone during the participant's activity window. The final ASU-PS will be administered to all participants using an accelerated schedule in 2010. See MOOP Section 3.6.1 for the timeline for administration of the 2010 ASU-PS.

For Office Use Only:

This section should be completed by the SC Coordinator prior to the screening visit.

Participant ID Label: Affix a PID label in the space provided.

Participant's Name: Write the participant's name in the designated space in the upper right corner of the sheet. (This is also the space where the PID label will be placed once the ASU is completed and returned.)

Screening Center ID: Record the two-digit SC ID number.

Screening Center Staff ID: Enter the four-digit SC staff ID number.

Study Year: Enter the current study year for the participant.

Specifications for completion of the form are given below. This section may be completed by the participant or administered by an SC staff member.

1.* In the period from (date) to the present, have you been diagnosed with cancer by a health care provider? (Do not include basal-cell or squamous-cell skin cancers.)

Instruct the participant to mark "Yes" or "No" depending on whether or not s/he was diagnosed with cancer during this time period. This does not include self-diagnosed cancer. The participant must have been told by a health care provider (health care provider, nurse, etc.) that s/he has cancer. The date on this question will either be pre-filled by an IDEAS directive or must be manually filled in by the SC. The date should be the date the last ASU or ASU-PS was completed or the randomization anniversary date, whichever is most recent.

**This question is a critical data item. If it is incomplete or not answered, data retrieval must be attempted. If data retrieval is successful, make any changes in a different color ink,*

and record your initials and the date of data retrieval in the white space next to the question. If data retrieval is unsuccessful, write "D.R. attempted," your initials, and the date of the data retrieval attempt in the white space next to the question.

2. What type of cancer was diagnosed? (Please record all cancers diagnosed during this period except basal-cell and squamous-cell skin cancers):

Instruct the participant to list each cancer that was diagnosed during the period of time outlined in Question 1. As noted in the question, basal-cell and squamous-cell skin cancers should not be recorded on the form. Also instruct the participant to complete the month, day, and year of the diagnosis and the hospital or clinic where the cancer was diagnosed. If the exact day is unknown, the participant should record the correct month or year and record "99" for the day.

The following instructions apply to the ASU-PS:

A. If Q.1 = Yes and no cancer is listed in Q.2 or if Q.1 = No or is blank and cancer is listed in Q.2, data retrieval needs to be performed.

B. If Q.1 = Yes and cancer is listed in Q.2, regardless of the type of cancer, a Cancer Diagnosis Form (CDF) must be completed. If the reported cancer is lung cancer, the CDF will trigger the expectation of a Diagnostic Evaluation Form (DE).

C. If Q.1 = Yes but the date in Q.2 is not within the time period covered by the ASU and the cancer has been previously reported, data retrieval can be performed by editing the participant's response (i.e. Q.1 = No). If the cancer has not previously been reported (regardless of the diagnosis date) or if it was diagnosed within the time period covered by the ASU, even if it has been reported or confirmed by another source, the participant's response to Q.1 cannot be edited and a CDF must be completed.

3. What is the name, phone number, and address of the health care provider who diagnosed the most recent cancer?

Instruct the participant to list the health care provider's name, phone number, and address.

4. Have you smoked any cigarettes, even a puff, in the last seven days?

Instruct the participant to mark yes or no to indicate if s/he has smoked any cigarettes in the past seven days.

When administering the ASU-PS via telephone, if the participant's response to Q.4 is "Yes", read the following information to the participant:

If you would like to quit smoking, we would like you to know that FREE information about quitting is available by calling 1-800/QUIT-NOW (1-800/784-8669) or by accessing www.smokefree.gov. They can provide information to you by mail or by telephone. They have helped many smokers, and, again, their services are free.

5. Who completed this questionnaire?

If the participant completed the form himself/herself, s/he should mark the box next to "Study Participant."

If the participant's spouse completed the form for the participant, s/he should mark the box next to "Spouse."

If the person who completed this form is not the participant or his/her spouse (e.g., brother, friend, neighbor, SC staff member), the respondent mark the box next to "Someone else" and specify the relationship to the participant on the line provided.

6. What is today's date?

The participant should write the month, day and year s/he completed this questionnaire in the space provided.

- If the participant left all parts of the date blank (month, day, and year), replace the blanks with the full receipt date (month, day, and year). Record this date in another color ink in the space provided.

- If the participant wrote a partial date (e.g., month, day only) or a partially incorrect date (e.g., month and day fall prior to date questionnaire was completed), replace what the participant wrote with the full receipt date (month, day, and year). Record this date in another color ink in the space provided. Do not replace part(s) of the completion date with part(s) of the receipt date.

- In the white space next to the question, record the fact that the date is the receipt date and your initials.

7. Comments:

The participant may use this space to record any other information or comments that s/he would like to communicate to the SC staff.

Upon receiving the form at the SC:

- If this form was administered by SC staff, thank the participant for answering the questions.
- If completed by the participant at the SC, instruct him/her to return it to the designated SC staff member or location. Thank the participant for completing the form.
- If the form is to be completed by the participant at home, instruct him/her to mail the form to the SC address at the bottom of the form. The SC should provide a self-addressed envelope for this purpose.
- Black out the participant's name in the PID label spot in the upper right corner of the form. Black out the name on both sides of the form. Affix a PID label in this space. Place it over the participant's name. **DO NOT** write the PID in.
- The form should be checked to make sure it is accurate, legible, and complete.

- The SC staff member who completed the form should write his/her initials in the space labeled "Initials Complete" in the box at the top of the first page.
- The SC staff member who checked the form for completion should write his/her initials in the space labeled "Initials QC" in the box at the top of the first page. This should not be the same SC staff member who completed the form.
- Enter the form into IDEAS.
- File the form in the participant's study file.
- If cancers were reported, complete a CDF for each cancer. Cancers reported to have been diagnosed on or before December 31, 2009 must be investigated by a medical record abstractor and the outcome documented on the CDF. Cancers reported to have been diagnosed on or after January 1, 2010 must be documented on a CDF with the estimated diagnosis date; however, the diagnosis does not need to be investigated and confirmed.

National Lung Screening Trial (NLST)

(Date)

(Participant Name)
(Participant Address)
(City, State, Zip Code)

Dear *(Participant Name)*:

Thank you for your participation in the National Lung Screening Trial (NLST). As you may recall, NLST participants are requested, on an annual basis, to inform study researchers of their medical history and to update their contact information.

Enclosed are two questionnaires: an **Annual Study Update** and a **Participant Contact Form**. The Annual Study Update requests information regarding your health, and the Participant Contact Form requests updates to the information we use to contact you, including your address and phone number, as well as your doctor's name. Please take a few moments to complete the Annual Study Update. Please review the Participant Contact Form and mark any necessary changes. Please return both the Annual Study Update and the Participant Contact Form (regardless of whether or not changes were made) in the postage-paid envelope provided. If you are unable to complete these forms, please contact the *(Local SC)* or have a member of your household contact the *(Local SC)* to advise us of your situation. Please be assured that all information you give will be kept confidential and will not be disclosed to anyone but the researchers conducting this study, except as otherwise required by law.

Again, we thank you for your cooperation. Your participation represents a valuable contribution to the study, and ultimately may help reduce the number of deaths each year from lung cancer.

If you have any questions about these forms or about any aspect of the National Lung Screening Trial, please do not hesitate to contact me or *(Name of SC Coordinator)* at (*Telephone Number*).

Sincerely yours,

(Name of Principal Investigator)
Principal Investigator
National Lung Screening Trial

Appendix 3-16 Sample Cover Letter for the Final Annual Study Update – Post Screening and Participant Contact Form

National Lung Screening Trial (NLST)

(Date)

(Participant Name)
(Participant Address)
(City, State, Zip Code)

Dear *(Participant Name)*:

Thank you for your participation in the National Lung Screening Trial (NLST). As you may recall, NLST participants are requested, on an annual basis, to inform study researchers of their medical history and to update their contact information. Enclosed are your final **Annual Study Update** and **Participant Contact Form**. Although it may have been less than one year since you completed your last Annual Study Update and Participant Contact Form, we are requesting the information at this time because we are nearing the end of the study.

The Annual Study Update requests information regarding your health, and the Participant Contact Form requests updates to the information we use to contact you, including your address and phone number, as well as your doctor's name. Please take a few moments to complete the Annual Study Update. Please review the Participant Contact Form and mark any necessary changes. Please return both the Annual Study Update and the Participant Contact Form (regardless of whether or not changes were made) in the postage-paid envelope provided. If you are unable to complete these forms, please contact the *(Local SC)* or have a member of your household contact the *(Local SC)* to advise us of your situation. Please be assured that all information you give will be kept confidential and will not be disclosed to anyone but the researchers conducting this study, except as otherwise required by law.

Again, we thank you for your cooperation. Your participation represents a valuable contribution to the study, and ultimately may help reduce the number of deaths each year from lung cancer.

If you have any questions about this form or about any aspect of the National Lung Screening Trial, please do not hesitate to contact me or *(Name of SC Coordinator)* at (*Telephone Number*).

Sincerely yours,

(Name of Principal Investigator)
Principal Investigator
National Lung Screening Trial

4. SPIRAL CT SCREENING EXAMINATION

4.1 Overview

Each participant in the spiral CT arm will receive three annual spiral CT screening examinations spaced one year apart. Screening Centers (SCs) are responsible for performing the spiral CT, having the spiral CT interpreted by a radiologist, and documenting the results of the spiral CT. This chapter describes these procedures. It also provides the NLST/LSS requirements for examiner training and certification and quality assurance procedures for this examination.

4.2 Participant Preparation

The following steps in the process of participant preparation will be standardized across all SCs. The participant will be told that the examination is a screening examination for lung cancer, not a complete physical examination, and that s/he should consult his/her health care provider for evaluation of any symptoms and for routine medical care. In addition, the participant will be told that s/he will receive written documentation of the results of the screening examination within three weeks, and will be contacted by telephone in the event of a positive screen or a negative screen with clinically significant abnormalities. The participant will be told that if s/he has a positive screen and does not have a health care provider, the SC will offer a list from which s/he may choose a health care provider. The participant will be given a brief description of the screening examination.

Participants who receive a pacemaker or internal defibrillator after randomization are eligible to receive CT scans with approval from their health care provider.

4.3 Examination Procedures

The participant will be asked to disrobe above the waist. Hospital gowns will be provided in accordance with standard procedures at the SC. The technologist will explain the procedure and position the participant. The participant will be instructed to hyperventilate for 20 seconds, and then to inhale deeply and to hold his/her breath while the spiral CT is taken. The entire lung region will be scanned in a

single breath-hold of approximately 20 seconds. If this is not possible, "cluster" helical scans may be obtained (ten seconds of scanning followed by a ten-second breathing break).

The technologist performing the spiral CT scan will make the initial judgment about the quality of the scan before the participant leaves the SC. The quality should be such that both lungs are completely scanned from apex through the lung bases, including both costophrenic angles. If the spiral CT scan is determined to be inadequate, the full scan should be repeated. If only part of the exam is inadequate, however, it is allowable to perform a partial repeat scan covering only the inadequate area. In this instance, the final adequate screening exam is comprised of the two images and they should be read in conjunction. The fact that a partial repeat scan was performed and the reason must be recorded in the Comments section of the Spiral CT Screening Examination Form. Reasons for inadequacy are listed in Section 4.7.2. When a repeat spiral CT is necessary, it should be taken during the same visit. However, no more than three CT scan attempts should be made in one visit. It may be necessary to arrange another screening visit to obtain an adequate spiral CT scan. This visit should occur as close to the initial visit as possible. No more than two visits are allowed to obtain a CT scan.

CT scans are then sent to the study radiologist for interpretation. If the radiologist determines that the CT scan examination is inadequate, the participant will be asked to return for a repeat examination. CT scans should be read by the study radiologist in a timely manner, so that the results can be reported to the participant within three weeks of the exam.

4.4 Equipment Specifications

The spiral CT scan should be obtained with a multi-channel helical CT scanner (minimum of four channels) with the capability of producing CT scans at 120-140 kVp with a range of 40 - 80 mAs and 20 - 60 effective mAs, and a scan time of at most one second using 2.5 mm collimation (maximum effective slice thickness 3.2), pitch of 1.25 – 2.0 or equivalent (dependent on model/type of scanner), and contiguous reconstructions. The display FOV should be the smallest diameter of the chest wall that will completely contain the lung parenchyma as measured from the widest point of outer rib to outer rib. In cases where the participant is obese, the radiologic technologist should use the lowest possible machine setting to obtain an adequate screen, and document the reason in the Comments section (Item A.6) of the SCT form. The Low Dose Chest CT Protocol Specifications are listed in Appendix 4-1.

Each technical parameter should be set to allow for all technical parameters to fall within their specified ranges. For example, the highest allowable mAs (80) could not be used with the lowest allowable pitch (1.25), because it would result in an effective mAs of 64, which is outside of the specified range. The CT dose should be as low as reasonably achievable while maintaining acceptable image quality. It is suggested that each site will tailor the CT dose to the size of the patient, with at least three preset protocols for small, medium, and large participants. For spiral CT exams, the mAs and effective mAs may operate below minimums if an adequate reason (e.g., higher kVp, less filtration, etc.) is documented in the Comments section of the Spiral CT Screening Examination Form. The maximum effective mAs may also be exceeded to achieve acceptable image quality for very large patients, as needed, and must be documented in the Comments section of the form.

Images will be obtained using a standard algorithm or reconstructed using a high-resolution bone algorithm. The GE Lung and other lung algorithms are not allowed, as they lead to difficulties in determining the presence or absence of calcification in a nodule. The reconstruction slice thickness will be between 1-2.5 mm, and the reconstruction interval should be 1-2.5 mm as well. Lung windows (standard width 1500, standard level -650) and mediastinal windows (standard width 400-500, standard level 10-30) will be provided for review. The standard width and level setting may be adjusted to optimize viewing. Filters may also be used. Image review will be conducted on soft copy display with a maximum of one on one for viewing and measuring. Magnification is encouraged for measuring.

In addition to these parameters, all equipment used on the NLST/LSS must meet the guidelines of the American College of Radiology (ACR). See Appendix 4-2 for the current ACR Guidelines. These guidelines can also be found at www.acr.org.

The SC is required to send documentation of equipment specifications to the CC. All documentation should also be maintained in the SC NLST/LSS files. The CC will forward all equipment specifications to the NCI for approval. The NCI will be responsible for reviewing equipment specifications from each SC and will make the final approval decision. Equipment specifications will also be reviewed by an NCI designated medical physicist who will make manufacturer specific recommendations for the dosing parameters to be used on each machine. This should be done before screening begins and whenever equipment is replaced during the course of the study.

4.5 Examiner Qualifications, Training, and Certification

The spiral CT examination requires three radiologic personnel: the radiologic technologist, the medical physicist, and the radiologist. The minimum qualifications for these individuals and the NLST/LSS training protocol are discussed in this section.

4.5.1 Minimum Qualifications for Examiners

Technologists will be American Registry of Radiologic Technologists (ARRT) certified radiologic technologists. The radiologists (interpreters and QA examiners) will be American Board of Radiology (ABR) certified or board-eligible (chest), and must have a valid active medical license in the state in which screening is performed. Radiologists at Federal sites must have an unrestricted active license to practice medicine in their clinical specialty, issued by one of the states, the District of Columbia, or a possession of the United States. Medical physicists must be certified by the American Board of Radiology in the subfield of Diagnostic Radiological Physics or the subfield of Radiological Physics. In addition to being appropriately certified, technologists, radiologists, and physicists must meet additional guidelines outlined by the American College of Radiology (ACR). See Appendix 4-2 or www.acr.org for current ACR Guidelines.

The SC must report the qualifications of each examiner by submitting a completed Record of Experience, Credentials, and Training (ECT, Appendix 11-5) to the CC. In lieu of submitting copies of diplomas and certificates, the SC may attach a letter from the department chairman stating that the technologist is an ARRT certified radiologic technologist, the physicist is ABR certified or board-eligible, or that the radiologist is ABR certified or board-eligible and holds a valid active medical license, and that additional ACR Guidelines have been met. For any technologist who is not ARRT certified or any physicist or radiologist who is not ABR certified, or for any technologist, physicist, or radiologist who do not meet the remaining ACR Guidelines, the SC Principal Investigator must document and certify adequate training and experience in a letter to be submitted with a completed ECT to the CC. The CC will review all ECTs and, if the qualifications meet the criteria, the CC will recommend approval to the NCI. If the qualifications do not match the requirements, the CC will request an exception approval from the NCI on a case-by-case basis. **The ECT must be approved by the NCI prior to the initiation of screening activities.**

4.5.2 Training Protocol

One radiologist from each SC will attend a central training session. The radiologists' training will utilize a training CD containing a variety of images designed to help standardize the interpretation of images across NLST/LSS sites. The radiologist will use the training CD to review the same interpretation guidelines with the remaining radiologists at the SC. Additionally, the radiologist will use the CD to train technologists at his/her SC on the correct procedures for conducting the screening exams for the NLST/LSS. The radiologists also will be trained on the screening exam forms. The SC Coordinator will be responsible for training the technologist on the use of the study forms and SC administrative procedures.

4.5.3 Examiner Certification

No additional qualifications for the technologist, physicist, or radiologist are necessary for this examination. Certification through ARRT (for technologists) and ABR (for physicists and radiologists), plus an active valid medical license (for radiologists) and adherence to additional ACR Guidelines (Appendix 4-2) will serve as the qualification for these examiners.

4.5.4 Updates to Qualifications for Radiologic Personnel

On an annual basis, SCs will be asked to submit updated qualifications for all radiologic personnel who continue to work on the NLST/LSS. For technologists, if an ARRT certification was submitted in the previous year, an updated and valid ARRT certification should be submitted. If a letter from the chair of the Radiology Department of the SC was sent to certify that the technologist was ARRT certified, then an updated letter, signed by the chair of the Radiology Department should be submitted. If updated credentials or a letter of certification is not submitted for annual review, the technologist will be unable to continue working on the NLST/LSS. Once screening operations have officially ended, as described in Section 3.4.3, updates to qualifications for radiologic personnel are no longer required.

4.6 Documentation of the Examination

Information documenting that the CT scan was taken and the interpretation was made by the radiologist will be recorded on the Spiral CT Screening Examination Form (SCT, Appendix 4-3). In addition to the examination result, the NLST/LSS images will be stored.

4.6.1 The Spiral CT Screening Examination Form (SCT)

The SCT form will be used to document the results and findings of the examination. Every screening visit must be documented, regardless of outcome. The form provides documentation that the examination was completed, whether the results were normal or abnormal, and a description of abnormal findings. The SC Coordinator or staff member should complete the Administrative Section on the first page of the form and the radiologic technologist should complete Part A. If adequate images are obtained, Parts B through E of the form should be completed by the radiologist. If the technologist does not obtain adequate images, Parts B and C should be left blank and the radiologist should complete Items D.1, D.3, and E.6. The radiologist should not complete a comparison review (Item E.3) if the image read in isolation is inadequate. If documentation of the exam, including exam images, is lost and cannot be recreated, Parts A and B and Items D.3 and E.6 must be completed. A Protocol and HIPAA Violation Form (PHVF) also must be completed. Specifications for Completion of the SCT Form are provided in Appendix 4-4. It is the responsibility of the SC Coordinator to train the technologists and radiologists in the use of the form.

After the form has been completed, the SC Coordinator should review it to ensure that it has been filled out completely, including items in the Administrative Section. The SCT form should be edited as necessary. Any data retrieval involving the examiner should be performed as expeditiously as possible since results reports must be sent to the participant and to his/her health care provider within three weeks of the screening visit. The SCT form should be entered into IDEAS and filed in the participant's study file.

4.6.2 Storage of Lung Screening Study Spiral CT Images

The spiral CT images should be labeled with the participant's name and PID number. The SC is responsible for storing the images for each of the participant's spiral CT screening examinations.

Inadequate images should be retained at the SC until adequate images are obtained. Upon collection of an adequate image, inadequate images may be discarded. Spiral CT images for the NLST/LSS should be stored in a manner that is consistent with the confidentiality agreement for the study. It is recommended that a participant's images not be stored with the participant's medical record or with other images that are not related to the NLST/LSS. If an SC wishes to store NLST/LSS data in the regular medical record, it must submit to the NCI (via the CC) documentation of the methods that will be used to maintain confidentiality of the data.

The spiral CT images are the photo documentation of the exam. It is acceptable for SCs to utilize digital storage of images (as in CR systems), but the capability to retrieve the images at any time must be maintained. If digital storage is used, a backup digital copy of the images should also be maintained. SC methods for utilizing digital storage must also comply with participant confidentiality standards. If the SC fails to maintain the original screening exam image (due to loss, corruption, or irreversible modification such that the image can no longer be read according to study protocol) and no backup copy exists, this is considered a protocol violation and a PHVF must be completed.

4.7 Interpretation of Findings

Each examination will be reviewed by a board certified or board-eligible chest radiologist who meets current ACR guidelines and holds a valid active medical license and the results of the review, including any abnormalities, will be recorded. The interpretation of findings will be recorded in two distinct steps on the SCT form. The Spiral CT Interpretation Results section (Part D) should reflect the current spiral CT examination findings only. The participant's prior medical history, prior radiologic examinations, or prior NLST/LSS screens should not be considered when assigning the examination result recorded in Part D of the SCT form. The Spiral CT Comparison Results section (Part E) will reflect the comparison of the current spiral CT examination with historical images for that participant, including NLST/LSS screens, any available non-NLST/LSS images, as well as any accompanying radiologic reports. At T_1 and T_2, the current examination must be compared to prior NLST/LSS screens, as well as any other available studies as described below. The result of the comparison read recorded in Item E.3a is considered to be the final result of the screening examination, and this is the result that will be communicated to both the participant and the participant's physician.

To complete Part E, T_1 screening exams must be compared with T_0 screening exams. T_2 screening exams must be compared with T_0 and T_1 exams. However, if the screening examinations from

all three study years are negative, then the T_2 screening examination may be compared with either the T_0 or T_1 screen, or both screens, at the radiologist's discretion. If the T_0 and T_1 exams are lost or are otherwise unavailable, the radiologist should mark "No Image Available" in Item E.1 and state the reason in the Comments section, Item E.5. In addition, a Protocol and HIPAA Violation Form should be completed. The type of protocol violation should be marked as "Other" and described in the space provided. State that the comparison read was not performed and provide the reason. For example, "T_1 comparison read not performed, T_0 exam was lost." The date the protocol violation occurred is the date that the current screening exam was read. If either the T_0 or T_1 screening exam was not completed, then the T_2 exam should be compared to the existing previous exam and no PHVF is required.

In the event that a screening exam is inadequate and a repeat screen is performed, the inadequate screen may be used as the comparison image for the repeat screen at the radiologist's discretion. For example, if a T_1 screen is inadequate and a repeat T_1 screen is performed, then both the T_0 and the inadequate T_1 screens may be used as comparison images for the repeat T_1 screen. An inadequate screen may also be used for comparison in later study years. In this instance, the use of the inadequate screen should be noted in the Comments section of the SCT form.

The following definitions of normal, abnormal, and inadequate findings are provided. These definitions will be used by the radiologist in recording his/her findings on the SCT form.

4.7.1 Classification and Definition of Abnormal Examination Results

Definitions of lung screening results are given below:

- **Positive Screen – Abnormalities suspicious for lung cancer:**

  The following abnormality is always considered a positive screen:

  - Non-calcified nodule/mass $\geq$ 4.0 mm

  Other abnormalities, or constellations of abnormalities, may be suggestive of lung cancer, but there is no absolute rule for coding other findings as suspicious for lung cancer. In these instances, the classification of a screening exam result as positive is left up to the radiologist.

  If, at the T_1 or T_2 study year, the current screen is positive and the abnormality identified appears not to have changed when compared to previous images at the comparison reading (Part E), the radiologist should record the result in the Spiral CT

Comparison Results section (Item E.3a) as B – "Abnormalities suspicious for lung cancer, no significant change."

When previous images from two successive study years have not changed and the third screen is positive and appears unchanged from the previous images, the radiologist may code that result as D – "Minor abnormalities not suspicious for lung cancer" at his/her discretion, rather than coding the image as suspicious for lung cancer. Additionally, the radiologist should specify in the Comments section (Item E.5) why the result was coded as D.

- **Negative Screen – Clinically significant abnormalities not suspicious for lung cancer:**

The review of the scan reveals that an abnormality is present and requires further evaluation, but is not suggestive of lung malignancy. It is up to the radiologist to determine whether an abnormality is clinically significant. If after baseline screening a clinically significant abnormality remains stable and unchanged on subsequent screening examinations, the abnormality may be coded as D – "Minor abnormalities not suspicious for lung cancer" at the discretion of the radiologist, rather than coding the image as a clinically significant abnormality. Additionally, the radiologist should specify in the Comments section (Item E.5) why the result was coded as a D.

- **Negative Screen – Minor abnormalities not suspicious for lung cancer:**

The review of the scan reveals a minor abnormality that is not suspicious for lung cancer. It is up to the radiologist to determine whether an abnormality is minor.

4.7.2 Criteria for Determination of a Negative or an Inadequate Spiral CT

- **Negative Screen – No significant abnormalities:**

The review of the scan reveals no significant abnormalities.

- **Inadequate:**

A spiral CT will be judged to be inadequate if the image does not include both lungs from apex through the lung bases, including both costophrenic angles. Reasons for inadequacy may include, but are not limited to:

- Participant refusal;
- Equipment malfunction;
- Poor image quality, including:
  - Motion or processing artifact;
  - Incomplete evaluation of the thorax;

- Inappropriate CT technique, and

- Excessive noise.

If the image is considered inadequate, but based on what is visible on the image there is an overt suspicion of lung cancer, the result of the screening exam should be recorded as positive.

4.8 Reporting Results to Participants and Health Care Providers

The SC should report results of a spiral CT screening examination in writing to the participant and to the participant's health care provider **within three weeks of the screening visit**. Results should be sent with a cover letter on SC letterhead. The SC may choose to incorporate results into the cover letter, may attach a copy of the radiologist's dictated report, or may produce a customized report of results. The SCT form should not be sent to the participant to report the results of the screening exam. The combination of documents sent must reflect the results of the examination. In addition to written notification, positive screens and negative screens with clinically significant abnormalities will be reported to participants by telephone. If the participant is unreachable by telephone, the results will be sent by certified mail with return receipt requested. Positive screens and negative screens with clinically significant abnormalities will be reported to the health care provider either by telephone, fax, or certified mail. If the fax method is chosen, it is recommended that the health care provider's office is telephoned and advised of the fax transmittal in advance. Other negative screens will be reported to the participant and his/her health care provider according to standard radiologic practice at the SC.

The guidelines provided above for reporting results to participants and health care providers are the minimum acceptable procedures, as set by the NCI. Individual institutional policies may require some SCs to take additional measures for reporting results. See Chapter 6 for additional information regarding reporting results of screening examinations.

Participants with a result of "Positive Screen" will be referred to their health care provider for further evaluation. If a participant does not have a health care provider, the SC will offer a list from which the participant may choose a health care provider to receive the results. In all cases where there is a positive spiral CT screen, referral will be recommended as outlined in Section 4.8.1. The SC will continue to monitor and follow up with all participants who have had a positive screening result.

4.8.1 Diagnostic Follow-up Recommendations

Participants with positive spiral CT screens will be referred to their health care providers. They and their health care providers will also be provided with general recommendations that the radiologist feels are appropriate for the findings from the screening examination. The status of the participant referral (e.g., saw health care provider; has not seen health care provider but appointment has been scheduled; plans to schedule appointment; has no plans for follow-up) should be monitored by the SC. If requested, the SC Coordinator will offer the participant a list from which s/he may choose a specialist.

The NCI does not provide recommendations for diagnostic follow-up of positive screens to the participant or to his/her health care provider. The recommended diagnostic options listed on the SCT form reflect typical options for follow-up in accordance with standard practices at the SC. In all communications it must be clear that the recommendations do not arise from and are not endorsed by the NCI. The SC should refer inquiries to providers that are considered to be experts in the field and provide the 1-800-4-CANCER hotline number as an additional source of information. It is expected that diagnostic evaluation will adhere to current medical standards of practice.

4.8.2 Lung Cancer Diagnosis

The final diagnosis of lung cancer will be made by histopathology or cytopathology, or in rare cases, by clinical examination only. Pathology reports that support the cancer diagnosis will be obtained for all participants. The cancer will be coded according to ICD-O-3 codes by a certified tumor registrar (CTR) at the SC. The diagnosis will be documented by the SC on the DE form (Appendix 7-2) and submitted to the CC.

4.8.3 Treatment Recommendations for Individuals Diagnosed with Lung Cancer

The NLST/LSS does not make specific treatment recommendations for individuals diagnosed with lung cancer. Participation in the NLST/LSS does not preclude a participant from involvement in any treatment protocol.

4.9 Examination Standardization and Quality Control

NLST/LSS has implemented a three-pronged approach to quality assurance and control to ensure standardization throughout the screening process. The quality assurance (QA) measures include equipment and personnel quality control (QC), image QA, and image interpretation QA. The NLST/LSS Screening QA Working Group developed and implemented the QA protocol. The Mallinckrodt Institute of Radiology at Washington University, the Quality Assurance Coordinating Center (QACC), is overseeing the administration of the QA protocol with support from the CC.

4.9.1 Quality Control of Equipment

Quality control (QC) of the equipment will be assured by the individual institution according to the guidelines for equipment quality control developed by the NLST/LSS Screening QA Working Group and the NLST Medical Physicist Working Group. The equipment quality control guidelines are based upon the guidelines outlined by the American College of Radiology (ACR) for ongoing equipment QC measures. Each SC must designate a qualified medical physicist to oversee the equipment QC and to ensure that ACR guidelines are met. The medical physicist will be required to complete and submit an ECT (Appendix 11-5) to the CC. It will be the primary responsibility of the medical physicist at each site to implement and document the equipment QC protocol. The SC should maintain records of equipment maintenance and QC activities that are readily available for auditing during site visits.

The quality control guidelines consist of the Low Dose Chest CT Protocol Specifications listed in Appendix 4-1, the CT Quality Assurance Information listed in Appendix 4-5, and the forms found in Appendices 4-6 through 4-9, which will be completed by the medical physicist at each SC and returned to the Screening QA Working Group to provide documentation of adherence to the CT protocol specifications and equipment testing requirements. Documentation of equipment characteristics is provided once for each piece of equipment and is updated as necessary. Attestation to performance testing and documentation of CT dosimetry measurements are provided annually and documentation of water phantom measurement is provided bi-monthly. Once screening operations have officially ended, as described in Section 3.4.3, completion of equipment QC tests and forms is no longer required.

4.9.2 Quality Control of Technologists

The CC will maintain a complete list of the radiologic technologists working at all SCs. The radiologic technologists are required to complete and submit an ECT (Appendix 11-5) to the CC. For each radiologic technologist, the CC will monitor the number of and reasons for inadequate screening examinations. The CC will consider the final result as inadequate if the screening examination cannot be repeated to obtain an adequate examination.

4.9.3 Image Quality Assurance

The goal of image QA is to establish consistency across the SCs in the adequacy of the screening images obtained and the appropriateness of the acquisition parameters. It is not the purpose of image QA to comment on the interpretation of the images by the radiologists. Information derived from image QA will be used to report on the adequacy of screening images and for educational and training purposes. The process of image QA is outlined below.

4.9.3.1 Image QA System Overview

Image QA will be performed using a Web-based system developed by the QACC. The QACC distributed a Clinical Studies Workstation (CSW) to each SC for use with image QA. The CSW consists of PC compatible hardware and software developed to assist with image anonymization and image collection for clinical trials. The QACC developed and distributed the *NLST/LSS Clinical Studies Workstation User's Guide* (Appendix 4-10) to the SCs to aid in the installation, use, and maintenance of the CSW. The SCs will transmit images from the CSW to the QACC using a Virtual Private Network (VPN) over the Internet. The QACC will then copy the images to a Web-based system that will be used by the radiologists for image review. A detailed overview of the image transmittal process can be found in Section 2 of the *CSW User's Guide*.

4.9.3.2 Image QA Radiologists

The image QA review process will be conducted by four NLST/LSS radiologists, all members of the NLST/LSS Screening QA Working Group. The QA radiologists are designated by the

NLST/LSS Screening QA Working Group with approval by NCI. Each QA radiologist will review approximately six to seven electronic image sets per week and will perform quarterly visits to those SCs that use screen film for chest x-ray images (refer to section 5.9.3.1 for details). The QA radiologists received separate training on the CSW for image transmittal and review. QA radiologists will also accompany NCI and the CC on annual site visits to the SCs. As part of the annual site visits, QA radiologists will observe screening exams, verify technical parameters being used for screening, meet with the SC lead radiologist, participate in the exit interview, and write a QA site visit report.

4.9.3.3 Selection of Images for QA

The number of images to be reviewed for image quality and correctness of image parameters is driven by two quantities: the acceptable percentage of inadequate images and the percentage of truly inadequate images that are detected as inadequate. An image set is considered to be inadequate if it is of substandard quality (i.e., does not include a clear view of the entire lung field) or its acquisition parameters lie outside the ranges set forth by the NLST protocol. The number of image sets chosen for image QA will be 430 for each screening arm (for a total of 860), which was calculated assuming a 1% acceptable inadequate rate and assuming that 3% of truly inadequate exams will not be detected as inadequate.

The CC will randomly select 72 image sets for QA review (36 SCT/36 XRY) on a monthly basis. Each of the image sets selected will be assigned to one of the four QA radiologists. QA radiologists will not review image sets from their own screening center. Image sets will be selected from exams recorded as being of adequate diagnostic quality on the SCT or XRY form and for which data has been received at the CC the month prior to the selection process. Repeat screening exams (due to the first exam failing image QA) will be eligible for future selection as a QA image set. Screen films will be identified from the XRY form and included in the selection process although the films will not be sent to the QACC. Screen films will be reviewed separately at site visits, as described in section 5.9.3.1.

The CC will send by e-mail the PID, type of image (digital vs. screen film), screening date, and ID number of the assigned reviewer to the QACC on the 15th day of every month (or closest business day). The CC also will send each SC a list of PIDs, type of image, and screening dates for selected images on the 15th day of every month. The SCs will only see their list of images selected for QA. After receiving the monthly list, each SC will have one week to transmit the requested image sets to the QACC.

4.9.3.4 Transmitting Images

The *CSW User's Guide* (Appendix 4-10) gives detailed instruction on transmitting image sets between the SC and the QACC. Depending on local protocol, these images are most likely stored on a Picture Archive and Communications System (PACS) in the Radiology Department or on a single-purpose storage device under the control of the screening center.

Once the CC e-mails the list of image sets selected for review, a designated staff member at the SC will transmit those images to the CSW at the SC. After the images are received at the CSW, a staff member removes the personal identifiers and transmits the image sets from the CSW to the QACC using a VPN over the Internet. While the PID remains on the image sets, no personal identifying information is included in the transmission.

A check-in process is performed as the image sets are received at the QACC, which includes assigning a unique accession number to each image set to replace the PID. Only the QACC has the key to cross-reference the PID and the accession number. The images are then copied to a Web-based system that is used by the radiologists for image quality review. At the same time, a second Web-based system is updated to give the QA radiologist a list of studies to review. The QA radiologist performing reviews will use a Web browser (Internet Explorer) and connect to the QACC through the same VPN software as used by the SCs to transmit images. Once the connection is made, the Web browser can connect to the Web server and provide images for review.

Although the CC will generate and send a list of images selected for QA review to the QACC and the SCs on a monthly basis, the QACC will submit a subset of the selected images to the four QA radiologists on weekly basis for review (approximately six to seven images per week per QA radiologist). This will help the QA radiologists avoid a backlog of images needing review. It is the responsibility of the QACC to track images submitted to the QACC from the SCs, to track images sent to the QA radiologists for review, and to track those images for which the review process is complete. The CC will assist the QACC in contacting SCs if image transmittal is delinquent.

4.9.3.5 Completing the Image Quality Review

Detailed instructions for the QA radiologists to complete the review process are outlined in Section 8 of the *CSW User's Guide*. QA review involves the use of two desktop windows, the *NLST QA Homepage* and *Easyweb Login*. After logging on the QA radiologist will see the image sets scheduled for his or her review and may then launch the image review application called *Easyweb*. The QA radiologist will be blinded to the PID number and its SC, and will only see an accession number provided by the QACC.

The QA radiologist will complete a simple, single-screen table for each selected image set. The table asks the QA radiologist to review the image in terms of appropriate acquisition parameters used and acceptable image quality. The QA radiologist also will state whether in his or her opinion a re-screen is necessary for the participant.

If a discrepancy exists between the QA radiologist and the screening radiologist as to the adequacy of the image set, or the acquisition parameters are found to lie outside the range specified by the NLST protocol, the image set is considered inadequate. Image sets that are found to be inadequate by initial review of the QA radiologist will be sent to the remaining QA radiologists for adjudication. The QA radiologists will be blind to the adjudication process; they will not know that the image set has previously "failed" the QA review. The majority opinion on the QA review will dictate the disposition of the image set.

If the acquisition parameters lie outside the range set forth in the NLST protocol, the QACC will contact the CC to obtain a PHVF from the SC where the image set was obtained. The QA radiologist will decide whether the participant needs to be re-screened when the image set is adequate yet the acquisition parameters are outside the specified range. An image set is considered unsatisfactory if the image set is inadequate, the acquisition parameters are out of range, or both.

It is the responsibility of the QACC to track unsatisfactory image sets being sent to the QA radiologists for subsequent review. In the event an image set "fails" the QA review process (two or more of the QA radiologists deem the image quality or acquisition parameters unsatisfactory), then the QACC will notify the CC with the PID of the unsatisfactory image set as soon as it is identified. The CC then will notify the SC regarding scheduling a repeat screening examination for the participant. The SC should contact the participant and schedule a repeat screening examination as soon as possible. The SC

will track those participants requiring a repeat screening examination due to image QA and document such on the screening exam form.

4.9.3.6 Ensuring Participant Anonymization

Section 10 of the *CSW User's Guide* outlines the participant anonymization process. At the SCs imaging studies are sent directly from the CT or CR scanners, or PACS to the CSW. The CSW stores the image sets with no modifications on the local disk system. The CSW software presents the participant's name to the SC user to help ensure that the proper studies are forwarded to the QACC.

When the CSW user transmits a study to the QACC, the workstation software automatically removes the participant identifiers from the DICOM headers. Before transmitting the image sets the user specifies the PIDs of the images being transmitted. The PID is required by the QACC to identify the proper study for QA. The CSW system uses a commercial VPN solution to connect the workstation to computer systems at the QACC behind a firewall. The VPN uses 128 bit encryption software on the workstation and a firewall system at the QACC.

The QACC will have only the PID to identify the image sets transmitted by the SCs. The QACC will have no mechanism to link these images to the participant. It is assumed that the SCs will have some means of linking PIDs with participant identifiers. Steps to ensure anonymization of images are designed to satisfy IRB or HIPAA requirements. The QACC will work with the SCs to ensure that their anonymization needs are met and that the proper documentation is available for IRB review.

4.9.3.7 Data Transmission, Management, and Reporting

The QACC will send data to the CC on a quarterly basis. The QACC and the CC have agreed to the type and format of the image QA data to be sent. The CC has created a separate QA database to manage all NLST/LSS QA activities, including tracking, scheduling, and reporting. The database will be used in conjunction with the QACC database and IDEAS. The NCI and the NLST/LSS Screening QA Working Group will designate type, substance, and frequency of reports to be generated from the image QA data. The CC will generate regular reports from the image QA review process.

4.9.4 Image Interpretation QA

The NLST/LSS Reader Variability Study (RVS) will assess Quality Control (QC) of spiral CT interpretation by determining the level of association between the results coded by the study radiologists at T_0. The study will be coordinated by the Quality Assurance Coordinating Center (QACC) in association with the CC. All NLST/LSS radiologists will be asked to participate in the study, which will be conducted during the first year of NLST.

The CC will randomly select PID numbers for images in the following categories and submit them to the SC Coordinators:

- 51 (non-calcified nodule/mass>/= 4mm)
- 52 (non-calcified nodule<4mm)
- 53 (benign lung nodule(s) (benign calcification)
- Cases coded >/= 54 (all other abnormal cases)

The SCs will be asked to forward the selected images to the QACC in the same manner in which they currently submit QA images. The QACC will compile all of the images on one CD and send it to the lead radiologist at each site. Reporting sheets will also be designed by the QACC and sent to the SC.

Radiologists will be asked to view all the images and classify them into one of the above categories. Images will be read using the built-in reader functions on the clinical workstation (CWS) provided by NLST/LSS to ensure standard monitor resolution and image quality. The radiologists will also be asked to measure the size of the nodule using tools built into the reader. The data will be anonymously submitted on the QA Web site using the form described above.

The QACC will gather and analyze the data and present it at an NLST/LSS Steering Committee Meeting. The results of the study will guide future NLST/LSS study activities including possible training and further research.

Appendices for Chapter 4

4-1 Low Dose Chest CT Protocol Specifications

4-2 American College of Radiology (ACR) Guidelines

4-3 Spiral CT Screening Examination Form (SCT)

4-4 Specifications for Completion of the Spiral CT Screening Examination Form

4-5 CT Quality Assurance Information

4-6 CT Equipment Characteristics Form

4-7 Attestation to CT Performance Testing Form

4-8 Bi-Monthly CT Water Phantom Measurement Form

4-9 CT Dosimetry Measurements Form

4-10 NSLT/LSS Clinical Studies Workstation User's Guide

4-11 NLST/LSS Screening Exam Form Data Handling Guidelines

NATIONAL LUNG SCREENING TRIAL (NLST)
EQUIPMENT QUALITY CONTROL

LOW DOSE CHEST CT PROTOCOL SPECIFICATIONS

NLST CT Specifications:

(agreed to at joint LSS/ACRIN NLST Medical Physicist Working Group Meeting (MPWG), June 6, 2003)

1. Only multi detector CT scanners with a minimum of four channels shall be used.

2. The CT kVp range shall be 120 – 140; 120 is preferred.

3. Reconstructed slice thickness may range from 1.0 – 2.5 mm.

4. Effective slice thickness (if known) may not exceed 3.2 mm.

5. CT pitch (i.e., table movement per rotation / total collimation) may range from 1.25 – 2.00.

6. The mAs (i.e., mA x scan rotation time) may range from 40*- 80.

7. The effective mAs (i.e., mAs / pitch) may range from 20*- 60, with the following stipulations pertaining to the dose / image quality balance.

* may operate below minimums if reason documented (e.g., higher kVp, less filtration, etc.)

- Sites should use the lowest effective mAs that achieves acceptable image quality.
- The effective mAs specification shall be reviewed by the MPWG in six months.

8. The specification of a maximum reference dose shall be reviewed after all sites have completed consistent dose (CTDI) measurements using NLST protocol techniques.

The MPWG recommends ancillary studies to address the question of maximum acceptable noise level at minimum dose.

9. The topogram “scout” view(s) technique should reflect the following:

- The initial scout view may be LAT or PA (not AP, to spare breast dose).
- A second scout view, PA or LAT, may be done if desired.
- Allowable scout techniques should be reviewed, and set as low as possible to minimize patient dose.

10. The total CT scan time should be kept to a maximum of 25 seconds to facilitate reasonable breath holds (LSS specification; not discussed at joint meeting).

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The American College of Radiology will periodically define new practice guidelines and technical standards for radiologic practice to help advance the science of radiology and to improve the quality of service to patients throughout the United States. Existing practice guidelines and technical standards will be reviewed for revision or renewal, as appropriate, on their fifth anniversary or sooner, if indicated.

Each practice guideline and technical standard, representing a policy statement by the College, has undergone a thorough consensus process in which it has been subjected to extensive review, requiring the approval of the Commission on Quality and Safety as well as the ACR Board of Chancellors, the ACR Council Steering Committee, and the ACR Council. The practice guidelines and technical standards recognize that the safe and effective use of diagnostic and therapeutic radiology requires specific training, skills, and techniques, as described in each document. Reproduction or modification of the published practice guideline and technical standard by those entities not providing these services is not authorized.

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ACR PRACTICE GUIDELINE FOR COMMUNICATION: DIAGNOSTIC RADIOLOGY

PREAMBLE

These guidelines are an educational tool designed to assist practitioners in providing appropriate radiologic care for patients. They are not inflexible rules or requirements of practice and are not intended, nor should they be used, to establish a legal standard of care. For these reasons and those set forth below, the American College of Radiology cautions against the use of these guidelines in litigation in which the clinical decisions of a practitioner are called into question.

The ultimate judgment regarding the propriety of any specific procedure or course of action must be made by the physician or medical physicist in light of all the circumstances presented. Thus, an approach that differs from the guidelines, standing alone, does not necessarily imply that the approach was below the standard of care. To the contrary, a conscientious practitioner may responsibly adopt a course of action different from that set forth in the guidelines when, in the reasonable judgment of the practitioner, such course of action is indicated by the condition of the patient, limitations on available resources or advances in knowledge or technology subsequent to publication of the guidelines. However, a practitioner who employs an approach substantially different from these guidelines is advised to document in the patient record information sufficient to explain the approach taken.

The practice of medicine involves not only the science, but also the art of dealing with the prevention, diagnosis, alleviation and treatment of disease. The variety and complexity of human conditions make it impossible to always reach the most appropriate diagnosis or to predict with certainty a particular response to treatment. It should be recognized, therefore, that adherence to these guidelines will not assure an accurate diagnosis or a successful outcome. All that should be expected is that the practitioner will follow a reasonable course of action based on current knowledge, available resources, and the needs of the patient to deliver effective and safe medical care. The sole purpose of these guidelines is to assist practitioners in achieving this objective.

I. INTRODUCTION

Communication is a critical component of the art and science of medicine and is especially important in diagnostic radiology. An official interpretation[1] shall be generated following any examination, procedure, or officially requested consultation. In addition, the interpreting physician and the referring physician or other health care provider have other opportunities to communicate directly with each other during the course of a patient's case management. Such communication should be encouraged because it promotes optimal patient

[1]The ACR Medical Legal Committee defines official interpretation as that written report (and any supplements or amendments thereto) that attach to the patient's permanent record. In healthcare facilities with a privilege delineation system, such a written report is prepared only by a qualified physician who has been granted specific delineated clinical privileges for that purpose by the facility's governing body upon the recommendation of the medical staff.

care and focuses attention on selection of appropriate and cost-effective imaging studies, clinical efficacy, and radiation exposure.

Diagnostic radiology practice is primarily a consultative physician service. The interests of both patients and their referring physicians are well served when the following are among the elements of the radiologic consultation and are completed in all practice settings: a) pre-examination evaluation of the patient by the referring physician; and b) a request for radiologic consultation that includes pertinent clinical findings, a working diagnosis, presenting signs or symptoms, and specific question to be answered by the radiology study. Such information assists both in promoting optimal patient care through interpretation of images based on appropriate clinical information and in enhancing the cost-effectiveness of diagnostic examinations by obtaining the optimal images.

Communication of patient information must be in accordance with federal and state privacy requirements.

II. THE DIAGNOSTIC RADIOLOGY REPORT

An official interpretation (final written report) shall be provided with all radiologic studies regardless of the site of performance (hospital, imaging center, physician office, mobile unit, etc.). The report should include the following items as a minimum:

A. Demographics

1. Name of patient and another identifier, such as social security number or hospital or office identification number.
2. Name of any referring physician(s) or other health care provider(s).
3. Name or type of examination.
4. Date of the examination.
5. Time of the examination, if relevant (e.g., for patients who are likely to have more than one of a given examination per day).
6. Inclusion of the following additional items is encouraged:
   a. Date of dictation
   b. Date of transcription
   c. Birth date or age
   d. Gender

B. Relevant clinical information and ICD-9 code as available

C. Body of the Report

1. Procedures and materials
   The report should include a description of the studies and/or procedures performed and any contrast media (including concentration and volume when applicable), medications, catheters, or devices used, if not recorded elsewhere. Any known significant patient reaction or complication should be recorded.
2. Findings
   The report should use precise anatomic, pathologic, and radiologic terminology to describe the findings accurately.
3. Potential limitations
   The report should, when appropriate, identify factors that may limit the sensitivity and specificity of the examination.
4. Clinical issues
   The report should address or answer any pertinent clinical issues raised in the request for the imaging examination.
5. Comparative data
   Comparison with relevant previous examinations and reports should be part of the radiologic consultation and report when appropriate and available.

D. Impression (Conclusion or Diagnosis)

1. Unless the report is brief, each report should contain an "impression" section.
2. A precise diagnosis should be given whenever possible.
3. A differential diagnosis should be given when appropriate.
4. Follow-up or additional diagnostic studies to clarify or confirm the impression should be suggested when appropriate.
5. Any significant patient reaction should be reported in the impression.

III. OFFICIAL INTERPRETATION (FINAL WRITTEN REPORT)

A. The final written report is considered to be the definitive means of communicating the results of an imaging examination or procedure to the referring physician. Other methods for direct or personal communication of results are encouraged in certain situations. The timeliness of reporting any radiologic examination varies with the nature and urgency of the clinical problem.

B. The final report should be proofread to minimize typographical errors, deleted words, and confusing or conflicting statements.

C. The final report should be completed in accordance with appropriate state and federal requirements (see the Final Regulations, Mammography Quality Standards Act for Mammography Reporting). Electronic or rubber-stamp signature devices, instead of a written signature, are acceptable if access to them is secure.

D. The final report should be sent to the referring physician or health care provider providing the clinical follow-up. It should be noted that the referring physician or health care provider also shares in the responsibility of obtaining results of imaging studies they have ordered.

E. When feasible, a copy of the final report should accompany the transmittal of relevant images to other health care professionals.

F. A copy of the final report should be kept as part of the patient's medical record (paper or electronic) and be retrievable for future reference. Retention of these records should be in accordance with state and federal regulations and facility policies.

IV. OTHER INTERPRETATIONS

A. If requested to render an interpretation of an imaging study obtained at another facility, radiologists are encouraged to document their interpretations either by means of a formal report or other written documentation.

B. If requested to render an interpretation of an imaging study obtained at the same facility and previously reported, and a discrepancy is noted, an addendum should be rendered.

V. COMMUNICATION

A. Direct communication is accomplished in person or by telephone to the referring physician or an appropriate representative. Documentation of direct communication is recommended. In those situations in which the interpreting physician feels that immediate patient treatment is indicated (e.g., tension pneumothorax), the interpreting physician should communicate directly with the referring physician, other health care provider, or an appropriate representative. If that individual cannot be reached, the interpreting physician should directly communicate the need for emergent care to the patient or responsible guardian, if possible.

B. Under some circumstances, practice constraints may dictate the necessity of a preliminary report before the final report is prepared. A significant change between the preliminary and final interpretation should be reported directly to the referring physician.

C. In those situations in which the interpreting physician feels that the findings do not warrant immediate treatment but constitute significant unexpected findings, the interpreting physician or his/her designee should communicate the findings to the referring physician, other healthcare provider, or an appropriate individual in a manner that reasonably insures receipt of the findings.

VI. SELF-REFERRED PATIENTS

Radiologists should recognize the potential obligations of assuming the care and treatment of patients who present themselves for imaging studies on a self-referred basis. Such obligations may include communicating the results of the imaging studies to the patient and the necessity of appropriate follow-up.

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ACR PRACTICE GUIDELINE FOR GENERAL RADIOGRAPHY

PREAMBLE

These guidelines are an educational tool designed to assist practitioners in providing appropriate radiologic care for patients. They are not inflexible rules or requirements of practice and are not intended, nor should they be used, to establish a legal standard of care. For these reasons and those set forth below, the American College of Radiology cautions against the use of these guidelines in litigation in which the clinical decisions of a practitioner are called into question.

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I. INTRODUCTION

Radiography is a proven and useful procedure that utilizes differences in X-ray attenuation to evaluate human anatomy and pathology. The goal of radiography is to establish the presence or absence and nature of disease by demonstration of the disease process itself or the effects of the disease process on the normal anatomy. The study should be done with the minimal radiation dose necessary to achieve an optimal study.

If an American College of Radiology (ACR) guideline or standard exists for the specific type of radiographic examination being performed, that guideline or standard as well as the general guidelines below would apply.

II. INDICATIONS AND CONTRAINDICATIONS

A. There are many indications for radiography, and these are dependent on the patient's clinical history and the disease processes that affect the anatomic area to be

studied. There should be a sufficient clinical indication to warrant performance of a study, and a reasonable anticipation that the results of the radiograph, normal or abnormal, will influence the treatment course of the patient. The indications should be communicated to the facility and the physician responsible for performance and interpretation of the radiographic study. The ACR Appropriateness Criteria™ should be considered when making these communications.

B. All imaging facilities should have policies and procedures to reasonably attempt to identify pregnant patients prior to the performance of any diagnostic examination involving ionizing radiation. If the patient is known to be pregnant, the potential radiation risks to the fetus and clinical benefits of the procedure should be considered before proceeding with the study (Res. 24, 1995).

III. QUALIFICATIONS AND RESPONSIBILITIES OF PERSONNEL

A. Physician

Radiographs must be obtained under the supervision of, and interpreted by, a licensed physician with the following qualifications:

1. Certification in Radiology or Diagnostic Radiology by the American Board of Radiology, the American Osteopathic Board of Radiology, the Royal College of Physicians and Surgeons of Canada, or Le College des Medecins du Quebec.

or

2. The physician shall have documented a minimum of 6 months of formal dedicated training in the interpretation and formal reporting of general radiographs, including patients of all ages, in an Accreditation Council for Graduate Medical Education (ACGME) approved residency program including radiographic training on all body areas.

and

3. The physician should have documented training and understanding of the physics of diagnostic radiography and experience with the equipment needed to safely produce the images. This should include general radiography, screen-film combinations, conventional image processing, and, where applicable, digital image processing.

and

4. The physician must be familiar with the principles of radiation protection, the hazards of radiation exposure to both patients and radiologic personnel, and radiation monitoring requirement.

and

5. The physician shall have documented training and understanding of other medical imaging modalities (fluoroscopy, computed tomography, ultrasound, magnetic resonance imaging, nuclear medicine, etc.) and their value relative to general radiography in order to best evaluate the patient's clinical symptoms.

B. Maintenance of Competence

All physicians performing general radiography examinations should demonstrate evidence of continuing competence in the interpretation and reporting of those examinations. If competence is assured primarily based on continuing experience, a minimum of 200 examinations per year is recommended in order to maintain the physician's skills. Because a physician's practice or location may preclude this method, continued competency can also be assured through monitoring and evaluation that indicates acceptable technical success, accuracy of interpretation, and appropriateness of evaluation.

Continuing Medical Education

The physician's continuing medical education should be in accordance with the ACR Practice Guideline for Continuing Medical Education (CME) and should include CME in general radiography as is appropriate to his/her practice.

C. Medical Physicist

A Qualified Medical Physicist is an individual who is competent to practice independently one or more of the subfields in medical physics. The ACR considers that certification and continuing education in the appropriate subfield(s) demonstrate that an individual is competent to practice one or more of the subfields in medical physics, and to be a Qualified Medical Physicist. The ACR recommends that the individual be certified in the appropriate subfield(s) by the American Board of Radiology (ABR).

The appropriate subfields of medical physics for this guideline are Therapeutic Radiological Physics, Diagnostic Radiological Physics, Medical Nuclear Physics, and Radiological Physics.

The continuing education of a Qualified Medical Physicist should be in accordance with the ACR Practice Guideline for Continuing Medical Education (CME).

D. Radiologic Technologist

Certification by the American Registry of Radiologic Technologists (ARRT) or an unrestricted state license is required.

IV. SPECIFICATIONS OF THE EXAMINATION

The written request for a radiographic examination should contain appropriate clinical history and the reason for the examination. This request should be completed under the supervision of the referring physician or other allied healthcare professional for whom this activity is within the scope of practice.

Technique

1. All radiographic studies should be permanently labeled with patient identification and date of the examination. The time of the examination should be included, if relevant. The side (right or left) of the anatomic site radiographed should be permanently labeled.

2. All facilities performing radiography should have protocols for standard views of each anatomic area that will be radiographed. These should be designed to optimize diagnostic information while minimizing radiation exposure.

3. Appropriate collimation should be used to limit exposure to the anatomic area of interest.

4. All facilities performing radiography should have technique charts listing exposure factors that will reliably produce diagnostic radiographs of anatomic parts of patients of different sizes to minimize the need for repeat exposures. Repeat rates should be part of the routine quality control process.

5. All radiographs should be reviewed for positioning and diagnostic quality at the facility before the patient is released. Repeat radiographs should be performed when necessary for diagnostic quality.

6. All facilities producing radiographs should have policies and procedures for appropriate shielding of patients.

7. Immobilization and assistance procedures appropriate for the age and size range of patients to be imaged should be available to ensure that images of diagnostic quality can be obtained in patients who are unable to cooperate, or unable to be positioned in the usual manner due to age or physical limitations, and without unnecessary irradiation of healthcare workers.

V. DOCUMENTATION

Reporting should be in accordance with the ACR Practice Guideline for Communication: Diagnostic Radiology.

VI. EQUIPMENT SPECIFICATIONS

A. The diagnostic radiographic equipment and facility should meet all applicable federal and state radiation standards.

B. Where an analog film system is used, appropriate screen-film and grid combinations should be available to obtain diagnostic radiographs of all anatomic areas to be imaged.

C. Where digital imaging is used, the equipment should meet the specifications described in the ACR Technical Standard for Digital Image Data Management.

D. Automated processing is preferred. Carefully controlled temperature and regular processor maintenance should be included in a quality control program. A constant time and temperature shall be maintained for manual processing.

VII. QUALITY CONTROL AND IMPROVEMENT, SAFETY, INFECTION CONTROL, AND PATIENT EDUCATION CONCERNS

Policies and procedures related to quality, patient education, infection control, and safety should be developed and implemented in accordance with the ACR Policy on Quality Control and Improvement, Safety, Infection Control, and Patient Education Concerns appearing elsewhere in the ACR Practice Guidelines and Technical Standards book.

Equipment performance monitoring should be in accordance with the ACR Technical Standard for Diagnostic Medical Physics Performance Monitoring of Radiologic and Fluoroscopic Equipment.

ACKNOWLEDGEMENTS

This guideline was revised according to the process described in the ACR Practice Guidelines and Technical Standards book by the Guidelines and Standards

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The American College of Radiology will periodically define new practice guidelines and technical standards for radiologic practice to help advance the science of radiology and to improve the quality of service to patients throughout the United States. Existing practice guidelines and technical standards will be reviewed for revision or renewal, as appropriate, on their fifth anniversary or sooner, if indicated.

Each practice guideline and technical standard, representing a policy statement by the College, has undergone a thorough consensus process in which it has been subjected to extensive review, requiring the approval of the Commission on Quality and Safety as well as the ACR Board of Chancellors, the ACR Council Steering Committee, and the ACR Council. The practice guidelines and technical standards recognize that the safe and effective use of diagnostic and therapeutic radiology requires specific training, skills, and techniques, as described in each document. Reproduction or modification of the published practice guideline and technical standard by those entities not providing these services is not authorized.

2001 (Res. 10)
Amended 2002 (Res. 2)
Effective 1/1/03

ACR PRACTICE GUIDELINE FOR PERFORMING AND INTERPRETING DIAGNOSTIC COMPUTED TOMOGRAPHY (CT)

PREAMBLE

These guidelines are an educational tool designed to assist practitioners in providing appropriate radiologic care for patients. They are not inflexible rules or requirements of practice and are not intended, nor should they be used, to establish a legal standard of care. For these reasons and those set forth below, the American College of Radiology cautions against the use of these guidelines in litigation in which the clinical decisions of a practitioner are called into question.

The ultimate judgment regarding the propriety of any specific procedure or course of action must be made by the physician or medical physicist in light of all the circumstances presented. Thus, an approach that differs from the guidelines, standing alone, does not necessarily imply that the approach was below the standard of care. To the contrary, a conscientious practitioner may responsibly adopt a course of action different from that set forth in the guidelines when, in the reasonable judgment of the practitioner, such course of action is indicated by the condition of the patient, limitations on available resources or advances in knowledge or technology subsequent to publication of the guidelines. However, a practitioner who employs an approach substantially different from these guidelines is advised to document in the patient record information sufficient to explain the approach taken.

The practice of medicine involves not only the science, but also the art of dealing with the prevention, diagnosis, alleviation and treatment of disease. The variety and complexity of human conditions make it impossible to always reach the most appropriate diagnosis or to predict with certainty a particular response to treatment. It should be recognized, therefore, that adherence to these guidelines will not assure an accurate diagnosis or a successful outcome. All that should be expected is that the practitioner will follow a reasonable course of action based on current knowledge, available resources, and the needs of the patient to deliver effective and safe medical care. The sole purpose of these guidelines is to assist practitioners in achieving this objective.

I. INTRODUCTION

Computed tomography (CT) is a proven radiologic modality that provides clinical information in the detection, differentiation, and demarcation of disease. CT is the primary diagnostic modality for a variety of presenting problems and is widely accepted as a supplement to other imaging techniques.

CT is a form of medical imaging that involves the exposure of patients to ionizing radiation. It should only be performed under the supervision of a physician with the necessary training in radiation protection to optimize examination safety. Radiation physicists and trained technical staff must be available.

CT examinations should be performed only for a valid medical reason and with the minimum exposure that provides the image quality necessary for adequate diagnostic information.

This guideline applies to all CT examinations performed in all settings.

(For pediatric considerations see Section IV.)

II. QUALIFICATIONS AND RESPONSIBILITIES OF PERSONNEL

Physicians who supervise, perform, and interpret CT examinations should be licensed medical practitioners who have a thorough understanding of the indications for CT as well as a familiarity with the basic physical principles and limitations of the technology of computed tomography imaging. They should be familiar with alternative and complementary imaging and diagnostic procedures and should be capable of correlating the results of these with CT findings. The physicians should have a thorough understanding of CT technology and instrumentation as well as radiation safety. Physicians responsible for CT examinations should be able to demonstrate familiarity with the anatomy, physiology, and pathophysiology of those organs or anatomic areas that are being examined. These physicians should provide evidence of training and requisite competence needed to perform CT examinations successfully.

A. Physician

All examinations must be performed under the supervision of and interpreted by a physician who has the following qualifications:

1. Certification in Radiology or Diagnostic Radiology by the American Board of Radiology, American Osteopathic Board of Radiology, the Royal College of Physicians and Surgeons of Canada, or Le College des Medecins du Quebec, and involvement with the supervision and/or performance of, as well as interpretation (and/or review) and reporting of, 300 CT examinations in the past 36 months.[1]

   or

   Completion of an accredited diagnostic radiology residency and involvement with the performance of, as well as interpretation and reporting of, 500 CT examinations in the past 36 months.[1]

   or

   For non-radiologists, the completion of an accredited residency in the specialty practiced plus 200 hours of Category I CME in the performance and interpretation of CT in the subspecialty where CT reading occurs, and 500 cases interpreted and reported during the past 36 months in a supervised situation.

   and

2. The physician shall have documented training in the physics of diagnostic radiology. Additionally, the physician must demonstrate training in the principles of radiation protection, the hazards of radiation exposure to both patients and radiologic personnel, and appropriate monitoring requirements.

   and

3. The physician should be thoroughly acquainted with the many morphologic and patho-physiologic manifestations and artifacts demonstrated on CT. Additionally, supervising physicians should have appropriate knowledge of alternative imaging methods, including the use and indications for general radiography and specialized studies such as angiography, ultra-sonography, magnetic resonance imaging, and nuclear medicine studies.

   and

4. The physician should be familiar with patient preparation for the examination. The physician must have had training in the recognition and treatment of adverse effects of contrast materials[2] used for these studies.

   and

5. The physician shall have the responsibility for reviewing all indications for the examination; specifying the use, dosage, and rate of administration of contrast agents[2]; specifying the imaging technique, including appropriate windowing and leveling; interpreting images; generating written reports; and maintaining the quality of both the images and interpretations.

Maintenance of Competence

All physicians performing CT examinations should demonstrate evidence of continuing competence in the interpretation and reporting of those examinations. If competence is assured primarily based on continuing experience, a minimum of 100 examinations per year is recommended in order to maintain the physician's skills. Because a physician's practice or location may preclude this method, continued competency can also be assured through monitoring and evaluation that indicates acceptable technical success, accuracy of interpretation, and appropriateness of evaluation.

Continuing Medical Education

The physician's continuing education should be in accordance with the ACR Practice Guideline for Continuing Medical Education (CME) and should include CME in CT as is appropriate to the physician's practice needs.

[1] Completion of an accredited radiology residency in the past 24 months will be presumed to be satisfactory experience for the reporting and interpreting requirement.

[2] See the ACR Practice Guideline for the Use of Intravascular Contrast Media.

B. Qualified Medical Physicist

A Qualified Medical Physicist is an individual who is competent to practice independently one or more of the subfields in medical physics. The ACR considers certification and continuing education in the appropriate subfield(s) to demonstrate that an individual is competent to practice one or more of the subfield(s) in medical physics and to be a Qualified Medical Physicist. The ACR recommends that the individual be certified in the appropriate subfield(s) by the American Board of Radiology (ABR).

The appropriate subfields of medical physics for computed tomography are Radiological Physics and Diagnostic Radiological Physics.

A Qualified Medical Physicist's continuing education should be in accordance with the ACR Practice Guideline for Continuing Education (CME).

C. Radiologic Technologist

The technologist should have the responsibility for patient comfort, preparing and positioning the patient for the CT examination, monitoring the patient during the examination, and obtaining the CT data in a manner prescribed by the supervising physician. If intravenous contrast material is to be administered, qualifications for technologists performing intravenous injections should be in compliance with current ACR policy statements[3,4] and existing operating procedures or manuals at the imaging facility. The technologist should also perform the regular quality control testing of the CT system under the supervision of a Qualified Medical Physicist.

Technologists performing CT examinations should be certified by the American Registry of Radiologic Technologists (ARRT) or have an unrestricted state license with documented training and experience in CT.

[3]See the ACR Practice Guideline for the Use of Intravascular Contrast Media.

[4]The American College of Radiology approves of the injection of contrast material and diagnostic levels of radiopharmaceuticals by certified and/or licensed radiologic technologists and radiologic nurses under the direction of a radiologist or his or her physician designee who is personally and immediately available, if the practice is in compliance with institutional and state regulations. There must be prior written approval by the medical director of the radiology department/service of such individuals; such approval process having followed established policies and procedures, and the radiologic technologists and radiologic nurses who have been so approved maintain documentation of continuing medical education related to the materials being injected and to the procedures being performed; 1987, 1997 (Res. 1-II).

III. EQUIPMENT SPECIFICATIONS

See the various anatomic CT procedure standards for definitive equipment specifications.

IV. QUALITY CONTROL AND IMPROVEMENT, SAFETY, INFECTION CONTROL, AND PATIENT EDUCATION CONCERNS

Policies and procedures related to quality, patient education, infection control and safety should be developed and implemented in accordance with the ACR Policy on Quality Control and Improvement, Safety, Infection Control, and Patient Education Concerns elsewhere in the ACR Practice Guidelines and Technical Standards book.

A comprehensive CT quality-control program should be documented and maintained at the CT facility. The program should help to minimize radiation risk to the patient, facility personnel, and the public, and to maximize the quality of diagnostic information. CT facility personnel must adhere to radiation safety regulations when inside the scanner room. Overall program responsibility should remain with the physician, but specific program implementation should be supervised by the medical physicist or service engineer in compliance with local and state regulations as well as manufacturer specifications. The facility should maintain a record of quality control tests, frequency of performance, and description of procedures, as well as a list of individuals or groups performing each test. Moreover, the parameters of technique, equipment testing, and acceptability of limits for each test should also be maintained, along with sample records for each test. Quantitative dose determination should be conducted periodically, in addition to equipment performance monitoring.

The supervising physician should review all practices and policies at least annually. Policies with respect to contrast and sedation must be administered in accordance with institutional policy as well as state and federal regulations. A physician should be available on-site whenever intravenous or intrathecal contrast or intravenous sedation is administered.

The lowest possible radiation dose consistent with acceptable image quality should be used in CT examinations of children. Radiation exposure levels and doses should be measured routinely using a reasonable sample of pediatric examinations performed. In all instances, the lowest possible exposure factors should be chosen that would produce images of diagnostic quality. Such factors should be appropriate for the size and age of the child to be examined. These factors may include

mAs, kVp, slice thickness, helical pitch, organs in the radiation field, and lead shielding, among others. Guides to technical factors that can be used effectively in children can be found in the published radiological literature.

All imaging facilities should have policies and procedures to reasonably attempt to identify pregnant patients prior to the performance of any diagnostic examination involving ionizing radiation. If the patient is known to be pregnant, the potential radiation risks to the fetus and clinical benefits of the procedure should be considered before proceeding with the study (Res. 24, 1995).

Equipment performance monitoring should be in accordance with the ACR Technical Standard for the Diagnostic Medical Performance Monitoring of Computed Tomography (CT) Equipment.

ACKNOWLEDGEMENTS

This guideline was developed according to the process described in the ACR Practice Guidelines and Technical Standards book by the Guidelines and Standards Committee of the General and Pediatric Radiology Commission.

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Each practice guideline and technical standard, representing a policy statement by the College, has undergone a thorough consensus process in which it has been subjected to extensive review, requiring the approval of the Commission on Quality and Safety as well as the ACR Board of Chancellors, the ACR Council Steering Committee, and the ACR Council. The practice guidelines and technical standards recognize that the safe and effective use of diagnostic and therapeutic radiology requires specific training, skills, and techniques, as described in each document. Reproduction or modification of the published practice guideline and technical standard by those entities not providing these services is not authorized.

1993 (Res. 2)
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ACR PRACTICE GUIDELINE FOR THE PERFORMANCE OF PEDIATRIC AND ADULT CHEST RADIOGRAPHY

PREAMBLE

These guidelines are an educational tool designed to assist practitioners in providing appropriate radiologic care for patients. They are not inflexible rules or requirements of practice and are not intended, nor should they be used, to establish a legal standard of care. For these reasons and those set forth below, the American College of Radiology cautions against the use of these guidelines in litigation in which the clinical decisions of a practitioner are called into question.

The ultimate judgment regarding the propriety of any specific procedure or course of action must be made by the physician or medical physicist in light of all the circumstances presented. Thus, an approach that differs from the guidelines, standing alone, does not necessarily imply that the approach was below the standard of care. To the contrary, a conscientious practitioner may responsibly adopt a course of action different from that set forth in the guidelines when, in the reasonable judgment of the practitioner, such course of action is indicated by the condition of the patient, limitations on available resources or advances in knowledge or technology subsequent to publication of the guidelines. However, a practitioner who employs an approach substantially different from these guidelines is advised to document in the patient record information sufficient to explain the approach taken.

The practice of medicine involves not only the science, but also the art of dealing with the prevention, diagnosis, alleviation and treatment of disease. The variety and complexity of human conditions make it impossible to always reach the most appropriate diagnosis or to predict with certainty a particular response to treatment. It should be recognized, therefore, that adherence to these guidelines will not assure an accurate diagnosis or a successful outcome. All that should be expected is that the practitioner will follow a reasonable course of action based on current knowledge, available resources, and the needs of the patient to deliver effective and safe medical care. The sole purpose of these guidelines is to assist practitioners in achieving this objective.

I. INTRODUCTION

Chest radiography is a proven and useful procedure for evaluation of the airways, pulmonary parenchyma and vessels, mediastinum, heart, pleura, and chest wall. The common and accepted practice consists of posteroanterior (PA) and left lateral radiographs obtained in the upright position. Under certain clinical circumstances and in certain patient populations (e.g., critically ill, postoperative, newborn), bedside (portable) chest radiography may be indicated and should be performed in accordance with the ACR Practice Guideline for the Performance of Pediatric and Adult Bedside Chest Radiography (Portable Chest Radiography).

(For pediatric considerations, see Section V.C.2.)

II. GOAL

The goal of the chest radiographic examination is to help establish the presence or absence and nature of disease involving the thorax or to follow its course.

III. INDICATIONS AND CONTRAINDICATIONS

Indications for chest radiography include, but are not limited to:

A. Signs and symptoms potentially related to the respiratory, cardiovascular, and upper gastrointestinal systems, and the musculoskeletal system of the thorax. The chest radiograph may also be helpful in evaluating diseases involving the thorax, including systemic and extrathoracic diseases that secondarily involve the thorax. Because the lungs are frequent sites of metastases, chest radiography is usually indicated in the staging of extrathoracic as well as intrathoracic tumors.

B. Follow-up of already diagnosed thoracic disease processes for the evaluation of improvement, resolution, or progression.

C. Monitoring of patients with life-support devices and patients who have undergone cardiac or thoracic surgery or other interventional procedures.

D. Compliance with government regulations that may mandate chest radiography. Examples include immigration chest films, chest films for coal miners, or other surveillance studies required by public health law.

E. Preoperative radiographic evaluation is indicated if cardiac or respiratory symptoms are present or if there is a significant potential for thoracic pathology that may compromise the surgical result or lead to increased perioperative morbidity or mortality.

All imaging facilities should have policies and procedures to reasonably attempt to identify pregnant patients prior to the performance of any diagnostic examination involving ionizing radiation. If the patient is known to be pregnant, the potential radiation risks to the fetus and clinical benefits of the procedure should be considered before proceeding with the study (Res. 24, 1995).

IV. QUALIFICATIONS AND RESPONSIBILITIES OF PERSONNEL

A. Physician

The examination must be performed under the supervision of and interpreted by a licensed physician(s) who has the following qualifications:

1. Certification in Radiology or Diagnostic Radiology by the American Board of Radiology, the American Osteopathic Board of Radiology, the Royal College of Physicians and Surgeons of Canada, or Le College des Medecins du Quebec.

   or

2. The physician shall have spent a minimum of 3 months in documented formal training in the interpretation and formal reporting of chest radiography in an approved residency program. If pediatric chest radiographs are to be interpreted, the physician should also have had 3 months of documented formal training in pediatric radiology, including interpretation and formal reporting of pediatric chest radiographs.

   or

3. Physicians whose residency or fellowship training did not include the above may still be considered qualified to interpret chest radiographs providing the following can be demonstrated:
   a. At least 2 years during which the physician supervised and interpreted chest radiographs.
   b. Generation of a written report for each study performed.

   and

4. The physician should have documented training and understanding of the physics of diagnostic radiology and the equipment needed to produce the images. These include conventional radiography, screen-film combinations, conventional image processing, and, where applicable, digital image processing.

   and

5. The supervising and interpreting physician must be familiar with the principles of radiation protection, the hazards of radiation exposure to both patients and radiographic personnel, and the monitoring requirements.

   and

6. The supervising and interpreting physician must be familiar with the disease processes for which the patient is being evaluated and must understand the many anatomic and physiologic manifestations of these diseases that may be reflected in the chest radiograph, as well as anatomic variants that may mimic disease.

   and

7. The physician supervising and interpreting the chest radiograph should have knowledge of complementary imaging techniques such as ultrasonography, computed tomography, nuclear medicine, magnetic resonance, and angiography, as well as other specialized procedures, in order to fulfill a consultative role.

Continuing Medical Education

The physician's continuing medical education should be in accordance with the ACR Practice Guideline for Continuing Medical Education (CME).

B. Radiologic Technologist

1. Certification by the American Registry of Radiologic Technologists or unrestricted state licensure is required.
2. Qualifications and performance of technologists should comply with procedure manuals at the imaging facility. CME programs and on-the-job training under the supervision of a qualified physician should be available.
3. If pediatric chest radiography is to be performed, documented training in pediatric chest radiography is required.

V. SPECIFICATIONS OF THE EXAMINATION

The written request for the chest radiographic examination should contain appropriate clinical history and the reason for the examination. This request should be completed under the supervision of the referring physician or other allied professionals for whom this activity is within their scope of practice.

A. A standard chest examination should include an erect PA and left lateral projection made during full inspiration (total lung capacity). The examination may be modified by the physician or qualified technologist depending on the clinical circumstances. Other techniques that may be used at times include supine, prone, oblique, decubitus, lordotic, expiratory, or views with nipple markers.

B. The chest radiograph should include both lung apices and both costophrenic angles. There should be appropriate definition of the vertebral bodies, and the left retrocardiac vascular pattern should be visible. The scapulae should be positioned outside the lung fields on the PA view and the arms elevated for the lateral view. The vertebral column should be centered between the clavicles. The radiographic beam should be appropriately collimated to include the structures listed while limiting exposure of the remainder of the patient and should not exceed the geometry of the image receptor.

C. Technical Factors

1. Adults: For a PA chest radiograph, the mean dose at skin entrance should not exceed 0.3 mGy per exposure, and the exposure time should not exceed 40 msec. A high-kilovoltage technique (120-150) should be employed. An anti-scatter technique (e.g., grid or air gap) should be used that reduces scatter at least as much as a 10:1 grid. Technique charts should be posted for use by technologists in the examination room. An optimally exposed radiograph presents the lung at a mid-gray level.

2. Newborns, infants, and children: In newborns and infants, a supine chest radiograph is preferred. For an AP/PA chest radiograph, the mean dose at skin entrance should range from 0.05 to 0.3 mGy per exposure, respectively, for a 1-year-old to adult-sized patient using a 200-speed image receptor. The kVp should be selected to provide adequate contrast; it should range from as low as 60 for infants to as high as 150 for adult-size patients. When using high-kVp techniques on larger patients, an anti-scatter technique (e.g., grid or air gap) should be selected to provide scatter reduction equivalent to that of a 10:1 grid. After establishing the correct kVp as a function of patient size, a tube current should be selected which minimizes patient motion during the exposure. The exposure time should be as short as feasible for fixed radiographic units. The selected mAs and kVp should produce a radiograph that presents the lung at a mid-gray level.

D. The following quality control procedures should be applied to all chest radiography:

1. When the examination is completed, the images should be checked either by a qualified physician or a qualified technologist.
2. Films not of diagnostic quality should be repeated as necessary.
3. Each film or image should be permanently marked with the patient's name, identification number, right or left side, patient position, and the date and time of the examination.

VI. DOCUMENTATION

It is important that new films be compared with prior chest examinations and/or other pertinent studies that may be available.

Reporting should be in accordance with the ACR Practice Guideline for Communication: Diagnostic Radiology.

VII. EQUIPMENT SPECIFICATIONS

The equipment required includes a diagnostic machine having a rotating anode tube with a tube filtration sufficient to achieve a half-value layer (HVL) greater than

3 mm of aluminum at 100 kVp. A grid should be used for adult radiography. At least a 10:1 grid with a minimum of 103 lines per in. (stationary) or 80 lines per in. (reciprocity) is recommended.

Radiographs shall be exposed only with equipment having a beam-limiting device that provides rectangular collimation.

There should be at least a 72-in. source-image distance (SID) to minimize magnification for routine upright imaging. A 40-in. SID may be used if clinically necessary (e.g., supine, stretcher, infants and young children, etc.).

The nominal source (focal spot) shall not exceed 2.0 mm; 0.6-1.2 mm is the recommended range.

For analog studies, intensifying screens shall be used. Any screen-film combination may be used that has a speed of at least 200.

Automatic processing is preferable with carefully controlled temperature and maintenance. A constant time and temperature shall be employed for manual processing.

Photostimulable plates or digital imaging techniques are an acceptable alternative to film-screen radiography, but require careful quality control.

VIII. QUALITY CONTROL AND IMPROVEMENT, SAFETY, INFECTION CONTROL, AND PATIENT EDUCATION CONCERNS

Policies and procedures related to quality, patient education, infection control, and safety should be developed and implemented in accordance with the ACR Policy on Quality Control and Improvement, Safety, Infection Control, and Patient Education Concerns appearing elsewhere in the ACR Practice Guidelines and Technical Standards book.

ACKNOWLEDGEMENTS

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ACR PRACTICE GUIDELINE FOR THE PERFORMANCE OF PEDIATRIC AND ADULT THORACIC COMPUTED TOMOGRAPHY (CT)

PREAMBLE

These guidelines are an educational tool designed to assist practitioners in providing appropriate radiologic care for patients. They are not inflexible rules or requirements of practice and are not intended, nor should they be used, to establish a legal standard of care. For these reasons and those set forth below, the American College of Radiology cautions against the use of these guidelines in litigation in which the clinical decisions of a practitioner are called into question.

The ultimate judgment regarding the propriety of any specific procedure or course of action must be made by the physician or medical physicist in light of all the circumstances presented. Thus, an approach that differs from the guidelines, standing alone, does not necessarily imply that the approach was below the standard of care. To the contrary, a conscientious practitioner may responsibly adopt a course of action different from that set forth in the guidelines when, in the reasonable judgment of the practitioner, such course of action is indicated by the condition of the patient, limitations on available resources or advances in knowledge or technology subsequent to publication of the guidelines. However, a practitioner who employs an approach substantially different from these guidelines is advised to document in the patient record information sufficient to explain the approach taken.

The practice of medicine involves not only the science, but also the art of dealing with the prevention, diagnosis, alleviation and treatment of disease. The variety and complexity of human conditions make it impossible to always reach the most appropriate diagnosis or to predict with certainty a particular response to treatment. It should be recognized, therefore, that adherence to these guidelines will not assure an accurate diagnosis or a successful outcome. All that should be expected is that the practitioner will follow a reasonable course of action based on current knowledge, available resources, and the needs of the patient to deliver effective and safe medical care. The sole purpose of these guidelines is to assist practitioners in achieving this objective.

I. INTRODUCTION

Computed tomography is a frequently used imaging modality for the evaluation of many thoracic diseases. Optimal performance of thoracic CT requires knowledge of normal anatomy, anatomic variants, pathophysiology, and CT techniques. This guideline outlines the principles for the performance of high-quality thoracic CT in adults and children.

(For pediatric thoracic CT specifically, refer to Sections IV, V. G, and V. H.)

II. GOAL

The goal of thoracic CT is to demonstrate normal and pathologic anatomy and physiology within the chest.

III. INDICATIONS AND CONTRAINDICATIONS

Chest CT may be a complementary examination to other imaging studies such as chest radiography (see the ACR Practice Guideline for the Performance of Pediatric and Adult Chest Radiography) or a stand-alone procedure. Indications for the use of thoracic CT include, but are not limited to:

A. Evaluation of abnormalities discovered on chest radiographs.
B. Evaluation of clinically suspected occult thoracic pathology.
C. Staging and follow-up of lung and other primary or secondary thoracic malignancies.
D. Evaluation for thoracic manifestations of known extrathoracic diseases.
E. Evaluation of known or suspected thoracic vascular abnormalities (congenital or acquired).
F. Evaluation of known or suspected congenital thoracic anomalies.
G. Evaluation and follow-up of pulmonary parenchymal and airway disease.
H. Evaluation of trauma.
I. Performance of CT-guided interventional procedures.

Computed tomography, using specialized techniques that are beyond the scope of this standard, can also be used for other thoracic applications such as evaluation for pulmonary embolus (See the ACR Practice Guideline for the Performance of Computed Tomography for the Detection of Pulmonary Embolism in Adults) and for more precise evaluation of a variety of pulmonary diseases (See the ACR Practice Guideline for the Performance of High-Resolution Computed Tomography (HRCT) of the Lungs in Adults).

There are no absolute contraindications to thoracic CT. As with all procedures, the relative benefits and risks of the procedure should be evaluated prior to the performance of thoracic CT with use of intravenous iodinated contrast. Appropriate precautions should be taken to minimize patient risks.

All imaging facilities should have policies and procedures to reasonably attempt to identify pregnant patients prior to the performance of any diagnostic examination involving ionizing radiation. If the patient is known to be pregnant, the potential radiation risks to the fetus and clinical benefits of the procedure should be considered before proceeding with the study (Res. 24, 1995).

IV. QUALIFICATIONS AND RESPONSIBILITIES OF PERSONNEL

See the ACR Practice Guideline for Performing and Interpreting Diagnostic Computed Tomography (CT).

V. SPECIFICATIONS OF THE EXAMINATION

A. A typical CT of the thorax should include axial images from the lung apices to the costophrenic sulci usually with 3 to 10 mm slice thickness and table increment or reconstruction interval equal to or less than the slice thickness. The examination may be tailored to specific clinical circumstances, to include 1-2 mm thin sections through focal areas of pathology, such as nodules. An adequate study may be performed with sequential single-slice technique, single detector helical (spiral) technique, or multidetector helical (spiral) technique.

B. During any single examination, all scans should be obtained in the same suspended state of respiration when possible. Scans should be obtained through the entire area of interest. The field of view should be optimized for each patient.

C. The examination may be conducted with or without contrast as clinically indicated.

D. Appropriate window and level settings should be used to view the lung parenchyma and the mediastinal structures. When skeletal pathology is suspected, window settings appropriate to visualize osseous structures should be used. In selected cases, soft copy review may facilitate evaluation of large data sets.

E. Although many of the operations of a CT scanner are automated, a number of technical parameters remain operator dependent and may significantly affect the diagnostic value of the CT examination. It is necessary for the supervising physician to acquire familiarity with the following:

1. Exposure factors.
2. Collimation and slice thickness.
3. Slice spacing, table increment, and pitch as appropriate.
4. Field of view.
5. Window and level settings.
6. Reconstruction algorithms.
7. Image reconstruction interval.

F. Optimization of the CT examination requires the supervising physician to develop appropriate CT protocols based on clinical indications.

G. Protocols should be prepared by organ system of interest and medical indication. Techniques should provide diagnostic image quality as well as acceptably low patient radiation exposure. For each study, the protocol should indicate at least the following:

1. Use of helical (spiral) or incremental slice acquisition.
2. If intravenous and/or oral contrast is used, the volume, rates of administration, and time delay between administration of contrast material and initiation of scan.
3. Collimation and slice thickness.
4. Slice spacing, table increment, and pitch as appropriate.
5. kVp and mAs per slice for small, medium, and large patients.
6. Superior and inferior extent of the area of interest to be imaged.
7. Reconstruction algorithm and level and window settings of permanent images.
8. Reconstruction interval (for helical exams).

These protocols should be reviewed and updated periodically.

H. For pediatric patients, efforts should be directed to:

1. Limit radiation dose when diagnostically feasible with increased table increment or pitch, use of low mA, and partial scans.
2. Minimize motion artifact with short scan times, partial scans, and appropriate sedation.

I. When sedation is used, it should be done in accordance with the ACR Practice Guideline for Adult Sedation/Analgesia or the ACR Practice Guideline for Pediatric Sedation/Analgesia.

VI. DOCUMENTATION

Reporting should be in accordance with the ACR Practice Guideline for Communication: Diagnostic Radiology.

VII. EQUIPMENT SPECIFICATIONS

A. Performance Standards

To achieve acceptable clinical CT scans of the thorax, a CT scanner should meet or exceed the following capabilities:

1. Scan times: ≤ 2 sec.
2. Slice thickness: ≤ 5 mm (≤ 2 mm is preferred).
3. Interscan delay: ≤ 5 sec (≤ 2 sec is preferred, but may be longer if no intravascular contrast used).
4. Limiting spatial resolution: ≥ 8 lp/cm for ≥ 32 cm display field of view (DFOV) and ≥ 10 lp/cm for < 24 cm DFOV.
5. Table pitch: no greater than 2:1 for single-row-detector helical scanners.

B. Emergency supplies, including appropriate medications and resuscitation equipment, must be immediately available to treat adverse reactions. If pediatric patients are examined, these supplies should include appropriate pediatric emergency devices and medication dosages. Policies and procedures should be in place for the regular review for currentness of emergency supplies.

VIII. EQUIPMENT QUALITY CONTROL

The quality control program for CT equipment should be designed to minimize patient, personnel, and public radiation risks and to maximize the diagnostic quality of the examination. The program should be supervised by a Qualified Medical Physicist. Each imaging facility should have documented policies and procedures that include:

1. A list of quality control tests and the frequency of performance.
2. A list of individuals or groups who will perform each test.
3. A written description of each testing procedure, to include technique factors, the equipment used, and the acceptability limits of and sample records from each test.

IX. QUALITY CONTROL AND IMPROVEMENT, SAFETY, INFECTION CONTROL, AND PATIENT EDUCATION CONCERNS

Policies and procedures related to quality, patient education, infection control, and safety should be developed and implemented in accordance with the ACR Policy on Quality Control and Improvement, Safety, Infection Control, and Patient Education Concerns appearing elsewhere in the ACR Practice Guidelines and Technical Standards book.

For specific issues regarding CT quality control, see the ACR Practice Guideline for Performing and Interpreting Computed Tomography (CT).

Equipment performance monitoring should be in accordance with the ACR Technical Standard for Diagnostic Medical Physics Performance Monitoring of Computed Tomography (CT) Equipment.

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2000 (Res. 10)
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ACR PRACTICE GUIDELINE FOR THE PERFORMANCE OF HIGH-RESOLUTION COMPUTED TOMOGRAPHY (HRCT) OF THE LUNGS IN ADULTS

PREAMBLE

These guidelines are an educational tool designed to assist practitioners in providing appropriate radiologic care for patients. They are not inflexible rules or requirements of practice and are not intended, nor should they be used, to establish a legal standard of care. For these reasons and those set forth below, the American College of Radiology cautions against the use of these guidelines in litigation in which the clinical decisions of a practitioner are called into question.

The ultimate judgment regarding the propriety of any specific procedure or course of action must be made by the physician or medical physicist in light of all the circumstances presented. Thus, an approach that differs from the guidelines, standing alone, does not necessarily imply that the approach was below the standard of care. To the contrary, a conscientious practitioner may responsibly adopt a course of action different from that set forth in the guidelines when, in the reasonable judgment of the practitioner, such course of action is indicated by the condition of the patient, limitations on available resources or advances in knowledge or technology subsequent to publication of the guidelines. However, a practitioner who employs an approach substantially different from these guidelines is advised to document in the patient record information sufficient to explain the approach taken.

The practice of medicine involves not only the science, but also the art of dealing with the prevention, diagnosis, alleviation and treatment of disease. The variety and complexity of human conditions make it impossible to always reach the most appropriate diagnosis or to predict with certainty a particular response to treatment. It should be recognized, therefore, that adherence to these guidelines will not assure an accurate diagnosis or a successful outcome. All that should be expected is that the practitioner will follow a reasonable course of action based on current knowledge, available resources, and the needs of the patient to deliver effective and safe medical care. The sole purpose of these guidelines is to assist practitioners in achieving this objective.

I. INTRODUCTION

High-resolution computed tomography (HRCT) of the lungs is a well-established imaging method for the evaluation of many pulmonary diseases. Optimal performance of HRCT requires knowledge of anatomy and pathophysiology, as well as familiarity with the basic physics and techniques of computed tomography. This guideline outlines the principles for performance of high-quality thoracic HRCT.

II. INDICATIONS

Indications for the use of thoracic HRCT include, but are not limited to the following:

1. Evaluation of diffuse pulmonary disease discovered on chest radiographs, including selection of the appropriate site for biopsy of diffuse lung disease.

2. Evaluation of the lungs in patients with clinically suspected pulmonary disorders that have normal or equivocal chest radiographs.
3. Evaluation of suspected small airway disease.
4. Evaluation of suspected bronchiectasis.
5. Quantification of the extent of diffuse lung disease for purposes of judging effectiveness of treatment.

There are no absolute contraindications to thoracic HRCT. Intravenous iodinated contrast is not used for routine HRCT but may be helpful in some cases for problem solving.

All imaging facilities should have policies and procedures to reasonably attempt to identify pregnant patients prior to the performance of any diagnostic examination involving ionizing radiation. If the patient is known to be pregnant, the potential radiation risks to the fetus and clinical benefits of the procedure should be considered before proceeding with the study (Res. 24, 1995).

III. QUALIFICATIONS AND RESPONSIBILITIES OF PERSONNEL

See the ACR Practice Guideline for Performing and Interpreting Diagnostic Computed Tomography (CT).

The physician shall have the responsibility for reviewing all indications for the examination; specifying the precise technical factors to be used for the HRCT study; generating written report; and monitoring and maintaining the quality of images and interpretation.

The physician should be thoroughly acquainted with the many anatomic and physiologic manifestations of intrathoracic disease. Additionally, supervising physicians should have appropriate knowledge of alternative imaging modalities, including available techniques for performing routine chest radiography and applications and indications for the use of specialized studies, such as standard thoracic computed tomography, angiography, ultrasonography, magnetic resonance imaging, and nuclear medicine studies.

IV. SPECIFICATIONS AND PERFORMANCE OF THE EXAMINATION

A. Although many of the operations of a CT scanner are automated, a number of technical parameters remain operator-dependent. As these factors can significantly affect the diagnostic value of the HRCT examination, it is necessary for the supervising physician to acquire familiarity with the following:

1. Radiation exposure factors.
2. Collimation (slice thickness).
3. Slice spacing (table increment).
4. Field of view.
5. Level and window settings.
6. Reconstruction algorithm.

B. Optimization of the CT examination requires the supervising physician to develop an appropriate CT protocol based on careful review of relevant patient history and clinical indications as well as all prior available imaging studies.

1. Protocols should be prepared according to the specific medical indication. Techniques should be selected that provide image quality consistent with the diagnostic needs of the exam at acceptably low radiation dose levels to the patient. For each indication, the protocol should include at least the following:
   a. Bone or high-spatial-frequency reconstruction algorithm.
   b. Collimation (slice thickness) $\leq$ 2 mm.
   c. Slice spacing (table increment).
   d. Field of view (FOV) for small, medium, and large patients.
   e. kVp and mAs per slice (120-140 kVp and approximately 240 mAs, although lower doses may be used with small patients or those receiving serial HRCT scans).
   f. Superior and inferior extent of the region of interest to be imaged.
   g. Level and window settings of hard-copy images.
   h. Patient positioning (supine and/or prone).
   i. State of respiration (inspiration and/or expiration).
2. These protocols should be reviewed and updated periodically.

V. DOCUMENTATION

Reporting should be in accordance with the ACR Practice Guideline for Communication: Diagnostic Radiology.

VI. EQUIPMENT SPECIFICATIONS

To achieve acceptable clinical HRCT scans of the thorax, a CT scanner should meet or exceed the following capabilities:

1. Scan times: $\leq$ 2 sec.
2. Slice thickness: $\leq$ 2 mm.
3. Algorithm available: bone or high-spatial frequency.
4. Spatial resolution should meet or exceed manufacturer's specifications.

VII. QUALITY CONTROL AND IMPROVEMENT, SAFETY, INFECTION CONTROL, AND PATIENT EDUCATION CONCERNS

Policies and procedures related to quality, patient education, infection control, and safety should be developed and implemented in accordance with the ACR Policy on Quality Control and Improvement, Safety, Infection Control, and Patient Education Concerns appearing elsewhere in the ACR Practice Guidelines and Technical Standards book.

Equipment performance monitoring should be in accordance with the ACR Technical Standard for Diagnostic Medical Physics Performance Monitoring of Computed Tomography (CT) Equipment.

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Each practice guideline and technical standard, representing a policy statement by the College, has undergone a thorough consensus process in which it has been subjected to extensive review, requiring the approval of the Commission on Quality and Safety as well as the ACR Board of Chancellors, the ACR Council Steering Committee, and the ACR Council. The practice guidelines and technical standards recognize that the safe and effective use of diagnostic and therapeutic radiology requires specific training, skills, and techniques, as described in each document. Reproduction or modification of the published practice guideline and technical standard by those entities not providing these services is not authorized.

1992 (Res. 11)
Amended 1994 (Res. 13)
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Effective 1/1/02

ACR TECHNICAL STANDARD FOR DIAGNOSTIC MEDICAL PHYSICS PERFORMANCE MONITORING OF RADIOGRAPHIC AND FLUOROSCOPIC EQUIPMENT

PREAMBLE

These guidelines are an educational tool designed to assist practitioners in providing appropriate radiologic care for patients. They are not inflexible rules or requirements of practice and are not intended, nor should they be used, to establish a legal standard of care. For these reasons and those set forth below, the American College of Radiology cautions against the use of these guidelines in litigation in which the clinical decisions of a practitioner are called into question.

The ultimate judgment regarding the propriety of any specific procedure or course of action must be made by the physician or medical physicist in light of all the circumstances presented. Thus, an approach that differs from the guidelines, standing alone, does not necessarily imply that the approach was below the standard of care. To the contrary, a conscientious practitioner may responsibly adopt a course of action different from that set forth in the guidelines when, in the reasonable judgment of the practitioner, such course of action is indicated by the condition of the patient, limitations on available resources or advances in knowledge or technology subsequent to publication of the guidelines. However, a practitioner who employs an approach substantially different from these guidelines is advised to document in the patient record information sufficient to explain the approach taken.

The practice of medicine involves not only the science, but also the art of dealing with the prevention, diagnosis, alleviation and treatment of disease. The variety and complexity of human conditions make it impossible to always reach the most appropriate diagnosis or to predict with certainty a particular response to treatment. It should be recognized, therefore, that adherence to these guidelines will not assure an accurate diagnosis or a successful outcome. All that should be expected is that the practitioner will follow a reasonable course of action based on current knowledge, available resources, and the needs of the patient to deliver effective and safe medical care. The sole purpose of these guidelines is to assist practitioners in achieving this objective.

I. INTRODUCTION

The performance of all radiographic and fluoroscopic equipment shall be evaluated upon installation and monitored at least annually by a Qualified Medical Physicist to ensure that the equipment is functioning properly and that patients are not exposed to unnecessary doses of radiation. Additional or more frequent monitoring may be necessary after repairs that might change the radiation exposure to patients or personnel or the imaging performance of the equipment. Although it is not possible to consider all possible variations of equipment performance to be monitored, adherence to this standard will assist in maximizing image quality and in

reducing patient radiation doses. Key points to consider are: performance characteristics to be monitored, patient radiation dose, qualifications of the personnel, and follow-up procedures.

II. GOAL

The goals are to produce the highest quality diagnostic image at the lowest reasonable radiation dose consistent with the clinical use of the equipment and the information requirement of the examination and to establish and maintain performance standards.

III. QUALIFICATIONS AND RESPONSIBILITIES OF PERSONNEL

A Qualified Medical Physicist is an individual who is competent to practice independently one or more of the subfields in medical physics. The American College of Radiology (ACR) considers that certification and continuing education in the appropriate subfield(s) demonstrate that an individual is competent to practice one or more of the subfields in medical physics, and to be a Qualified Medical Physicist. The ACR recommends that the individual be certified in the appropriate subfield(s) by the American Board of Radiology (ABR).

The appropriate subfields for this standard are Diagnostic Radiological Physics and Radiological Physics.

The continuing education of a Qualified Medical Physicist should be in accordance with the ACR Practice Guideline for Continuing Medical Education.

Understanding of the relationship between image quality and patient radiation dose is essential to proper monitoring of equipment performance. The medical physicist must be familiar with the principles of imaging physics and of radiation protection; the current guidelines of the National Council on Radiation Protection and Measurements (NCRP); laws pertaining to the performance of the equipment being tested; the function, clinical uses, and performance specifications of the imaging equipment; and calibration processes and limitations of the instruments used for testing performance.

The Qualified Medical Physicist may be assisted by other properly trained individuals in obtaining test data for performance monitoring. These individuals must be properly trained and approved by the Qualified Medical Physicist in the techniques of performing the tests, the function and limitations of the imaging equipment and test instruments, the reasons for the tests, and the importance of the test results. The Qualified Medical Physicist must be available at the facility during initial and annual surveys and must review, interpret, and approve all data measurements and provide a signed report.

IV. SPECIFICATIONS OF THE MONITORING PROCESS

A. Equipment Characteristics To Be Monitored

The following characteristics shall be evaluated for the equipment to which they apply:

1. Integrity of unit assembly
2. Collimation and radiation beam alignment
3. Fluoroscopic system resolution
4. Automatic exposure control system performance
5. Image artifacts
6. Fluoroscopic phantom image quality
7. KVp accuracy and reproducibility
8. Linearity of exposure vs. mA
9. Exposure reproducibility
10. Timer accuracy
11. Beam quality assessment (half-value layer)
12. Fluoroscopic exposure rates
13. Image receptor entrance exposure
14. Fluoroscopic alignment test
15. Equipment radiation safety functions
16. Patient dose monitoring system calibration, if present
17. Video and digital monitor performance
18. Digital image receptor performance.

B. Monitoring of Technologist's Quality Control Program

The following aspects of a technologist's quality control program shall be reviewed as deemed applicable:

1. Appropriateness of technique factors
2. Dark-room and screen cleanliness
3. Processor quality control
4. Film-screen speed matching
5. Viewboxes and viewing conditions
6. Phantom images
7. Visual equipment checklists
8. Repeat analysis
9. Analysis of fixer retention
10. Darkroom fog
11. Screen-film contact
12. Laser film printer quality control
13. Personnel radiation monitoring.

C. Radiation Dose and Patient Safety

Patient radiation dose shall be evaluated for radiographic and fluoroscopic equipment at least annually. Tables of patient radiation exposure for representative examinations shall be prepared and supplied to the facility. These tables

shall be prepared using measured radiation output data and imaging techniques provided by the facility. These results shall be compared with appropriate guidelines or recommendations when they are available. The Qualified Medical Physicist should assist facilities in developing policies and procedures to evaluate patient, personnel, and physician risk from studies and interventions requiring prolonged radiation exposure. Electrical safety of the equipment should be tested by appropriate personnel prior to initial clinical use and periodically thereafter.

D. Acceptance Testing

Acceptance testing shall be performed upon installation and should be completed before clinical use. This testing shall be more comprehensive than periodic performance and compliance testing and shall be consistent with current acceptance testing practices.

E. Follow-up Procedures

The Qualified Medical Physicist shall report the findings to the responsible professional in charge of obtaining or providing necessary service to the equipment and, if appropriate, initiate the required service. Action shall be taken immediately by verbal communication if there is imminent danger to patients or staff using the equipment due to either unsafe conditions or unacceptably poor image quality. Written reports shall be provided in a timely manner consistent with the importance of any adverse findings. The Qualified Medical Physicist shall confirm that the unit is performing in a safe or acceptable fashion as soon as possible after the required service has been performed.

ACKNOWLEDGEMENTS

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1998 (Res. 14)
Revised 2002 (Res. 21)
Effective 1/1/03

ACR TECHNICAL STANDARD FOR DIAGNOSTIC MEDICAL PHYSICS PERFORMANCE MONITORING OF COMPUTED TOMOGRAPHY (CT) EQUIPMENT

PREAMBLE

These guidelines are an educational tool designed to assist practitioners in providing appropriate radiologic care for patients. They are not inflexible rules or requirements of practice and are not intended, nor should they be used, to establish a legal standard of care. For these reasons and those set forth below, the American College of Radiology cautions against the use of these guidelines in litigation in which the clinical decisions of a practitioner are called into question.

The ultimate judgment regarding the propriety of any specific procedure or course of action must be made by the physician or medical physicist in light of all the circumstances presented. Thus, an approach that differs from the guidelines, standing alone, does not necessarily imply that the approach was below the standard of care. To the contrary, a conscientious practitioner may responsibly adopt a course of action different from that set forth in the guidelines when, in the reasonable judgment of the practitioner, such course of action is indicated by the condition of the patient, limitations on available resources or advances in knowledge or technology subsequent to publication of the guidelines. However, a practitioner who employs an approach substantially different from these guidelines is advised to document in the patient record information sufficient to explain the approach taken.

The practice of medicine involves not only the science, but also the art of dealing with the prevention, diagnosis, alleviation and treatment of disease. The variety and complexity of human conditions make it impossible to always reach the most appropriate diagnosis or to predict with certainty a particular response to treatment. It should be recognized, therefore, that adherence to these guidelines will not assure an accurate diagnosis or a successful outcome. All that should be expected is that the practitioner will follow a reasonable course of action based on current knowledge, available resources, and the needs of the patient to deliver effective and safe medical care. The sole purpose of these guidelines is to assist practitioners in achieving this objective.

I. INTRODUCTION

All computed tomography (CT) equipment shall be evaluated upon installation and subsequently monitored at least annually, or as required by state or local regulatory agencies, by a Qualified Medical Physicist to ensure that it is functioning properly. Additional or more frequent performance monitoring may be necessary after any service that may change the radiation exposure to patients or personnel or the image quality. Although it is not possible to consider all possible variations of equipment performance to be monitored, adherence to this standard will assist in maximizing image quality and in reducing patient radiation dose(s). Key points to consider are: performance characteristics to be monitored, patient radiation dose, qualifications of personnel, and follow-up procedures.

II. GOAL

The goal is to produce the highest quality diagnostic image at the lowest reasonable dose consistent with the clinical use of the equipment and the information requirement of the examination, and to establish performance standards.

III. QUALIFICATIONS AND RESPONSIBILITIES OF PERSONNEL

A Qualified Medical Physicist is an individual who is competent to practice independently in one or more of the subfields in medical physics. The American College of Radiology (ACR) considers that certification and continuing education in the appropriate subfield(s) demonstrate that an individual is competent to practice in one or more of the subfields in medical physics and to be a Qualified Medical Physicist. The ACR recommends that the individual be certified in the appropriate subfield(s) by the American Board of Radiology (ABR).

The appropriate subfields of medical physics for this standard are Diagnostic Radiological Physics and Radiological Physics.

The continuing education of a Qualified Medical Physicist should be in accordance with the ACR Practice Guideline for Continuing Medical Education (CME).

The Qualified Medical Physicist must be familiar with the principles of imaging physics and of radiation protection; the guidelines of the National Council on Radiation Protection and Measurements (NCRP); laws and regulations pertaining to the performance of the equipment being tested; the function, clinical uses, and performance specifications of the imaging equipment; and calibration processes and limitations of the instruments used for testing performance.

The Qualified Medical Physicist may be assisted by properly trained individuals in obtaining data. These individuals must be approved by the Qualified Medical Physicist in the techniques of performing tests, the function and limitations of the imaging equipment and test instruments, the reason for the tests, and the importance of the test results. The Qualified Medical Physicist is responsible for and must be present during initial and annual surveys and must review, interpret, and approve all data as well as provide a signed report of conclusions.

IV. PERFORMANCE CHARACTERISTICS TO BE MONITORED

A. Characteristics to be Monitored

Performance monitoring must be performed on each CT unit at least annually. This evaluation should include, but not be limited to, the following:

1. Alignment light accuracy
2. Alignment of table to gantry
3. Table/gantry tilt
4. Slice localization from scanned projection radiograph (localization image)
5. Table incrementation accuracy
6. Slice thickness
7. Image quality
   a. High-contrast (spatial) resolution
   b. Low-contrast sensitivity/resolution
   c. Image uniformity
   d. Noise
   e. Artifact evaluation
8. CT number accuracy and linearity
9. Display devices
   a. Image display monitor(s)
   b. Hard-copy display unit(s), if available
10. Dosimetry
    a. CT dose index (CTDI)
    b. Patient radiation dose for representative examinations
11. Safety evaluation
    a. Visual inspection
    b. Work load assessment
    c. Scatter and stray radiation measurements (if work load and other related parameters have changed since acceptance testing)
    d. Audible/visual signals
    e. Posting requirements
12. Other tests as required by state and/or local regulations.

B. Patient Radiation Dose

Patient radiation dose for CT equipment shall be evaluated at least annually. Tables of patient radiation absorbed dose for representative examinations (e.g., head, thorax, abdomen, and pelvis) shall be prepared and supplied to the facility. These results shall be compared with appropriate guidelines or recommendations when they are available.

V. QUALITY CONTROL PROGRAM

A continuous quality control (QC) program shall be established for all CT units with the assistance of a Qualified Medical Physicist. The Qualified Medical Physicist should determine the frequency of each test and who should perform each test based upon the facility and CT usage. An on-site radiologic technologist shall be identified to be responsible for conducting routine QC.

The QC program should include, but not be limited to, the following:

1. Alignment light accuracy
2. Slice thickness
3. Image quality
   a. High contrast (spatial) resolution
   b. Low-contrast sensitivity/resolution
   c. Image uniformity
   d. Noise
   e. Artifact evaluation
4. CT number accuracy and linearity
5. Display devices.

The result of the QC program shall be monitored annually by the Qualified Medical Physicist. If measured values of QC parameters fall outside the control limits, the physicist shall initiate appropriate investigative or corrective actions. A Qualified Medical Physicist should be available to assist in prescribing corrective actions for unresolved problems.

VI. ACCEPTANCE TESTING

Initial performance testing shall be performed upon installation and should be completed before clinical use. This testing shall be more comprehensive than periodic performance and compliance testing and should be consistent with current acceptance testing practices.

VII. FOLLOW-UP PROCEDURES/WRITTEN SURVEY REPORTS

The Qualified Medical Physicist shall report the findings to the physician(s), to the responsible professional(s) in charge of obtaining or providing necessary service to the equipment, and, in the case of the consulting physicist(s), to the representative of the hiring party, and, if appropriate, initiate the required service. Action shall be taken immediately by verbal communication, if there is imminent danger to patients or staff using the equipment due to unsafe conditions. Written survey reports shall be provided in a timely manner consistent with the importance of any adverse findings.

ACKNOWLEDGEMENTS

This standard was revised according to the process described in the ACR Practice Guidelines and Technical Standards book by the Guidelines and Standards Committee of the Medical Physics Commission.

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Appendix 4-3 Spiral CT Screening Examination Form (SCT)

National Lung Screening Trial / Lung Screening Study (NLST/LSS)

SPIRAL CT SCREENING EXAMINATION FORM (SCT)

Administrative Section

Screening Center ID: |___|___|

Date of Examination: |___|___| / |___|___| / |_2_|_0_|___|___|
Month Day Year

Study Year (T_0 - T_2): T |___|

Visit Number: ☐ One ☐ Two

Reason for repeat visit _____

Interval Follow Up Information:

Has the participant had any imaging studies since the previous screening exam that may be useful for the radiologist to review if needed? ☐ Yes ☐ No ☐ N/A

If YES, dates obtained (Month /Year): |___|___| / |___|___|___|___|
|___|___| / |___|___|___|___|

Initials Complete: _____

Initials QC: _____

SCT

Participant ID Label

PART A. SPIRAL CT EXAMINATION FINDINGS (COMPLETED BY TECHNOLOGIST)

1. Number of Attempts:
☐ None (GO TO A.3)
☐ One
☐ Two
☐ Three

2. Adequate Scan Obtained:
☐ No
☐ Yes (GO TO A.4)

3. Reason for Inadequate or No Scan: (MARK ALL THAT APPLY)
☐ Participant refusal
☐ Equipment malfunction
☐ Poor image quality
☐ Other (SPECIFY)
_____

4. Technical Parameters:
A. |___|___|___| kVp
B. |___|___|___| mAs
C. |___|___|___| mA
D. |___|___| Display FOV
E. |___|___| Effective mAs
F. |___|.|___|___| Pitch

5. Indicate CT reconstruction algorithm/filter:
☐ GE Bone
☐ GE Standard
☐ GE, other: _____
☐ Philips D
☐ Philips C
☐ Philips, other: _____
☐ Siemens B50F
☐ Siemens B30
☐ Siemens, other: _____
☐ Toshiba FC10
☐ Toshiba FC51
☐ Toshiba, other: _____

6. Comments: ☐ No ☐ Yes

_____

☐ Continued

7. Tech ID:

|___|___|___|___| **Signature:** _____

Appendix 4-3 Spiral CT Screening Examination Form (SCT)

PARTS B, C, D AND E COMPLETED BY RADIOLOGIST

PART B. SPIRAL CT OVERALL DIAGNOSTIC QUALITY (COMPLETED BY RADIOLOGIST)

1. Indicate the overall diagnostic quality of the CT image acquisition sequence:

- ☐ A. Diagnostic CT (GO TO C.1)
- ☐ B. Limited CT, but interpretable (COMPLETE B.2 AND GO TO C.1)
- ☐ C. Non-diagnostic CT exam, reschedule CT (COMPLETE B.2 AND GO TO D.1)
- ☐ D. No image available (GO TO D.3, COMMENTS)

2. Which of the following affected the quality of the limited or non-diagnostic CT? (MARK ALL THAT APPLY)

- ☐ Submaximal inspiratory breath-hold
- ☐ Motion artifact
- ☐ Respiratory misregistration
- ☐ Incorrect technical parameter(s)
- ☐ Lungs not completely imaged
- ☐ Severe beam hardening artifact
- ☐ Excessive quantum mottle or graininess
- ☐ Other (SPECIFY)_____

PART C. SPIRAL CT EXAMINATION FINDINGS (COMPLETED BY RADIOLOGIST)

1. Radiologic Abnormality Noted:

- ☐ No (GO TO D.1 AND MARK RESULT "E")
- ☐ Yes (COMPLETE C.2. RECORD INFORMATION FOR EACH ABNORMALITY)

2. Record Information for Each Abnormality:

Abn #	Description of Abnormality		Complete for Code 51 Only: CT Slice	Location of Epicenter	Longest Diameter (mm)	Longest Perpendicular Diameter (mm)	Margins	Predominant Attenuation
	51 = Non-calcified nodule/mass ≥ 4 mm (MUST MARK "A" IN D.1) 52 = Non-calcified nodule < 4 mm 53 = Benign lung nodule(s) (benign calcification) 54 = Atelectasis, segmental or greater 55 = Pleural thickening or effusion 56 = Non-calcified hilar/mediastinal adenopathy/mass ≥ 10 mm short axis 57 = Chest wall abnormality (e.g. bone destruction, metastasis) 58 = Consolidation 59 = Reticular/reticulonodular opacities, honeycombing, fibrosis, scar 62 = 6 or more nodules, not suspicious for cancer (opacities ≥ 4mm) (ANY SUSPICIOUS NODULES MUST BE CODED AS 51) 63 = Emphysema 64 = Significant cardiovascular abnormality (SPECIFY) 70 = Other significant abnormality above the diaphragm (SPECIFY) 71 = Other significant abnormality at/below the diaphragm (SPECIFY) 72 = Other minor abnormality noted (SPECIFY IF DESIRED)		Record slice number containing abnormality's greatest diameter	1 = RUL 2 = RML 3 = RLL 4 = LUL 5 = Lingula 6 = LLL 8 = Other, SPECIFY (in Comments section)	999 = Unable to determine	(same CT slice) 999 = Unable to determine	1 = Spiculated (Stellate) 3 = Smooth 4 = Poorly defined 9 = Unable to determine	1 = Soft tissue 2 = Ground glass 3 = Mixed 4 = Fluid/ water 6 = Fat 7 = Other 9 = Unable to determine
	CHECK BOX IF IDENTIFIED AFTER COMPARISON WITH HISTORICAL IMAGES:							
1	|___|___|	☐	|___|___|___|	|___|	|___|___|___|	|___|___|___|	|___|	|___|
2	|___|___|	☐	|___|___|___|	|___|	|___|___|___|	|___|___|___|	|___|	|___|
3	|___|___|	☐	|___|___|___|	|___|	|___|___|___|	|___|___|___|	|___|	|___|
4	|___|___|	☐	|___|___|___|	|___|	|___|___|___|	|___|___|___|	|___|	|___|
5	|___|___|	☐	|___|___|___|	|___|	|___|___|___|	|___|___|___|	|___|	|___|
6	|___|___|	☐	|___|___|___|	|___|	|___|___|___|	|___|___|___|	|___|	|___|

Appendix 4-3 Spiral CT Screening Examination Form (SCT)

PART D. SPIRAL CT INTERPRETATION RESULTS (COMPLETED BY RADIOLOGIST)

1. Lung Screening Result:

☐ A. **Positive Screen – Abnormalities suspicious for lung cancer**
☐ C. **Negative Screen** – Clinically significant abnormalities not suspicious for lung cancer (GO TO D.3)
☐ D. **Negative Screen** – Minor abnormalities not suspicious for lung cancer (GO TO D.3)
☐ E. **Negative Screen** – No significant abnormalities (GO TO D.3)
☐ F. **Inadequate** (COMPLETE PART D.3 AND GO TO E.6)

2. Other Significant Abnormalities (in addition to lung screening results) that need to be reported:

☐ No ☐ Yes (SPECIFY IN D.3)

3. Comments: ☐ No ☐ Yes

____

____ ☐ Continued

PART E. SPIRAL CT COMPARISON RESULTS – COMPLETE FOR ALL LUNG SCREENING RESULTS (COMPLETED BY RADIOLOGIST)

1. Comparison Image: (MARK ALL THAT APPLY)

☐ No image available (GO TO E.4)
☐ T_0
☐ T_1
☐ T_2 Inadequate scan
☐ Previous scan not completed as part of NLST (RECORD SCAN TYPE AND DATES FOR UP TO 3 PREVIOUS SCANS)

Scan Types
1 = CT
2 = CXR
3 = MRI

Previous Scan Type(s):	**Date(s) of Previous Scan(s) (MONTH/DAY/YEAR)**
|___|	|___|___| / |___|___| / |___|___|___|___|
|___|	|___|___| / |___|___| / |___|___|___|___|
|___|	|___|___| / |___|___| / |___|___|___|___|

2. Enter abnormality number and code for <u>all</u> Code 51 abnormalities AND other significant abnormalities seen on this screening exam. (IF NONE, GO TO E.3)

		Was Abnormality Pre-existing?		COMPLETE FOR CODE 51 ABNORMALITIES ONLY		COMPLETE FOR OTHER SIGNIFICANT ABNORMALITIES ONLY
Abn. # (FROM ITEM C.2.)	**Abn.Code** (FROM ITEM C.2)	1 = No 2 = Yes 9 = Unable to determine	**Earliest Date Visible** (COMPLETE ONLY FOR PRE-EXISTING ABNORMALITIES) **(Month/Day/Year)** 99/99/9999 = Unable to determine	**Interval Growth of Abnormality?** 1 = No 2 = Yes 9 = Unable to determine	**Interval suspicious change in attenuation?** 1 = No 2 = Yes 9 = Unable to determine	**Interval change warrants further investigation?** 1 = No 2 = Yes 9 = Unable to determine
|___|	|___|___|	|___|	|___|___| / |___|___| / |___|___|___|___|	|___|	|___|	|___|
|___|	|___|___|	|___|	|___|___| / |___|___| / |___|___|___|___|	|___|	|___|	|___|
|___|	|___|___|	|___|	|___|___| / |___|___| / |___|___|___|___|	|___|	|___|	|___|
|___|	|___|___|	|___|	|___|___| / |___|___| / |___|___|___|___|	|___|	|___|	|___|
|___|	|___|___|	|___|	|___|___| / |___|___| / |___|___|___|___|	|___|	|___|	|___|
|___|	|___|___|	|___|	|___|___| / |___|___| / |___|___|___|___|	|___|	|___|	|___|

Appendix 4-3 Spiral CT Screening Examination Form (SCT)

3a. Lung Screening Comparison Result:

- ☐ A. **Positive Screen –** Abnormalities suspicious for lung cancer
- ☐ B. **Positive Screen –** Abnormalities suspicious for lung cancer, no significant change
- ☐ C. **Negative Screen –** Clinically significant abnormalities not suspicious for lung cancer (GO TO E.4)
- ☐ D. **Negative Screen –** Minor abnormalities not suspicious for lung cancer (GO TO E.4)
- ☐ E. **Negative Screen –** No significant abnormalities (GO TO E.4)

3b. Other Significant Abnormalities (in addition to lung screening results) that need to be reported:

☐ No ☐ Yes (SPECIFY IN E.5)

4. Which of the following diagnostic procedures for screening examination results should the screening result letter include?

(MARK ALL THAT APPLY)

- ☐ No diagnostic intervention necessary
- ☐ Continue NLST screening CT
- ☐ Comparison with historical images (NOTE: CHECK OTHER PROCEDURES IN CASE HISTORICAL IMAGES UNAVAILABLE)
- ☐ Low dose CT with NLST parameters at:

(MARK ALL THAT APPLY)
- ☐ 3 months
- ☐ 6 months
- ☐ 3-6 months
- ☐ 12 months
- ☐ 24 months

(MARK AN AREA OF FOCUS)
- ☐ Limited
- ☐ Entire chest

- ☐ Diagnostic chest CT
- ☐ Contrast-enhanced CT nodule densitometry
- ☐ FDG-PET
- ☐ Tech 99m depreotide scintigraphy
- ☐ Biopsy (percutaneous, thoracoscopic, open, etc.)
- ☐ Other (SPECIFY)_____

5. Comments: ☐ No ☐ Yes

_____

_____

☐ Continued

6. Radiologist ID: |___|___|___|___| **Date:** |___|___| / |___|___| / |2|0|___|___|
MO DAY YEAR

_____
Signature

National Lung Screening Trial (NLST)

Specifications for Completion of the Spiral CT Screening Examination Form (SCT)

This form is to be completed by the SC Coordinator or staff member, and the examiners (technologist and radiologist). The SC Coordinator or staff member will complete the Administrative Section, the technologist will complete Part A, and the radiologist will complete Parts B through E of the form. This form should be completed in black or blue ink. An SCT form must be completed for every screening visit by a participant, regardless of the outcome. If documentation of the exam, including exam images, is lost and cannot be recreated, Parts A and B, and Items D.3 and E.6 must be completed.

Please refer to the NLST/LSS Screening Exam Data Handling Guidelines in Appendix 4-11 for details about making changes to data on the screening exam forms. Items pertaining to technical parameters must be changed by the technologist who performed the screening exam and items pertaining to exam results must be changed by the radiologist who read the screening exam. The remaining items may be changed by the SC Coordinator or other designated staff member. All data changes must be initialed and dated in pen on the screening exam form by the staff member making the change. Cross out erroneous data with one line, do not black out or use correction fluid to conceal the original data.

Specifications for completing each item of the form are given below:

Administrative Section:

Participant ID Label: Affix a PID label in the space provided in the upper right-hand corner of the form.

Screening Center ID: Record the two-digit SC ID number.

Date of Examination: Record the date of the examination. The month, day, and the last two digits of the year should be recorded (e.g., 02/07/2002). The date of examination should not be recorded in advance of the participant's study visit.

Study Year ($T_0 – T_2$): Record the participant's study year (T_0, T_1, or T_2).

Visit Number: Record the number of times the participant visited the SC to complete this examination in the current study year. There should be no more than two visits to the SC to complete the spiral CT examination in any one study year. If an exam form is completed for visit two, there must also be a completed form for visit one.

Reason for Repeat Visit: If this is a repeat visit, record the reason for the repeat visit. Refer to the examination form from the previous visit(s) for this information. The purpose of this item is to provide potentially useful information to the examiner regarding why the participant is returning for a repeat visit. Some example reasons:

"Prior scan was of poor quality."

This might be entered if the participant's prior scan was of poor quality during the previous visit, but s/he was willing to return to the SC for a repeat scan. This information will alert the examiner to explore the reasons for this problem.

"Participant out of time. Unable to complete spiral CT exam."

This might be entered if the participant's schedule did not allow him/her to remain at the SC to complete the spiral CT screening examination during a previous visit, and the examination was rescheduled.

Interval Follow-Up Information: This section indicates whether the participant has had any imaging studies since the previous screening exam. This section is intended to be a tool for the SCs to collect interval follow-up information and transmit it easily to the radiologists. However, some SCs may have alternate internal methods for obtaining and transmitting interval follow-up information.

The SC may complete this section using information received during the DE process, contact with the participant during the year, or questioning the participant when s/he comes to the clinic for the current screening exam. This information may be referenced by the radiologist if needed when completing Part E of the form.

Has the participant had any imaging studies since the previous screening exam that may be useful for the radiologist to review if needed?

- **Yes:** The SC should mark this box to indicate that the participant has had at least one imaging study since his or her previous screening exam.

- **No:** The SC should mark this box to indicate that the participant has not had at least one imaging study since his or her previous screening exam.

- **N/A:** For SCs where interval follow-up information is collected and transmitted to the radiologists through an alternate method, the SC should mark this box to indicate that the question is not applicable.

  For SCs using this question to capture interval follow-up information, the SC should mark this box to indicate that interval follow-up information is not available.

If YES, dates obtained (month and year): Record the date that any interval images were obtained. The month and the last two digits of the year should be recorded (e.g., 02/2002). If the date is unknown, enter 99/9999. If no interval images were obtained or if N/A is marked, the dates may be left blank.

Part A. Spiral CT Examination Findings (Completed by Technologist):

1. **Number of Attempts:** Mark the box corresponding to the number of attempts made to complete the spiral CT. Three attempts are allowed per visit.

   - **None:** This might apply if the participant entered the dressing room to prepare for the examination, but for some reason there was no attempt to obtain the spiral CT image (participant became ill, could not wait, etc.). (Go to Item A.3.)

     If the participant never prepared for the examination in any way, the examination is considered "Not Done." The SCT form would not be filled out in such cases.

- **One:** The spiral CT is attempted once, regardless of whether it is successfully completed.

- **Two:** The spiral CT is attempted twice, regardless of whether it is successfully completed.

- **Three:** The spiral CT is attempted three times, regardless of whether it is successfully completed.

2. **Adequate Scan Obtained:** Before the participant leaves the SC, the technologist will evaluate the spiral CT for quality. All scans are then sent to the study radiologist, who will also judge their adequacy. A scan will be considered to be adequate if both lungs are completely scanned, from apex through the lung bases, including both costophrenic angles. Responses are explained below:

   - **No:** The scan is judged to be inadequate. (The technologist should complete Part A. Parts B and C should be skipped and the radiologist should complete Items D.1, D.3, and E.6.)

   - **Yes:** The scan is judged to be adequate. (The technologist should complete Part A. The radiologist should complete Parts B through E.)

3. **Reason for Inadequate or No Scan:** This item is completed only if the answer to Item A.1 is "None," or the answer to Item A.2 is "No." Mark one or more boxes to indicate the reason(s) for not obtaining the scan or for obtaining inadequate scans. An explanation of each reason for inadequate scans is given below:

   - **Participant Refusal:** The participant is unwilling to cooperate, i.e., lie in the proper position, hold breath, etc.

   - **Equipment Malfunction:** This includes any problem with the equipment that prevents the successful completion of the spiral CT scan.

   - **Poor Image Quality:** An image is obtained, but it is not adequate for interpretation. Poor image quality may be due to motion artifact, incomplete evaluation of the thorax, inappropriate CT technique, or excessive noise.

   - **Other (SPECIFY):** In the space provided, describe any other situation in which adequate scans could not be obtained.

4. **Technical Parameters**: Record the parameters used to complete the spiral CT scan. If any of the parameters are lower or higher than the acceptable range, provide a comment to explain in Item A.6 and complete a PHVF. A PHVF is not required if the mAs or effective mAs is lower than the acceptable range when 1) a lower dose is desired due to patient size, or 2) higher kVp, less filtration, etc. are used along with the lower mAs or effective mAs to attain adequate image quality. Refer to MOOP Sections 3.9.3, 4.4, and Appendix 4-1 for further details. If documentation of the exam, including exam images, has been lost and cannot be recovered or recreated, "9"s can be recorded for the missing technical parameter values.

A. kVp: Record the kVp at which the image was obtained. The kVp must always be recorded; it is **not** acceptable to fill with "999" unless documentation of the exam has been lost and cannot be recreated. The acceptable range is 120-140 kVp.

B. mAs: Record the mAs for the image obtained. For two-digit doses, zero-fill the first digit (i.e., 018). If the mAs is not available, record 999. The acceptable range is 40-80 mAs. A setting of 40 mAs should be used for non-obese participants. If the participant is obese, a higher mAs setting may be used. Either the mAs and pitch or effective mAs must be recorded; if effective mAs is blank then mAs and pitch must be recorded.

C. mA: Record the mA for the image obtained. For two-digit doses, zero-fill the first digit (i.e., 018). If the mA is not available, record 999. The mA setting should allow for the mAs to fall within the exposure range and times specified in the protocol.

D. Display FOV: Record the display field of view, in centimeters. The dFOV should be the smallest diameter of the chest wall that will completely contain the lung parenchyma as measured from the widest point of outer rib to outer rib. If the dFOV is unknown or not available, record 99.

E. Effective mAs: Record the effective mAs for the image obtained. If effective mAs is not available, record 99. Effective mAs may be calculated by dividing mAs by the pitch. The allowable range for effective mAs is 20-60. Either the mAs and pitch or effective mAs must be recorded; if mAs is blank then effective mAs must be recorded.

F. Pitch: Record the pitch for the image obtained. If the pitch is not available, record 9.99. The allowable range for pitch is 1.25-2.0. If mAs is recorded, then pitch must also be recorded.

4. Indicate CT reconstruction algorithm/filter: Check the box that corresponds to the manufacturer of the spiral CT machine used and the reconstruction algorithm used to obtain the image. Images may be obtained using a standard algorithm or reconstructed using a high-resolution bone algorithm. The GE Lung and other lung algorithms are <u>not</u> acceptable for NLST/LSS spiral CT scan because they lead to difficulties with determining the calcification of a nodule.

5. Comments: The comments box should be used to record information that may help clarify a situation, provide further information for an item in another part of the form, and to record additional "Other (SPECIFY)" information, if needed.

If there are no additional comments, mark the box next to "No." If there are additional comments, mark the box next to "Yes." Enter the item number to which the comments are related. The item number should include a letter indicating the part of the form, and a number indicating the item within that part (e.g., A.3). If the comment is not related to a specific item in Part A of the form, use the item number for the Comments section itself (A.6). Then enter the comments in the space provided to the right of the item number.

6. Tech ID: The technologist should enter his/her four-digit staff ID number and sign the form in the space provided.

Part B. Spiral CT Overall Diagnostic Quality (Completed by Radiologist)

Part B is to be completed by the radiologist. At some SCs, the SC staff will complete this section using the radiologist's written report. Also, the SC staff may complete Item B.1 if the answer is D, "No images available." If Item A.2 is answered, "No," Parts B and C should be left blank, and Items D.1, D.3, and E.6 should be completed.

1. Indicate the overall diagnostic quality of the CT image acquisition sequence:

A. Diagnostic CT: The spiral CT image is of diagnostic quality. Go to C.1 to record examination findings.

B. Limited CT, but interpretable: The spiral CT image is of limited diagnostic quality, but it can be interpreted. The radiologist should record the factors affecting the quality of the spiral CT in B.2, and should complete C.1 to record the examination findings. If an abnormality suspicious for lung cancer or a clinically significant abnormality is noted, the result in D.1 should be recorded as A or C. The result in D.1 may not be recorded as F.

C. Non-diagnostic CT exam, reschedule CT: The spiral CT image is not acceptable for interpretation, and must be repeated. Record the factors affecting the quality of the image in B.2. Then complete D.1 (record Result F) and D.3, and go to Item E.6. No abnormalities may be recorded for a screening exam of non-diagnostic image quality. If the exam is not of diagnostic quality but an abnormality suspicious for lung cancer or a clinically significant abnormality is noted, then select "B. Limited CT, but interpretable" and record the abnormality in C.1 as described above. However, if a minor non-suspicious abnormality is noted, the diagnostic quality should be recorded as "C. Non-diagnostic CT exam, reschedule CT" and the minor abnormality should not be recorded in C.1.

D. No image available: The spiral CT image is not available for review. Instances in which the participant underwent a screening examination but the image sets were either lost or inadvertently destroyed and not available for review by the radiologist should be recorded as "No image available." Record the reason that images are not available for review in Item D.3 (Comments). After detailing the reason the images were not available, complete Item E.6. Having no images available for review is considered a protocol violation, therefore a Protocol and HIPAA Violation Form (PHVF) must be completed and submitted to the CC.

2. Which of the following affected the quality of the limited or non-diagnostic CT? Mark the box(es) to indicate the factor(s) that contributed to the limited diagnostic quality spiral CT. Mark all that apply.

- Submaximal inspiratory breath-hold
- Motion artifact
- Respiratory misregistration
- Incorrect technical parameter(s)
- Lungs not completely imaged
- Severe beam hardening artifact
- Excessive quantum mottle or graininess

- Other (SPECIFY)

Part C. Spiral CT Examination Findings (Completed by Radiologist):

Part C is to be completed by the radiologist. Any finding that could impact follow-up (i.e. result codes "A," "B," and "C") must be in the dictated report and recorded in Part C of the screening exam form. Minor abnormalities that do not require follow-up may be included in the dictated report but do not need to be recorded on the screening exam form. Any abnormality recorded on the screening exam form must be noted in the dictated report. If item A.2 is answered "No," Parts B and C should be left blank and Items D.1, D.3, and E.6 should be completed.

1. **Radiologic Abnormality Noted:**

   - **No:** No abnormality was seen. Go to Item D.1 and mark Result "E."

   - **Yes:** An abnormality (either suspicious for lung cancer or abnormal for any other reason) was seen. Record information for each (up to six) abnormality in the chart (C.2).

2. **Record Information for Each Abnormality:** Complete this item for up to six abnormalities. If more than six are identified, record the six most serious abnormalities. Complete the chart by recording the appropriate number(s) in the designated spot. Enter information about the most serious abnormality in the row labeled "1," the second most serious abnormality in the row labeled "2," and so on.

   Description of Abnormality: For each abnormality, mark **one** number that corresponds to it from the list below. Please note that **code 51 (in bold) is considered to be a positive screen for lung cancer and always should be listed first if multiple abnormalities are identified**. For this abnormality, the examination result in Item D.1 must be coded "Positive Screen – Abnormalities suspicious for lung cancer." If, however, the non-calcified nodule/mass ≥ 4 mm is not discovered until the comparison exam, it is possible that code 51 will not be listed first and that the examination result in Item D.1 will not be "Positive Screen – Abnormalities suspicious for lung cancer."

   Code 52, "Non-calcified nodules < 4 mm," should be used to document nodules present at T_0 as well as incident nodules at T_1 and T_2. If the nodule is noted at T_2, the radiologist may wish to recommend that the participant receive an annual CT until no further change is observed, however no study-wide recommendations have been established.

   Please note that codes 70 and 71, "Other significant abnormality (SPECIFY)" should be used to designate all other significant abnormalities not listed below, including, but not limited to, any other abnormalities suspicious for malignancy. Code 72, "Other minor abnormality noted" should be used to designate all other minor abnormalities noted. Specifying the minor abnormalities designated by code 72 is optional.

   51 = Non-calcified nodule/mass ≥ 4 mm (MUST MARK "A" IN D.1)
   For this abnormality, the examination result in Item D.1 must be coded "Positive Screen – Abnormalities suspicious for lung cancer."

   52 = Non-calcified nodule < 4 mm
   New, small nodules observed at T_1 or T_2 are to be coded as "D – Negative Screen, Minor abnormalities not suspicious for lung cancer."

   53 = Benign lung nodule(s) (benign calcification)

54 = Atelectasis, segmental or greater
55 = Pleural thickening or effusion
56 = Non-calcified hilar/mediastinal adenopathy/mass ≥ 10 mm short axis
57 = Chest wall abnormality (e.g. bone destruction, metastasis)
58 = Consolidation
59 = Reticular/reticulonodular opacities, honeycombing, fibrosis, scar
62 = 6 or more nodules, not suspicious for cancer (opacities ≥ 4 mm) (ANY SUSPICIOUS NODULES MUST BE CODED AS 51)

Code 62 should be used in cases where there are at least six nodules not suspicious for cancer. "Not suspicious for cancer" is defined as round, well-defined, and similar in size. Any nodules that are suspicious MUST be coded as 51; should this leave a total of fewer than six non-suspicious nodules, each nodule must be individually recorded.

63 = Emphysema
64 = Significant cardiovascular abnormality (SPECIFY)

Code 64 should be used to record a significant cardiovascular abnormality, such as a thoracic aortic aneurysm, aortic dissection, marked cardiomegaly, pulmonary hypertension, coronary artery calcifications, or valvular calcifications (exclude mitral annular calcification). The abnormality should be specified in the space provided to the right of the two-digit box for the abnormality code.

70 = Other significant abnormality above the diaphragm (SPECIFY)

The abnormality should be specified in the space provided to the right of the two-digit box for the abnormality code.

71 = Other significant abnormality at or below the diaphragm (SPECIFY)

The abnormality should be specified in the space provided to the right of the two-digit box for the abnormality code.

72 = Other minor abnormality noted (SPECIFY IF DESIRED)

The abnormality may be specified in the space provided to the right of the two-digit box for the abnormality code, if desired.

Check box if identified after comparison with historical images: This box indicates when the abnormality listed in the table was identified. Check the box for any abnormality that was found on the current spiral CT only after comparing it with any historical image. If an abnormality was identified during the initial (isolated) review of the current spiral CT, this box is left blank.

The remaining information under Description of Abnormality (CT Slice, Location of Epicenter, Longest Diameter, Longest Perpendicular Diameter, Margins, and Predominant Attenuation) must be recorded for abnormalities coded as 51 only.

- **CT Slice:** Record the slice number that contains the greatest diameter of the abnormality or identify a representative slice. This will be used primarily to identify the location of the abnormality for follow-up. The CT slice number where an abnormality is seen must be recorded.
- **Location of Epicenter:** Record the code that corresponds to the approximate center of the location of the abnormality in the appropriate lobe. Select one location for each abnormality.

- **RUL (Right Upper Lobe):** The abnormality was found in the upper 1/3 of the right lobe.
- **RML (Right Middle Lobe):** The abnormality was found in the middle 1/3 of the right lobe.
- **RLL (Right Lower Lobe):** The abnormality was found in the lower 1/3 of the right lobe.
- **LUL (Left Upper Lobe, excluding lingula):** The abnormality was found in the upper 1/3 of the left lobe, excluding the lingula.
- **Lingula:** The abnormality was found in the lingula.
- **LLL (Left Lower Lobe):** The abnormality was found in the lower 1/3 of the left lobe.
- **Other (SPECIFY):** This choice is used when it is difficult to identify the lung section containing the epicenter. If the lung section containing the epicenter cannot be identified, specify a more general location (i.e., upper lobe).

- **Longest Diameter (mm):** Record the length of the abnormality's maximum dimension in millimeters using whole integers. Zero-fill all measurements (e.g., 005). If dimensions are not available, record 999.
- **Longest Perpendicular Diameter (mm):** Record the length of the maximum perpendicular dimension (that is, the longest length that is perpendicular to the maximum dimension) in millimeters using whole integers. Zero-fill all measurements (e.g., 005). If dimensions are not available, record 999.
- **Margins**: Record the code that corresponds to whether the lesion is spiculated (stellate), smooth, or poorly defined. If the morphology cannot be determined, code "unable to determine."
- **Predominant Attenuation**: The radiologist will categorize, when possible, the appearance of the abnormality by recording the code that corresponds to the attenuation. *(Note: "Mixed attenuation" refers to nodules of mixed soft tissue (solid) and ground glass attenuation, also referred to as "semi-solid.")*

Part D. Spiral CT Interpretation Results (Completed by Radiologist):

Part D is to be completed by the radiologist. At some SCs, the SC staff will complete this section using the radiologist's written report. In cases where an adequate scan was not obtained (A.2 = No), Items D.1 and D.3 must be completed by the radiologist.

Part D documents the results of the current screening examination only. The participant's prior medical history, prior radiologic examinations, or prior NLST/LSS screens should not be considered when assigning the lung screening result in Part D. The result of comparing the current spiral CT image with historical images will be recorded in Part E.

Note: The focus of the screening examination is to identify abnormalities that are suspicious for lung cancer. Although other clinically significant findings may be found incidentally during the screening, the Results section is meant to reflect a hierarchy of examination findings in regard to lung cancer. Result

categories A, C, D, E, and F in Part D, Item 1 are in hierarchical order. Thus, a positive screen is at the highest end of findings, a clinically significant abnormality is at the next level, and so on, throughout the results category.

1. **Lung Screening Result:** Mark the box corresponding to the result of the current spiral CT examination. Definitions of lung screening results are given below:

   A. Positive Screen – Abnormalities suspicious for lung cancer:

   The following abnormality (C.2, #51) is always considered a positive screen and Item D.1 must always be marked "A":

   - Non-calcified nodule/mass $\geq$ 4.0 mm

   Other abnormalities, or constellations of abnormalities, may be suggestive of lung cancer, but there is no absolute rule for coding other findings as suspicious for lung cancer. In these instances, the classification of a screening exam result as positive is left up to the radiologist. Any other clinically significant abnormalities may be reported in Item D.2.

   C. Negative Screen – Clinically significant abnormalities not suspicious for lung cancer:

   The review of the scan reveals that an abnormality is present and requires further evaluation, but is not suggestive of lung malignancy. It is up to the radiologist to determine whether an abnormality is clinically significant. Complete Item D.3 and then go to Part E.

   D. Negative Screen – Minor abnormalities not suspicious for lung cancer:

   The review of the scan reveals minor abnormalities that are not suspicious for lung cancer. It is up to the radiologist to determine whether an abnormality is minor. Complete Item D.3 and then go to Part E. In the instance of a nodule(s) < 4mm, the result must be coded a "D" – "Negative Screen, Minor abnormalities not suspicious for lung cancer."

   E. Negative Screen – No significant abnormalities:

   The review of the scan reveals no significant abnormalities. Complete Item D.3 and then go to Part E.

   F. Inadequate:

   The spiral CT scans were inadequate and sufficient information could not be obtained to determine the examination result. Complete Item D.3 and then go to E.6.

   If the image is considered inadequate, but based on what is visible on the image, there is an overt suspicion of lung cancer, the result of the screening exam should be recorded as positive. The radiologist should record that the image is positive in Item D.1 of the SCT. The radiologist must comment in Item D.3 that although the result is positive, the overall quality of the image is inadequate. Part E should be completed as outlined below.

2. **Other Significant Abnormalities (in addition to lung screening results) that need to be reported:** Complete D.2 only if the Lung Screening Result in D.1 was "A. Positive Screen."

   No: The spiral CT did not reveal other significant abnormalities other than the lung screening result.

   Yes: The spiral CT revealed a significant abnormality in addition to the positive lung screening result; for example, a breast mass was seen in addition to nodules that are suspicious for lung cancer.

3. **Comments:** The comments box should be used to record information from Parts B, C, and D that may help clarify a situation, provide further information for an item in another part of the form, and to record additional "Other (SPECIFY)" information, if needed.

   If there are no additional comments, mark the box next to "No." If there are additional comments, mark the box next to "Yes." Enter the item number to which the comments are related. The item number should include a letter indicating the part of the form, and a number indicating the item within that part (e.g., B.2). If the comment is not related to a specific item in Parts B, C, or D of the form, use the item number for the Comments section itself (D.3). Then enter the comments in the space provided to the right of the item number.

   Note that if a dictated report is not provided, the Comments section should be used to describe significant and minor abnormalities occurring with a negative screen.

   If Item D.2 is marked "Yes," the Comments section should be used to describe the other clinically significant abnormality.

Part E. Spiral CT Comparison Results – Complete for All Lung Screening Results (Completed by Radiologist)

Part E is to be completed by the radiologist and must be completed for ALL screening examinations.

Part E documents the comparison of the current spiral CT with any available historical images for the participant. Comparison to previous images may or may not lead to a change in the lung screening result. Historical images for the T_0 prevalence screen will be obtained according to local practice at the SC. Cases where a participant does not have an historical image to be used for a comparison read should be recorded in "E.5. Comments." If a previous screening exam was not performed, then not doing the comparison is not considered a protocol violation. For example, not performing the comparison read at T_1 is not considered a protocol violation if the T_0 exam was never obtained and an MDF was submitted for the T_0 SCT or form. However, if the previous screening exam was performed but the images are not compared to the current screening exam, a Protocol and HIPAA Violation Form must be completed.

If historical images can be obtained, they should be used to conduct a comparison review for the T_0 prevalence screen. For T_1 screening examinations, the comparison image is the T_0 screen. For T_2 screening examinations the comparison images are the T_0 and T_1 screens. However, if the screening examinations from all three study years are negative, then the T_2 screening examination may be compared with either the T_0 or T_1 screen, or both screens, at the radiologist's discretion.

In the event that a screen is inadequate and a repeat screen is performed, the inadequate screen may be used as the comparison image for the repeat screen at the radiologist's discretion. In this instance, check the box for the current study year in Item E.1. If an inadequate screen is used for comparison in later study years, that fact should be noted in the Comments section. A comment is not required if using an

inadequate screen for comparison in the same study year. For example, if a T_1 screen is inadequate and a repeat T_1 screen is performed, then both the T_0 and the inadequate T_1 screens may be used as comparison images for the repeat T_1 screen. If the inadequate screen is used as a comparison image at T_2, then it should be noted in the Comments section. Once the comparison has been made and the data recorded, the results of the comparison are recorded in Item E.3a.

Should the comparison with historical images lead to a change in the lung screening result, the radiologist should record the new result in Part E. For example, a minor abnormality documented in Part C may lead to the Lung Screening Result "D" in Item D.1. However, upon comparison with historical images, the radiologist may decide that there has been a significant change in the abnormality. In this instance, the radiologist would complete Part E, recording the information concerning the abnormality in Table E.2, and record the Lung Screening Comparison Result "C" in E.3a.

Should the comparison with historical images identify an abnormality that was not previously seen on the image read in isolation, the abnormality should be recorded in Item C.2, and the box which reads "Check Box If Identified After Comparison With Historical Images" should be checked. If the abnormality is coded as a "51" or other significant abnormality, then these newly identified abnormalities should be recorded in Item E.2.

Likewise, should the comparison with historical images result in an abnormality that differs (more severe or less severe) from what was seen on the image read in isolation, the abnormality should be coded according to the comparison image and recorded in Item C.2. For example, an abnormality is coded as a "72 – Other minor abnormality noted" for the image read in isolation. But in comparison with the historical image, the abnormality now appears to be a "71 – Other significant abnormality at/below the diaphragm." The abnormality should be recorded as a "71" in Item C.2, and the box which reads "Check Box If Identified After Comparison With Historical Images" should be checked. The change in the abnormality as a result of the comparison with historical images should be documented in the Comments section of Part E (Item E.5). Item E.2 should then be completed according to the guidelines outlined below. Any findings from historical images used as comparisons that are <u>not present at the current screening exam</u> (i.e. a 51 present at T_0 but not at T_1) should be noted as a comment in E.5.

1. Comparison Image: Check the box to indicate the source of the comparison image. Mark all boxes for which a comparison image is available.

No image available – There is no historical image available. If checked, this should be the only box checked. Go to E.4.

T_0 – The comparison image is the NLST/LSS T_0 exam. The current spiral CT scan is the T_1 or T_2 examination. In instances where the T_0 screen is inadequate and a repeat screen is performed, the inadequate T_0 screen may be used as the comparison image for the repeat T_0 screen at the radiologist's discretion. If the inadequate T_0 screen is used as a comparison image at the T_1 or T_2 examination, record that fact in the Comments section.

T_1 – The comparison image is the NLST/LSS T_1 exam. The current spiral CT scan is the T_2 examination. In instances where the T_1 screen is inadequate and a repeat screen is performed, the inadequate T_1 screen may be used as the comparison image for the repeat T_1 screen at the radiologist's discretion. If the inadequate T_1 screen is used as a comparison image at the T_2 examination, record that fact in the Comments section.

T_2 Inadequate scan – The comparison image is the NLST/LSS T_2 inadequate scan. The current spiral CT exam is the T_2 repeat examination.

Previous scan not completed as part of NLST – The comparison image was not done as part of the NLST/LSS. Record the code that corresponds to the type of scan for which the images are available, and the date of the scan. A total of three non-NLST/LSS scans may be recorded.

2. Enter abnormality number and code for all Code 51 abnormalities AND other significant abnormalities seen on this screening exam. This chart records the result of the comparison of each abnormality seen on the current spiral CT with any available historical images. Transfer the abnormality number and code from Item C.2 for each code 51 abnormality and/or other significant abnormality, including any abnormalities that have been determined to be significant only after comparison with historical images. Any new abnormality that is identified during the comparison must be recorded in Item C.2. Complete the following:

Was abnormality pre-existing? Record the single-digit code to indicate whether or not the abnormality was seen on any historical image.

1 = No: The abnormality is not visible on any previous image. Do not complete the rest of the table; go to E.3.

2 = Yes: The abnormality can be seen on a previous image. The remainder of Item E.2 should be completed.

9 = Unable to determine: It cannot be determined whether or not the abnormality can be seen on a previous image. Do not complete the rest of the table; go to E.3.

Earliest date visible: Record the month, day, and year of the earliest historical image which shows the abnormality listed.

Complete for Code 51 Abnormalities Only: If the abnormality was recorded as code 51, complete the following:

Interval Growth of Abnormality?: Record the single digit code that indicates if the abnormality has grown since its appearance on the previous image.

Interval suspicious change in attenuation?: Record the single digit code that indicates if there has been a suspicious change in attenuation between the historical image and the current one. A suspicious change in attenuation is an increase in attenuation from ground glass to a combination of ground glass and soft tissue or to pure soft tissue attenuation.

Interval change warrants further investigation?: If the abnormality was recorded as any other significant abnormality or is being re-classified as a significant abnormality due to the comparison with historical images, record the single digit code that indicates if there has been a significant change that warrants further investigation.

3a. Lung Screening Comparison Result: Check the box to indicate the result of comparison of the current spiral CT exam with the historical images available. This is the result that will be reported to the participant and the participant's health care provider, and should take into

account the radiologist's assessment of the current scan in the context of the participant's available historical images.

If the current screen is positive and the abnormality identified appears not to have changed when compared to previous images at the comparison reading (Part E), the radiologist should record the result in Item E.3a as B – "Abnormalities suspicious for lung cancer, no significant change."

However, when previous images from two successive study years have not changed and the third image is positive and appears unchanged from the previous images, the radiologist may code that result as D – "Minor abnormalities not suspicious for lung cancer" at his/her discretion as described below, rather than using result code B. Additionally, the radiologist should specify in the Comments section (Item E.5) why the result was coded as D. Likewise, if after baseline screening a clinically significant abnormality remains stable and unchanged on subsequent screening examinations, the abnormality may be coded at T_2 as D - "Minor abnormalities not suspicious for lung cancer" at the discretion of the radiologist, rather than coding the image as a clinically significant abnormality. Additionally, the radiologist should specify in the Comments section (Item E.5) why the result was coded as a D.

Any new nodules less than 4 mm that are identified on the T_1 or T_2 screening exam are to be recorded as "D" in Item E.3a as "Negative Screen, Minor abnormalities not suspicious for lung cancer." If other abnormalities are present which are suspicious for lung cancer either on their own or in conjunction with the new nodule, a result of "A – Positive screen-Abnormalities suspicious for lung cancer" should be recorded in section E.3a.

3b. Other Significant Abnormalities (in addition to lung screening results) that need to be reported: Complete E.3b only if the Lung Screening Result in E.3a was "A. Positive Screen" or "B. Positive Screen, no significant change."

No: The spiral CT did not reveal other significant abnormalities other than the lung screening result.

Yes: The spiral CT revealed a significant abnormality in addition to the positive lung screening result; for example, a breast mass was seen in addition to nodules that are suspicious for lung cancer.

4. Which of the following diagnostic procedures for screening examination results should the screening result letter include? Mark the box to indicate recommended follow-up options for this participant. More than one item may be marked. If the participant reported previous chest images but those images were not immediately available for comparison, "Comparison with historical images" may be marked, indicating that the comparison should still be attempted. If "Comparison with historical images" is marked, other follow-up diagnostic procedures MUST be indicated as well, in case the historical images cannot be obtained. If "Low dose CT with NLST parameters" is marked, the radiologist must indicate when the follow-up CT should be performed by marking one or more time intervals from the list below. The radiologist must also select the area of focus, applicable to any time period chosen. Only one box may be marked for area of focus; both may not be marked and both may not be blank. "Limited" focus refers to the abnormal region only, as opposed to the entire chest. There are no study-wide recommendations for T_2 nodules that have been stable for two years; however radiologists may make recommendations at their own discretion.

New nodules identified at T_2 will be documented on a DE Form and followed for 24 months as described in section 7.2 of the MOOP.

5. **Comments:** This comments box should be used to record comments for any item in Part E that may help clarify a situation, provide further information for an item in another part of the form, and to record additional "Other (SPECIFY)" information, if needed.

   If there are no additional comments, mark the box next to "No." If there are additional comments, mark the box next to "Yes." Enter the item number to which the comments are related. The item number should include a letter indicating the part of the form, and a number indicating the item within that part (e.g., E.2). If the comment is not related to a specific item in Part E of the form, use the item number for the Comments section itself (E.5). Then enter the comments in the space provided to the right of the item number.

6. **Radiologist ID:** This item should be completed by the radiologist. The radiologist should enter his/her four-digit staff ID number, record the date the form was completed, and sign the form in the space provided. If this section was completed by a member of the SC staff using the radiologist's written report, the SC staff member should enter the radiologist's name and staff ID number, then sign his/her own name below the name of the radiologist.

After completing the form:

- The form should be checked to make sure it is accurate, legible, and complete.
- The SC staff member who completed the form should write his/her initials in the space labeled "Initials Complete" in the box at the top of the first page.
- The SC staff member who checked the form for completion should write his/her initials in the space labeled "Initials QC" in the box at the top of the first page. This should not be the same SC staff member who completed the form.
- Enter the form into the IDEAS.
- File the form in the participant's study file.

NATIONAL LUNG SCREENING TRIAL (NLST)
EQUIPMENT QUALITY CONTROL

CT QUALITY ASSURANCE INFORMATION

The following information is required for CT quality assurance.

1. **LSS protocol CT specifications.**
2. **Confirmation of screening site adherence to CT specifications.**
3. **CT equipment characteristics.**
4. **Physicist attestation to ongoing performance testing (annual).**
5. **CT water phantom image quality scan (bi-monthly).**
6. **CT dosimetry measurements (annual, and after tube change).**

NATIONAL LUNG SCREENING TRIAL (NLST)
EQUIPMENT QUALITY CONTROL

CT EQUIPMENT CHARACTERISTICS

Site physicist: Please provide the following information, as possible, for each CT scanner being used in this study.

LSS SCREENING CENTER NAME: _____ Site #: _____

SITE MAILING ADDRESS: _____

I. PI (Radiologist) : _____

ID#: _____ Tel#: _____ Email: _____

II. Chief CT Technologist: _____

ID#: _____ Tel#: _____ Email: _____

III. Medical Physicist: _____

ID#: _____ Tel#: _____ Email: _____

	CT EQUIPMENT LOCATION:
1.	Manufacturer:
2.	Model Name:
3.	Date of Manufacture:
4.	Detector Type: __Solid State Xenon Gas
5.	Available kVp's:
6.	Maximum Available Channels (#) :
7.	Minimum Available Channel Collimation (MM):
8.	Minimum Tube Rotation Time (sec)_____

AVAILABLE DOSE REDUCTION OPTIONS: _____

NATIONAL LUNG SCREENING TRIAL (NLST)
EQUIPMENT QUALITY CONTROL

ATTESTATION TO CT PERFORMANCE TESTING

Site physicist: For each CT Scanner being used in this study, please provide the following information regarding performance testing. Copies of your reports should be available for site inspectors.

I SITE NAME: _____

II CT SCANNER: _____ **MACHINE #:** _____ **VENDOR:** _____ **MODEL#:** _____

III LOCATION OF INSTALLATION: _____

IV DATE OF INSTALLATION: _____

	PERFORMANCE TEST	TESTED AT INSTALLATION	LAST DATE TESTED	TEST NOT DONE
1.	Laser Accuracy	☐ Yes ☐ No ☐ Unknown	__/__/____	
2.	Table Movement	☐ Yes ☐ No ☐ Unknown	__/__/____	
3.	Gantry Tilt	☐ Yes ☐ No ☐ Unknown	__/__/____	
4.	Slice Thickness	☐ Yes ☐ No ☐ Unknown	__/__/____	
5.	Dose Profile	☐ Yes ☐ No ☐ Unknown	__/__/____	
6.	Scout Accuracy	☐ Yes ☐ No ☐ Unknown	__/__/____	
7.	Tube Output & Linearity	☐ Yes ☐ No ☐ Unknown	__/__/____	
8.	Half Value Layer	☐ Yes ☐ No ☐ Unknown	__/__/____	
9.	Patient Dosimetry (CTDI)	☐ Yes ☐ No ☐ Unknown	__/__/____	
10.	Geometric Distortion	☐ Yes ☐ No ☐ Unknown	__/__/____	
11.	CT# Uniformity & Nose	☐ Yes ☐ No ☐ Unknown	__/__/____	
12.	CT# Linearity	☐ Yes ☐ No ☐ Unknown	__/__/____	
13.	Spatial Resolution	☐ Yes ☐ No ☐ Unknown	__/__/____	
14.	Low Contrast Detectability	☐ Yes ☐ No ☐ Unknown	__/__/____	
15.	Artifact Evaluation	☐ Yes ☐ No ☐ Unknown	__/__/____	
16.	Display Devices	☐ Yes ☐ No ☐ Unknown	__/__/____	
17.	Scatter Exposure	☐ Yes ☐ No ☐ Unknown	__/__/____	

PLEASE INDICATE BELOW THE TYPE AND FREQUENCY OF ANY ONGOING QC PROCEDURES.

ATTESTED TO:

_____**(Physicist)** _____**(Date)**

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NATIONAL LUNG SCREENING TRIAL (NLST)
EQUIPMENT QUALITY CONTROL

BI-MONTHLY CT WATER PHANTOM MEASUREMENT

SITE PHYSICIST: PLEASE COMPLETE ONE COPY OF THIS FORM, EVERY TWO MONTHS, FOR EACH CT SCANNER USED IN THE NLST/LSS STUDY.

1. DATE: _____
2. LSS SITE NAME : _____ SITE #_____
3. CT SCANNER ID# AND LOCATION: _____
4. CT VENDOR & MODEL: _____
5. PERSON PERFORMING TESTS: _____ ID#_____
6. TITLE: _____ TEL#: _____ E-MAIL: _____

PURPOSE:

Bi-monthly water phantom tests will be performed on all CT scanners used in the NLST/LSS study.

This is done to ensure that the scanner is operating optimally at the acquisition parameters being used for the low dose CT protocol, and that any degradations in performance can be recognized and corrected in a timely manner.

These water phantom tests will monitor CT# calibration, field uniformity, noise, and artifacts.

SETUP:

The standard (approx. 20 cm diameter) water phantom supplied by your vendor for routine quality control will be used for these tests.

Using the CT alignment lights, and the vendor supplied phantom holder (if available), align and center the phantom in the gantry. Align the axial light, indicating slice position zero, to the mid thickness point of the phantom. If you must rest the phantom on the table (i.e., no holder), avoid placing it over any metal in the table, and be sure that the phantom is secured with tape or velcro.

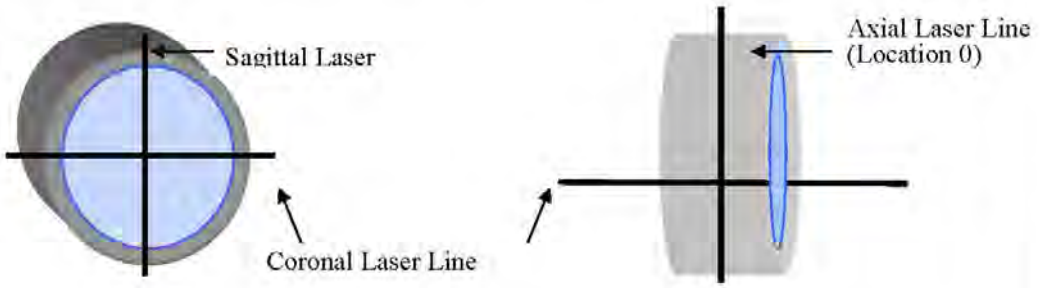

Figure 1. Front and side views of water phantom. Note that the axial laser line is located directly over the center of the water phantom.

SCANNING THE PHANTOM:

- Prescribe a short helical scan that covers the entire thickness of the water phantom.
- Use your LSS acquisition parameters for an average size patient, and reconstruct with a non-sharp algorithm.
  - Use a display field of view close to, but not smaller than the diameter of the water phantom.

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CT WATER PHANTOM MEASUREMENT

MEASUREMENTS OF WATER CT#, UNIFORMITY, AND NOISE; ARTIFACT EVALUATION:

- Select one reconstructed image that represents the center of the water phantom (axial location "0").
- View the image with window width = 100, and window level = 0.
- Place an ROI of approximately 400 mm^2 at the center, 12:00, and 3:00 positions.
- Make sure that the peripheral ROI's are approximately 2 cm from the edge, and fully within the water (avoid air bubble at 12:00).

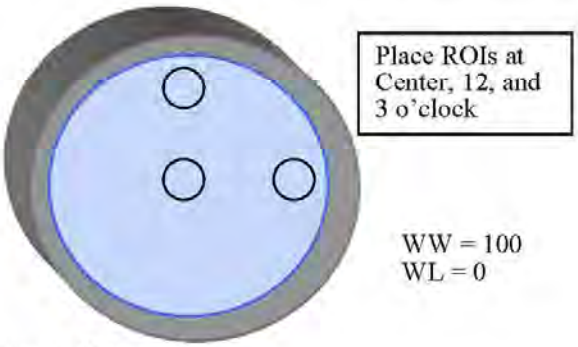


Figure 2. Measurement of CT# and Noise; Artifact evaluation.

- Record the mean CT# and standard deviation for each ROI on the attached data sheet. With room lights lowered, carefully examine the image for artifacts, and note the results.

SAVING WATER PHANTOM IMAGES:

- Image data from all slices of the water phantom should be saved and made available on request for future inclusion in the image archive library.
- When acquiring the study use the following:

  Last Name: PHANTOM
  First Name: WATER
  MRN: Site # -99999 (i.e. 04-99999 for Henry Ford)

CT WATER PHANTOM MEASUREMENT

PLEASE ENTER YOUR ACQUISITION PARAMETERS HERE:

WATER PHANTOM TEST

	PARAMETER*	(EXAMPLE)	YOUR TEST
A	LSS Site	Univ of Colorado	
B	Test Date	09/28/03	
C	Tester	F. Larke	
D	CT Scanner	Siemens Vol Zoom	
E	KVP	120	
F	Gantry Rotation Time	0.5	
G	MA		
H	MAS		
I	Effective MAS	30	
J	Number of Channels Used	4	
K	Channel Collimation (MM)	1.0	
L	Table Movement (MM Per Rotation)	8.0	
M	Pitch		
N	Reconstructed Slice Width (MM)	2.0	
O	Reconstruction Interval (MM)	2.0	
P	Reconstruction Algorithm (Filter)	b30f med smooth	
Q	Display Field Of View (MM)	250	

*** RECORD WHICHEVER PARAMETERS APPEAR ON YOUR CONTROL CONSOLE.**

PLEASE ENTER YOUR TEST RESULTS HERE:

EXAMPLE:

PARAMETER	CT#	STD DEV	CT# DIFF*	LIMITS		LSS REVIEW
CENTER ROI	-1.1	21.8		0 +/- 4; 15-40	OK?	ACTION REQ'D?
12:00 ROI	-1.5		0.4	</= 7	OK?	ACTION REQ'D?
3:00 ROI	-2.3		1.2	</= 7	OK?	ACTION REQ'D?
ARTIFACTS	RING?	STREAK?	OTHER?			
OBSERVED?	NO	NO	NO	NO ARTIFACTS	OK?	ACTION REQ'D?

* = ABS (CT#edge - CT#center)

YOUR TEST:

PARAMETER	CT#	STD DEV	CT# DIFF*	LIMITS		LSS REVIEW
CENTER ROI				0 +/- 4; 15-40	OK?	ACTION REQ'D?
12:00 ROI				</= 7	OK?	ACTION REQ'D?
3:00 ROI				</= 7	OK?	ACTION REQ'D?
ARTIFACTS	RING?	STREAK?	OTHER?			
OBSERVED?				NO ARTIFACTS	OK?	ACTION REQ'D?

* = ABS (CT#edge - CT#center)

NATIONAL LUNG SCREENING TRIAL (NLST)
EQUIPMENT QUALITY CONTROL

CT DOSIMETRY MEASUREMENTS

SITE PHYSICIST: PLEASE COMPLETE ONE COPY OF THIS FORM ANNUALLY, AND AFTER ANY X-RAY TUBE, OR MAJOR COMPONENT CHANGE, FOR EACH CT SCANNER USED IN THE NLST/LSS STUDY.

1. **DATE:** _____
2. **LSS SITE NAME:** _____
3. **CT SCANNER ID# AND LOCATION:** _____
4. **CT VENDOR & MODEL:** _____
5. **PHYSICIST PERFORMING TESTS:** _____
6. **TITLE:** _____ **TEL#:** _____ **E-MAIL:** _____

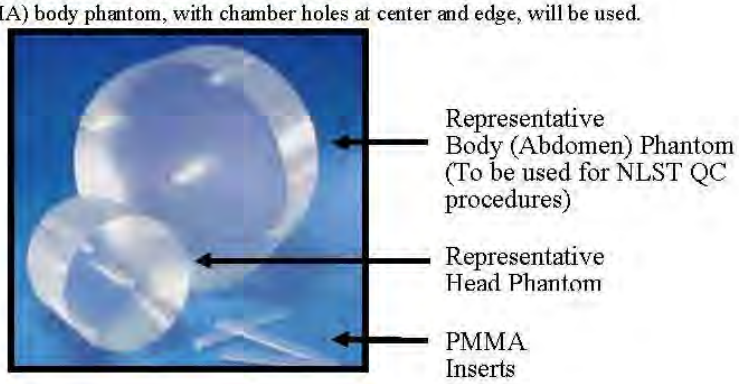
PURPOSE:

- Annual, and post tube or major component change, dose measurements will be performed by a qualified medical physicist on all CT scanners used in the NLST/LSS study, using the acquisition parameters of the low dose CT protocol. This will ensure consistent and accurate measurement of dose across all LSS sites, allowing valid comparisons, and pinpointing possible problem areas.
- Measurements shall be made using the technique factors employed for screening examinations.
- The appropriate equations and a dosimetry form are provided to facilitate consistent calculations.

SETUP:

CT DOSE INDEX (CTDI):

- The standard procedure for measuring CTDI should be utilized.
- A calibrated CT pencil ionization chamber, and associated electrometer are required.
- The 32 cm diameter (PMMA) body phantom, with chamber holes at center and edge, will be used.



- All tube warm-up, and daily calibration and QC scans should be done prior to scanning the body phantom.
- Remove the table pad, and use the scanner alignment lights to center the body phantom in the gantry.
- Align the axial light, indicating slice position zero, to the mid thickness point of the phantom.
- Be sure the phantom is secured from rolling. Avoid any metal in the table.
- Connect the pencil ionization chamber to the electrometer, and fully insert the chamber into the center hole of the phantom.
- Place the PMMA acrylic rods into the other holes.

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Appendix 4-9 CT Dosimetry Measurements Form

CT DOSIMETRY MEASUREMENTS

SCANNING THE PHANTOM AND ACQUIRING DOSE INFORMATION:

- CTDI dose information must be acquired using single axial scan acquisitions.
- Acquire one axial scan at the center of the phantom, with no table movement, using your LSS low dose technique factors for an average size patient; i.e., kVp, mA, rotation time, # of channels, and channel collimation. (Note: Siemens users may wish to use the service mode for this.)

IMPORTANT NOTE:

- The mA and time should reflect the actual mAs (mA x rotation time), NOT an effective mAs that includes the effect of pitch , (i.e., eff mAs = mAs / pitch).
- The effect of "pitch" on dose in a helical scan will be accounted for on the dosimetry form in the calculation of
- "CTDIvol" = CTDIw / pitch.
- Also, it is imperative that the detector configuration (i.e., # of channels and individual channel collimation - 4x1.0, 16x1.5, 4x2.5, etc), be the same as in the low dose protocol, as it will affect dose.

ON THE FORM PROVIDED:

- Record your technique factors and average exposure reading (i.e., avg. of three rdgs).
- Move the chamber to the 12:00 position, replacing the acrylic rod in the center position, and repeat the above procedure for an average exposure reading.
- Adjust your technique (mAs) to reflect a large patient, and repeat the above scans. (this is done as a dose verification and mAs linearity check.)

For each LSS technique (avg. and large), please record the vendor specified dose and units, for comparison.

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Appendix 4-9 CT Dosimetry Measurements Form

CT DOSIMETRY MEASUREMENTS				
PLEASE ENTER YOUR CTDI SCAN PARAMETERS AND RESULTS HERE:				
LSS MAS RANGE IN USE AT YOUR SITE:		(40 - 80)	**Your Scanner:** ( )	
	Single Scan Axial CTDI:	**Example**	**Average Patient**	**Large Patient**
	LSS Screening Site / #	Univ of Colo / 01		
	Date	09/28/03		
	Tester	F.J. Larke		
	CT Scanner	Siemens Vol Zoom		
	Location / Room Number	AOP1241		
	X-ray tube Identifier #	CT3		
	kVp	120		
	mA	120		
	Exposure time per rotation (sec)	0.5		
	mAs	60		
	Number of data channels used (= N)	4		
	Nominal collimation per channel (mm) (= T)	1.0		
	Pencil Ionization Chamber Active Length (mm) (=ACL)	100		
	Chamber correction factor at stp (mR/rdg) (=CF) *	1.02		
	Temperature and Pressure Correction, (=Ctp)	1.22		
	32 cm Phantom Center Position:			
	Average of 3 meter readings (=AVGRDG)	11.8		
	$CTDI_{tissue}$ at phantom center (mGy)**	3.5		
	32 cm Phantom 12 o'clock position:			
	Average of 3 meter readings (=AVGRDG)	26.0		
	$CTDI_{tissue}$ at phantom surface (mGy)**	7.7		
Average Tissue Dose:				
	CTDIw (mGy) (= 1/3 CENTER + 2/3 SURFACE)	6.3		
Clinical Exam Dose Estimates:				
	Table Increment per rotation (mm) (= I) used in LSS Protocol	8.0		
	Calculated Pitch (= I/NT) used in LSS Protocol	2.0		
	Effective mAs (= mAs / Pitch) used in LSS Protocol	30.0		
Average Tissue Dose - LSS Protocol:				
	CTDIvol (mGy) =CTDIw / Pitch	3.2		
	Vendor specified protocol dose (mGy) (incl pitch)	3.4		
	DLP (mGy-cm) for 40 cm scan =CTDIvol*40	128.0		
	Effective Whole Body Dose (mSv) =DLP*0.017	2.2		
*** CF is the correction factor needed to convert your meter reading to mR at standard temperature & pressure.**				
****($CTDI_{tissue}$ (mGy) = (AVGRDG * CF(mR/RDG @ stp) * Ctp * (ACL / NT) * .0094 mGy/mR)**				

Version 1 03/11/05

NLST/LSS Clinical Studies Workstation User's Guide

Revision 1.2.1
February 6, 2003

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CONTENTS

1 Introduction

The Clinical Studies Workstation (CSW) is a PC compatible computer with custom software developed to assist in image anonymization and collection for clinical trials. The NLST version of this system includes a special display card and monitor that are important for Quality Assurance work performed.

This manual describes how to install, use and maintain this workstation. It includes sections on hardware installation as well as software configuration for participant anonymization.

2 System Overview

Figure 2.1 below shows a diagram of the components found at the screening center and Quality Assurance Coordinating Center (QACC). Some components are omitted from the diagram.

Participants are screened on a CT, CR or other device. Depending on local protocol, these images are probably stored on a Picture Archive and Communications System (PACS) in the radiology department or they may be stored on a single-purpose storage device under the control of the study coordinator for the screening center.

At some time after the participant screening, Westat will inform both the screening center and the QACC of a list of studies to be transmitted for quality assurance. A staff member at the screening center will transmit those studies from the storage system (or imaging modality) to the Clinical Studies Workstation that is present at the screening center.

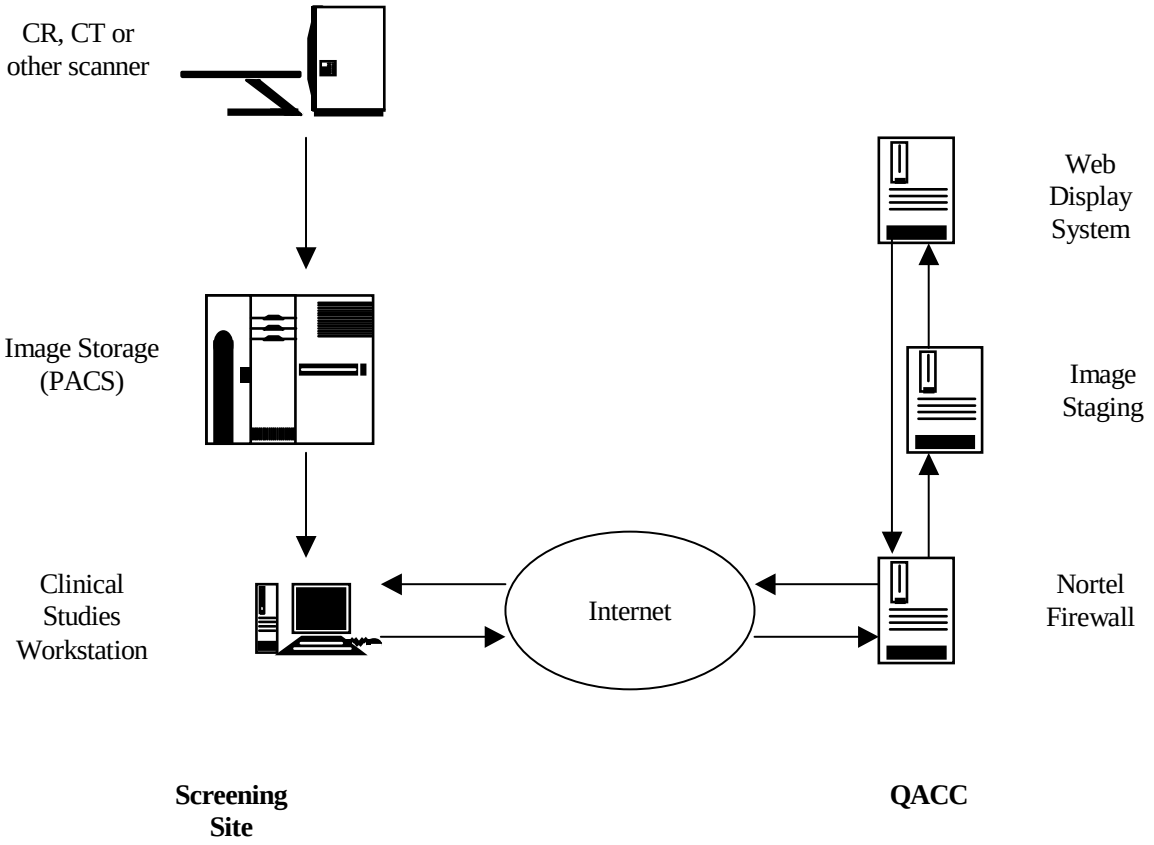


Figure 2.1 Block Diagram of Components at Screening Site and QACC

After the studies are received at the CSW, another staff member (possibly the same staff member as above) modifies the demographics and transmits those studies to the QACC using a Virtual Private Network (VPN) over the Internet. No identifying information (PHI in HIPAA terms) is included in the transmission.

QACC members perform a check-in process and copy the images to a web-based system that is used by radiologists for image review. At the same time, a second web-based system is updated to give the QA radiologist a list of studies to review.

QA radiologists performing review use a Web browser (Internet Explorer) and connect to the QACC through the same VPN software. Once the connection is made, the Web browser can connect to the web server and provide images for review.

3 Site Installation

The CSW was configured and tested at the Electronic Radiology Laboratory at the Mallinckrodt Institute Of Radiology. This section describes those steps needed for site installation.

3.1 Connecting the Color Monitor

[1] Face the rear of the monitor.

[2] Attach the 1/3 tail of the gray-beige 3-tailed cable to the left-most receptacle labeled "Input 1 DVI-D".

[3] Do not attach the 2/4 tail. Attach the remaining tail to the rear of the PC.

[4] Attach the power cord. Monitor's power switch is on left side of monitor when facing front.

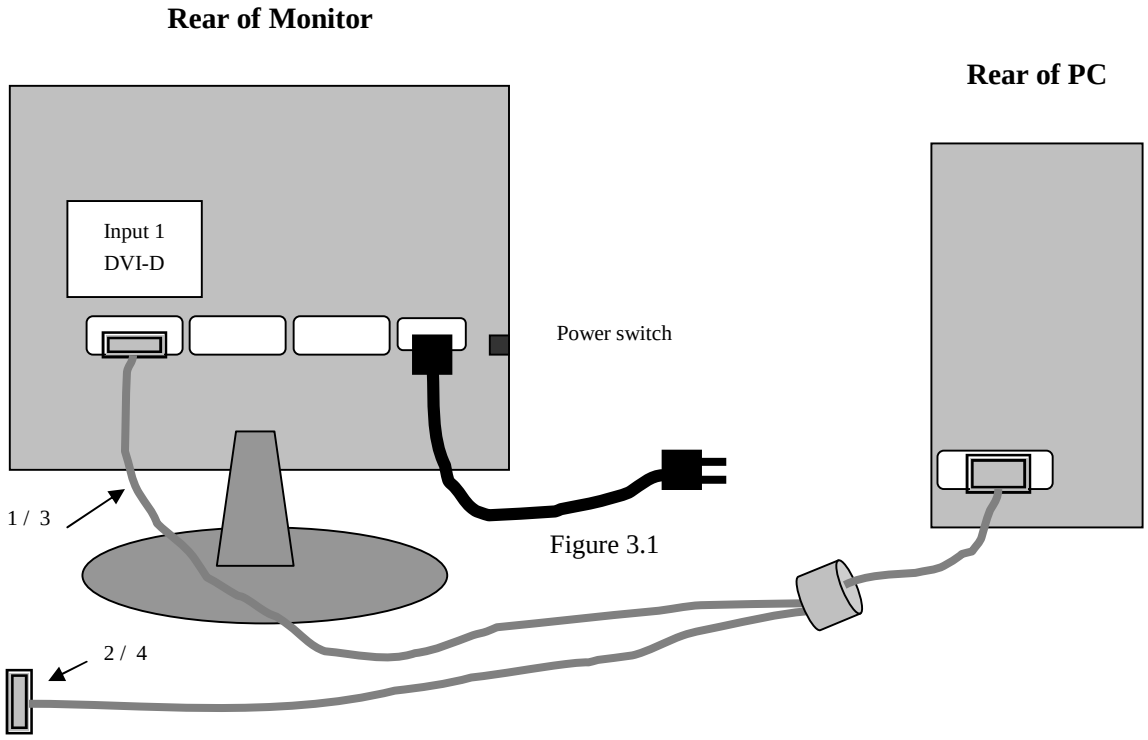


Figure 3.1

3.2 Administrator Changes

1. Logon to the system using the Administrator account. The system shipped to you has the administrator password set to _____. Change this password according to local convention.
2. The hostname of the system is _____. Please leave the hostname unchanged, but you should change the network settings for your institution. Use the Control Panel to get access to the Network Settings for this system, and change the following per your local configuration:
    a. IP address
    b. Subnet mask
    c. Default router
    d. DNS Service Search Order

    This PC will operate best with a fixed IP address. That can be managed through the network settings. If your site uses DHCP, you need to get a fixed IP address through your DHCP mechanism. This is because computer systems in Radiology (CT, Chest X-Ray) will likely only understand a fixed IP address and will not be able to send images to this system if the IP address changes.
3. The system is shipped with a user account (Power User) under the name of the PI from your institution. That account name is _____ and password is _____. You are free to use this account for day to day activity or to create other accounts for individual users. To use the CSW software, these other accounts should be members of the Power Users group.
4. Some sites may want to reconfigure their PC and place it in a cluster with other systems. Do not do this with this PC. The VPN software that is used will cause problems with shared network drives, and the clustering software will disrupt the performance of the system. Use this PC as a standalone system as it was shipped.

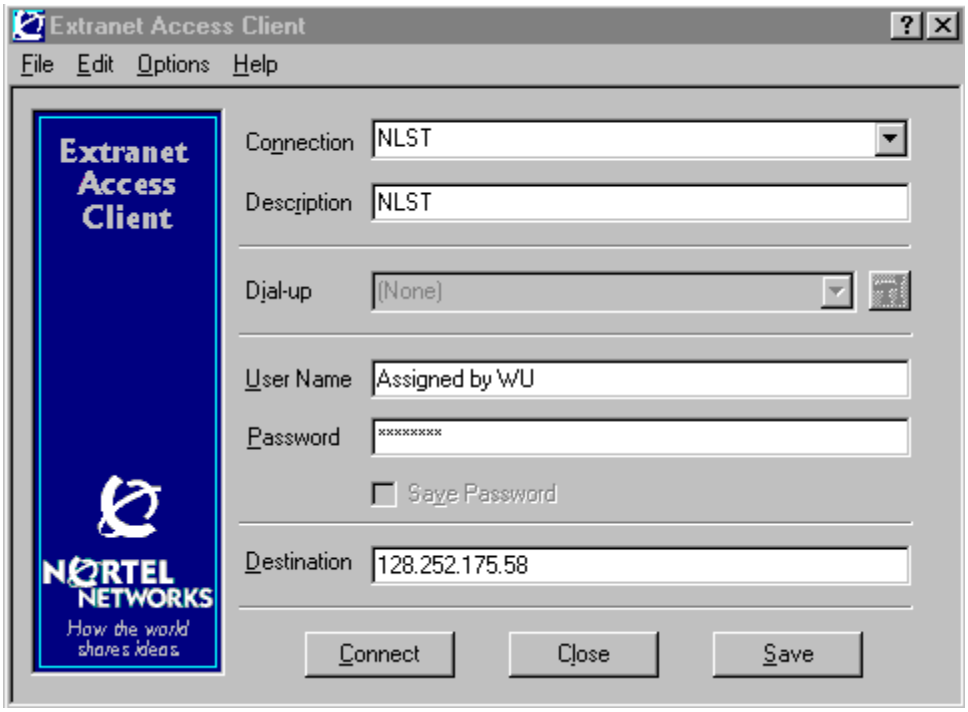
3.3 Test the VPN Software

This test can be performed using the Administrator account or a user account.

1. Make sure your system has network access to the Nortel firewall system at Washington University. Open a Command Prompt (DOS) window and ping the firewall system:
    ping 128.252.175.58
    The VPN software will not work if you cannot ping this system.
2. Activate the Nortel VPN client software. Use the desktop icon provided for the default user account or activate from the Start menu (Start->Programs->Nortel Networks->Extranet Access Client).
3. The Nortel client will present a display as shown in figure 3.2 below. The User Name and Password are fixed by Washington University. Your User Name is _____ and Password is _____. Leave the destination as is (128.252.175.58)

and connect to the VPN. Upon success, you should see the window as shown in figure 3.3 below. Select the OK button to dismiss the success window.

4. Test connectivity to a system using the VPN software. Use the Command Prompt window and ping the system 172.20.219.7. If that succeeds, the VPN software if operational.
5. Disconnect the VPN connection. The Nortel VPN icon will be displayed in the tool tray in the lower right hand corner of your display. Double click that icon to bring the display to your screen. Select the Disconnect button.




Security Banner
NLST
Any unauthorized use of the system is unlawful, and may be subject to civil and/or criminal penalties.
This system may be logged or monitoredwithout further notice, and that the resulting logs may be used as evidence in court.
OK
Cancel

4 PACS/Modality Configuration Information

The CSW software includes a DICOM receiver that accepts images from a scanner (CT, CR, MR) or PACS and stores those images on local disk. The software starts when the system is turned on and remains active.
In order to receive images, you will need to inform the PACS manager of the parameters that describe this machine. These parameters include a port number, IP address and DICOM Application Entity title. The port number and DICOM Application Entity title are configured by Washington University. Your system administrator assigns the IP address at your institution.

1. Inform the PACS manager or appropriate person of your system parameters. These are listed below:
   Host Name: _____
   IP address: _____
   Port Number: _____**2301**_____
   DICOM AE Title: _____
2. Ask the manager to send a sample study from each system that will be used during the NLST study. Because this is QA performed after the fact, we presume that these studies will be archived somewhere and then sent to the workstation. That is, even though the workstation supports this mode, we do not expect radiology to send studies directly from the scanner itself.
3. Logon to the system, anonymize the images, and send them as test cases to Washington University. The contact person for testing is Steve Moore (moores@mir.wustl.edu).

4.1 Reading Images from CD ROM

Because of network or other issues, some institutions may not be able to send DICOM images over a network to the CSW. Some institutions may have the ability to produce a DICOM Part 10 compatible CD ROM that can be read by software included with the CSW. These software was not designed as part of the GUI and is not an integrated part of the CSW application. This section of the document will describe the several steps needed to send images from a Part 10 CD ROM to the CSW application.

There is a set of one-time steps needed to modify the PATH variable for your account (or for the system) to include the CSW installation directory. You probably want assistance from a system administrator to perform these steps. The workstation shipped from MIR should have been shipped with an account with the PATH variable set as described below. Use that account or modify your account as follows:

1. Select the "Start" menu and then select Settings->Control Panel.
2. From the Control Panel folder, open the System icon.
3. A System Properties window should appear. Select the Advanced tab.
4. From the Advanced table, select the button for Environment variables.

5. You need to add a variable in the area reserved for User Variables (not system variables). In the User Variables area, select the button for New variable. Enter the name PATH for the variable and the following for the value: `%PATH%;C:\Program Files\CSW`
6. Close the system properties window (use the OK button)
7. Open a command prompt window (Start->Programs->Accessories->Command Prompt). In the window, type `dicom_echo <Enter>`. The system should tell you the parameters for the application. If the system tells you that it cannot find the application, then the %PATH% variable is not set properly.

Here are the instructions for sending the images to the workstation.

1. Insert the CDROM into your CD reader. Some CD ROMs have automatic software that starts a viewing application. Exit that application (this will leave the CD ROM mounted).
2. Use the Windows Explorer application on the workstation to open the CD ROM and search for files. If you try to open the CD using the drive designation from "My Computer", you are likely to launch the viewing application on the CD.
3. The CD contains DICOM images in files that are roughly 500 KBytes in length. The CD also contains other files used by the vendor to display the images or serve as an index for the images. Our software will try to open the non-image files and will have a problem. Copy all of the image files from the CD to a temporary folder on your hard drive. If you want, you can copy the entire CD and then go back and delete the non-image files on the local, temp directory.
4. Open a command prompt window. In that window, change directories to the temp directory where you just copied the image files. It could be that you created several sub-directories because the CD was formatted with sub-directories. That is OK; just change to the top-level directory that you created: (eg, `cd \cd-images`).
5. Type this command to make sure the local DICOM receiver is running:

   ```
   dicom_echo localhost 2301
   ```

   It should print a status message that looks like this:

   ```
   Echo context: Context
   Verification Response
     Message ID Responded to:    1
     Verification Status:     0000
   Echo Response
   Message ID Responded To: 1
   Data Set Type:           0101
   Status:                  0000  Status Information:-
        Successful operation
   Class UID:               1.2.840.10008.1.1
   ```

6. Send the images to the local workstation by typing the following command in the command prompt window:

   ```
   send_image –q –a CDROM –Z localhost 2301 . (that is a
   period)
   ```

   This command tells the system to send all images in the current directory and below to the CSW server.

7. Assuming the transfers are successful, each image should be sent with the send_image program printing a success message. An example is included below.

   ```
   Store Response
   Message ID Resp:1
   Data Set Type:  0101
   Status:         0000  Status Information:-
        Successful operation
   Class UID:      1.2.840.10008.5.1.4.1.1.2
   Instance UID:
   1.3.12.2.1107.5.1.4.24535.6.0.135608519411846
   ```

8. If any of the files cannot be transmitted, *send_image* will stop with an error message. This normally indicates that one of the files was not a proper image file. Find the errant file, delete the file and invoke the *send_image* program again. It does not matter if you send the same images multiple times. The CSW software will discard duplicate copies of images.

5. User Login Instructions

These are the login instructions for users of the NLST CSW. The Washington University QA group created one user account on your system. Your administrator may have created a separate account for you. Check with the administrator to determine the account name and password.

Account Name _____

Password _____

1. When no one is logged on the computer, you should see a screen as shown in figure 4.1 below. If the screen is dark (blank), press the Shift key or space bar.
2. As indicated in the figure, press the Ctrl, Alt and Delete keys simultaneously. This will bring you to the login screen. Use the login and password for your account.
3. To logout, use the mouse to select the Start menu (lower left corner of the screen). Select the Shutdown option and from there, select logoff (not shutdown or restart).

6 Washington University VPN Instructions

The Washington University Virtual Private Network (VPN) uses a hardware server from Nortel and client software on your PC to encrypt data sent across the Internet. The hardware server is located at Washington University. When the user wants to communicate with the imaging systems at Washington University, the VPN software must be enabled. The imaging functions include:

- Transmitting QA cases to the QA center
- Reviewing QA cases using a web browser and EasyWeb software

Users should be able to login and log off the Washington University VPN using these instructions.

1. You should already be logged on to the PC using the instructions given in section 5. Your account can be a standard user account and need not be the Administrator account.
2. Activate the Nortel VPN client software. Use the desktop icon provided for the default user account or activate from the Start menu (Start->Programs->Nortel Networks->Extranet Access Client).
3. The Nortel client will present a display as shown in figure 6.1 below. The User Name and Password are fixed by Washington University. Your User Name is _____ and Password is _____. Leave the destination as is (128.252.175.58) and connect to the VPN. Upon success, you should see the window as shown in figure 6.2 below. Select the OK button to dismiss the success window.
4. When the VPN software is active, you will not be able to contact other computers on your local network or the Internet. This means that modality systems (CT, Chest X-Ray) cannot send images to you, nor can you connect to public web servers such as www.rsna.org.
5. When you are finished using the CSW software, you need to disconnect the Virtual Private Network. The Nortel VPN icon will be displayed in the tool tray in the lower right hand corner of your display. Double click that icon to bring the display to your screen. Select the Disconnect button.
6. After the VPN software is disconnected, you may choose to log off the PC or perform other tasks.

7. Forwarding Studies to QACC

The Clinical Studies Workstation application presents a graphical user interface (GUI) to the user to allow the user to modify demographic information in images and to forward those images to the Quality Assurance Coordinating Center (QACC) at Washington University. To use this software, follow these instructions.

1. Log on to the computer using a standard user account; you do not need the Administrator account.
2. Activate the CSW application (Start Menu->Programs->CSW) as shown in figure 7.1 below.

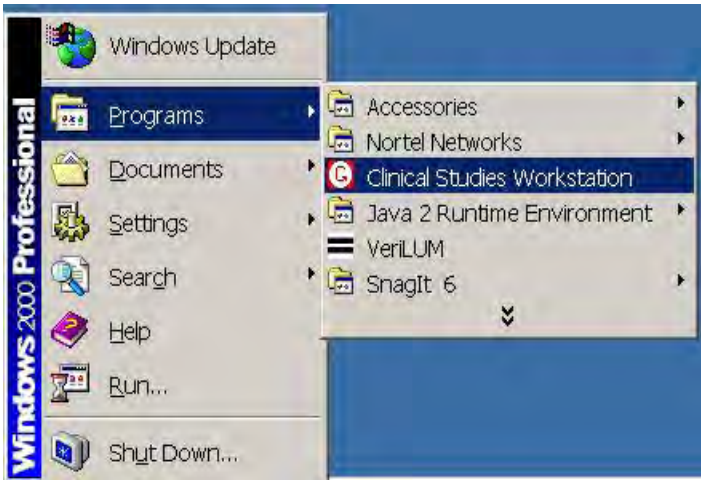


Figure 7.1: Launching CSW Application

3. The CSW application will present you with a list of studies stored on the workstation as shown in figure 7.2 below. The studies include demographics transmitted by the scanner (CT, CR) or by the PACS. Select one study for transmission (single click).
4. Enter the Westat ID for the participant in the Patient ID box. A Westat ID has three fields separated by the dash symbol. An example is 11-12345-1. You do not need to modify any other fields. The CSW software will automatically erase the Patient Name, Date of Birth and Sex.
5. Press the Commit button. This signals the workstation software to remember your changes in local memory; the images on disk are not changed.
6. Immediately after committing the changes, press the Enqueue button. This will place the study in a queue for transmission to the QACC.
7. In order to see what entries are in the queue to be transferred, select the "Queue" entry from the "Settings" pulldown.
8. The images stay in the queue until completely transmitted to the QACC at Washington University. You will need to activate the Virtual Private Network software and leave that

software active until all images are transferred. To make sure all images have been transferred, select the Study view and then Queue view again.

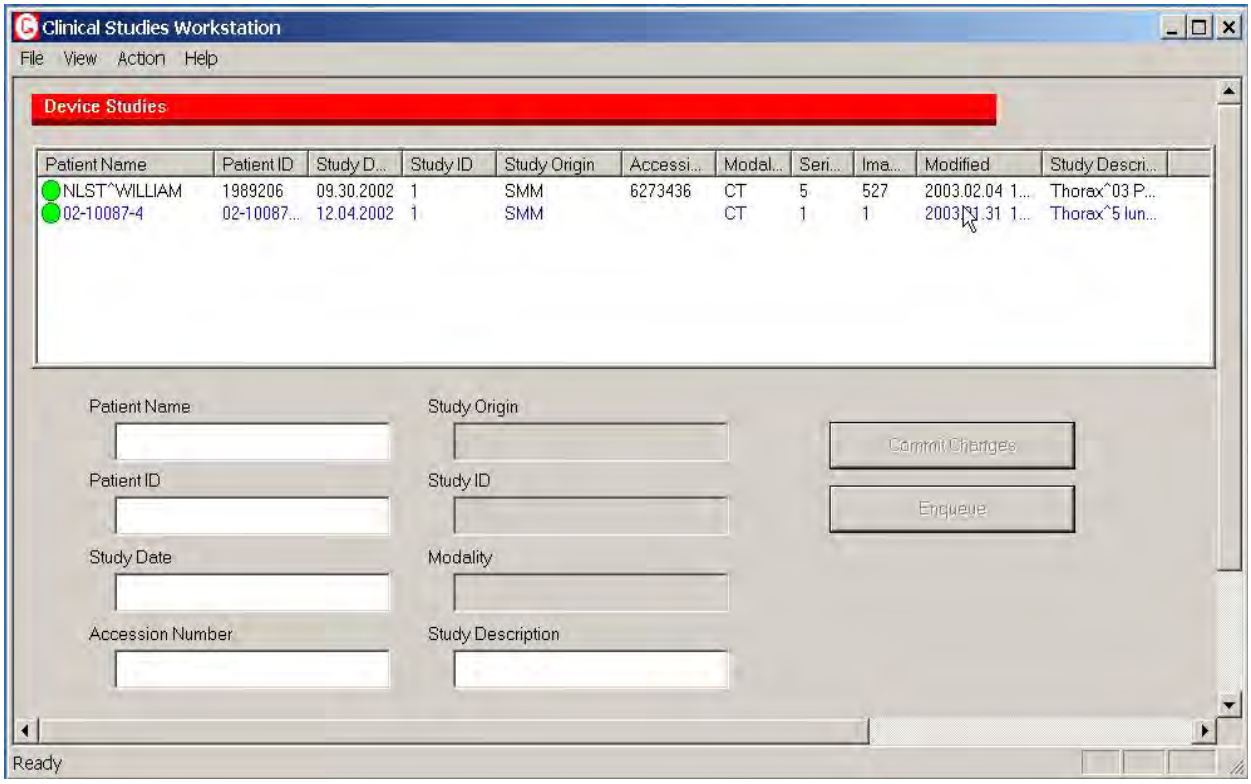


Figure 7.2: Study View of the CSW Application

8 QA Review Instructions

These instructions are included for sites with QA radiologists. Sites not participating in the QA process may skip this section. Furthermore, sites without QA responsibilities will not have the required logins to access the QA servers.

The QA process involves separate web-based systems that must be used by the QA reviewer. These are the NLST QA web system developed specifically by the QA center and a Philips Easyweb system. The latter is a commercial image viewing application supported by the Philips Corporation that is used as an "off the shelf" component.

The QA radiologist should follow these directions:

1. Log on to the CSW using a standard user account. You do not need administrator privileges to carry out this step.
2. Activate the Nortel client software and establish a VPN connection with Washington University. This will require typing in a second password to enable the VPN software.
3. Make a connection to the NLST QA web server by activating the desktop icon labeled *NLST QA Home Page*. Figure 8-1 below shows the initial window that will be shown by Internet Explorer.
4. Once the home page has been displayed, select the entry in the left tab labeled *QA Review*. This will cause the QA system to popup a window that requests the user to login. Please login to this window using the login/password supplied by the QACC. This login is necessary so that the QACC can supply you with the proper list of studies to review. Figure 8-2 below shows an example list of studies for review.
5. Make a connection to the Philips EasyWeb system using the desktop icon labeled *Easyweb Login*. This will require another login that will authenticate you as a user and allow you to see those studies that are scheduled for your review.
6. Each entry on the QA web server should have a corresponding study on the EasyWeb system. Select one entry on the QA web server. Note the accession number and select the corresponding study on the EasyWeb system.
7. After you have reviewed the study, select the appropriate Y/N response for each question. The questions are all supposed to be worded so that a 'Y' response means that the parameter or image quality is what you expect for a study that is "acceptable". The only exception is the single question that asks if a rescan is necessary. For an acceptable study, the answer would be 'N' (no rescan is required).
8. In the event that a rescan is required, please enter a comment indicating why the rescan is necessary. If the parameters and image quality are acceptable, no comment is required.
9. There may be cases where you want to make a comment. For example, there may be problems with the parameters (kVp is too high), but you would not want to ask the site to rescan the participant. Make your comment in the comment section; those comments will be relayed to Westat.

As of now, the only sites needing these instructions are those with QA radiologists. Nonetheless, the instructions are provided here for future reference.
QA review involves the use of two desktop windows, both launched with desktop icons labeled NLST QA Home Page **and** Easyweb Login**. Clicking on the** NLST QA Home Page **launches a multi-frame window whose left frame looks like:**

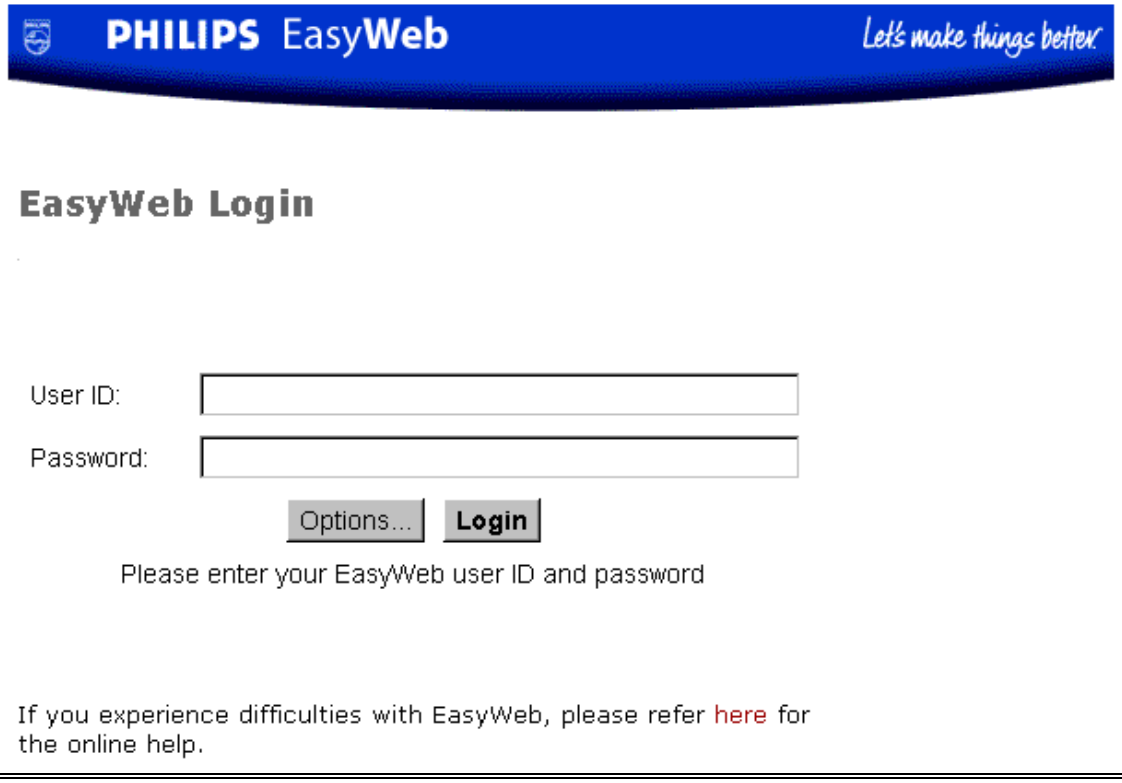
The radiologist logs on and then sees studies scheduled for his or her review. The radiologist then clicks on the Easyweb Login **icon to launch the image-review application called Easyweb. The following pages include instructions for launching and leaving Easyweb. These pages do not include the use of Easyweb. On-site training in the use of Easyweb will be provided by QACC personnel, and substantial on-line Help is available within the Easyweb application. The radiologist is given her/his own Easyweb logon name and password. The radiologist may change the password at anytime within the application.**

Launching Easyweb

[1] If you have not already established a VPN connection back to Washington University, do so now by clicking on the "Wash Univ VPN" icon on the desktop. Login and password as directed in the VPN Configuration Instructions.

[2] Click on the "Easyweb" or "Easyweb Login" on your desktop. You see the following screen:

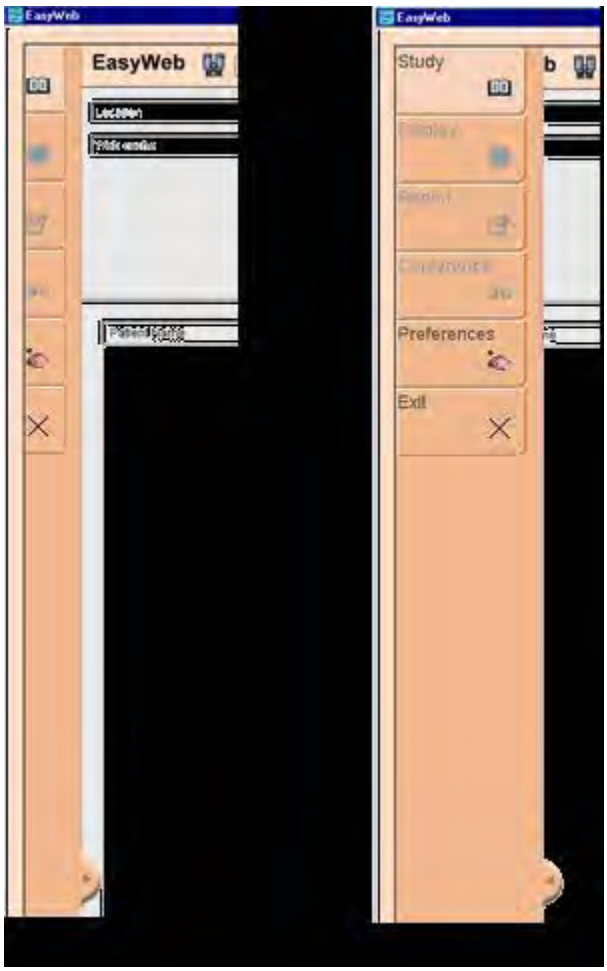
==========



[3] Enter the User ID: _____

[4] Enter the Password: _____

[5] Click the "Login" button. After a slight delay, you'll see the Easyweb base screen, the left-hand side of which appears below. In the left half of the figure below is a vertical array of buttons, not all of which are very intuitive. By clicking the semi-circular arrow tab near the bottom, the button array expands to look like the right side of the figure below. Clicking again returns to the cryptic state.



[6] To exit the Easyweb application, click on the "X" button of the vertical toolbar.

9. Calibration Documentation

{ separate documents }

10 Participant Anonymization Overview

The Clinical Studies Workstation is designed to operate under the control of sites participating in the NLST study. Imaging studies are sent directly from scanners (CT, CR) or from a PACS to the workstation. The workstation stores the images with no modification on the local disk system.

The user of the CSW is assumed to be a study coordinator or other staff member at a screening site. Those staff members are assumed to have access to the demographics of participants in the study. The workstation software presents the participant name to the user to help ensure that the proper studies are forwarded to the QACC.

When the CSW user transmits a study to the QACC, the workstation software automatically replaces the following DICOM attributes with empty strings:

```
0010 0010 Patient Name
0010 0030 Patient Date of Birth
0010 0040 Patient Sex
```

Before transmitting the images, the user specifies a new patient identifier that is the Westat Participant Identifier. This number is required by the QACC to identify the proper study for quality assurance.

The CSW software is configured to remove a number of private groups from the DICOM images during the transmission process. This is done because some vendors copy patient demographics into those private groups. Screening sites that identify further attributes to be removed should contact the QACC for instructions on updating the CSW configuration.

The CSW system uses a commercial VPN solution to connect the workstation to computer systems at the QACC behind a firewall. This VPN solution uses 128 bit encryption software on the workstation and a firewall system at the QACC.

The QACC will only have the Westat number to identify the images transmitted by the screening site. The QACC will have no mechanism to link these images to the human participant. It is expected that screening sites will have some mechanism to link the Westat identifier to the participant.

The steps described above are designed to satisfy IRB or HIPAA requirements for participant anonymization. If a screening site requires further anonymization steps or documentation, please contact the QACC data coordinator:

Ken Clark (clarkk@mir.wustl.edu)
Mallinckrodt Institute Of Radiology
510 South Kingshighway Blvd.
St. Louis, MO 63110

Phone: 314.362.6965 Fax: 314.362.6971

A: Password Management

Using the CSW and associated services requires a number of different accounts and passwords used by various applications. This appendix describes the accounts and passwords.

A.1: CSW Computer Login

The CSW computer is a Windows 2000 computer system with normal user accounts. The QACC ships the CSW computer with one account established for users. Each site is free to add more accounts as they see fit. If any new accounts are added, the user must be a "Power User" to take advantage of software that must modify registry settings.

A.2: Virtual Private Network Software

The CSW uses a Virtual Private Network solution from Nortel. A client application on the workstation requires a login and password that are assigned and managed by the QACC site. Each screening center is given one login and one password that should be shared by users at that site. Screening centers are not allowed to modify passwords.

A.3: QA Web System

The QA Web system is managed by the QACC and is used by radiologists for their quality assurance process. Some of the pages are password protected and require an account/password that are managed by the QACC. These login/password combinations are assigned by the QACC and can be only changed by the QACC.

A.4: Philips EasyWeb Image Display

The EasyWeb system is used during the QA process. Each QA radiologist is assigned a login/password by the QACC. Radiologists may modify the EasyWeb password using tools provided by that application.

Appendix 4-11 NLST/LSS Screening Exam Form Data Handling Guidelines

Item No.	Item Name	Personnel Required to Approve Edit	Additional Guidelines and Exceptions
	Administrative Section	SCC*	
A1	Number of Attempts	Tech	
A2	Adequate Scan Obtained	Tech	If A2 is blank but A3 is completed, SCC may mark A2 as "No."
A3	Reason for Inadequate or No Scan	Tech	
A4	Technical Parameters	Tech	If technical parameters are out of range, a comment is required. If no comment is recorded, the confirmation of the value must be obtained from the tech and a comment added that it has been confirmed.
A5	CT Reconstruction Algorithm/Filter (SCT) OR CXR System Used (XRY)	Tech	
A6	Comments	SCC	If comments are provided, SCC may check "Yes." If comments are blank, SCC may check "No" if other items in Part A are unremarkable. If there was more than one attempt or technical parameters are out of range, then the SCC should ask the tech whether a comment is required.
A7	Tech ID and Signature	Tech	If signature is present and legible, the SCC may enter the Tech ID.
B1	Diagnostic Quality of CT or CXR Image	Radiologist	
B2	Items that Affected Image Quality	Radiologist	
C1	Radiologic Abnormality Noted	SCC	If C1 is blank and abnormalities are recorded in C2, the SCC may check the box for "Yes" in C1. If no abnormalities are recorded in C2 and the SC has the dictated report which confirms that no abnormalities were noted on the exam, the SCC may check "No" in C1. If the SCC does not have the dictated report, or if the dictated report indicates that abnormalities were noted, then item C1 must be corrected by the radiologist.
C2	Abnormality Information	Radiologist	The SCC may not use information in the dictated report to record abnormality information in C2. If discrepancies are noted between the dictated report and C.2, the data must be verified by the radiologist.

Appendix 4-11 NLST/LSS Screening Exam Form Data Handling Guidelines

D1	Lung Screening Result	Radiologist	
D2	Other Significant Abnormalities to be Reported	Radiologist	If D2 is blank and a clinically significant abnormality is recorded in C2, the SCC may mark D2 as "Yes." If no clinically significant abnormalities are recorded, the SCC may mark D2 as "No."
D3	Comments	SCC	If comments are provided, SCC may check "Yes." If comments are blank, and D2 is marked "No," SCC may check "No" in D3. However, if D2 is marked "Yes" then the SCC must request a comment from the radiologist. If A2 is marked “No” and D1 is marked “A,” the SCC must request a comment from the radiologist regarding the overall quality of the image.
E1	Comparison Image	Radiologist	
E2	Abnormality Information	Radiologist	The SCC <u>may not</u> use information in the dictated report to record abnormality information in E2. If discrepancies are noted between the dictated report and E.2, the data must be verified by the radiologist.
E3a	Lung Screening Comparison Result	Radiologist	
E3b	Other Significant Abnormalities to be Reported	Radiologist	If E3b is blank and a clinically significant abnormality is recorded in E2, the SCC may mark E3b as "Yes." If no clinically significant abnormalities are recorded, the SCC may mark E3b as "No."
E4	Recommended Follow-up Procedures	Radiologist	If "Low Dose CT with NLST parameters" is not checked, but a time interval (months) and an area of focus is checked on the SCT form or an area of focus is checked on the XRY form, then the SCC may check the box for "Low Dose CT with NLST parameters." Also, if "Other" is not checked but follow-up is specified in the line provided, the SCC may check the box for "Other."
E5	Comments	SCC	If comments are provided, SCC may check "Yes." If comments are blank, and E3b is marked "No," SCC may check "No" in E5. However, if E3b is marked "Yes," then the SCC must request a comment from the radiologist.
E6	Radiologist ID, Date, and Signature	Radiologist	If signature is present and legible, the SCC may enter the Radiologist ID. Date and signature must be recorded by the radiologist.

5. CHEST X-RAY SCREENING EXAMINATION

5.1 Overview

Each participant in the chest x-ray arm will receive three annual chest x-ray screening examinations spaced one year apart. Screening Centers (SCs) are responsible for taking the x-ray, having the x-ray interpreted by a radiologist, and documenting the results of the x-ray. This chapter describes these procedures. It also provides the NLST/LSS requirements for examiner training and certification and quality assurance procedures for this examination.

5.2 Participant Preparation

The following steps in the process of participant preparation will be standardized across all SCs. The participant will be told that the examination is a screening examination for lung cancer, not a complete physical examination, and that s/he should consult his/her health care provider for evaluation of any symptoms and for routine medical care. In addition, the participant will be told that s/he will receive written documentation of the results of the screening examination within three weeks, and will be contacted by telephone in the event of a positive screen or a negative screen with clinically significant abnormalities. The participant will be told that if s/he has a positive screen and does not have a health care provider, the SC will offer a list from which s/he may choose a health care provider. The participant will be given a brief description of the screening examination.

5.3 Examination Procedures

A postero-anterior (PA) x-ray will be taken at a tube-to-receiver distance of six to ten feet. The participant will be asked to disrobe above the waist. Hospital gowns will be provided in accordance with standard procedures at the SC. The technologist will explain the procedure and position the participant. The participant will be instructed to inhale deeply and to hold his/her breath while the x-ray is taken. If a participant has a condition such as severe kyphosis that precludes a PA view of the lung, it is acceptable to do an antero-posterior (AP) view of the lung. The fact that an AP film was taken and the reason for it must be recorded in the Comments section of the Chest X-ray Screening Examination Form.

The technologist performing the x-ray will make the initial judgment about the quality of the x-ray before the participant leaves the SC. The quality should be such that the lung vessels are clearly visible and the mediastinal structures are sufficiently penetrated to allow for adequate visualization. The image should include both lung apices and costophrenic angles, adequate definition of the vertebral bodies, the left retrocardiac pulmonary vessels, lateral wall of descending aorta, and left hemidiaphragm. If the entire chest of a large participant cannot be viewed with one chest x-ray, then two chest x-rays may be taken in order to view the entire chest. In this case, the two views count as one attempt and two exposures. The fact that two chest x-rays were taken and the reason must be recorded in the Comments section of the Chest X-ray Screening Examination Form. If the x-ray is determined to be inadequate, it should be repeated. In the case of two views for large participants as described above, the repeat x-ray would count as a second attempt and two additional exposures, for a total of four exposures in two attempts. Reasons for inadequacy are described in Section 5.7.2. When a repeat x-ray is necessary, it should be taken during the same visit. However, no more than three x-ray attempts should be made in one visit. It may be necessary to arrange another screening visit to obtain an adequate x-ray. This visit should occur as close to the initial visit as possible. No more than two visits are allowed to obtain an x-ray.

X-rays examinations are then sent to the study radiologist for interpretation. If the radiologist determines that the x-ray examination is inadequate, the participant will be asked to return for a repeat examination. X-rays should be read by the study radiologist in a timely manner, so that the results can be reported to the participant within three weeks of the exam.

5.4 Equipment Specifications

The chest x-ray should be obtained using high-kVp equipment (100-150 kVp) at a tube-to-receiver distance of six to ten feet. Vendor machines that do not comply will be reviewed on a case by case basis. Film should be wide latitude type with a ten to one standard grid or higher. Computed radiography (CR), or digital radiography (DR) chest x-ray systems may be used in addition to screen-film systems. The image will be obtained at 0.1-20 mAs. The maximum of 20 mAs may be exceeded for very large patients to achieve acceptable image quality as long as the reason is documented in the Comments section (Item A.6) of the XRY Form. While there is no upper bound for the mAs for larger participants the lowest mAs with acceptable image quality should be used. The maximum exposure time is 40 msec.

Exposure indicators associated with digital systems (e.g., Fuji S#) will be recorded, however, no ranges will be set at this time. The Chest X-ray Protocol Specifications are listed in Appendix 5-1.

The image review should be done with soft copy images if available, otherwise hard copy images are acceptable. If a soft copy image is used, a maximum of one on one image display is to be used for viewing and measuring. Magnification is encouraged for measuring.

In addition to these parameters, all equipment used on the NLST/LSS must meet the guidelines of the American College of Radiology (ACR). See Appendix 4-2 for the current ACR Guidelines. These guidelines can also be found at www.acr.org.

The SC is required to send documentation of equipment specifications, including information on film type (e.g., symmetric or asymmetric film screen combination) to the CC. All documentation should also be maintained in the SC NLST/LSS files. The CC will forward all equipment specifications to the NCI for approval. The NCI will be responsible for reviewing equipment specifications from each SC and will make the final approval decision. Equipment specifications will also be reviewed by an NCI designated medical physicist who will make manufacturer specific recommendations for the parameters to be used on each machine. This should be done before screening begins and whenever equipment is replaced during the course of the study.

5.5 Examiner Qualifications, Training, and Certification

The chest x-ray examination requires three radiologic personnel: the radiologic technologist, the medical physicist, and the radiologist. The minimum qualifications for these individuals and the NLST/LSS training protocol are discussed in this section.

5.5.1 Minimum Qualifications for Examiners

Technologists will be American Registry of Radiologic Technologists (ARRT) certified radiologic technologists. The radiologists (interpreters and QA examiners) will be American Board of Radiology (ABR) certified or board-eligible (chest) and must have a valid active medical license in the state in which screening is performed. Radiologists at Federal sites must have an unrestricted active

license to practice medicine in their clinical specialty, issued by one of the states, the District of Columbia, or a possession of the United States. Medical physicists must be certified by the American Board of Radiology in the subfield of Diagnostic Radiological Physics or the subfield of Radiological Physics. In addition to being appropriately certified, technologists, radiologists, and physicists must meet additional guidelines outlined by the American College of Radiology (ACR). See Appendix 4-2 or www.acr.org for current ACR Guidelines.

The SC must report the qualifications of each examiner by submitting a completed Record of Experience, Credentials, and Training (ECT, Appendix 11-5) to the CC. In lieu of submitting copies of diplomas and certificates, the SC may attach a letter from the department chairman stating that the technologist is an ARRT certified radiologic technologist, the physicist is ABR certified or board-eligible, or that the radiologist is ABR certified or board-eligible and holds a valid active medical license, and that additional ACR guidelines have been met. For any technologist who is not ARRT certified or any physicist or radiologist who is not ABR certified, or for any technologist, physicist, or radiologist who does not meet the remaining ACR guidelines, the SC Principal Investigator must document and certify adequate training and experience in a letter to be submitted with a completed ECT to the CC. The CC will review all ECTs and, if the qualifications meet the CC criteria, the CC will recommend approval to the NCI. If the qualifications do not match the requirements, the CC will request an exception approval from the NCI on a case-by-case basis. **The ECT must be approved by the NCI prior to the initiation of screening activities.**

5.5.2 Training Protocol

One radiologist from each SC will attend a central training session. The radiologists' training will utilize a training CD containing a variety of images designed to help standardize the interpretation of images across NLST/LSS sites. The radiologist will use the training CD to review the same interpretation guidelines with the remaining radiologists at the SC. Additionally, the radiologist will use the CD to train technologists at his/her SC on the correct procedures for conducting the screening exams for the NLST/LSS. The radiologists also will be trained on the screening exam forms. The SC Coordinator will be responsible for training the technologist on the use of the study forms and SC administrative procedures.

5.5.3 Examiner Certification

No additional qualifications for the technologist, physicist, or radiologist are necessary for this examination. Certification through ARRT (for technologists) and ABR (for physicists and radiologists), plus an active valid medical license (for radiologists) and adherence to additional ACR guidelines (Appendix 4-2) will serve as the qualification for these examiners.

5.5.4 Updates to Qualifications for Radiologic Personnel

On an annual basis, SCs will be asked to submit updated qualifications for all radiologic personnel who continue to work on the NLST/LSS. For technologists, if an ARRT certification was submitted in the previous year, an updated and valid ARRT certification should be submitted. If a letter from the chair of the Radiology Department of the SC was sent to certify that the technologist was ARRT certified, then an updated letter, signed by the chair of the Radiology Department should be submitted. If updated credentials or a letter of certification is not submitted for annual review, the technologist will be unable to continue working on the NLST/LSS. Once screening operations have officially ended, as described in Section 3.4.3, updates to qualifications for radiologic personnel are no longer required.

5.6 Documentation of the Examination

Information documenting that the chest x-ray was taken and the interpretation was made by the radiologist will be recorded on the Chest X-ray Screening Examination Form (XRY, Appendix 5-2). In addition to the examination result, the NLST/LSS images will be stored.

5.6.1 Chest X-ray Screening Examination Form (XRY)

The XRY form will be used to document the results and findings of the examination. Every screening visit must be documented, regardless of outcome. The form provides documentation that the examination was completed, whether the results were normal or abnormal, and a description of abnormal findings. The SC Coordinator or staff member should complete the Administrative Section on the first page of the form and the radiologic technologist should complete Part A. If adequate images are

obtained, Parts B through E of the form should be completed by the radiologist. If the technologist does not obtain adequate images, Parts B and C should be left blank and the radiologist should complete Items D.1, D.3, and E.6. The radiologist should not complete a comparison review (Item E.3) if the image read in isolation is inadequate. CR or DR chest x-ray systems (including Thoravision) may be used in addition to conventional systems. The type of chest x-ray system used is noted on the form. For CR and DR systems, the x-ray machines (or x-ray examination rooms) at each SC will be assigned a two-digit number that will be recorded on the XRY form for every examination. This will link the recorded technical parameters to the machine used to obtain the image, thus enabling verification that proper technical parameters were used for the examination. SCs must maintain a link between the machine number and the manufacturer/model information. If documentation of the exam, including exam images, is lost and cannot be recreated, Parts A and B and Items D.3 and E.6 must be completed. A Protocol and HIPAA Violation Form (PHVF) also must be completed. Specifications for Completion of the XRY Form are provided in Appendix 5-3. It is the responsibility of the SC Coordinator to train the technologists and radiologists in the use of the form.

After the form has been completed, the SC Coordinator should review it to ensure that it has been filled out completely, including the items in the Administrative Section. The XRY form should be edited as necessary. Any data retrieval involving the examiner should be performed as expeditiously as possible since results reports must be sent to the participant and to his/her health care provider within three weeks of the screening visit. The XRY form should be entered into IDEAS and filed in the participant's study file.

5.6.2 Storage of Lung Screening Study Chest X-ray Images

The x-ray images should be labeled with the participant's name and PID number. The SC is responsible for storing the images for each of the participant's chest x-ray screening examinations. Inadequate images should be retained at the SC until adequate images are obtained. Upon collection of an adequate image, inadequate images may be discarded. Chest x-ray images for the NLST/LSS should be stored in a manner that is consistent with the confidentiality agreement for the study. It is recommended that a participant's images not be stored with the participant's medical record or with other images that are not related to the NLST/LSS. If an SC wishes to store NLST/LSS data in the regular medical record, it must submit to the NCI (through the CC) documentation of the methods that will be used to maintain confidentiality of the data.

The chest x-ray images are the photo documentation of the exam. It is acceptable for SCs to utilize digital storage of images (as in CR and DR systems), but the capability to retrieve the images at any time must be maintained. If digital storage is used, a backup digital copy of the images should also be maintained. SC methods for utilizing digital storage must also comply with participant confidentiality standards. If the SC fails to maintain the original screening exam image (due to loss, corruption, or irreversible modification such that the image can no longer be read according to study protocol) and no backup copy exists, this is considered a protocol violation and a PHVF must be completed.

5.7 Interpretation of Findings

Each examination will be reviewed by a board certified or board-eligible chest radiologist who meets current ACR guidelines and holds a valid active medical license and the results of the review, including any abnormalities, will be recorded. The interpretation of findings will be recorded in two distinct steps on the XRY form. The Chest X-ray Interpretation Results Section (Part D) should reflect the current chest x-ray examination findings only. The participant's prior medical history, prior radiologic examinations, or prior NLST/LSS screens should not be considered when assigning the examination result recorded in Part D of the XRY form. The Chest X-ray Comparison Results Section (Part E) will reflect the comparison of the current chest x-ray examination with historical images for that participant, including NLST/LSS screens, any available non-NLST/LSS images, as well as any accompanying radiologic reports. At T_1 and T_2, the current examination must be compared to prior NLST/LSS screens, as well as any other available studies, as described below. The result of the comparison read recorded in Item E.3a is considered to be the final result of the screening examination, and this is the result that will be communicated to both the participant and the participant's physician.

To complete Part E, T_1 screening exams must be compared with T_0 screening exams. T_2 screening exams must be compared with T_0 and T_1 exams. However, if the screening examinations from all three study years are negative, then the T_2 screening examination may be compared with either the T_0 or T_1 screen, or both screens, at the radiologist's discretion. If the T_0 and T_1 exams are lost or are otherwise unavailable, the radiologist should mark "No Image Available" in Item E.1 and state the reason in the Comments section, Item E.5. In addition, a Protocol and HIPAA Violation Form should be completed. The type of protocol violation should be marked as "Other" and described in the space provided. State that the comparison read was not performed and provide the reason. For example, "T_1

comparison read not performed, T_0 exam was lost." The date the protocol violation occurred is the date that the current screening exam was read. If either the T_0 or T_1 screening exam was not completed, then the T_2 exam should be compared to the existing previous exam and no PHVF is required.

In the event that a screening exam is inadequate and a repeat screen is performed, the inadequate screen may be used as the comparison image for the repeat screen at the radiologist's discretion. For example, if a T_1 screen is inadequate and a repeat T_1 screen is performed, then both the T_0 and the inadequate T_1 screens may be used as comparison images for the repeat T_1 screen. An inadequate screen may also be used for comparison in later study years. In this instance, the use of the inadequate screen should be noted in the Comments section of the XRY form.

The following definitions of normal, abnormal, and inadequate findings are provided. These definitions will be used by the radiologist in recording his/her findings on the XRY form.

5.7.1 Classification and Definition of Abnormal Examination Results

Definitions of lung screening results are given below:

- **Positive Screen – Abnormalities suspicious for lung cancer:**

  The following abnormality is always considered a positive screen:

  - Non-calcified visible nodule/mass

  Other abnormalities, or constellations of abnormalities, may be suggestive of lung cancer, but there is no absolute rule for coding other findings as suspicious for lung cancer. In these instances, the classification of a screening exam result as positive is left up to the radiologist.

  If, at the T_1 or T_2 study year, the current screen is positive and the abnormality identified appears not to have changed when compared to previous images at the comparison reading (Part E), the radiologist should record the result in the Chest X-ray Comparison Result section (Item E.3a) as B – "Abnormalities suspicious for lung cancer, no significant change."

  When previous images from two successive study years have not changed and the third screen is positive and appears unchanged from the previous images, the radiologist may code that result as D – "Minor abnormalities not suspicious for lung cancer" at his/her discretion, rather than coding the image as suspicious for lung

cancer. Additionally, the radiologist should specify in the Comments section (Item E.5) why the result was coded as D.

- **Negative Screen – Clinically significant abnormalities not suspicious for lung cancer:**

  The review of the film reveals that an abnormality is present and requires further evaluation, but is not suggestive of lung malignancy. It is up to the radiologist to determine whether an abnormality is clinically significant. If after baseline screening the clinically significant abnormality remains stable and unchanged on subsequent screening examinations, the abnormality may be coded as D – "Minor abnormalities not suspicious for lung cancer" at the discretion of the radiologist, rather than coding the image as a clinically significant abnormality. Additionally, the radiologist should specify in the Comments section (Item E.5) why the result was coded as a D.

- **Negative Screen – Minor abnormalities not suspicious for lung cancer:**

  The review of the film reveals a minor abnormality that is not suspicious for lung cancer. It is up to the radiologist to determine whether an abnormality is minor.

5.7.2 Criteria for Determination of a Negative or an Inadequate Chest X-ray

- **Negative Screen – No significant abnormalities:**

  The review of the film reveals no significant abnormalities.

- **Inadequate:**

  An image should display adequate definition of vertebral bodies, the left retrocardiac pulmonary vessels, the lateral wall of the descending aorta, and the left hemidiaphragm. The image quality should be such that the lung vessels are clearly visible and the mediastinal structures are sufficiently penetrated to allow for adequate visualization. The image should include both lung apices and costophrenic angles, adequate definition of the vertebral bodies, the left retrocardiac pulmonary vessels, lateral wall of descending aorta, and left hemidiaphragm. Reasons for inadequacy may include, but are not limited to:

  - Participant refusal;
  - Equipment malfunction;
  - Poor film quality, including:
    - Motion or processing artifact;

- Inadequate inspiration;
- Excessive rotation, and
- Over or under penetration.

If the image is considered inadequate, but based on what is visible on the image, there is an overt suspicion of lung cancer, the result of the screening exam should be recorded as positive.

5.8 Reporting Results to Participants and Health Care Providers

The SC should report results of a chest x-ray screening examination in writing to the participant and to the participant's health care provider **within three weeks of the screening visit**. Results should be sent with a cover letter on SC letterhead. The SC may choose to incorporate results into the cover letter, may attach a copy of the radiologist's dictated report, or may produce a customized report of results. The XRY form should not be sent to the participant to report the results of the screening exam. The combination of documents sent must reflect the results of the examination. In addition to written notification, positive screens and negative screens with clinically significant abnormalities will be reported to participants by telephone. If the participant is unreachable by telephone, the results will be sent by certified mail with return receipt requested. Positive screens and negative screens with clinically significant abnormalities will be reported to the health care provider either by telephone, fax, or certified mail. If the fax method is chosen, it is recommended that the health care provider's office is telephoned and advised of the fax transmittal in advance. Other negative screens will be reported to the participant and his/her health care provider according to standard radiologic practice at the SC.

The guidelines provided above for reporting results to participants and health care providers are the minimum acceptable procedures, as set by the NCI. Individual institutional policies may require some SCs to take additional measures for reporting results. See Chapter 6 for additional information regarding reporting results of screening examinations.

Participants with a result of "Positive Screen" will be referred to their health care provider for further evaluation. If a participant does not have a health care provider, the SC will offer a list from which the participant may choose a health care provider to receive the results. In all cases where there is a positive chest x-ray screen, referral will be recommended as outlined in Section 5.8.1. The SC will continue to monitor and follow up with all participants who have had a positive screening result.

5.8.1 Diagnostic Follow-up Recommendations

Participants with positive chest x-ray screens will be referred to their health care providers. They and their health care providers will also be provided with general recommendations that the radiologist feels are appropriate for the findings from the screening examination. The status of the participant referral (e.g., saw health care provider; has not seen health care provider but appointment has been scheduled; plans to schedule appointment; has no plans for follow-up) should be monitored by the SC. If requested, the SC Coordinator will offer the participant a list from which s/he may choose a specialist.

The NCI does not provide recommendations for diagnostic follow-up of positive screens to the participant or to his/her health care provider. The recommended diagnostic options listed on the XRY form reflect typical options for follow-up in accordance with standard practices at the SC. In all communications it must be clear that the recommendations do not arise from and are not endorsed by the NCI. The SC should refer inquiries to providers that are considered to be experts in the field and provide the 1-800-4-CANCER hotline number as an additional source of information. It is expected that diagnostic evaluation will adhere to current medical standards of practice.

5.8.2 Lung Cancer Diagnosis

The final diagnosis of lung cancer will be made by histopathology or cytopathology, or in rare cases, by clinical examination only. Pathology reports that support the cancer diagnosis will be obtained for all participants. The cancer will be coded according to ICD-O-3 codes by a certified tumor registrar (CTR) at the SC. The diagnosis will be documented by the SC on the DE form (Appendix 7-2) and submitted to the CC.

5.8.3 Treatment Recommendations for Individuals Diagnosed with Lung Cancer

The NLST/LSS does not make specific treatment recommendations for individuals diagnosed with lung cancer. Participation in the NLST/LSS does not preclude a participant from involvement in any treatment protocol.

5.9 Examination Standardization and Quality Control

NLST/LSS has implemented a three-pronged approach to quality assurance and control to ensure standardization throughout the screening process. The quality assurance (QA) measures include equipment and personnel quality control (QC), image QA, and image interpretation QA. The NLST/LSS Screening QA Working Group developed and implemented the QA protocol. The Mallinckrodt Institute of Radiology at Washington University, the Quality Assurance Coordinating Center (QACC), is overseeing the administration of the QA protocol with support from the CC.

5.9.1 Quality Control of Equipment

Quality control (QC) of the equipment will be assured by the individual institution according to the guidelines for equipment quality control developed by the NLST/LSS Screening QA Working Group and the NLST Medical Physicist Working Group. The equipment quality control guidelines are based upon the guidelines outlined by the American College of Radiology (ACR) for ongoing equipment QC measures. Each SC must designate a qualified medical physicist to oversee the equipment QC and to ensure that ACR guidelines are met. The medical physicist will be required to complete and submit an ECT (Appendix 11-5) to the CC. It will be the primary responsibility of the medical physicist at each site to implement and document the equipment QC protocol. The SC should maintain records of equipment maintenance and QC activities that are readily available for auditing during site visits.

The quality control guidelines consist of the Chest X-ray Protocol Specifications listed in Appendix 5-1, the Chest X-ray Quality Assurance Information listed in Appendix 5-4, and the forms found in Appendices 5-5 through 5-7, which will be completed by the medical physicist at each SC and returned to the Screening QA Working Group to provide documentation of adherence to the chest x-ray protocol specifications and equipment testing requirements. Documentation of equipment characteristics

is provided once for each piece of equipment and is updated as necessary. Attestation to performance testing and documentation of chest x-ray exposure measurements are provided annually. Once screening operations have officially ended, as described in Section 3.4.3, completion of equipment QC tests and forms is no longer required.

5.9.2 Quality Control of Technologists

The CC will maintain a complete list of the radiologic technologists working at all SCs. The radiologic technologists are required to complete and submit an ECT (Appendix 11-5) to the CC. For each radiologic technologist, the CC will monitor the number of and reasons for inadequate screening examinations. The CC will consider the final result as inadequate if the screening examination cannot be repeated to obtain an adequate examination.

5.9.3 Image Quality Assurance

The image quality QA process is the same for the soft copy chest x-ray and spiral CT images. These processes are described in section 4.9.3, Image Quality Assurance, and subsections. Image quality QA processes for hard copy screen films are described below, when they differ from the image quality QA process described in Chapter 4.

5.9.3.1 Image Quality Assurance of Screen Films

Chest x-ray screen films will undergo a comparable quality assurance process as the digital chest x-ray images and the spiral CT image sets. Since screen films can not be distributed to the QA radiologists for review, the QA radiologists will visit each SC that utilizes screen films three or four times per year, depending on volume. For each SC, one visit will coincide with the SC's annual NCI/CC site visit, and the remaining visits will occur every three to four months solely for image QA purposes. The QA radiologist will be responsible for submitting a brief site visit report to NCI and the CC summarizing the findings of each visit. When attending annual NCI/CC site visits, the QA radiologist will present the QA findings and any recommendations during the NCI exit interview.

Before each QA visit, the CC will send the SC a list of the hard copy images that have been randomly selected for QA review. This list should be given to the QA radiologist when s/he performs the QA review. The SC will acquire the selected images and ensure that they have been adequately de-identified before the arrival of the QA radiologist. The SC should ensure that the lead radiologist is available for some portion of the QA visit to meet with the QA radiologist.

At each visit, the QA radiologist should observe spiral CT and chest x-ray screening exams, and ensure that the technical parameter settings are appropriate. The QA radiologist will then be brought to a work station to view screen films. A Chest X-ray Image QA Form (XQA) (Appendix 5-8) should be completed for each image reviewed. Any technical parameter settings used to obtain the image that are not printed on the image are available on the listing of images selected for QA that was sent to the SC by the QACC. When the QA review is completed, the QA radiologist should send the XQA forms to the CC for data entry at the following address:

Ellen Martinusen
9274 Gaither Road, GA 26A
Gaithersburg, MD 20877
tel: 301/963-5409

In the event that a QA radiologist disagrees with the image quality as documented by the initial reading by the radiologist at the SC, whether adequate or inadequate, the QA radiologist should document such differences of opinion in the site visit report. These images should be reviewed by a third radiologist for adjudication. Since original hard copy images can not be sent to another QA radiologist, the third radiologist will be internal to the SC. This tie-breaker review may occur at the time of the QA visit, or after the visit is complete. The resolution to the discrepant readings should be submitted to NCI in writing by the lead radiologist or PI. The letter should note the result of the third review, describe whether the participant will be re-screened, and provide reasons for not re-screening if applicable. If the third review occurs during the QA visit, and if that review resolves all discrepancies, then documentation in the QA radiologist's site visit report is adequate.

When the image QA process results in a change to data previously submitted on the XRY form (from "adequate" exam to "inadequate" exam or vice versa), the CC will generate a CC Edit Form. The CC Edit Form will be sent to the SC requesting the change to the XRY form.

Appendices for Chapter 5

NATIONAL LUNG SCREENING TRIAL / LUNG SCREENING STUDY (NLST/LSS)

EQUIPMENT QUALITY CONTROL

CHEST X-RAY PROTOCOL SPECIFICATIONS

NLST CXR Specifications:

1. The chest x-ray kVp range shall be 100 – 150.

2. The Source to Image Distance (SID) may range from 6 to 10 feet. A vendor machine with a SID outside this range shall be reviewed on a case by case basis.

3. The maximum exposure time shall be 40 msec, consistent with ACR guidelines.

4. Anti scatter grids shall have a minimum grid ratio of 10:1.

5. The mAs may range from 0.1 to 20. The maximum of 20 may be exceeded for very large patients to achieve acceptable image quality. While there is no upper bound for the mAs for larger participants, the lowest mAs with acceptable image quality should be used.

6. The specification of maximum reference dose(s) will be reviewed after all sites have completed consistent dose measurements and/or estimates.

7. Exposure indicators associated with digital systems (e.g., Fuji S#) shall be recorded. However, no ranges will be set at this time.

8. No specification for chest film optical density or measurement will be set at this time. Sites are expected to provide films of adequate density and contrast, and are subject to reviewer feedback if density is deemed inadequate.

Appendix 5-2 Chest X-Ray Screening Examination Form (XRY)

National Lung Screening Trial / Lung Screening Study (NLST/LSS)

CHEST X-RAY SCREENING EXAMINATION FORM (XRY)

Administrative Section

Screening Center ID: |___|___|

Date of Examination: |___|___| / |___|___| / |_2_|_0_|___|___|
Month Day Year

Study Year (T_0 - T_2): T |___|

Visit Number: ☐ One ☐ Two

Reason for repeat visit _____

Interval Follow Up Information:

Has the participant had any imaging studies since the previous screening exam that may be useful for the radiologist to review if needed? ☐ Yes ☐ No ☐ N/A

If YES, dates obtained (Month /Year): |___|___| / |__|__|___|___|
|___|___| / |__|__|___|___|

Initials Complete: _____

Initials QC: _____

XRY

Participant ID Label

PART A. CHEST X-RAY EXAMINATION FINDINGS (COMPLETED BY TECHNOLOGIST)

1. Number of Attempts:

☐ None (GO TO A.3)
☐ One
☐ Two
☐ Three

2. Adequate Image Obtained:

☐ No
☐ Yes (GO TO A.4)

3. Reason for Inadequate or No Image:

(MARK ALL THAT APPLY)

☐ Participant refusal
☐ Equipment malfunction
☐ Poor film quality
☐ Other (SPECIFY)
_____

4. Technical Parameters:

A. |___|___|___| kVp

B. |___|___|.|___| mAs

C. |___|___|___| mA

D. |___|___| Time (msec)

E. |___|___|___|___|
Exposure Value

5. CXR system used:

☐ Screen-Film (SF)
|___|___| Machine Number

☐ Computed Radiography (CR)
|___|___| Machine Number

☐ Direct Digital Radiography (DR)
|___|___| Machine Number

6. Comments: ☐ No ☐ Yes
_____ ☐ Continued

7. Tech ID: |___|___|___|___| **Signature:** _____

Appendix 5-2 Chest X-Ray Screening Examination Form (XRY)

PARTS B, C, D AND E COMPLETED BY RADIOLOGIST

PART B. CHEST X-RAY OVERALL DIAGNOSTIC QUALITY (COMPLETED BY RADIOLOGIST)

1. Indicate the overall diagnostic quality of CXR:

- ☐ A. Diagnostic CXR (GO TO C.1)
- ☐ B. Limited CXR, but interpretable (COMPLETE B.2 AND GO TO C.1)
- ☐ C. Non-diagnostic CXR, reschedule CXR (COMPLETE B.2 AND GO TO D.1)
- ☐ D. No image available (GO TO D.3, COMMENTS)

2. Which of the following affected the quality of the limited or non-diagnostic CXR? (MARK ALL THAT APPLY)

- ☐ Low lung volumes
- ☐ Lungs incompletely imaged
- ☐ Poor positioning
- ☐ Motion degradation
- ☐ Incorrect exposure or other technical parameter
- ☐ Artifacts obscure anatomy
- ☐ Incorrect processing algorithm
- ☐ High image noise
- ☐ Other (SPECIFY) _____

PART C. CHEST X-RAY EXAMINATION FINDINGS (COMPLETED BY RADIOLOGIST)

1. Radiologic Abnormality Noted:

- ☐ No (GO TO D.1 AND MARK RESULT "E")
- ☐ Yes (COMPLETE C.2. RECORD INFORMATION FOR EACH ABNORMALITY)

2. Record Information for Each Abnormality:

Abn #	Description of Abnormality		Complete for Code 51 Only: Location of Epicenter	Nodule /mass dimensions: Longest Diameter (mm)	Nodule /mass dimensions: Longest Perpendicular Diameter (mm)	Nodule/Mass Margins
	51 = Non-calcified visible nodule/mass (MUST MARK "A" IN D.1) 53 = Benign lung nodule(s) (benign calcification) 54 = Atelectasis, segmental or greater 55 = Pleural thickening or effusion 56 = Non-calcified hilar/mediastinal adenopathy/mass ≥ 10 mm short axis 57 = Chest wall abnormality (e.g. bone destruction, metastasis) 58 = Consolidation 59 = Reticular/reticulonodular opacities, honeycombing, fibrosis, scar 62 = 6 or more nodules, not suspicious for cancer (opacities ≥ 4mm) (ANY SUSPICIOUS NODULES MUST BE CODED AS 51) 63 = Emphysema 64 = Significant cardiovascular abnormality (SPECIFY) 70 = Other significant abnormality above the diaphragm (SPECIFY) 71 = Other significant abnormality at/below the diaphragm (SPECIFY) 72 = Other minor abnormality noted (SPECIFY IF DESIRED)		1 = Rt upper zone 2 = Rt middle zone 3 = Rt lower zone 4 = Lt upper zone 5 = Lt middle zone 6 = Lt lower zone 8 = Other, SPECIFY (in Comments section)	999 - Unable to determine	999 - Unable to determine	1 = Spiculated (Stellate) 2 = Smooth 3 = Poorly defined 9 = Unable to determine
	CHECK BOX IF IDENTIFIED AFTER COMPARISON WITH HISTORICAL IMAGES:					
1	|___|___|	☐	|___|	|___|___|___|	|___|___|___|	|___|
2	|___|___|	☐	|___|	|___|___|___|	|___|___|___|	|___|
3	|___|___|	☐	|___|	|___|___|___|	|___|___|___|	|___|
4	|___|___|	☐	|___|	|___|___|___|	|___|___|___|	|___|
5	|___|___|	☐	|___|	|___|___|___|	|___|___|___|	|___|
6	|___|___|	☐	|___|	|___|___|___|	|___|___|___|	|___|

Appendix 5-2 Chest X-Ray Screening Examination Form (XRY)

PART D. CHEST X-RAY INTERPRETATION RESULTS (COMPLETED BY RADIOLOGIST)

1. Lung Screening Result:

☐ A. **Positive Screen – Abnormalities suspicious for lung cancer**
☐ C. **Negative Screen** – Clinically significant abnormalities not suspicious for lung cancer (GO TO D.3)
☐ D. **Negative Screen** – Minor abnormalities not suspicious for lung cancer (GO TO D.3)
☐ E. **Negative Screen** – No significant abnormalities (GO TO D.3)
☐ F. **Inadequate** (COMPLETE PART D.3 AND GO TO E.6)

2. Other Significant Abnormalities (in addition to lung screening results) that need to be reported:

☐ No ☐ Yes (SPECIFY IN D.3)

3. Comments: ☐ No ☐ Yes

____

____ ☐ Continued

PART E. CHEST X-RAY COMPARISON RESULTS – COMPLETE FOR ALL LUNG SCREENING RESULTS (COMPLETED BY RADIOLOGIST)

1. Comparison Image: (MARK ALL THAT APPLY)

☐ No image available (GO TO E.4)
☐ T_0
☐ T_1
☐ T_2 Inadequate scan
☐ Previous scan not completed as part of NLST (RECORD SCAN TYPE AND DATES FOR UP TO 3 PREVIOUS SCANS)

Scan Types
1 = CT
2 = CXR
3 = MRI

Previous Scan Type(s):	**Date(s) of Previous Scan(s) (MONTH/DAY/YEAR)**
|___|	|___|___| / |___|___| / |___|___|___|___|
|___|	|___|___| / |___|___| / |___|___|___|___|
|___|	|___|___| / |___|___| / |___|___|___|___|

2. Enter abnormality number and code for <u>all</u> Code 51 abnormalities AND other significant abnormalities seen on this screening exam. (IF NONE, GO TO E.3)

Abn. # (FROM PART C.2.)	Abn.Code (FROM PART C.2)	Was Abnormality Pre-existing?	Earliest Date Visible (COMPLETE ONLY FOR PRE-EXISTING ABNORMALITIES)	COMPLETE FOR CODE 51 ABNORMALITIES ONLY		COMPLETE FOR OTHER SIGNIFICANT ABNORMALITIES ONLY
		1 = No 2 = Yes 9 = Unable to determine	(Month/Day/Year) 99/99/9999 = Unable to determine	Interval Growth of Abnormality? 1 = No 2 = Yes 9 = Unable to determine	Interval suspicious change in attenuation? 1 = No 2 = Yes 9 = Unable to determine	Interval change warrants further investigation? 1 = No 2 = Yes 9 = Unable to determine
|___|	|___|___|	|___|	|___|___| / |___|___| / |___|___|___|___|	|___|	|___|	|___|
|___|	|___|___|	|___|	|___|___| / |___|___| / |___|___|___|___|	|___|	|___|	|___|
|___|	|___|___|	|___|	|___|___| / |___|___| / |___|___|___|___|	|___|	|___|	|___|
|___|	|___|___|	|___|	|___|___| / |___|___| / |___|___|___|___|	|___|	|___|	|___|
|___|	|___|___|	|___|	|___|___| / |___|___| / |___|___|___|___|	|___|	|___|	|___|
|___|	|___|___|	|___|	|___|___| / |___|___| / |___|___|___|___|	|___|	|___|	|___|

Appendix 5-2 Chest X-Ray Screening Examination Form (XRY)

3a. Lung Screening Comparison Result:

- ☐ A. **Positive Screen** – Abnormalities suspicious for lung cancer
- ☐ B. **Positive Screen** – Abnormalities suspicious for lung cancer, no significant change
- ☐ C. **Negative Screen** – Clinically significant abnormalities not suspicious for lung cancer (GO TO E.4)
- ☐ D. **Negative Screen** – Minor abnormalities not suspicious for lung cancer (GO TO E.4)
- ☐ E. **Negative Screen** – No significant abnormalities (GO TO E.4)

3b. Other Significant Abnormalities (in addition to lung screening results) that need to be reported:

☐ No ☐ Yes (SPECIFY IN E.5)

4. Which of the following diagnostic procedures for screening examination results should the screening result letter include?

(MARK ALL THAT APPLY)

- ☐ No diagnostic intervention necessary
- ☐ Comparison with historical images (NOTE: CHECK OTHER PROCEDURES IN CASE HISTORICAL IMAGES UNAVAILABLE)
- ☐ Chest X-ray, with or without additional views to confirm abnormality and location
- ☐ Chest fluoroscopy to confirm abnormality and location
- ☐ Low kVp chest X-ray to determine abnormality calcification
- ☐ Chest X-ray in 3 months
- ☐ Low dose CT with NLST parameters:
  (MARK AN AREA OF FOCUS)
  - ☐ Limited
  - ☐ Entire chest
- ☐ Diagnostic CT
- ☐ FDG-PET
- ☐ Tech 99m depreotide scintigraphy
- ☐ Biopsy (percutaneous, thoracoscopic, open, etc.)
- ☐ Other (SPECIFY)_____

5. Comments: ☐ No ☐ Yes

_____

_____

_____

☐ Continued

6. Radiologist ID: |___|___|___|___|

Date: |___|___| / |___|___| / |2|0|___|___|
MO DAY YEAR

_____
Signature

National Lung Screening Trial (NLST)

Specifications for Completion of the Chest X-ray Screening Examination Form (XRY)

This form is to be completed by the SC Coordinator or staff member, and the examiners (technologist and radiologist). The SC Coordinator or staff member will complete the Administrative Section, the technologist will complete Part A, and the radiologist will complete Parts B through E. This form should be completed in black or blue ink. An XRY form must be completed for every screening visit by a participant, regardless of the outcome. If documentation of the exam, including exam images, is lost and cannot be recreated, Parts A and B and Items D.3 and E.6 must be completed.

Please refer to the NLST/LSS Screening Exam Data Handling Guidelines in Appendix 4-11 for details about making changes to data on the screening exam forms. Items pertaining to technical parameters must be changed by the technologist who performed the screening exam and items pertaining to exam results must be changed by the radiologist who read the screening exam. The remaining items may be changed by the SC Coordinator or other designated staff member. All data changes must be initialed and dated in pen on the screening exam form by the staff member making the change. Cross out erroneous data with one line, do not black out or use correction fluid to conceal the original data.

Specifications for completing each item of the form are given below:

Administrative Section:

Participant ID Label: Affix a PID label in the space provided in the upper right-hand corner of the form.

Screening Center ID: Record the two-digit SC ID number.

Date of Examination: Record the date of the examination. The month, day, and the last two digits of the year should be recorded (e.g., 02/07/2002). The date of examination should not be recorded in advance of the participant's study visit.

Study Year (T_0 - T_2): Record the participant's study year (T_0, T_1, or T_2)

Visit Number: Record the number of times the participant visited the SC to complete this examination in the current study year. There should be no more than two visits to the SC to complete the chest x-ray examination in any one study year. If an exam form is completed for visit two, there must also be a completed form for visit one.

Reason for Repeat Visit: If this is a repeat visit, record the reason for the repeat visit. Refer to the examination form from the previous visit(s) for this information. The purpose of this item is to provide potentially useful information to the examiner regarding why the participant is returning for a repeat visit. Some example reasons:

"*Prior image was of poor quality*."

This might be entered if the participant's prior image was of poor quality during the previous visit, but s/he was willing to return to the SC for a repeat image. This information will alert the examiner to explore the reasons for this problem.

"Participant out of time. Unable to complete chest x-ray exam."

This might be entered if the participant's schedule did not allow him/her to remain at the SC to complete the chest x-ray screening examination during a previous visit, and the examination was rescheduled.

Interval Follow-up Information: This section indicates whether the participant has had any imaging studies since the previous screening exam. This section is intended to be a tool for the SCs to collect interval follow-up information and transmit it easily to the radiologists. However, some SCs may have alternate internal methods for obtaining and transmitting interval follow-up information.

The SC may complete this section using information received during the DE process, contact with the participant during the year, or questioning the participant when s/he comes to the clinic for the current screening exam. This information may be referenced by the radiologist if needed when completing Part E of the form.

Has the participant had any imaging studies since the previous screening exam that may be useful for the radiologist to review if needed?

- **Yes:** The SC should mark this box to indicate that the participant has had at least one imaging study since his or her previous screening exam.

- **No:** The SC should mark this box to indicate that the participant has not had at least one imaging study since his or her previous screening exam.

- **N/A:** For SCs where interval follow-up information is collected and transmitted to the radiologists through an alternate method, the SC should mark this box to indicate that the question is not applicable.

  For SCs using this question to capture interval follow-up information, the SC should mark this box to indicate that interval follow-up information is not available.

If YES, dates obtained (month and year): Record the date that any interval images were obtained. The month and the last two digits of the year should be recorded (e.g., 02/2002). If the date is unknown, enter 99/9999. If no interval images were obtained or if N/A is marked, the dates may be left blank.

Part A. Chest X-ray Examination Findings (Completed by Technologist):

1. **Number of Attempts:** Mark the box corresponding to the number of attempts made to complete the chest x-ray. Three attempts are allowed per visit. If the entire chest of a large participant cannot be viewed with one chest x-ray, then two chest x-rays may be taken in order to view the entire chest. In this case, the two views count as one attempt and two exposures. The fact that two chest x-rays were taken and the reason must be recorded in the Comments section.

- **None:** This might apply if the participant entered the dressing room to prepare for the examination, but for some reason there was no attempt to obtain the chest x-ray image (participant became ill, could not wait, etc.). (Go to Item A.3.)

  If the participant never prepared for the examination in any way, the examination is considered "Not Done." The XRY form would not be filled out in such cases.

- **One:** The chest x-ray is attempted once, regardless of whether it is successfully completed.

- **Two:** The chest x-ray is attempted twice, regardless of whether it is successfully completed.

- **Three:** The chest x-ray is attempted three times, regardless of whether it is successfully completed.

2. **Adequate Image Obtained:** Before the participant leaves the SC, the technologist will evaluate the chest x-ray for quality. All images are then sent to the study radiologist, who will also judge their adequacy. An image will be considered adequate if the lung vessels are clearly visible, and the mediastinal structures are sufficiently penetrated to allow for adequate visualization. Responses are explained below:

   - **No:** The image is judged to be inadequate. (The technologist should complete Part A. Parts B and C should be skipped and the radiologist should complete Items D.1, D.3, and E.6).

   - **Yes:** The image is judged to be adequate. (The technologist should complete Part A. The radiologist should complete Parts B through E.)

3. **Reason for Inadequate or No Image:** This item is completed only if the answer to Item A.1 is "None," or the answer to Item A.2 is "No." Mark one or more boxes to indicate the reason(s) for not obtaining the images or for obtaining inadequate images. An explanation of each reason for inadequate images is given below:

   - **Participant Refusal:** The participant is unwilling to cooperate, i.e., stand in the proper position, hold breath, etc.

   - **Equipment Malfunction:** This includes any problem with the equipment that prevents the successful completion of the chest x-ray exam.

   - **Poor Film Quality:** An image is obtained, but it is not adequate for interpretation. Poor image quality may be due to excessive rotation, inadequate inspiration, motion or processing artifact, over or under penetration, or exclusion of parts of the lung and mediastinal structures from the image.

   - **Other (SPECIFY):** In the space provided, describe any other situation in which adequate images could not be obtained.

4. **Technical Parameters:** Record the technical parameters used for obtaining the x-ray image. If any of the parameters are lower or higher than the acceptable range, provide a comment to explain in Item A.6 and complete a PHVF. If documentation of the exam, including exam

images, has been lost and cannot be recovered or recreated, "9"s can be recorded for the missing technical parameter values.

A. kVp: Record the kVp at which the image was obtained. The acceptable range is 100-150 kVp.

B. mAs: Record the mAs for the image obtained. Zero-fill the boxes (i.e., 02.2). If however, the mAs are not available, record 99.9. The acceptable range for mAs is 0.1-20 mAs. The maximum of 20 mAs may be exceeded for very large patients to achieve acceptable image quality. While there is no upper bound for the mAs for larger participants, the lowest mAs with acceptable image quality should be used.

C. mA: Record the mA for the image obtained. For two-digit doses, zero-fill the first digit (i.e., 020). If the mA is not available, record 999. The mA setting should allow for the mAs to fall within the exposure range and times specified in the protocol.

D. Time: Record the time for the image obtained in milliseconds. If unavailable, enter 99. The maximum exposure time is 40 msec.

E. Exposure Value: Record the exposure value for the image obtained. Depending on the manufacturer and model of the x-ray equipment used to obtain the image, the exposure value may be either the S-value or an exposure index value. If the Exposure Value is not available, enter 9999.

5. CXR system used: Mark the box corresponding to the type of x-ray system used for the specific chest x-ray. For all systems, record the two-digit machine number used for this participant's x-ray exam. If the SC has designated room numbers instead of machine numbers for the chest x-ray, record the room number in the boxes labeled "machine number." Zero-fill all boxes.

6. Comments: The comments box should be used to record information that may help clarify a situation, provide further information for an item in another part of the form, and to record additional "Other (SPECIFY)" information, if needed.

If there are no additional comments, mark the box next to "No." If there are additional comments, mark the box next to "Yes." Enter the item number to which the comments are related. The item number should include a letter indicating the part of the form, and a number indicating the item within that part (e.g., A.3). If the comment is not related to a specific item in Part A of the form, use the item number for the Comments section itself (A.6). Then enter the comments in the space provided to the right of the item number.

7. Tech ID: The technologist should enter his/her four-digit staff ID number and sign the form in the space provided.

Part B. Chest X-ray Overall Diagnostic Quality (Completed by Radiologist)

Part B is to be completed by the radiologist. At some SCs, the SC staff will complete this section using the radiologist's written report. Also, the SC staff may complete Item B.1 if the answer is D, "No images available." If Item A.2 is answered, "No," Parts B and C should be left blank, and Items D.1, D.3, and E.6 should be completed.

Appendix 5-3 Specifications for Completion of the Chest X-ray Screening Examination Form (XRY)

1. Indicate the overall diagnostic quality of CXR:

A. Diagnostic CXR: The chest x-ray image is of diagnostic quality. Go to C.1 to record examination findings.

B. Limited CXR, but interpretable: The chest x-ray image is of limited diagnostic quality, but it can be interpreted. The radiologist should record the factors affecting the quality of the chest x-ray in B.2, and should complete C.1 to record the examination findings. If an abnormality suspicious for lung cancer or a clinically significant abnormality is noted, the result in D.1 should be recorded as A or C. The result in D.1 may <u>not</u> be recorded as F.

C. Non-diagnostic CXR, reschedule CXR: The chest x-ray image is not acceptable for interpretation, and must be repeated. Record the factors affecting the quality of the image in B.2. Then complete D.1 (record Result "F") and D.3, and go to Item E.6. No abnormalities may be recorded for a screening exam of non-diagnostic image quality. If the exam is not of diagnostic quality but an abnormality suspicious for lung cancer or a clinically significant abnormality is noted, then select "B. Limited CXR, but interpretable" and record the abnormality in C.1 as described above. However, if a minor non-suspicious abnormality is noted, the diagnostic quality should be recorded as "C. Non-diagnostic CXR exam, reschedule CXR" and the minor abnormality should <u>not</u> be recorded in C.1.

D. No image available: The chest x-ray image is not available for review. Instances in which the participant underwent a screening examination but the image sets were either lost or inadvertently destroyed and not available for review by the radiologist should be recorded as "No image available." Record the reason that images are not available for review in Item D.3 (Comments). After detailing the reason the images were not available, complete Item E.6. Having no images available for review is considered a protocol violation, therefore a Protocol and HIPAA Violation Form (PHVF) must be completed and submitted to the CC.

2. Which of the following affected the quality of the limited or non-diagnostic CXR? Mark the box(es) to indicate the factor(s) that contributed to the limited diagnostic quality of the chest x-ray. Mark all that apply.

- ■ Low lung volumes
- ■ Lungs incompletely imaged
- ■ Poor positioning
- ■ Motion degradation
- ■ Incorrect exposure or other technical parameter
- ■ Artifacts obscure anatomy
- ■ Incorrect processing algorithm
- ■ High image noise
- ■ Other (SPECIFY)

Part C. Chest X-ray Examination Findings (Completed by Radiologist):

Part C is to be completed by the radiologist. Any finding that could impact follow-up (i.e. result codes "A," "B," and "C") must be in the dictated report and recorded in Part C of the screening exam form. Minor abnormalities that do not require follow-up may be included in the dictated report but do not need to be recorded on the screening exam form. Any abnormality recorded on the screening exam form must be noted in the dictated report. If Item A.2 is answered "No," Part C should be left blank and Items D.1, D.3, and E.6 should be completed.

1. Radiologic Abnormality Noted:

- **No:** No abnormality was seen. Go to Item D.1 and mark Result "E."
- **Yes:** An abnormality (either suspicious for lung cancer or abnormal for any other reason) was seen. Record information for each (up to six) abnormality in the chart (C.2).

2. Record Information for Each Abnormality: Complete this item for up to six abnormalities. If more than six are identified, record the six most serious abnormalities. Complete the chart by recording the appropriate number(s) in the designated spot. Enter information about the most serious abnormality in the row labeled "1," the second most serious abnormality in the row labeled "2," and so on.

Description of Abnormality: For <u>each</u> abnormality, mark **one** number that corresponds to it from the list below. Please note that **code 51 (in bold) is considered to be a positive screen for lung cancer and always should be listed first if multiple abnormalities are identified**. For this abnormality, the examination result in Item D.1 must be coded "Positive Screen – Abnormalities suspicious for lung cancer." If, however, the non-calcified visible nodule/mass is not discovered until the comparison exam, it is possible the code 51 will not be listed first and that the examination result in Item D.1 will not be "Positive Screen – Abnormalities suspicious for lung cancer."

Please note that codes 70 and 71 – "Other significant abnormality (SPECIFY)" should be used to designate <u>all</u> other significant abnormalities not listed below, including, but not limited to, any other abnormalities suspicious for malignancy. Code 72 "Other minor abnormality noted" should be used to designate all other minor abnormalities noted. Specifying the minor abnormalities designated by code 72 is optional.

51 = Non-calcified visible nodule/mass (MUST MARK "A" IN D.1)
For this abnormality, the examination result in item D.1 must be coded "Positive Screen – Abnormalities suspicious for lung cancer."
53 = Benign lung nodule(s) (benign calcification)
54 = Atelectasis, segmental or greater
55 = Pleural thickening or effusion
56 = Non-calcified hilar/mediastinal adenopathy/mass ≥ 10 mm short axis
57 = Chest wall abnormality (e.g. bone destruction, metastasis)
58 = Consolidation

59 = Reticular/reticulonodular opacities, honeycombing, fibrosis, scar

62 = 6 or more nodules, not suspicious for cancer (opacities ≥ 4 mm) (ANY SUSPICIOUS NODULES MUST BE CODED AS 51)

Code 62 should be used in cases where there are at least six nodules not suspicious for cancer. "Not suspicious for cancer" is defined as round, well-defined, and similar in size. Any nodules that are suspicious MUST be coded as 51; should this leave a total of fewer than six non-suspicious nodules, each nodule must be individually recorded.

63 = Emphysema

64 = Significant cardiovascular abnormality (SPECIFY)

Code 64 should be used to record a significant cardiovascular abnormality, such as a thoracic aortic aneurysm, aortic dissection, marked cardiomegaly, pulmonary hypertension, coronary artery calcifications, or valvular calcifications (exclude mitral annular calcification). The abnormality should be specified in the space provided to the right of the two-digit box for the abnormality code.

70 = Other significant abnormality above the diaphragm (SPECIFY)

The abnormality should be specified in the space provided to the right of the two-digit box for the abnormality code. (**Note:** Abnormalities identified on chest x-ray that are suspicious for lung cancer but cannot be recorded using codes 51-59, such as ground glass opacities, may be coded as a 70 with an "A – Positive Screen – Abnormalities suspicious for lung cancer" at the discretion of the radiologist. In such cases the SC must contact User Support at the CC to implement a manual override in IDEAS since abnormality code 70 normally cannot be entered as a positive screen in IDEAS).

71 = Other significant abnormality at or below the diaphragm (SPECIFY)

The abnormality should be specified in the space provided to the right of the two-digit box for the abnormality code.

72 = Other minor abnormality noted (SPECIFY IF DESIRED)

The abnormality may be specified in the space provided to the right of the two-digit box for the abnormality code, if desired.

Check box if identified after comparison with historical images: This box indicates when the abnormality listed in the table was identified. Check the box for any abnormality that was found on the current chest x-ray only after comparing it with any historical image. If an abnormality was identified during the initial (isolated) review of the current chest x-ray image, this box is left blank.

The remaining information under Description of Abnormality (Location of Epicenter, Longest Diameter, Longest Perpendicular Diameter, and Nodule/Mass Margins) must be recorded for abnormalities coded as 51 only.

- **Location of Epicenter**: Record the code that corresponds to the approximate center of the location of the abnormality in the appropriate zone or lung field. For simplicity, the lungs are divided into thirds, with upper, middle, and lower zones. Select one location for each abnormality.

  - **Rt Upper Zone**: The abnormality was found in the upper 1/3 of the right lung field.

- **Rt Middle Zone:** The abnormality was found in the middle 1/3 of the right lung field.
- **Rt Lower Zone**: The abnormality was found in the lower 1/3 of the right lung field.
- **Lt Upper Zone**: The abnormality was found in the upper 1/3 of the left lung field.
- **Lt Middle Zone**: The abnormality was found in the middle 1/3 of the left lung field.
- **Lt Lower Zone**: The abnormality was found in the lower 1/3 of the left lung field.
- **Other (SPECIFY)**: This choice is used when it is difficult to identify the lung section containing the epicenter. If the lung section containing the epicenter cannot be identified, specify a more general location (i.e., upper lobe).

- **Longest Diameter (mm):** Record the length of the abnormality's maximum dimension in millimeters. If dimensions are not available or are not applicable, record 999. Zero-fill all measurements (e.g., 005). Use whole numbers only.

- **Longest Perpendicular Diameter (mm):** Record the length of the maximum perpendicular dimension (that is, the longest length that is perpendicular to the maximum dimension) in millimeters. If dimensions are not available or not applicable, record 999. Zero-fill all measurements (e.g., 005). Use whole numbers only.

- **Nodule/Mass Margins:** Record the code that corresponds to whether the lesion is spiculated (stellate), smooth, or poorly defined. If the morphology cannot be determined, code "unable to determine."

Part D: Chest X-ray Interpretation Results (Completed by Radiologist):

Part D is to be completed by the radiologist. At some SCs, the SC staff will complete this section using the radiologist's written report. In cases where an adequate scan was not obtained (A.2 = No), Items D.1 and D.3 must be completed by the radiologist.

Part D documents the results of the current screening examination only. The participant's prior medical history, prior radiologic examinations, or prior NLST/LSS screens should not be considered when assigning the lung screening result in Part D. The result of comparing the current chest x-ray with historical images will be recorded in Part E.

Note: The focus of the screening examination is to identify abnormalities that are suspicious for lung cancer. Although other clinically significant findings may be found incidentally during the screening, the Results section is meant to reflect a hierarchy of examination findings in regard to lung cancer. Result categories A, C, D, E, and F in Part D, Item 1 are in hierarchical order. Thus, a positive screen is at the highest end of findings, a clinically significant abnormality is at the next level, and so on, throughout the results category.

Appendix 5-3 Specifications for Completion of the Chest X-ray Screening Examination Form (XRY)

1. Lung Screening Result: Mark the box corresponding to the result of the current chest x-ray examination. Definitions of lung screening results are given below:

A. Positive Screen – Abnormalities suspicious for lung cancer:

The following abnormality (C.2, #51) is always considered a positive screen and Item D.1 must always be marked "A:"

- Non-calcified visible nodule/mass

Other abnormalities, or constellations of abnormalities, may be suggestive of lung cancer, but there is no absolute rule for coding other findings as suspicious for lung cancer. In these instances, the classification of a screening exam result as positive is left up to the radiologist. Any other clinically significant abnormalities may be reported in Item D.2.

C. Negative Screen – Clinically significant abnormalities not suspicious for lung cancer:

The review of the image reveals that an abnormality is present and requires further evaluation, but is not suggestive of lung malignancy. It is up to the radiologist to determine whether an abnormality is clinically significant. Complete Item D.3, then go to Part E.

D. Negative Screen – Minor abnormalities not suspicious for lung cancer:

The review of the image reveals minor abnormalities that are not suspicious for lung cancer. It is up to the radiologist to determine whether an abnormality is minor. Complete Item D.3, then go to Part E.

E. Negative Screen – No significant abnormalities:

The review of the image reveals no significant abnormalities. Complete Item D.3 and then go to Part E.

F. Inadequate:

The chest x-ray images were inadequate and sufficient information could not be obtained to determine the examination result. Complete Item D.3 and then go to E.6.

If the image is considered inadequate, but based on what is visible on the image, there is an overt suspicion of lung cancer, the result of the screening exam should be recorded as positive. The radiologist should record that the image is positive in Item D.1 of the XRY. The radiologist must comment in Item D.3 that although the result is positive, the overall quality of the image is inadequate. Part E should be completed as outlined below.

2. Other Significant Abnormalities (in addition to lung screening results) that need to be reported: Complete D.2 only if the Lung Screening Result in D.1 was "A. Positive Screen."

No: The chest x-ray did not reveal other significant abnormalities other than the lung screening result.

Yes: The chest x-ray revealed a significant abnormality in addition to the positive lung screening result; for example, a breast mass was seen in addition to nodules that are suspicious for lung cancer.

3. Comments: The comments box should be used to record information from Parts B, C, and D that may help clarify a situation, provide further information for an item in another part of the form, and to record additional "Other (SPECIFY)" information, if needed.

If there are no additional comments, mark the box next to "No." If there are additional comments, mark the box next to "Yes." Enter the item number to which the comments are related. The item number should include a letter indicating the part of the form, and a number indicating the item within that part (e.g., B.2). If the comment is not related to a specific item in Parts B, C, or D of the form, use the item number for the Comments section itself (D.3). Then enter the comments in the space provided to the right of the item number.

Note that if a dictated report is not provided, the Comments section should be used to describe significant and minor abnormalities occurring with a negative screen.

If Item D.2 is marked "Yes," the Comments section should be used to describe the other clinically significant abnormality.

Part E. Chest X-ray Comparison Results – Complete for All Lung Screening Results (Completed by Radiologist)

Part E is to be completed by the radiologist. Part E is to be completed for ALL screening examinations.

Part E documents the comparison of the current chest x-ray with any available historical images for the participant. Comparison to previous images may or may not lead to a change in the lung screening result. Historical images for the T_0 prevalence screen will be obtained according to local practice at the SC. Cases where a participant does not have an historical image to be used for a comparison read should be recorded in "E.5. Comments." If a previous screening exam was not performed, then not doing the comparison is not considered a protocol violation. For example, not performing the comparison read at T_1 is not considered a protocol violation if the T_0 exam was never obtained and an MDF was submitted for the T_0 XRY form. However, if the previous screening exam was performed but the images are not compared to the current screening exam, a Protocol and HIPAA Violation Form must be completed.

If historical images can be obtained, they should be used to conduct a comparison review for the T_0 prevalence screen. For T_1 screening examinations, the comparison image is the T_0 screen. For T_2 screening examinations the comparison images are the T_0 and T_1 screens. However, if the screening examinations from all three study years are negative, then the T_2 screening examination may be compared with either the T_0 or T_1 screen, or both screens, at the radiologist's discretion.

In the event that a screen is inadequate and a repeat screen is performed, the inadequate screen may be used as the comparison image for the repeat screen at the radiologist's discretion. In this instance, check the box for the current study year in Item E.1. If an inadequate screen is used for comparison in later study years, that fact should be noted in the Comments section. A comment is not required if using an

inadequate screen for comparison in the same study year. For example, if a T_1 screen is inadequate and a repeat T_1 screen is performed, then both the T_0 and the inadequate T_1 screens may be used as comparison images for the repeat T_1 screen. If the inadequate screen is used as a comparison image at T_2, then it should be noted in the Comments section. Once the comparison has been made and the data recorded, the results of the comparison are recorded in Item E.3a.

Should the comparison with historical images lead to a change in the lung screening result, the radiologist should record the new result in Part E. For example, a minor abnormality documented in Part C may lead to the Lung Screening Result "D" in Item D.1. However, upon comparison with historical images, the radiologist may decide that there has been a significant change in the abnormality. In this instance the radiologist would complete Part E, recording the information concerning the abnormality in Item E.2, and record the Lung Screening Comparison Result "C" in E.3a.

Should the comparison with historical images identify an abnormality that was not previously seen on the image read in isolation, the abnormality should be recorded in Item C.2, and the box which reads "Check Box If Identified After Comparison With Historical Images" should be checked. If the abnormality is coded as a "51" or other significant abnormality, then these newly identified abnormalities should be recorded in Item E.2.

Likewise, should the comparison with historical images result in an abnormality that differs (more severe or less severe) from what was seen on the image read in isolation, the abnormality should be coded according to the comparison image and recorded in Item C.2. For example, an abnormality is coded as a "72 – Other minor abnormality noted" for the image read in isolation. But in comparison with the historical image, the abnormality now appears to be a "71 – Other significant abnormality at/below the diaphragm." The abnormality should be recorded as a "71" in Item C.2, and the box which reads "Check Box If Identified After Comparison With Historical Images" should be checked. The change in the abnormality as a result of the comparison with historical image should be documented in the Comments section of Part E (Item E.5). Item E.2 should then be completed according to the guidelines outlined below. Any findings from historical images used as comparisons that are <u>not present at the current screening exam</u> (i.e. a 51 present at T_0 but not at T_1) should be noted as a comment in E.5.

1. **Comparison Image:** Check the box to indicate the source of the comparison image. Mark all boxes for which a comparison image is available.

   No image available – There is no historical image available. If checked, this should be the only box checked. Go to E.4.

   T_0 – The comparison image is the NLST/LSS T_0 exam. The current chest x-ray exam is the T_1 or T_2 examination. In instances where the T_0 screen is inadequate and a repeat screen is performed, the inadequate T_0 screen may be used as the comparison image for the repeat T_0 screen at the radiologist's discretion. If the inadequate T_0 screen is used as a comparison image at the T_1 or T_2 examination, record that fact in the Comments section.

   T_1 – The comparison image is the NLST/LSS T_1 exam. The current chest x-ray exam is the T_2 examination. In instances where the T_1 screen is inadequate and a repeat screen is performed, the inadequate T_1 screen may be used as the comparison image for the repeat T_1 screen at the radiologist's discretion. If the inadequate T_1 screen is used as a comparison image at the T_2 examination, record that fact in the Comments section.

   T_2 Inadequate scan – The comparison image is the NLST/LSS T_2 inadequate scan. The current chest x-ray exam is the T_2 repeat examination.

Previous scan not completed as part of NLST – The comparison image was not done as part of the NLST/LSS. Record the code that corresponds to the type of scan for the images available, and the date(s) of the scan(s). A total of three non-NLST/LSS scans may be recorded.

2. Enter abnormality number and code for <u>all</u> Code 51 abnormalities AND other significant abnormalities seen on this screening exam. This chart records the result of the comparison of each abnormality seen on the current chest x-ray with any available historical images. Transfer the abnormality number and code from Item C.2 for each code 51 abnormality and/or other significant abnormality, including any abnormalities that have been determined to be significant only after comparison with historical images. Any new abnormality that is identified during the comparison must be recorded in Item C.2. Complete the following:

Was abnormality pre-existing? Record the single-digit code to indicate whether or not the abnormality was seen on any historical image.

1 = No: The abnormality is not visible on any previous image. Do not complete the rest of the table; go to E.3.

2 = Yes: The abnormality can be seen on a previous image. The remainder of Item E.2 should be completed.

9 = Unable to determine: It cannot be determined whether or not the abnormality can be seen on a previous image. Do not complete the rest of the table; go to E.3.

Earliest date visible: Record the month, day, and year of the earliest historical image that shows the abnormality.

Complete for Code 51 Abnormalities Only: If the abnormality was recorded as code 51, complete the following:

Interval Growth of Abnormality: Record the single digit code that indicates if the abnormality has grown since its appearance on the previous image.

Interval suspicious change in attenuation: Record the single digit code that indicates if there has been a suspicious change in attenuation between the historical image and the current one. A suspicious change in attenuation is an increase in attenuation from ground glass to a combination of ground glass and soft tissue or to pure soft tissue attenuation.

Interval change warrants further investigation?: If the abnormality was coded as an other significant abnormality or is being re-classified as a significant abnormality due to the comparison with historical images, complete the following: record the single digit code that indicates if there has been a significant change that warrants further investigation.

3a. Lung Screening Comparison Result: Check the box to indicate the result of comparison of the current chest x-ray exam with the historical images available. This is the result that will be reported to the participant and the participant's health care provider, and should take into

account the radiologist's assessment of the current screen in the context of the participant's available historical images.

If the current screen is positive and the abnormality identified appears not to have changed when compared to previous images at the comparison reading (Part E), the radiologist should record the result in Item E.3a as B – "Abnormalities suspicious for lung cancer, no significant change."

However, when previous images from two successive study years have not changed and the third image is positive and appears unchanged from the previous images, the radiologist may code that result as D – "Minor abnormalities not suspicious for lung cancer" at his/her discretion as described below, rather than using result code B. Additionally, the radiologist should specify in the Comments section (Item E.5) why the result was coded as D. Likewise, if after baseline screening a clinically significant abnormality remains stable and unchanged on subsequent screening examinations, the abnormality may be coded as D – "Minor abnormalities not suspicious for lung cancer" at the discretion of the radiologist, rather than coding the image as a clinically significant abnormality. Additionally, the radiologist should specify in the Comments section (Item E.5) why the result was coded as a D.

3b. Other Significant Abnormalities (in addition to lung screening results) that need to be reported: Complete E.3b only if the Lung Screening Result in E.3a was "A. Positive Screen" or "B. Positive Screen, no significant change."

No: The chest x-ray did not reveal other significant abnormalities other than the lung screening result.

Yes: The chest x-ray revealed a significant abnormality in addition to the positive lung screening result; for example, a breast mass was seen in addition to nodules that are suspicious for lung cancer.

4. Which of the following diagnostic procedures for screening examination results should the screening result letter include? Mark the box to indicate recommended follow-up options for this participant. More than one item may be marked. If the participant reported previous chest images but those images were not immediately available for comparison, "Comparison with historical images" may be marked, indicating that the comparison should still be attempted. If "Comparison with historical images" is marked, other follow-up diagnostic procedures MUST be indicated as well, in case the historical images cannot be obtained. If "Low dose CT with NLST parameters" is marked, the radiologist must also select the area of focus. Only one box may be marked for area of focus; both may not be marked and both may not be blank. "Limited" focus refers to the abnormal region only, as opposed to the entire chest. There are no study-wide recommendations for T_2 nodules that have been stable for two years; however radiologists may make recommendations at their own discretion. New nodules identified at T_2 will be documented on a DE Form and followed for 24 months as described in section 7.2 of the MOOP.

5. Comments: This comments box should be used to record comments for any item in Part E that may help clarify a situation, provide further information for an item in another part of the form, and to record additional "Other (SPECIFY)" information, if needed.

If there are no additional comments, mark the box next to "No." If there are additional comments, mark the box next to "Yes." Enter the item number to which the comments are related. The item number should include a letter indicating the part of the form, and a number indicating the item within that part (e.g., E.2). If the comment is not related to a specific item in Part E of the form, use the item number for the Comments section itself (E.5). Then enter the comments in the space provided to the right of the item number.

6. **Radiologist ID:** This item should be completed by the radiologist. The radiologist should enter his/her four-digit staff ID number, record the date the form was completed, and sign the form in the space provided. If this section was completed by a member of the SC staff using the radiologist's written report, the SC staff member should enter the radiologist's name and staff ID number, then sign his/her own name below the name of the radiologist.

After completing the form:

- The form should be checked to make sure it is accurate, legible, and complete.
- The SC staff member who completed the form should write his/her initials in the space labeled "Initials Complete" in the box at the top right corner of the first page.
- The SC staff member who checked the form for completion should write his/her initials in the space labeled "Initials QC" in the box at the top right corner of the first page. This should not be the same SC staff member who completed the form.
- Enter the form into IDEAS.
- File the form in the participant's study file.

NATIONAL LUNG SCREENING TRIAL (NLST)
EQUIPMENT QUALITY CONTROL

CHEST X-RAY QUALITY ASSURANCE INFORMATION

The following information is required for CXR quality assurance.

1. **LSS protocol CXR specifications.**
2. **Confirmation of screening site adherence to CXR specifications.**
3. **CXR equipment characteristics.**
4. **Physicist attestation to ongoing performance testing (annual).**
5. **CXR exposure measurements (annual, and after tube change).**

NATIONAL LUNG SCREENING TRIAL (NLST)
EQUIPMENT QUALITY CONTROL

CHEST X-RAY EQUIPMENT CHARACTERISTICS

PLEASE HAVE YOUR PHYSICIST PROVIDE THE FOLLOWING INFORMATION FOR EACH X-RAY UNIT.

LSS SITE NAME: _____

SITE MAILING ADDRESS: _____

I. **PI (Radiologist) :** _____

Tel#: _____ **Email:** _____

II. **Chief CXR Technologist:** _____

Tel#: _____ **Email:** _____

III. **Medical Physicist:** _____

Tel#: _____ **Email:** _____

	CXR EQUIPMENT			
1.	Manufacturer:			
2.	Model Name:			
3.	Date of Manufacture:			
4.	Detector Type:	☐ DR	☐ CR	☐ Screen/Film
5.	Dedicated chest unit:	☐ Yes	☐ No	
6.	SID:			
7.	Grid ratio:			
8.	Film/screen combination:			
9.	Processor manufacturer and model:			
10.	CR Reader manufacturer and model:			

Appendix 5-6 Attestation to Chest X-ray Performance Testing

NATIONAL LUNG SCREENING TRIAL (NLST)
EQUIPMENT QUALITY CONTROL

ATTESTATION TO CHEST X-RAY PERFORMANCE TESTING

PLEASE HAVE YOUR PHYSICIST PROVIDE THE FOLLOWING INFORMATION REGARDING PERFORMANCE TESTING OF EACH OF YOUR CHEST X-RAY UNITS. A COPY OF THE PHYSICIST'S REPORT SHOULD BE KEPT ON SITE, AND BE AVAILABLE FOR SITE INSPECTORS.

I. SITE NAME: _____

II. CXR MACHINE #_____ MAKE & MODEL:_____

III. DATE OF INSTALLATION: _____

	PERFORMANCE TEST	TESTED AT INSTALLATION?	LATEST DATE TESTED	TEST NOT DONE?
1.	Collimation	☐ Yes ☐ No	__/__/__	
2.	Linearity with mA	☐ Yes ☐ No	__/__/__	
3.	kVp accuracy and repro.	☐ Yes ☐ No	__/__/__	
4.	Exposure repro. and mR/mAs output	☐ Yes ☐ No	__/__/__	
5.	AEC performance	☐ Yes ☐ No	__/__/__	
6.	Entrance skin exposure	☐ Yes ☐ No	__/__/__	
7.	Beam quality - HVL	☐ Yes ☐ No	__/__/__	
8.	Artifact evaluation	☐ Yes ☐ No	__/__/__	
9.	Focal spot size	☐ Yes ☐ No	__/__/__	
10.	CR reader (if applicable)	☐ Yes ☐ No	__/__/__	

PLEASE INDICATE BELOW THE TYPE AND FREQUENCY OF ANY ONGOING QC PROCEDURES.

ATTESTED TO

_____ **(Physicist)**
_____ **(Physicist ID#)**
_____ **(Date)**

Appendix 5-7 Annual Chest X-ray Exposure Measurements

NATIONAL LUNG SCREENING TRIAL (NLST)
EQUIPMENT QUALITY CONTROL

ANNUAL CHEST X-RAY EXPOSURE MEASUREMENTS

DATE: _____

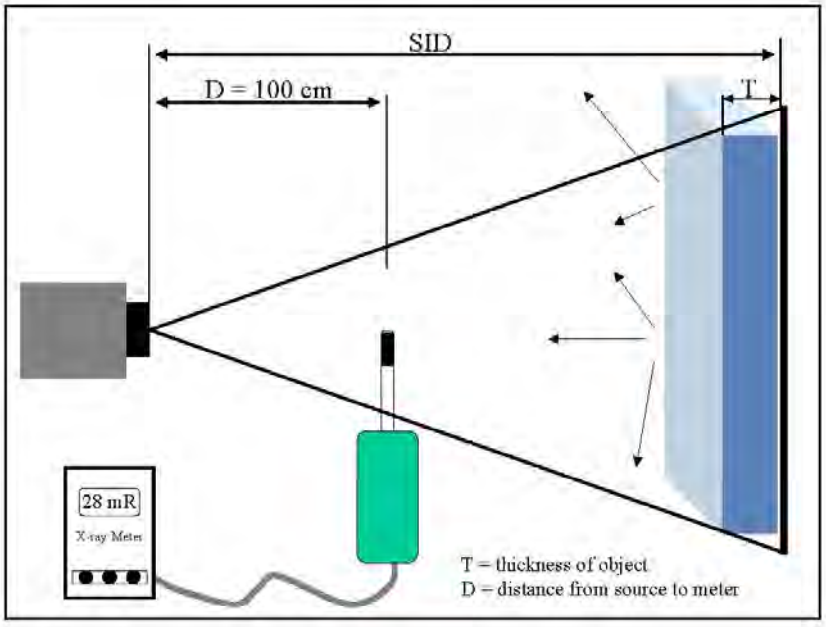
LSS SITE NAME: _____

CXR MANUFACTURER AND MODEL: _____

PHYSICIST PERFORMING TESTS: _____

TITLE: _____ **TEL#:** _____ **EMAIL:** _____

A.	**Exposure Output Instructions**
1.	Select focal spot, kVp, and mA station clinically used by this machine for PA chest
2.	Manually select an exposure time sufficient to produce reproducible exposures (at least 10 milliseconds - recommend 100 milliseconds).
3.	Place appropriate ion chamber 100 cm (40 inches) from tube focal spot.
4.	Collimate to an area sufficient to cover the ion chamber.
5.	Record exposure (mR) and mAs.



Appendix 5-7 Annual Chest X-ray Exposure Measurements

ANNUAL CXR EXPOSURE MEASUREMENTS (continued)

B.		(Example)	(Your site)
1.	LSS SITE	Wash. U.	
2.	TEST DATE	8/19/03	
3.	TESTER	G. Fletcher	
4.	CXR MACHINE	ThoraVision	
5.	SID (cm)	180	
6.	kVp	140	
7.	HVL at kVp in line #6	10.5	
8.	MA	500	
9.	TIME (mSEC)	20	
10.	mAs	10	
11.	OUTPUT AT 40 CM (mR)	200	
12.	mR/mAs	20	

Appendix 5-8 Chest X-ray Image QA Form (XQA)

National Lung Screening Trial (NLST)

CHEST X-RAY IMAGE QA FORM (XQA)

ADMINISTRATIVE SECTION

PID: |___|___| -|___|___|___|___|___| - |___|

Screening Date: |___|___| / |___|___| / |2|0|___|___|

Reviewer ID: |___|___|___|___| Reviewer:_____

Review Date: |___|___| / |___|___| / |2|0|___|___|

PART A. Technical Parameters

Field	Value	Adequate?
kVp	|___|___|___|	☐Yes ☐No
mAs	|___|___|.|___|	☐Yes ☐No
mA	|___|___|___|	☐Yes ☐No
Time	|___|___| msec	☐Yes ☐No

PART B. Image Quality

Review Item	Adequate?
Collimation	☐Yes ☐No
Vertebral body definition	☐Yes ☐No
Left retrocardiac pulmonary vessels	☐Yes ☐No
Lateral wall of descending aorta	☐Yes ☐No
Left hemidiaphragm	☐Yes ☐No
R/L marker present	☐Yes ☐No
Motion absent	☐Yes ☐No
Other artifact absent (technical, external)	☐Yes ☐No
Positioning (rotation, centering, scapulae, lordosis)	☐Yes ☐No
Inspiratory level adequate	☐Yes ☐No

PART C. Overall

X-ray technical parameters adequate?	☐Yes ☐No
Image quality adequate?	☐Yes ☐No
Repeat screening exam suggested?	☐Yes ☐No

Comments (Include reason for suggested repeat screening exam):

6. REPORTING RESULTS OF SCREENING TESTS

6.1 Overview

The SC is responsible for reporting the results of all baseline and annual screening examinations to the participant and to the participant's health care provider within three weeks of the screening visit. Participants with abnormal results that are suspicious for lung malignancy (positive screens) will be urged to speak with their health care provider regarding whether or not they need to follow up with a specialist. A participant with abnormal findings that are *not* suspicious for lung malignancy will be referred according to the standard practices of the SC. The SC is also responsible for reporting the results of follow-up of positive screens to the CC. To facilitate accurate results reporting, the CC will provide a module in IDEAS for generating screening examination results letters as well as documenting the screening examination results and the dates that results letters were mailed.

This chapter details the procedures for providing notification to participants and their health care providers, including creating cover letters; providing examination results reports; making referrals when necessary; and tracking, reporting, and monitoring notification tasks.

6.2 Notifying Participants and Health Care Providers

The SC will report all screening results in writing to the participant and to the participant's health care provider **within three weeks of the screening visit.** At the minimum, positive screens and negative screens with clinically significant abnormalities will also be reported to participants by telephone. If the participant is unreachable by telephone, results will be sent via certified mail with return receipt requested. Positive screens and negative screens with clinically significant abnormalities may be reported to the health care provider by telephone, fax, or certified mail. If the fax method is chosen, it is recommended that the health care provider's office is telephoned and advised of the fax transmittal in advance. If the participant does not wish to have a medical professional informed of his/her screening results and has signed a Results Withheld Statement (Appendix 3-3), only the participant will receive the results. In this case, the participant's results letter should indicate that the results were not sent to a health care provider. A copy of the participant results letter and the health care provider results letter, if sent, should be kept in the participant's study file.

6.2.1 Documents for Reporting Results of the Screening Examinations

The SC is responsible for reporting results of the screening examinations. The SC will send the results to participants and their health care providers with a cover letter as described in the following section. The SC may choose to incorporate results into the cover letter, may attach a copy of the radiologist's dictated report, or may produce a customized report of results. The combination of documents sent must reflect the results of the examination. A copy of the exam form should not be sent to the participant or the health care provider. The SC may provide the participant with a copy of the screening examination image, upon his/her request, to take to his/her health care provider for follow-up.

6.2.2 Letters for Reporting Results of the Screening Examinations

The SC will send screening examination results to participants and their health care providers with a separate results letter. Each SC is responsible for drafting its own letters using SC letterhead. Sample participant results letters for each result type (positive screen, positive screen with small nodules [0.4 – 0.9 cm], positive screen with no significant change since the previous exam, negative screen with clinically significant abnormalities, negative screen with minor abnormalities, negative screen with no significant abnormalities, or an inadequate screen) are presented as Appendices 6-1 through 6-7. Sample health care provider results letters are presented as Appendices 6-8 through 6-14. The SC specific results letter for each type of result must be submitted to the CC and approved by the NCI prior to use at the SC. The letters must include the following elements.

The participant letter must include:

- A disclaimer stating that the screening examination was not intended to be a complete physical examination or a substitute for a visit to a health care provider;
- A statement providing the overall result of the screening examination ("positive screen with abnormalities suspicious for lung cancer," a "positive screen with abnormalities suspicious for lung cancer that have not changed significantly since the previous exam," a "negative screen with clinically significant abnormalities not suspicious for lung cancer," a "negative screen with minor abnormalities not suspicious for lung cancer," a "negative screen with no significant abnormalities," or an "inadequate screen") with reference to any attached supplemental report for further details;

- For positive screening examination results, a statement indicating that the exact follow-up time intervals and methods have not been established and a list of common methods of follow-up;

- A statement stating the costs of diagnostic tests are not covered by the trial in the case of a positive screening exam or negative screening exam with clinically significant abnormalities;

- A statement urging the participant to see his/her health care provider and talk with him/her about whether s/he should see a recognized specialist for further evaluation of exam results in the case of positive screening exam results;

- A statement recommending that the participant see his/her health care provider to discuss his/her examination results in the case of a negative screening exam with clinically significant abnormalities;

- A statement that the results have been sent to his/her health care provider or a statement that the results were not sent to a health care provider (if the participant does not have health care provider or does not want his/her health care provider notified of the results and has signed a Results Withheld Statement), and

- The SC telephone number and the SC Coordinator's and Principal Investigator's names for any questions or concerns the participant may have.

The health care provider letter must include:

- A statement that the NLST/LSS is a NCI-sponsored scientific study designed to evaluate screening exams for lung cancer;

- The name and date of birth of the participant for whom results are being reported;

- The date of the screening examination;

- A disclaimer stating that the screening examination was not intended to be a complete physical examination or a substitute for a visit to a health care provider;

- A statement providing the overall result of the screening examination ("positive screen with abnormalities suspicious for lung cancer," a "positive screen with abnormalities suspicious for lung cancer that have not changed significantly since the previous exam," a "negative screen with clinically significant abnormalities not suspicious for lung cancer," a "negative screen with minor abnormalities not suspicious for lung cancer," a "negative screen with no significant abnormalities," or an "inadequate screen") with reference to any attached supplemental report for further details;

- For positive screening examination results, a statement indicating that the exact follow-up time intervals and methods have not been established and a list of common methods of follow-up;

- A statement indicating that the participant was urged to seek medical attention in the case of positive screening examination results;
- A statement encouraging the health care provider to see the participant for diagnostic follow-up of positive screening exams;
- A statement indicating that the participant received a recommendation to discuss his/her examination results with his/her health care provider in the case a negative screen with clinically significant abnormalities;
- A statement stating the costs of diagnostic tests are not covered by the trial in the case of a positive screening exam or negative screening exam with clinically significant abnormalities;
- For positive screening examination results, a statement advising the health care provider to contact the SC if more information regarding the diagnosis and treatment of lung cancer is desired, and
- The SC telephone number and the SC Coordinator's and Principal Investigator's names for any questions or concerns the health care provider may have.

When reporting the result of a positive screen from a spiral CT screening exam, the SC has the option of providing the health care provider with the low-dose CT scan technique that was used to obtain the screen. Use of these or similar settings may facilitate comparison to the previous examination, and help limit cumulative radiation exposure to the participant**.** The template CT Scan Technique Information Sheet for Health Care Providers is found in Appendix 6-15. The template should be customized by each SC to contain the actual settings that were used to obtain the participant's screening exam.

6.2.2.1 IDEAS Support for the Production of Results Letters

IDEAS provides two options for producing results letters. One option is to generate the results letters within IDEAS itself, without the need to export data. Detailed information about this process is provided in the *NLST/LSS IDEAS User's Guide*. The second option is to use the IDEAS export function to download the results of the screening examinations, participant data, and health care provider data from IDEAS to the SC's own system. IDEAS will capture the date of the merge file download and the SC will enter a mailing date for the letters. The mailing date will be used to monitor the time elapsed from screening to mailing of results letters. To generate results letters, the SC will be required to download the exam results file(s) and use them directly (as in a mail-merge process) when preparing the

results letters. Using the exam results file from IDEAS allows the SCs to transfer the examination data directly to the appropriate version of a results letter, thereby reducing the chance of sending incorrect results to both participants and their health care providers. It is important to note that even if the SC develops its own mailing and reporting process, the SC is required to use the examination results from IDEAS.

6.3 Making Referrals for Screening Examinations

Each SC is responsible for referring participants to appropriate medical professionals in accordance with standards of practice at the SC. Each participant with a positive screening examination result should be urged to speak with his/her health care provider regarding whether or not s/he needs to see a specialist. In some cases, the SC may wish to review a positive result with a medical professional associated with the SC. Participants with negative screening examination results but one or more significant abnormalities may also be referred for follow-up at the discretion of the SC.

6.4 Correcting an Erroneous Results Report

If it is discovered that erroneous results were sent to the participant or his/her health care provider, the correct results must be reported along with an explanation of the circumstances, regardless of the type of error (underestimate or overestimate of seriousness). The manner and timing of this reporting should be handled on a case by case basis at the discretion of the SC. In addition to reporting the correct results, the SC should also report this error to the CC as a protocol violation, as described in Chapter 11, Section 11.5.2.

Errors in notification may also be identified through quality assurance checks performed by the CC. Some of these efforts are described in Section 6.6. If errors are found through these checks, the SC will be notified to perform data retrieval to correct any errors. Details regarding data retrieval procedures and follow-up are also described in Chapter 11, Section 11.6.1.

6.5 Ensuring Diagnostic Work-up for Positive Screens

The SC Coordinator is responsible for verifying that a participant follows up with his/her health care provider in the case of a positive screen. The SC will contact the participant within four weeks of the initial screening examination to determine whether a follow-up examination has been scheduled. If follow-up has not yet been scheduled, the SC will contact the participant four weeks later (eight weeks after the screening examination) to determine whether a follow-up appointment has been scheduled. The SC will maintain a manual or automatic tracking system on the follow-up of these participants. Approximately four weeks after confirming with the participant that a follow-up appointment has been scheduled, the SC will re-contact the participant to determine if follow-up occurred and to assess the status of the work-up. When the work-up is complete, or at the three month intervals, whichever is first, the SC should contact the health care provider and/or hospital to obtain information regarding diagnostic tests (to be abstracted and recorded on a DE form, Appendix 7-2).

It is anticipated that up to 10% of participants will be under-insured or uninsured. Efforts must therefore be made wherever possible to ensure that diagnostic and therapeutic options are identified and that participants who are without other means to pay for necessary diagnostic evaluation and treatment are able to find resources for medical care.

6.6 Quality Assurance of Results Reporting

The CC will perform quality assurance on the results reporting activities. The CC will choose an initial random selection of results letters by PID, stratified by SC and result code. The CC will request from the SCs copies of these results letters with personal identifiers removed. The CC will perform checks to ensure that there are no discrepancies in results reporting between the screening examination form and the results notification letters sent. If necessary, additional random selections of results letters will be selected for QA by the CC.

6.7 Tracking, Reporting, and Monitoring Notification Activities

The SC Coordinator will develop a system to track the mailings of written notifications of screening examination results. This is to ensure that the participant and his/her health care provider

receive the results of the screening examination within three weeks. The SC Coordinator should keep all documentation concerning the certified mailings, including the original certified mail receipt with postmark and the return receipt cards signed by the addressee that are returned to the SC. If no receipt card has been received after two weeks of the postmark of the mailing to a participant or health care provider, the SC Coordinator will follow up to determine whether the notification was received. If the participant or health care provider confirms that it has not been received, the SC Coordinator will resend the notification.

The Screening Exam Results Report (Appendix 11-19) will be available to assist the SC in monitoring notification activities and identifying any problems with notification procedures.

Appendices for Chapter 6

Appendix 6-1 Sample Results Letter to Participants:
Positive Screen - Abnormalities suspicious for lung cancer

National Lung Screening Trial / Lung Screening Study (NLST/LSS)

(Date)

(Participant Name)
(Participant Address)
(City, State, Zip Code)

Dear (*Participant Name)*:

Recently you received a lung cancer screening examination as part of the National Lung Screening Trial. **Your** *(chest x-ray/spiral CT)* **examination revealed abnormalities in your lungs. The possibility that these abnormalities represent lung cancer cannot be ruled out.** The attached report provides you with detailed results of your examination.

Among physicians, it is agreed that this abnormality requires a follow-up evaluation. The exact follow-up time interval and method have not been scientifically established, but common methods may include: *(list all that apply).* Your physician may have alternative methods of evaluation within the range of current practice.

The costs for any diagnostic tests beyond the screening examination are not covered by the trial and must come from your insurance or other sources.

It is necessary for you to receive additional medical attention. I strongly recommend that you see your health care provider in a timely fashion. A copy of your test results has been mailed to your health care provider if you listed one at the time you started in the study. If you do not have a health care provider, or would like your records sent to another health care provider or a recognized specialist, please contact us and we will help you to identify health care providers and arrange to have your records sent.

The screening examination was not intended to be a complete physical examination or a substitute for a visit to a health care provider.

If you have any questions about your examination results or any other aspect of the National Lung Screening Trial, please do not hesitate to call *(Name of SC Coordinator),* National Lung Screening Trial Study Coordinator, at *(Telephone Number).*

Thank you for your participation in the National Lung Screening Trial.

Sincerely,

(Name of Principal Investigator)
Principal Investigator
National Lung Screening Trial

Appendix 6-2 Sample Results Letter to Participants:
Positive Screen – Nodules 0.4 – 0.9 cm

National Lung Screening Trial / Lung Screening Study (NLST/LSS)

(Date)

(Participant Name)
(Participant Address)
(City, State, Zip Code)

Dear (*Participant Name)*:

Recently you received a lung cancer screening examination as part of the National Lung Screening Trial. **Your Spiral CT examination revealed one or more small nodules in your lungs that require further monitoring. These nodules are usually benign (non-cancerous) but in a minority of people may be a lung cancer. A biopsy is not usually done on these small nodules, but if a subsequent exam shows they are growing then further evaluation would be recommended.**

This abnormality requires a follow-up evaluation. The exact follow-up time interval and method have not been scientifically established, but common methods may include: *(list all that apply)*. Your physician may have alternative methods of evaluation within the range of current practice.

The costs for any diagnostic tests beyond the screening examination are not covered by the trial and must come from your insurance or other sources.

It is important that you receive additional medical attention and I strongly recommend that you see your health care provider. A copy of your examination results has been mailed to your health care provider if you listed one at the time you enrolled in the study. If you do not have a health care provider, or would like your records sent to another health care provider or a specialist, please contact us and we will help you to identify a health care provider and arrange to have your records sent.

The screening examination was not intended to be a complete physical examination or a substitute for a visit to a health care provider.

If you have any questions about your examination results or any other aspect of the National Lung Screening Trial, please do not hesitate to call *(Name of SC Coordinator),* National Lung Screening Trial Study Coordinator, at *(Telephone Number).*

Thank you for your participation in the National Lung Screening Trial.

Sincerely,

(Name of Principal Investigator)
Principal Investigator
National Lung Screening Trial

Appendix 6-3 Sample Results Letter to Participants:
Positive Screen – Abnormalities suspicious for lung cancer, no significant change

National Lung Screening Trial / Lung Screening Study (NLST/LSS)

(Date)

(Participant Name)
(Participant Address)
(City, State, Zip Code)

Dear (*Participant Name)*:

Recently you received a lung cancer screening examination as part of the National Lung Screening Trial. The result of your *(chest x-ray/spiral CT)* examination reveals **an abnormality that has not changed significantly since your previous study exam. Although the possibility of lung cancer cannot be ruled out, lack of a change in the abnormality over one year does make it less likely.**

Because there is a chance that the abnormality represents lung cancer, it is important for you to discuss these findings with your primary care physician, who may recommend additional medical follow-up. The exact time interval and method for follow-up have not been scientifically established, but common methods may include: (*list all that apply*).

Your physician may have alternative methods of evaluation within the range of current practice. The costs for any diagnostic tests beyond the screening examination are not covered by the trial and must come from your insurance or other sources.

A copy of your examination results has been mailed to your health care provider if you listed one at the time you enrolled in the study. If you do not have a health care provider, or would like your records sent to another health care provider or a specialist, please contact us and we will help you to identify a health care provider and arrange to have your records sent.

The screening examination was not intended to be a complete physical examination or a substitute for a visit to a health care provider.

If you have any questions about your examination results or any other aspect of the National Lung Screening Trial, please do not hesitate to call *(Name of SC Coordinator)*, Study Coordinator, at *(Telephone Number).*

Sincerely,

(Name of Principal Investigator)
Co-Principal Investigator
National Lung Screening Trial

Appendix 6-4 Sample Results Letter to Participants:
Negative Screen - Clinically significant abnormalities not suspicious for lung cancer

National Lung Screening Trial / Lung Screening Study (NLST/LSS)

(Date)

(Participant Name)
(Participant Address)
(City, State, Zip Code)

Dear *(Participant Name)*:

Recently you received a lung cancer screening examination as part of the National Lung Screening Trial. The result of your *(chest x-ray/spiral CT)* examination was found to be negative for lung cancer; however, other abnormalities were found. The attached report provides you with detailed results of your examination. It is important that you see your physician to discuss follow-up of these abnormalities.

The costs for any diagnostic tests beyond the screening examination are not covered by the trial and must come from your insurance or other sources.

The screening examination was not intended to be a complete physical examination or a substitute for a visit to a health care provider. We recommend that you make an appointment with your health care provider to have these results fully evaluated. A copy of the examination results has been mailed to your health care provider if you listed one at the time you started in the study. If you do not have a health care provider or would like us to recommend one, please contact us.

If you have any questions about the examination results or any other aspect of the National Lung Screening Trial, please do not hesitate to call *(Name of SC Coordinator)*, National Lung Screening Trial Study Coordinator, at *(Telephone Number).*

Thank you for your participation in the National Lung Screening Trial.

Sincerely,

(Name of Principal Investigator)
Principal Investigator
National Lung Screening Trial

Appendix 6-5 Sample Results Letter to Participants:
Negative Screen - Minor abnormalities not suspicious for lung cancer

National Lung Screening Trial / Lung Screening Study (NLST/LSS)

(Date)

(Participant Name)
(Participant Address)
(City, State, Zip Code)

Dear *(Participant Name)*:

Recently you received a lung cancer screening examination as part of the National Lung Screening Trial. The result of your *(chest x-ray/spiral CT)* examination was found to be negative for lung cancer although minor abnormalities were found. The attached report provides you with detailed results of your examination. Although you may want to discuss the abnormality with your health care provider at your next routine visit, there is no need for any immediate follow-up or evaluation.

The screening examination was not intended to be a complete physical examination or a substitute for a visit to a health care provider. A copy of the examination results has been mailed to your health care provider if you listed one at the time you started in the study.

If you have any questions about the examination results or any other aspect of the National Lung Screening Trial, please do not hesitate to call *(Name of SC Coordinator)*, National Lung Screening Trial Study Coordinator, at *(Telephone Number).*

Thank you for your participation in the National Lung Screening Trial.

Sincerely,

(Name of Principal Investigator)
Principal Investigator
National Lung Screening Trial

Appendix 6-6 Sample Results Letter to Participants:
Negative Screen - No significant abnormalities

National Lung Screening Trial / Lung Screening Study (NLST/LSS)

(Date)

(Participant Name)
(Participant Address)
(City, State, Zip Code)

Dear *(Participant Name)*:

Recently you received a lung cancer screening examination as part of the National Lung Screening Trial. The result of your *(chest x-ray/spiral CT)* examination was found to be negative for lung cancer. No abnormal findings were seen.

The screening examination was not intended to be a complete physical examination or a substitute for a visit to a health care provider. A copy of the examination results has been mailed to your health care provider if you listed one at the time you started in the study. No further follow-up or evaluation is necessary at this time.

If you have any questions about the examination results or any other aspect of the National Lung Screening Trial, please do not hesitate to call *(Name of SC Coordinator)*, National Lung Screening Trial Study Coordinator, at *(Telephone Number).*

Thank you for your participation in the National Lung Screening Trial.

Sincerely,

(Name of Principal Investigator)
Principal Investigator
National Lung Screening Trial

Appendix 6-7 Sample Results Letter to Participants: Inadequate

National Lung Screening Trial / Lung Screening Study (NLST/LSS)

(Date)

(Participant Name)
(Participant Address)
(City, State, Zip Code)

Dear *(Participant Name)*:

Recently you received a lung cancer screening examination as part of the National Lung Screening Trial. The results of your *(chest x-ray/spiral CT)* examination were uninterpretable. We will contact you shortly to attempt to reschedule a screening examination at a convenient time.

The screening examination was not intended to be a complete physical examination or a substitute for a visit to a health care provider. A copy of the examination results has been mailed to your health care provider if you listed one at the time you started in the study.

If you have any questions about the examination results or any other aspect of the National Lung Screening Trial, please do not hesitate to call *(Name of SC Coordinator)*, National Lung Screening Trial Study Coordinator, at *(Telephone Number).*

Thank you for your participation in the National Lung Screening Trial.

Sincerely,

(Name of Principal Investigator)
Principal Investigator
National Lung Screening Trial

Appendix 6-8 Sample Results Letter to Health Care Providers:
Positive Screen - Abnormalities suspicious for lung cancer

National Lung Screening Trial / Lung Screening Study (NLST/LSS)

(Date)

(Physician Name)
(Physician Address)
(City, State, Zip Code)

RE: Participant Name: (*Participant Name)*
Date of Birth: (*Date of Birth)*
Date of Examination: *(Date of Exam)*

Dear *(Health Care Provider's Name)*:

Recently (*Participant Name)* received a lung cancer screening examination as part of the National Lung Screening Trial. This is an NCI-sponsored scientific study designed to compare chest x-ray and spiral CT as potential screening tests for lung cancer.

(*Participant Name)*'s *(chest x-ray/spiral CT)* examination revealed **abnormal findings. The possibility that these findings represent lung cancer cannot be ruled out.** At the participant's request, we are sending you the attached report, documenting the results of the examination.

It is generally agreed that this abnormality requires a follow-up evaluation. The exact follow-up time interval and method have not been scientifically established, but common methods may include: *(list all that apply)*. You may have alternative methods of evaluation within the range of current practice.

We have contacted (*Participant Name)* and recommended that s/he contact you to discuss these findings. We encourage you to see him/her as soon as possible and discuss diagnostic follow-up options. You may wish to refer *(Participant Name)* to a recognized specialist.

Diagnostic tests that may be indicated for abnormal screening results are beyond the scope of the National Lung Screening Trial. Their costs are not covered by the trial and must come from the participant's insurance or other sources.

If you would like additional information regarding the diagnosis and treatment of lung cancer, including the names of specialists in your area, please contact the *Screening Center*. Since the participant is enrolled in an NCI-sponsored study, it is important that we receive follow-up information. We may be contacting your office at a later date to obtain information on the participant's health status.

We appreciate your cooperation in this important study. If you have any questions about the examination results or any other aspect of the National Lung Screening Trial, please do not hesitate to call *(Name of SC Coordinator)*, National Lung Screening Trial Study Coordinator, at *(Telephone Number).*

Sincerely,

(Name of Principal Investigator)
Principal Investigator
National Lung Screening Trial

Appendix 6-9 Sample Results Letter to Health Care Providers:
Positive Screen – Nodules 0.4 to 0.9 cm

National Lung Screening Trial / Lung Screening Study (NLST/LSS)

(Date)

(Physician Name)
(Physician Address)
(City, State, Zip Code)

RE: Participant Name: (*Participant Name)*
Date of Birth: (*Date of Birth)*
Date of Examination: *(Date of Exam)*

Dear *(Health Care Provider's Name)*:

Recently (*Participant Name)* received a lung cancer screening examination as part of the National Lung Screening Trial. This is an NCI-sponsored scientific study designed to compare chest x-ray and spiral CT as potential screening tests for lung cancer.

(*Participant Name)*'s spiral CT examination revealed **one or more small nodules in the lungs that require further monitoring. Although such small nodules are usually benign, the possibility that these findings represent lung cancer cannot be ruled out.** At the participant's request, we are sending you the attached report, documenting the results of the examination.

It is generally agreed that this abnormality requires a follow-up evaluation. The exact follow-up time interval and method have not been scientifically established, but common methods may include: *(list all that apply)*. You may have alternative methods of evaluation within the range of current practice.

We have contacted (*Participant Name)* and recommended that s/he contact you to discuss these findings. We encourage you to see him/her as soon as possible and discuss diagnostic follow-up options. You may wish to refer *(Participant Name)* to a recognized specialist.

Diagnostic tests that may be indicated for abnormal screening results are beyond the scope of the National Lung Screening Trial. Their costs are not covered by the trial and must come from the participant's insurance or other sources.

If you would like additional information regarding the diagnosis and treatment of lung cancer, including the names of specialists in your area, please contact the *Screening Center*. Since the participant is enrolled in an NCI-sponsored study, it is important that we receive follow-up information. We may be contacting your office at a later date to obtain information on the participant's health status.

We appreciate your cooperation in this important study. If you have any questions about the examination results or any other aspect of the National Lung Screening Trial, please do not hesitate to call *(Name of SC Coordinator)*, National Lung Screening Trial Study Coordinator, at *(Telephone Number).*

Sincerely,

(Name of Principal Investigator)
Principal Investigator
National Lung Screening Trial

Appendix 6-10 Sample Results Letter to Health Care Providers:
Positive Screen – Abnormalities suspicious for lung cancer, no significant change

National Lung Screening Trial / Lung Screening Study (NLST/LSS)

(Date)

(Physician Name)
(Physician Address)
(City, State, Zip Code)

RE: Participant Name: *(Participant Name)*
Date of Birth: *(Date of Birth)*
Date of Examination: *(Date of Exam)*

Dear (*Health Care Provider's Name)*:

Recently *(Participant Name)* received a lung cancer screening examination as part of the National Lung Screening Trial. This is an NCI-sponsored scientific study designed to compare chest x-ray and spiral CT as potential screening tests for lung cancer.

(Participant Name)'s *(chest x-ray/spiral CT)* examination revealed **an abnormality that has not changed significantly since the previous study exam. Although the possibility of lung cancer cannot be ruled out, lack of a change in the abnormality over one year does make it less likely.** At the participant's request, we are sending you the attached report, documenting the results of the examination.

Because there is a chance that the abnormality represents lung cancer, it is generally agreed that this abnormality requires a follow-up evaluation. The exact time interval and method for follow-up have not been scientifically established, but common methods may include: *(list all that apply)*. You may have alternative methods of evaluation within the range of current practice.

We have contacted *(Participant Name)* and recommended that s/he contact you to discuss these findings. We encourage you to see him/her as soon as possible and discuss follow-up options. You may wish to refer *(Participant Name)* to a recognized specialist. The costs for any diagnostic tests beyond the screening examination are not covered by the trial and must come from the participant's insurance or other sources.

If you would like additional information regarding the diagnosis and treatment of lung cancer, including the names of specialists in your area, please contact the *Screening Center*. Since the participant is enrolled in an NCI-sponsored study, it is important that we receive follow-up information. We may be contacting your office at a later date to obtain information on the participant's health status.

We appreciate your cooperation in this important study. If you have any questions about the examination results or any other aspect of the National Lung Screening Trial, please do not hesitate to call *(Name of SC Coordinator)*, National Lung Screening Trial Study Coordinator, at *(Telephone Number).*

Sincerely,

(Name of Principal Investigator)
Co-Principal Investigator
National Lung Screening Trial

Appendix 6-11 Sample Results Letter to Health Care Providers:
Negative Screen – Clinically significant abnormalities not suspicious for lung cancer

National Lung Screening Trial / Lung Screening Study (NLST/LSS)

(Date)

(Physician Name)
(Physician Address)
(City, State, Zip Code)

RE: Participant Name: (*Participant Name)*
Date of Birth: (*Date of Birth)*
Date of Examination: *(Date of Exam)*

Dear *(Health Care Provider's Name)*:

Recently (*Participant Name)* received a lung cancer screening examination as part of the National Lung Screening Trial. This is an NCI-sponsored scientific study designed to compare chest x-ray and spiral CT as potential screening tests for lung cancer.

(*Participant Name)*'s *(chest x-ray/spiral CT)* examination was found to be negative for lung cancer; however, other abnormalities were found. At the participant's request, we are sending you the attached report, documenting the results of the examination. We have recommended that *(Participant Name)* contact you to discuss follow-up of these abnormalities.

This screening examination was not intended to be a complete physical examination or a substitute for a visit to a health care provider. We have contacted (*Participant Name)* and recommended that s/he contact you to discuss these findings and we encourage you to see (*Participant Name)* for any diagnostic follow-up you deem necessary.

Diagnostic tests that may be indicated for any abnormalities observed on the screening examination are beyond the scope of the National Lung Screening Trial. Their costs are not covered by the trial and must come from the participant's insurance or other sources.

We appreciate your cooperation in this important study. If you have any questions about the examination results or any other aspect of the National Lung Screening Trial, please do not hesitate to call *(Name of SC Coordinator),* National Lung Screening Trial Study Coordinator, at *(Telephone Number).*

Sincerely,

(Name of Principal Investigator)
Principal Investigator
National Lung Screening Trial

Appendix 6-12 Sample Results Letter to Health Care Providers:
Negative Screen - Minor abnormalities not suspicious for lung cancer

National Lung Screening Trial / Lung Screening Study (NLST/LSS)

(Date)

(Physician Name)
(Physician Address)
(City, State, Zip Code)

RE: Participant Name: (*Participant Name)*
Date of Birth: (*Date of Birth)*
Date of Examination: *(Date of Exam)*

Dear *(Health Care Provider's Name)*:

Recently (*Participant Name)* received a lung cancer screening examination as part of the National Lung Screening Trial. This is an NCI-sponsored scientific study designed to compare chest x-ray and spiral CT as potential screening tests for lung cancer.

(*Participant Name)*'s *(chest x-ray/spiral CT)* examination was found to be negative for lung cancer although minor abnormalities were found. At the participant's request, we are sending you the attached report, documenting the results of the examination. We have sent the results of this examination to (*Participant Name).* We notified him/her that the findings require no immediate follow-up or evaluations, and suggested that s/he discuss these findings with you at his/her next routine visit, if so desired.

This screening examination was not intended to be a complete physical examination or a substitute for a visit to a health care provider.

We appreciate your cooperation in this important study. If you have any questions about the examination results or any other aspect of the National Lung Screening Trial, please do not hesitate to call *(Name of SC Coordinator),* National Lung Screening Trial Study Coordinator, at *(Telephone Number).*

Sincerely,

(Name of Principal Investigator)
Principal Investigator
National Lung Screening Trial

Appendix 6-13 Sample Results Letter to Health Care Providers:
Negative Screen - No significant abnormalities

National Lung Screening Trial / Lung Screening Study (NLST/LSS)

(Date)

(Physician Name)
(Physician Address)
(City, State, Zip Code)

RE: Participant Name: (*Participant Name)*
Date of Birth: (*Date of Birth)*
Date of Examination: *(Date of Exam)*

Dear *(Health Care Provider's Name)*:

Recently (*Participant Name)* received a lung cancer screening examination as part of the National Lung Screening Trial. This is an NCI-sponsored scientific study designed to compare chest x-ray and spiral CT as potential screening tests for lung cancer.

(*Participant Name)*'s *(chest x-ray/spiral CT)* examination was found to be negative for lung cancer. No abnormal findings were seen. At the participant's request, we are sending you the attached report, documenting the results of the examination. We have written to (*Participant Name)* to notify him/her of these findings and that no further follow-up or evaluations are necessary at this time.

This screening examination was not intended to be a complete physical examination or a substitute for a visit to a health care provider.

We appreciate your cooperation in this important study. If you have any questions about the examination results or any other aspect of the National Lung Screening Trial, please do not hesitate to call *(Name of SC Coordinator),* National Lung Screening Trial Study Coordinator, at *(Telephone Number).*

Sincerely,

(Name of Principal Investigator)
Principal Investigator
National Lung Screening Trial

Appendix 6-14 Sample Results Letter to Health Care Providers: Inadequate

National Lung Screening Trial / Lung Screening Study (NLST/LSS)

(Date)

(Physician Name)
(Physician Address)
(City, State, Zip Code)

RE: Participant Name: (*Participant Name)*
Date of Birth: (*Date of Birth)*
Date of Examination: *(Date of Exam)*

Dear *(Health Care Provider's Name)*:

Recently (*Participant Name)* received a lung cancer screening examination as part of the National Lung Screening Trial. This is an NCI-sponsored scientific study designed to compare chest x-ray and spiral CT as potential screening tests for lung cancer.

(*Participant Name)*'s *(chest x-ray/spiral CT)* examination was uninterpretable. At the participant's request, we are sending you the attached report documenting the results of the examination. We have written to (*Participant Name)* to notify him/her of these findings and that we will attempt to reschedule the examination at his/her earliest convenience.

This screening examination was not intended to be a complete physical examination or a substitute for a visit to a health care provider.

We appreciate your cooperation in this important study. If you have any questions about the examination results or any other aspect of the National Lung Screening Trial, please do not hesitate to call *(Name of SC Coordinator)*, National Lung Screening Trial Study Coordinator, at *(Telephone Number).*

Sincerely,

(Name of Principal Investigator)
Principal Investigator
National Lung Screening Trial

National Lung Screening Trial / Lung Screening Study (NLST/LSS)

CT Scan Technique Information Sheet for Health Care Providers

The CT scan settings below are used for low dose CT screening examinations performed in the NLST at *Screening Center (Local SC).* If follow-up CT examinations are performed, this may be useful information for your local radiology department. Use of these or similar settings may facilitate comparison to the previous examination, and help limit cumulative radiation exposure. If other screen-detected abnormalities also need to be evaluated, different scanner settings or intravenous contrast may be needed.

Screening Center (Local SC) NLST personnel can be reached at *(Telephone Number)* for any questions or assistance.

Screening Center (Local SC) NLST CT Scan Technique

(Record the technical parameters used at the Local SC in the spaces provided below.)

Scanner type: *(Record number of channels.)* multislice

kVp: *(Record kVp.)*

mA: *(Record mA; if using more than one scanner type, specify mA for each.)*

Scan time: *(Number of seconds)*

mAs: *(Record mAs; if using more than one scanner type, specify mAs for each.)*

Detector collimation: *(Record collimation in mm; if using more than one scanner type, specify collimation for each.)*

Table increment: *(Record table increment in mm/rotation; if using more than one scanner type, specify table increment for each.)*

Pitch [table increment/(detector collimation x number of channels)]**:** *(Record pitch; if using more than one scanner type, specify pitch for each.)*

Effective mAs: *(Record effective mAs.)*

Intravenous contrast: None

Reconstructed slice thickness: *(Record reconstructed slice thickness in mm.)*

Slice reconstruction interval: *(Record slice reconstruction interval in mm.)* (contiguous)

7. FOLLOW-UP OF A POSITIVE SCREENING EXAMINATION AND OTHER REPORTED LUNG CANCERS

7.1 Overview of Diagnostic Evaluation and Treatment Information Procedures

Each SC will implement procedures to collect diagnostic evaluation information, including cancer diagnosis, on all participants who have had a positive screening examination. This information is to be obtained in a timely manner following the screening visit. For each confirmed case of primary invasive lung cancer, treatment and cancer progression information will be collected. Certified Tumor Registrars (CTRs) and Medical Record Abstractors (MRAs) from each SC will review the participant's medical records and abstract all diagnostic information regarding follow-up of the positive screen onto the Diagnostic Evaluation (DE) form, all treatment information onto the Treatment Information (TI) form, and all information on progression of the cancer onto the Cancer Progression (CP) form. DE and TI forms will also be completed for all cases of confirmed lung cancer diagnosed on or before December 31, 2009 that arise from sources other than a positive screening examination. CP forms will be completed annually through 2009 for confirmed lung cancers. Additional information regarding these situations can be found in Chapter 8.

Primary cancers of the trachea are classified as primary lung cancers for medical record abstraction purposes. As such, DE, TI, and CP forms are to be completed for these diagnoses.

This chapter will present procedures for the collection and abstraction of the diagnostic evaluation and treatment information by SCs and the tracking of medical record acquisition. Quality assurance measures for medical record abstraction are discussed. In addition, this chapter describes the DE, TI, and CP forms and the letter to request medical records.

7.2 Timeframe for Collection of Medical Records

Medical records documenting diagnostic evaluation should be collected for all participants with positive screening examinations. Documentation of diagnostic evaluation procedures that occur after a positive T_0 or T_1 screen but prior to the earliest of three milestones listed below should be collected. This also applies to those participants with positive screens who were administered the incorrect screening examination. The three milestones are as follows:

- A conclusive diagnosis (either cancer or non-cancer) has been made;
- Twelve months from the date of the positive screen, or
- The next screening examination.

Participants with a positive screening examination at T_2 will be followed from the time of the positive screen and diagnostic evaluation information will be collected until the first of the following situations:

- A conclusive diagnosis (either cancer or non-cancer) has been made;
- Twelve months from the date of the positive screen, if the positive nodule has been stable for at least one year (Comparison result code = B), or
- Twenty-four months from the date of the positive screen, if the positive nodule is newly discovered or has changed (Comparison result code = A). In these instances, a T_3 DE form must be completed in addition to the T_2 DE form. If, however, a conclusive diagnosis (either cancer or non-cancer) is recorded on the T_2 DE form, the T_3 DE form will not be required.

In some instances, diagnostic evaluation procedures relating to a given study year's positive exam will occur in the next year's activity window. In that instance, record the procedures on the DE form for the study year in which the positive screen occurred. For example, diagnostic evaluation procedures that occur during the T_1 activity window but occur as a result of a T_0 positive screen should be recorded on the T_0 DE form. An exception to this occurs when a T_3 DE form is required for a T_2 positive screen with a result code "A," for which no conclusive diagnosis has been determined within twelve months. In this case, the T_3 DE form should include any procedures that occurred after completion of the T_2 DE form and up to twenty-four months after the T_2 screening exam.

The completion of the DE is not limited to those with a positive screening exam. Those participants with a confirmed report of lung cancer after screening has concluded, or those with a negative screening exam but with a confirmation of lung cancer should have medical records collected from the time there is a suspicion of cancer through staging procedures and treatment. This applies to confirmed lung cancers with a diagnosis date on or before December 31, 2009. Medical records will not be collected for lung cancers diagnosed after December 31, 2009. See Chapter 8 for more information on documenting these cancers.

All staging information related to the initial diagnosis should be collected, even if a staging procedure was performed after the date of the initial diagnosis or after the first definitive treatment.

Staging procedures that are recorded should correspond to the TNM or stage of disease classifications recorded in Part C of the DE form. Staging information on cancer recurrence should not be collected.

In the instance of a confirmed primary invasive lung cancer, medical records will be collected to complete the Treatment Information (TI) form. Medical records will also be collected on an annual basis through 2009 in order to complete the Cancer Progression (CP) form.

The SC should conduct a review of all cases with pending medical record requests on a regular basis. It is recommended that the SC check the status of diagnostic evaluation at least every three months. This review will allow adequate time before the window closes to request medical records either not received from an earlier request or inadvertently not requested earlier. In many cases, follow-up to a positive screen will have been completed within six months of the screen.

7.3 Procedures for Contacting Health Care Providers and Hospitals

Information regarding diagnostic procedures, treatment information, or cancer progression should be obtained from a health care provider or hospital. Information should be obtained from the participant when other sources are unavailable, with at least verification of the procedures by reference in the medical records (or verbally) by a health care provider, should the original report of the procedure, treatment, or cancer progression not be available. An exception to this is Item A.1 on the DE form (Did participant undergo diagnostic procedures?), in which the response may be based on participant self-report without subsequent health care provider verbal or written verification. For additional details see the Specifications for Completion of the Diagnostic Evaluation (DE) Form, Appendix 7-3.

If the participant has a follow-up after a positive screen, the SC should collect all records related to the evaluation.

The following lists the contact procedures for obtaining the participant's medical records by mail.

1. The SC will contact the participant four weeks after the result letter has been sent to determine whether follow-up has begun (Section 6.5).

2. The SC will confirm the health care provider's name and office address and establish a contact person at the office prior to mailing the letter requesting medical records. The SC will also confirm information regarding hospitals and their medical records departments.

3. A letter requesting the release of medical records, along with a signed Medical Record Release Authorization Form (Appendix 3-4), will be sent to each health care provider four weeks after the SC has confirmed with the participant that diagnostic follow-up has begun.

4. The SC will re-contact the participant to obtain a more recent Medical Record Release Authorization Form, if needed.

5. The SC will check on the status of the request to the health care provider within three to five business days after the mailing.

6. The SC will re-contact the participant at least every three months to check the status of diagnostic evaluation, if incomplete, until the window of data collection closes.

7. If necessary, the SC will make additional requests for information regarding diagnostic procedures and treatment information related to a positive screen in order to obtain the complete history of the participant's follow-up.

7.4 Letter to Request Medical Records

The CC will provide the SCs with a sample letter to request the participant's medical records (Appendix 7-1). This letter should be adapted by the SC, copied onto SC letterhead, and signed by the Principal Investigator at the SC. The participant's date of birth and the date of the screening visit are included in the letter to assist the health care provider in locating the correct medical records for the participant. The letter requests that the health care provider send photocopies of the patient's medical records dated from the time of the screening visit to the present. The initial request for medical records will be sent approximately two months after the screening visit. This request may need to be sent to multiple health care providers concurrently. In addition, some health care providers may require multiple requests before the complete records are provided. Because it may not be possible to request the complete record, certain key parts have been identified that are needed to complete the DE, TI, and CP forms. These include (for each request):

- Admission history for diagnosis and initial treatment
- History and physical
- Treatment history or reports
- Discharge summary for all hospitalizations related to diagnosis and treatment
- Operative reports
- Radiology reports

- Pathology reports
- Lab reports
- Progress notes and reports of diagnostic work-up and treatment

The letter should also contain the SC Coordinator's name and telephone number in case there are questions.

The SC must enclose a copy of the participant's Medical Record Release Authorization Form (Appendix 3-4) with the letter. The Medical Record Release Authorization Form should also be on SC letterhead and the copy must be legible. The original Medical Record Release Authorization Form must be kept in the participant's study file at the SC. In some instances, the health care provider may not accept the Medical Record Release Authorization Form as sufficient for release of the records. Additional authorization may need to be requested from the participant or the participant's next of kin. In addition, some institutions may require a recent authorization (within six months, for example) or may require the original authorization form. In some cases, hospitals or insurance plans may require the authorization in a specific format. In these special situations, the participant may need to be re-contacted by the SC to obtain a new authorization form.

7.4.1 Collection of Medical Records

The collection of medical records to complete the DE form may involve contacting the health care provider to determine the status of screening follow-up as well as collecting medical records to document the participant's cancer status. **A DE form should always be completed for participants who had a positive screening examination, even if cancer was not diagnosed**. If lung cancer was diagnosed, the SC MRA should obtain diagnostic evaluation and staging information, including the pathology report, as well as lung cancer treatment information. Additionally, the SC MRA should collect information on cancer progression for confirmed primary invasive lung cancers on an annual basis through 2009.

In some cases, the SC may be charged a fee for obtaining copies of medical record documentation. Since the NLST is federally funded research, the SC may be able to obtain a waiver of fees from some institutions.

All medical records collected should be labeled with the PID and kept in the participant's study file. The SC should maintain a telephone log on which the SC staff records comments from the health care provider, clinic, or participant, and the log should also be kept in the participant's study file with the medical records.

7.4.2 Tracking Medical Record Acquisition

Each SC is responsible for tracking the requests to participants for signed Medical Records Release Authorization Forms and to the health care providers for copies of the medical records. The tracking may be done manually using methods such as tickler files or using an automated system. The SC Coordinator will determine the tracking method. The procedures used to obtain medical records and the timeliness with which these procedures are conducted will be monitored by the CC during site visits.

7.5 Abstraction of the Medical Records

Once the records have been obtained, it should be verified that they are in reference to the correct participant and are organized chronologically. A PID label should be attached to each page of the records. Each document should be reviewed for legibility and completeness. Consistency of information between documents should be checked and, if necessary, the health care provider should be contacted to resolve any problems. If the records are not complete, the diagnosing health care provider may need to be contacted for additional information.

The medical record abstraction forms include the DE form (Appendix 7-2), the TI form (Appendix 7-4), and the CP form (Appendix 7-6). The DE form has been developed to standardize the documentation of information concerning diagnostic evaluation and cancer diagnosis, including pathology, histology, and staging evaluation. The Specifications for Completion of the DE Form are provided in Appendix 7-3. The TI form has been developed to document information concerning initial cancer treatments. The Specifications for Completion of the TI Form are provided in Appendix 7-5. The CP form has been developed to document disease progression for all confirmed primary invasive lung cancers. The CP form should be completed during the first two months of the study year following the study year with which the TI form is associated. For example, if the date of a positive T_0 screen is 02/01/03, the DE is completed on 10/15/03, and the TI is completed on 03/01/04 (T_1 study year), then the CP should be completed during the first two months of the T_2 study year and during the first two months

of every following study year through 2009. No CP forms will be expected in 2010. The Specifications for Completion of the CP are provided in Appendix 7-7.

A trained and approved medical record abstractor will abstract information regarding diagnostic evaluation, cancer confirmation, initial treatment, and cancer progression onto the appropriate medical record abstract forms. A nosologist will code non-cancer diagnoses. A certified tumor registrar (CTR), or CTR-eligible individual, is required for coding cancer diagnoses.

7.5.1 Diagnostic Evaluation of Positive Screens and Other Reported Lung Cancers

After organizing the medical records as described in Section 7.5, all diagnostic procedures should be documented on the DE form. Information will be abstracted about the procedures performed to make a diagnosis.

The Diagnostic Evaluation (DE) form is organized into five sections. These sections are described below.

- **Part A: Diagnostic Evaluation and Staging** - This section is used to document procedures performed for the evaluation of suspicion of lung cancer and staging for confirmed primary cancers. In Part A the MRA will document the medical complications of the diagnostic evaluation and staging if primary invasive lung cancer is confirmed and is the final result of the diagnostic evaluation.

- **Part B: Diagnosis Information for Any Condition Other Than Primary Invasive Lung Cancer** - This section is used to record the diagnosis of any abnormality other than primary invasive lung cancer, including date of diagnosis and the ICD-9-CM or ICD-O-3 classification. Diagnosis of cancers other than primary invasive lung cancer should be coded with the appropriate ICD-O-3 code.

- **Part C: Primary Invasive Lung Cancer Diagnosis Information** - This section is used to document the source of the primary invasive lung cancer confirmation, the date and description of the primary invasive lung cancer diagnosis, the ICD-O-3 code, the histologic classification, and TNM staging.

- **Part D: Comments** - This section is used to document notes, comments, and any overflow information while abstracting from the participant's medical record.

- **Part E: Health Care Provider/Hospital Location Information** - This section is used to document all health care providers or hospitals where the participant received diagnostic evaluation for lung cancer.

In conducting medical record abstractions for lung cancer, the SC may encounter some special situations:

- **When no follow-up procedures were performed based on a health care provider's decision that follow-up of a positive screening examination was not necessary:** In such cases, the SC should complete a DE form and document the result of the diagnostic evaluation as "No malignancy." The SC must also record verbatim in Item D.18 (Comments) what the health care provider stated (whether written or verbal) regarding follow-up and the date the health care provider made the statement. In the situation where only a participant's report can be obtained that his/her health care provider decided not to conduct follow-up on a positive screening examination, this information should be collected and the reason recorded in Item D.18 (Comments). Refer to the Specifications for Completion of the DE form (Appendix 7-3) for specific instructions for completing the form in such situations.

- **When the participant receives an A result – "Abnormalities suspicious for lung cancer," or a B result – "Abnormalities suspicious for lung cancer, no significant change," and chooses not to follow up further with his/her health care provider:** In such cases the SC should encourage the participant to follow up with his/her health care provider either in person or by telephone as recommended in the A and B results letters, the premise being that the decision for follow-up care ultimately lies with the participant's health care provider. If the participant ultimately chooses to follow up with his/her health care provider by telephone or in person, the SC must complete a DE form as outlined above. If the participant still does not follow up with his/her health care provider either by telephone or in person, then an MDF should be completed for the DE form.

- **When the participant begins diagnostic evaluation but then decides (against the recommendation of his/her health care provider) not to continue:** In such cases, the SC should complete a DE form and document the result of the diagnostic evaluation as "No information available" and provide an explanation of the situation. Refer to the Specifications for Completion of the DE form (Appendix 7-3) for specific instructions for completing the form in such situations.

- **When the decision of the health care provider is to not pursue a diagnostic work-up following a positive screen immediately, but to observe the participant for any change that might prompt an evaluation (i.e., "watchful waiting"):** In such cases, the SC should wait to complete the DE form until twelve months following the screening examination or until the participant's next screening exam, whichever occurs first. The SC must then determine if any work-up has occurred in the interim, and, if so, obtain copies of the medical records. If no specific plan for follow-up has occurred within twelve months of the screening examination or by the time of the next screening examination, the SC should complete a DE form and document the result of the diagnostic evaluation as "No malignancy, determined by clinical evaluation only – no pathologic proof."

- **When a participant is diagnosed with a cancer that is metastatic to the lung:** Only **primary invasive lung cancer** should be recorded in the cancer section of the DE form. If the diagnostic evaluation for a suspected lung cancer reveals a lung malignancy that is a metastasis from another cancer site, the result of the diagnostic

evaluation should be recorded as either "Malignancy other than primary invasive lung cancer, with or without lung metastasis, confirmed by histology or cytology," or "Malignancy other than primary invasive lung cancer, with or without lung metastasis, diagnosed by clinical evaluation only – no pathologic proof," and the primary cancer type should be recorded in Part B of the DE form.

- **When the record indicates that an abnormality was identified and no conclusive diagnosis was made:** The health care provider indicates that it is necessary to re-evaluate the abnormality with a procedure that might make a conclusive diagnosis two to three months after the regular window of data collection has ended for that study year. The result of the diagnostic evaluation should be coded as "Further follow-up required." There must be a heightened suspicion for the possibility of primary invasive lung cancer, but the evaluation was not completed prior to the close of the study year window. This code should not be used when the record clearly indicates that follow-up, or "active surveillance," is scheduled on a regular basis, such as every six months, to ensure stability of an abnormality. The reasons for further follow-up should be written in Item D.18 (Comments) of the DE form. In these instances, the SC must continue to collect medical records and update the DE form when more information becomes available. A DE form with a result of "Further follow-up required" must be updated before the close of the next study year window (i.e. a T_1 DE form with "Further follow-up required" must be updated before the end of the T_2 study year.)

The DE form should always be completed before the TI and CP forms because the TI and CP forms are only required when a primary invasive lung cancer has been confirmed and documented on the DE form. The follow-up of positive screening examinations may show that the participant had a non-malignant condition or other cancer. In such situations, the TI and CP forms should not be completed.

Note: In the event a participant is given an incorrect screening exam that yields a positive result, a DE form should be completed. The SC should NOT enter this DE form into IDEAS, but rather hold the DE form in the participant's file. The CC will maintain an internal monitoring report to track DE forms of participants who were given incorrect screening examinations. It also is the responsibility of each SC to monitor these participants and ensure adequate follow-up for the positive screening examination.

7.5.2 Collection of Treatment Information for Confirmed Lung Cancers

The Treatment Information (TI) form is organized into three sections. These sections are described below.

- **Part A: Initial Treatment Information** - This section is used to document all **initial** treatment information for the primary invasive lung cancer diagnosis.

- **Part B: Comments** - This section is used to document notes, comments, and any overflow information while abstracting from the participant's medical record.

- **Part C: Health Care Provider/Hospital Location Information** - This section is used to document all health care providers or hospitals where the participant received treatment for lung cancer.

Initial treatment is defined as the first course of treatment for confirmed primary invasive lung cancer. Usually this is treatment that begins within six months of diagnosis. If treatment begins after six months, it is possible that this treatment is not related to the initial disease, but perhaps to a recurrence of the disease. Cases in which primary therapy is begun *after* the initial six-month period should be referred to the SC Principal Investigator for adjudication. If it is unclear as to whether the treatment is primary therapy, photocopies of the appropriate information should be sent to the MRA Coordinator at the CC, who will send the information to the NCI for final adjudication. NCI will decide with the CC the best way in which to handle each specific case.

7.5.3 Collection of Cancer Progression Information for Confirmed Lung Cancers

The Cancer Progression (CP) form is organized into two sections. These sections are described below.

- **Part A: Progressive Disease Following Treatment of First Primary Invasive Lung Cancer –** This section is used to document any progression of the confirmed primary invasive lung cancer in terms of enlargement of the original tumor, metastatic disease, or recurrence of the lung cancer.

- **Part B: Development of Second Primary Invasive Lung Cancer –** This section is used to document the occurrence of a second primary invasive lung cancer after the participant has received treatment for the first primary invasive lung cancer.

Information on cancer progression for participants with confirmed primary invasive lung cancers will be collected annually through 2009.

7.5.4 Timeframe for Abstraction of Medical Records

The SC should complete and submit the DE form, and in the case of primary invasive lung cancer, the TI and CP forms, in a timely manner. For a DE form, for an abnormal suspicious nodule discovered at T_0 or T_1, the endpoint for data collection following a positive screen is when a conclusive

diagnosis is made, twelve months from the date of the positive screening exam, or the date of the next screening exam, whichever occurs first. For an abnormal suspicious nodule newly discovered at T_2, the diagnostic information will be collected until the first of the following situations: a conclusive diagnosis (either cancer or non-cancer) has been made, or twenty-four months from the date of the positive screen, (Result code = A). For a TI form, the endpoint for data collection is one year from the date of cancer diagnosis. A TI form can usually be submitted much earlier than this, as data are collected on only the first course of treatment, which usually begins within six months of the date of cancer diagnosis. The CP form should be submitted on an annual basis through 2009 beginning in the study year immediately following the study year in which the TI form was submitted. The CP form should be submitted within two months of the opening of the next study year window for the participant. SCs may want to get the information regarding cancer progression at the time information for the ASU is obtained.

Information on medical complications should be collected for twelve months after the start of diagnostic evaluation for cancer cases other than primary invasive lung cancer, and for six months after a diagnosis for primary invasive lung cancer cases. Any complications noted after the DE form has been entered into IDEAS should be added to the DE form and entered into IDEAS. Medical complications that result from the treatment of a primary invasive lung cancer should not be recorded on the DE form.

7.6 Missing Data Form

In some cases, the SC will not be able to complete a DE, TI, or CP form. The following are the conditions under which an MDF should be completed (refer to Chapter 11 for additional information on the completion of the MDF):

- When the participant receives an A result – "Abnormalities suspicious for lung cancer," or a B result - "Abnormalities suspicious for lung cancer, no significant change," and the participant informs the SC that he/she does not intend to get follow-up. In such cases the SC should encourage the participant to follow up with his/her health care provider either in person or by telephone as recommended in the A and B results letters. If the participant ultimately chooses to follow up with his/her health care provider by telephone or in person, then the SC must complete a DE form. However, if the participant still does not follow up with his/her health care provider either by telephone or in person, then an MDF should be completed for the DE form. The reason why the participant did not receive follow-up should be determined and the appropriate code should be recorded on the MDF. If no reason is given, code 19 (No reason given) should be used. If the reason does not fall into one of the specified codes, code 88 (Other, SPECIFY) should be used. If the participant explicitly states that s/he refuses to follow up, the MDF-DE can be completed at the time of refusal. Otherwise, the MDF can be completed when the SC determines that the lack of action

on the participant's part indicates that s/he will not be obtaining diagnostic follow-up. An MDF should not be completed for a participant who begins diagnostic evaluation, but discontinues the evaluation before a diagnosis has been made. In these cases, a DE form should be completed with a result of "No information available."

- When the participant does not see the utility in following up with his or her health care provider by phone or in person following a positive screening exam. The reason code on the MDF should be, "No perceived benefit," code 26.

- When a participant refuses treatment following a diagnosis of primary invasive lung cancer, an MDF for the TI form should be completed. If the reason why the participant did not receive treatment can be determined, the appropriate code on the MDF should be selected. If there is no reason given, code 19 (No reason given) should be used. If the reason does not fall into one of the specified codes, code 88 (Other, SPECIFY) should be used.

- When the participant had no follow-up for a positive lung screen due to other, more critical illnesses, complete an MDF for the DE form with a reason code of 10 (Physical illness/cognitive impairment).

- When the SC is unable to locate the participant to determine whether or not s/he had follow-up for a positive screen, code 02 (Can't locate) should be recorded on the MDF, or when the SC is unable to locate the participant to obtain consent to collect medical records, code 02 (Can't locate) should be recorded on the MDF.

- When the participant dies before seeking follow-up for a positive lung screen, complete an MDF for the DE form with a reason code of 03 (Deceased).

- When the participant sought follow-up attention but has subsequently died and the SC is unable to contact the participant's family for consent to obtain medical records, or the participant's family is contacted, but refuses to consent to the release of the participant's medical records, code 22 (Family refuses to release medical records) should be recorded on the MDF.

- When the medical records necessary for the completion of the DE, TI, or CP forms are not available because the records cannot be located, code 25 (Medical records lost) should be recorded on the MDF.

- When the medical records necessary for the completion of the DE, TI, or CP forms are not available because of institutional refusal, or foreign or non-local institution, code 23 (Health care provider refuses to release medical records) or code 24 (Health care provider does not respond to record requests) should be recorded on the MDF.

- When a participant refuses to sign a Medical Record Release Authorization Form for the SC to obtain medical records to document diagnostic follow-up procedures, code 21 (Participant refuses to release medical records) should be recorded on the MDF.

An MDF should <u>not</u> be completed in place of the DE form if the SC or the participant consults a health care provider for follow-up and the health care provider indicates, based on the screening examination result and/or a review of the participant's medical record, that no follow-up is

necessary (see Section 7.5.1). In this situation, a DE form should be completed as described in the form completion specifications (Appendix 7-3).

7.7 Quality Assurance of Medical Record Abstraction

The quality assurance plan for medical record abstraction consists of two components: the registration and training of SC staff and the central re-abstraction of lung cancer cases and a certain percentage of positive screens regardless of outcome by medical record abstractors at the CC. These components are described in detail in the following sections.

7.7.1 Registration and Training of SC Staff

Each abstractor and certified tumor registrar (CTR) will be required to submit qualifications, training, and certification to the CC for review. The Record of Experience, Credentials, and Training Form (ECT, Appendix 11-5) must be completed and sent to the CC for each abstractor and nosologist to document the abstractor's and nosologist's qualifications to perform competently for the NLST/LSS. The CC will review the ECTs. If the qualifications meet the NLST/LSS criteria, the CC will recommend approval to the NCI. If the qualifications do not meet the requirements, the CC will request an exception approval from the NCI if appropriate.

The medical record abstractor should have knowledge of medical record terminology, anatomy, physiology, and concepts of disease in addition to basic medical coding instruction. The abstractor must have a minimum of two years on-the-job experience abstracting medical records. The nosologist should possess at least one of the following credentials from each list for ICD-9-CM and ICD-O-3 coding.

<u>For ICD-9-CM coding (in order of desirability):</u>

a. Certified Coding Specialist (CCS) - This individual has obtained sufficient coding expertise either through education, experience, or a combination of the two to pass an advanced coding examination and become certified.

b. Registered Health Information Technician (RHIT) - A RHIT has at least an associate's degree in Medical Record Science and has passed an accreditation examination. This individual must meet RHIT continuing education requirements to maintain accreditation.

c. Registered Health Information Administrator (RHIA) - A RHIA has at least a bachelor's degree in Medical Record Science and has passed a registration examination. This individual must meet RHIA continuing education requirements to maintain registration. If a person is a RHIA and is currently doing medical coding, then s/he may be qualified to conduct medical coding. If, however, a RHIA is doing supervisory work, then s/he may not be up-to-date on medical coding.

For ICD-O-3 coding and TNM staging:

a. Certified Tumor Registrar (CTR or CTR-eligible) - A CTR is an individual who has passed the Certification Examination for Cancer Registrars, which is offered by the National Cancer Registrars Association's (NCRA) Council on Certification. To maintain a certified status, a CTR must meet current continuing education requirements of the NCRA. To be eligible to take the Certification Examination, an individual must meet one of the following requirements as of the application deadline:

   - Two years full-time equivalent experience in the cancer registry field and a high school or GED diploma and two semesters/three quarters of college-level courses in human anatomy and/or physiology, one semester of medical science/biology and one semester of medical terminology.

   - Successful completion of an NCRA Accredited Formal Education Program curriculum, plus 160 hour practicum.

   - One year full-time equivalent experience in the cancer registry field and successful completion of a minimum of an Associate's degree or equivalent in an approved college level curriculum in a recognized allied health field as determined by NCRA's Council on Certification.

   - One year full-time equivalent experience in the cancer registry field and successful completion of a minimum of an Associate's degree or equivalent and license or certification in a recognized allied health field as determined by NCRA's Council on Certification.

   - One year full-time equivalent experience in the cancer registry field and successful completion of a Master's degree or higher college level curriculum in a recognized allied health field as determined by NCRA's Council on Certification.

The staff person in charge of medical record abstraction at the CC will facilitate regular communication between the SCs and the NCI on medical record abstraction issues and problem resolution as well as coordinate training. A staff person at each SC will assist the CC in monitoring internal quality assurance at their SC and provide input for resolution of medical record abstraction issues.

7.7.2 Central Re-abstraction of Selected Lung Cancer Cases

The goal of re-abstracting medical records at the CC is to provide feedback to the medical record abstractors, to standardize the abstracting process, and to ensure a high level of accuracy. Appendix 7-8 presents the Medical Records Abstraction Quality Assurance Plan that will be followed at the CC.

For NLST/LSS, all SCs will be asked to submit to the CC a copy of the medical records for the first ten cancer and the first ten non-cancer cases completed. For all SCs, one hundred percent (100%) of the cases with primary invasive lung cancer will be re-abstracted. Five percent (5%) of all non-lung cancer cases following a positive screen will be randomly selected for re-abstraction. In addition, each year a selected number of TI and CP forms will be randomly selected for QA review. The proportion of non-cancer cases that are re-abstracted may change as the study continues, depending on the performance of the SC MRAs. The CC MRA Coordinator will identify cases for re-abstraction and request copies of the medical records for each case. When requested, the SC MRA will send a legible, chronologically organized copy of the medical record, with all participant identifiers removed, including the date of birth. The medical record should be submitted to the CC within two weeks of the request. The CC MRAs, who are also trained in the study protocol, will re-abstract the selected medical records. The CC MRA Coordinator will review the results, note any discrepancies between the CC and SC forms, and provide the results to the SC and to the NCI. A CC Edit Form (see Appendix 11-7) will be sent electronically to the SC to address any issues. The SC will make updates to the hard copy form and to the IDEAS database as needed. Should the SC MRA disagree with the suggested changes, s/he will contact the CC to discuss the issue. The goal of the CC will be to re-abstract the records and to provide follow-up of any discrepancies within eight weeks of receipt. If recurrent errors with abstracting the medical records persist despite feedback, the CC MRA Coordinator, after consultation with the NCI, may begin closer monitoring of the MRA efforts at the particular SC and consider the need for remedial training and/or additional review.

7.8 Tracking, Reporting, and Monitoring Medical Record Abstraction Activities

DE, TI, and CP forms should be manually edited at the SC. See Chapter 11, Section 11.6.1 for information regarding editing of forms. Upon completion of the forms, they should be entered into IDEAS. The original DE, TI, and CP forms, as well as the medical records and CC Edit Forms, should be filed in the participant's study file. If required, the medical records should be copied, with the copy retained and the original returned to the health care provider or institution from which they were

requested. The SC Coordinator should use the Expected Forms Report (Appendix 11-18) and/or the Medical Abstraction Report (Appendix 11-22) to track the completion of the DE, TI, and CP forms.

Appendices for Chapter 7

Appendix 7-1 Sample Letter to Request Medical Records

National Lung Screening Trial / Lung Screening Study (NLST/LSS)

(Date)

(Name of Institution)
(Address of Institution)
(City, State, Zip Code)

RE: *(Name of Participant)*
Date of Birth: *(Participant DOB)*
Date of Screening Visit: *(Date of Visit)*

Dear *(Physician/Head of Medical Records Department)*:

The person named above is a participant in the National Lung Screening Trial, an NCI-sponsored study of lung cancer screening, and has indicated that s/he was intending to be seen at your institution for follow-up of an abnormal *(chest x-ray/spiral CT exam).*

We would appreciate receiving copies of medical records pertaining to the abnormal chest x-ray/ spiral CT screening exam. Please include all relevant records from the date of the screening exam to the present time. Enclosed you will find a copy of the consent form authorizing release of information. Please send the following information in regards to any diagnostic follow-up done after *(Date of spiral CT/chest x-ray exam).*

- ____ Admission history
- ____ History and physical
- ____ Discharge summary for all hospitalizations related to diagnosis
- ____ Operative reports
- ____ Radiology reports
- ____ Pathology reports
- ____ Lab reports
- ____ Progress notes and reports of diagnostic work-up
- ____ Treatment records or summaries

If you have no records for this patient, please check here (___ we have no records) and return this letter.

Thank you for the time and effort involved in complying with our request. If you have any questions, please do not hesitate to call *(Name of SC Coordinator)* at *(Telephone Number).*

Sincerely yours,

(Name of Principal Investigator)
Principal Investigator
National Lung Screening Trial

Appendix 7-2 Medical Record Abstract Diagnostic Evaluation Form (DE)

National Lung Screening Trial / Lung Screening Study (NLST/LSS)

MEDICAL RECORD ABSTRACT
DIAGNOSTIC EVALUATION FORM (DE)

Administrative Section

☐ Please mark box if another DE form has been submitted for this participant.

Date Abstracted: |__|__| / |__|__| / |2|0|__|__|

Abstractor ID: |___|___|___|___|

Screening Center ID: |___|___|

Study Year: T|___|

☐ Please mark box if T_3 completion is due to T_2 positive screen.

Date of Screening Exam or CDF Completion Date:
|__|__| / |__|__| / |2|0|__|__|

Purpose of Abstract:
☐ Initial Abstract
☐ Re-abstract for QA

Multiple DE #_____

Initials Complete: _____

Initials QC: _____

DE

Participant ID Label

PART A: DIAGNOSTIC EVALUATION AND STAGING

1. Did participant undergo diagnostic procedures?
   ☐ Yes
   ☐ No, Physician Report (GO TO A.5)
   ☐ No, Participant Self-Report (GO TO A.5)

2. Reason for initial visit for diagnostic evaluation: (Mark all that apply)
   ☐ Symptomatic
   ☐ Follow-up of positive NLST screen
   ☐ Other (SPECIFY)_____

3. Diagnostic Evaluations **(DO NOT RECORD RESULTS OF SCREENING SPIRAL CT SCAN OR CHEST X-RAY EXAM)**

PROCEDURE #	DATE OF PROCEDURE (MO/DAY/YR)	TYPE OF PROCEDURE (USE PROCEDURE CODES ON THE NEXT PAGE)
1	|__|__|-|__|__|-|2|0|__|__|	|__|__|
2	|__|__|-|__|__|-|2|0|__|__|	|__|__|
3	|__|__|-|__|__|-|2|0|__|__|	|__|__|
4	|__|__|-|__|__|-|2|0|__|__|	|__|__|
5	|__|__|-|__|__|-|2|0|__|__|	|__|__|
6	|__|__|-|__|__|-|2|0|__|__|	|__|__|
7	|__|__|-|__|__|-|2|0|__|__|	|__|__|
8	|__|__|-|__|__|-|2|0|__|__|	|__|__|
9	|__|__|-|__|__|-|2|0|__|__|	|__|__|
10	|__|__|-|__|__|-|2|0|__|__|	|__|__|
11	|__|__|-|__|__|-|2|0|__|__|	|__|__|
12	|__|__|-|__|__|-|2|0|__|__|	|__|__|
13	|__|__|-|__|__|-|2|0|__|__|	|__|__|
14	|__|__|-|__|__|-|2|0|__|__|	|__|__|
15	|__|__|-|__|__|-|2|0|__|__|	|__|__|
16	|__|__|-|__|__|-|2|0|__|__|	|__|__|
17	|__|__|-|__|__|-|2|0|__|__|	|__|__|
18	|__|__|-|__|__|-|2|0|__|__|	|__|__|

Appendix 7-2 Medical Record Abstract Diagnostic Evaluation Form (DE)

PROCEDURE CODES	
01 = Biopsy – Endobronchial	29 = Lymphadenectomy/lymph node sampling
04 = Biopsy – Lymph node, scalene (supraclavicular) nodes	30 = Mediastinoscopy/Mediastinotomy
03 = Biopsy – Lymph node, other **(Specify)**	62 = MRI – Abdomen (or liver)
09 = Biopsy – Open surgical	31 = MRI – Bone
52 = Biopsy – Percutaneous adrenal	32 = MRI – Brain
02 = Biopsy – Percutaneous liver	33 = MRI – Chest
53 = Biopsy – Percutaneous transthoracic yielding histology	35 = MRI – Other **(Specify)**
50 = Biopsy – Thoracoscopic	39 = Pulmonary function tests/spirometry
10 = Biopsy – Transbronchial	11 = Radiograph – Bone
08 = Biopsy – Other **(Specify)**	13 = Radiograph – Chest
54 = Bronchoscopy without biopsy or cytology	15 = Radiograph – Comparison with historical images
14 = Clinical evaluation	37 = Radiograph – Other **(Specify)**
55 = CT – Abdomen (or liver)	40 = Radionuclide scan – Bone
17 = CT – Abdomen and pelvis	41 = Radionuclide scan – Brain
18 = CT – Brain	63 = Radionuclide scan – FDG-PET scan
56 = CT – Chest, plus contrast-enhanced nodule densitometry	68 = Radionuclide scan – Fusion PET/CT scan
57 = CT – Chest, diagnostic	64 = Radionuclide scan – Gallium
69 = CT – Chest, low dose spiral	42 = Radionuclide scan – Liver
23 = CT – Chest, limited thin section of nodule	65 = Radionuclide scan – Somatostatin receptor
70 = CT – Chest, limited thin section of entire lung	66 = Radionuclide scan – Ventilation/perfusion lung
71 = CT – Chest and abdomen	67 = Radionuclide scan - Other **(Specify)**
72 = CT – Chest, abdomen, and pelvis	43 = Resection
22 = CT – Other **(Specify)**	47 = Thoracentesis
58 = Cytology – Bronchoscopic	49 = Thoracoscopy
59 = Cytology – Percutaneous transthoracic	46 = Thoracotomy
25 = Cytology – Sputum	48 = Ultrasound **(Specify)**
60 = Cytology – Other **(Specify)**	36 = Other **(Specify)**
61 = Echocardiography	99 = Unknown
27 = Fluoroscopy	

COMPLICATION CODES	
01 = Acute respiratory failure	17 = Hospitalization post procedure
02 = Allergic reaction	37 = Infection requiring antibiotics
03 = Anaphylaxis	31 = Injury to vital organ or vessel
05 = Blood loss requiring transfusion	21 = Myocardial Infarction
06 = Bronchopulmonary fistula	22 = Pain requiring referral to a pain specialist
29 = Bronchial stump leak requiring tube thoracostomy or other drainage for >4 days	23 = Pneumothorax requiring tube placement
	32 = Prolonged mechanical ventilation over 48 hours post-operatively
07 = Bronchospasm	25 = Respiratory arrest
08 = Cardiac arrest	26 = Rib fracture(s)
09 = Cardiac arrhythmia requiring medical intervention	33 = Thromboembolic complications requiring intervention
10 = Cerebral vascular accident (CVA)/stroke	34 = Vaso-vagal reaction
11 = Congestive heart failure (CHF)	27 = Vocal cord immobility/paralysis
12 = Death	28 = Wound dehiscence
30 = Empyema	36 = Wound infection
14 = Fever requiring antibiotics	35 = Other **(Specify)**
16 = Hemothorax requiring tube placement	99 = Unknown

4. Were there any medical complications as a result of diagnostic evaluation and staging?

☐ No **(Go to A.5)** ☐ Yes (COMPLETE TABLE BELOW) ☐ Unknown

DATE OF COMPLICATION MO	DAY	YEAR	MEDICAL COMPLICATIONS (USE COMPLICATION CODES ON PREVIOUS PAGE; LIST MORE THAN ONE IF NEEDED.)
☐☐	☐☐	20☐☐	____
☐☐	☐☐	20☐☐	____
☐☐	☐☐	20☐☐	____
☐☐	☐☐	20☐☐	____
☐☐	☐☐	20☐☐	____

5. Result of Diagnostic Evaluation for Primary Invasive Lung Cancer:

- ☐ No malignancy, confirmed by histology or cytology
- ☐ No malignancy, determined by clinical evaluation only-no pathologic proof
- ☐ Primary invasive lung malignancy confirmed histologically
- ☐ Primary invasive lung malignancy confirmed cytologically
- ☐ Primary invasive lung malignancy diagnosed by clinical examination only-no pathologic proof
- ☐ Malignancy other than primary invasive lung cancer, with or without lung metastasis, confirmed by histology or cytology
- ☐ Malignancy other than primary invasive lung cancer, with or without lung metastasis, diagnosed by clinical evaluation only – no pathologic proof
- ☐ Diffuse idiopathic pulmonary neuroendocrine hyperplasia
- ☐ Neoplasm of uncertain behavior
- ☐ Carcinoma in situ
- ☐ Squamous dysplasia
- ☐ Atypical adenomatous hyperplasia
- ☐ Further follow-up required **(Go to PART D)**
- ☐ No information available **(Go to PART D)**

PART B: DIAGNOSIS INFORMATION FOR ANY CONDITION OTHER THAN PRIMARY INVASIVE LUNG CANCER

6a. Non-Cancer Diagnosis ☐ Yes ☐ No

ICD-9-CM Classification:

_____ . _____ Nosologist/Abstractor ID #: _____

6b. Date of Diagnosis: _____

____ / ____ / 20__

7a. Cancer Diagnosis, Site other than primary invasive lung ☐ Yes ☐ No

ICD-O-3 Cancer Classification: (TO BE COMPLETED BY CTR OR CTR-ELIGIBLE STAFF)

C___ - ____ - __ - __

TOPOGRAPHY MORPHOLOGY BEHAVIOR GRADE

7b. ____ / ____ / 20__ ____

Date of Diagnosis CTR ID #

7c. Is this Cancer Metastatic to Lung? ☐ Yes ☐ No

PART C: PRIMARY INVASIVE LUNG CANCER DIAGNOSIS INFORMATION

8. Date of Primary Invasive Lung Cancer Diagnosis (Mo/Day/Year):
|___|___| / |___|___|/ |_2_|_0_|___|___|

9. Photocopy of Report Confirming Primary Invasive Lung Cancer (**MARK ONE**):

- ☐ No Report/Clinical Examination (**COMPLETE C10**)
- ☐ Histology/Histopathology (**GO TO C11**)
- ☐ Cytology/Cytopathology (**GO TO C11**)
- ☐ Report exists but cannot be obtained (**COMPLETE C10**)

10. Verbatim Description of Primary Invasive Lung Cancer Diagnosis:
(COMPLETE ONLY WHEN ANSWER TO C9 IS "NO REPORT/CLINICAL EXAMINATION," or "REPORT EXISTS BUT CANNOT BE OBTAINED.")

11a. ICD-O-3 Cancer Classification: **(TO BE COMPLETED BY CTR OR CTR-ELIGIBLE STAFF)**

|_C_|___|___|___| - |___|___|___|___| - |___| - |___|
TOPOGRAPHY MORPHOLOGY BEHAVIOR GRADE

CTR ID #
(For Items C.11a, b, & C14-C17 only)
|___|___|___|___|

11b. Source: ☐ Cytology ☐ Histology ☐ Combined (CYTOLOGY and HISTOLOGY) ☐ Clinical
(IF COMBINED or CLINICAL, MUST COMMENT IN D.18)

12. Primary Tumor Location (**MARK ALL THAT APPLY**):

- ☐ Right upper lobe
- ☐ Right middle lobe
- ☐ Right lower lobe
- ☐ Left upper lobe
- ☐ Left lower lobe
- ☐ Lingula
- ☐ Right hilum
- ☐ Left hilum
- ☐ Right main stem bronchus
- ☐ Left main stem bronchus
- ☐ Carina
- ☐ Mediastinum
- ☐ Unknown
- ☐ Other: **(SPECIFY):**_____

13. Pathology Lesion Size (maximum dimension): |__|__|__| mm

14a. Pathologic Type for Primary Invasive Lung Cancer: (TO BE COMPLETED BY CTR OR CTR-ELIGIBLE STAFF)

|__|__|__|__|__|/|__|

14b. Date of Pathologic Confirmation: |__|__| / |__|__|/ |2|0|__|__|

15. Grade of Primary Invasive Lung Cancer: (TO BE COMPLETED BY CTR OR CTR-ELIGIBLE STAFF)

- ☐ Grade cannot be assessed (GX)
- ☐ Well differentiated (G1)
- ☐ Moderately differentiated (G2)
- ☐ Poorly differentiated (G3)
- ☐ Undifferentiated (G4)
- ☐ Unspecified in pathology report
- ☐ Unknown – Pathology report missing

16. TNM Staging for Primary Invasive Lung Cancer: (TO BE COMPLETED BY CTR OR CTR-ELIGIBLE STAFF)

16a. TNM Clinical Staging:
(MARK ONE BOX ONLY IN EACH COLUMN.)

☐ YES ☐ NO

16b. TNM Pathological Staging:
(MARK ONE BOX ONLY IN EACH COLUMN.)

☐ YES ☐ NO

Neoadjuvant therapy prior to staging?

☐ YES ☐ NO

Primary Tumor (T) Codes:	Nodal Involvement (N) Codes:	Distant Metastases (M) Codes:	Primary Tumor (T) Codes:	Nodal Involvement (N) Codes:	Distant Metastases (M) Codes:
☐ T_x	☐ N_x	☐ M_x	☐ T_x	☐ N_x	☐ M_x
☐ T_0	☐ N_0	☐ M_0	☐ T_1	☐ N_0	☐ M_0
☐ T_1	☐ N_1	☐ M_1	☐ T_2	☐ N_1	☐ M_1
☐ T_2	☐ N_2	☐ Not available	☐ T_3	☐ N_2	☐ Not available
☐ T_3	☐ N_3		☐ T_4	☐ N_3	
☐ T_4	☐ Not available		☐ Not available	☐ Not available	
☐ Not available					

17. Record Stage: COMPLETE ONLY IF ANY PART OF THE TNM PATHOLOGICAL STAGING IS UNKNOWN.
(TO BE COMPLETED BY CTR OR CTR-ELIGIBLE STAFF)

Stage Only:

- ☐ Occult Carcinoma
- ☐ IA
- ☐ IB
- ☐ IIA
- ☐ IIB
- ☐ IIIA
- ☐ IIIB
- ☐ IV
- ☐ Not available

VALCSG (Small Cell only):

- ☐ Limited
- ☐ Extensive
- ☐ Not available

Summary Staging:

- ☐ Localized
- ☐ Regional
- ☐ Distant
- ☐ Not available

Appendix 7-2 Medical Record Abstract Diagnostic Evaluation Form (DE)

PART D: COMMENTS

18. Comments: ☐ No ☐ Yes (SPECIFY)

☐ Continued

Appendix 7-2 Medical Record Abstract Diagnostic Evaluation Form (DE)

PART E: HEALTH CARE PROVIDER/HOSPITAL LOCATION INFORMATION

19. HEALTH CARE PROVIDER FOR DIAGNOSTIC EVALUATION:

a. NAME: MR./MRS./MISS/MS./DR. | FIRST | MIDDLE | LAST | (JR., SR., etc.)

STREET ADDRESS 1 | STREET ADDRESS 2 | SUITE OR OFFICE NO

CITY | STATE | ZIP

TELEPHONE 1 ( ) | TELEPHONE 2 ( ) | FAX NUMBER: ( )

Medical Record / Chart Number

b. NAME: MR./MRS./MISS/MS./DR. | FIRST | MIDDLE | LAST | (JR., SR., etc.)

STREET ADDRESS 1 | STREET ADDRESS 2 | SUITE OR OFFICE NO

CITY | STATE | ZIP

TELEPHONE 1 ( ) | TELEPHONE 2 ( ) | FAX NUMBER: ( )

Medical Record / Chart Number

20. HOSPITAL OR CLINIC FOR DIAGNOSTIC EVALUATION:

a. NAME OF HOSPITAL OR CLINIC

STREET ADDRESS 1 | STREET ADDRESS 2 | SUITE OR OFFICE NO

CITY | STATE | ZIP

TELEPHONE 1 ( ) | TELEPHONE 2 ( ) | FAX NUMBER: ( )

Medical Record / Chart Number

b. NAME OF HOSPITAL OR CLINIC

STREET ADDRESS 1 | STREET ADDRESS 2 | SUITE OR OFFICE NO

CITY | STATE | ZIP

TELEPHONE 1 ( ) | TELEPHONE 2 ( ) | FAX NUMBER: ( )

Medical Record / Chart Number

Specifications for Completion of the Medical Record Abstract Diagnostic Evaluation Form (DE)

This form is to be completed by the SC Coordinator, Medical Record Abstractor, and a Tumor (or Cancer) Registrar who is also a Certified Tumor Registrar (CTR) or CTR-eligible. Items that are to be completed by a nosologist, CTR, or CTR-eligible individual are specified. The abstractor should complete all other non-administrative items. The nosologist will be required to complete Items B.6a and B.6b. The CTR or CTR-eligible individual will be required to complete Items B.7a and B.7b and C.11a and C.11b (ICD-O-3 Cancer Classification and Source), C.14a & C.14b (Histopathologic Type for Primary Invasive Lung Cancer), C.15 (Histopathologic Grade for Primary Invasive Lung Cancer), C.16a & C.16b (TNM Staging for Primary Invasive Lung Cancer), and C.17 (Stage). The SC Coordinator should complete the Administrative Section. This form should be completed in black or blue ink.

Some guidelines for general abstracting are presented below:

- Sources of information for abstracting the variable items on the form should be used in priority order by best source. The preferred sources of information are a physician, hospital, or tumor registry; information should only be obtained from the participant when other sources are unavailable. Written documentation from the physician or the medical record is preferable to obtaining information verbally. An exception to this is Item A.1 (Did participant undergo diagnostic procedures?), in which the response may be based on participant self-report. Any information obtained verbally needs to be documented on a telephone log or memo with SC letterhead to provide details and serve as a record in lieu of medical records, and should be placed in the participant's file.

- Medical records documenting diagnostic evaluation and staging procedures should be collected for all positive screens and for all reported lung cancers confirmed by a Cancer Diagnosis Form (CDF). For positive screens at T_0 and T_1, records should be collected on all diagnostic and staging procedures until a conclusive diagnosis is made, the next screening exam is completed, or twelve months from the date of the positive screen, <u>whichever comes first</u>. For the time frame for DE's collected at T_2 see Chapter 7, Section 7.2. Medical records documenting complications of diagnostic evaluations or staging procedures should also be collected. These records should be collected for complications that occur up to twelve months from the time diagnostic procedures began for participants without a diagnosis of primary invasive lung cancer. In the event of a cancer diagnosis, medical complications related to the diagnostic or staging procedures should be collected for an additional six months after the diagnosis. Medical complications that result from treatment of a primary invasive lung cancer should not be recorded.

- Before beginning abstraction, the medical record documents should be placed in chronological order. The diagnostic/staging procedures should be abstracted chronologically. If, however, a diagnostic or staging procedure is identified and added after the form has been completed, it is not necessary to shift all of the data to maintain the chronological order; the new procedure may be added at the end of the appropriate item.

- This form includes items requiring that data be entered verbatim, such as recording "other (Specify)" and recording information in Item D.18 (Comments). The abstractor should be sure to use clear and legible handwriting when completing these items.

- If the medical record contains unclear, discrepant, or conflicting information for any item, the SC Coordinator and/or Principal Investigator should first be consulted for a resolution and for making an appropriate coding decision, prior to contacting the CC.

- When recording information in the Comments section (Item D.18), it is necessary to appropriately identify to which item the comment refers. Appropriate identification will aid in the analysis of Comments data. Throughout the specifications, identifying phrases have been suggested for use when recording information in Comments.

Below are some guidelines for the collection of diagnostic evaluation information:

- If the DE form is being completed as a result of a positive screen, the screening examination should not be recorded as a part of the diagnostic evaluation. In addition, the comparison read conducted as part of the NLST screening exam should not be recorded.

- If the DE form is being completed as a result of a positive screen, information regarding diagnostic procedures that occurred prior to the participant's screening date should not be recorded. If the DE form is being completed for a reported lung cancer that has been confirmed by a Cancer Diagnosis Form, all diagnostic evaluations and staging procedures should be recorded.

- If the diagnostic evaluation has not resulted in a final diagnosis of malignancy or a diagnosis of one of the specific lung conditions listed in A.5, record the result of the diagnostic evaluation as either "No malignancy, confirmed by histology or cytology" or "No malignancy, determined by clinical evaluation only -- no pathologic proof." There are two exceptions to this:

  - When the diagnostic evaluation procedures are discontinued by the participant and it cannot be determined conclusively whether the participant had a malignancy. In this situation it is not appropriate to record a conclusive diagnosis, but rather to record "No information available" and a verbatim description of the situation in Item D.18 (Comments).

  - When the diagnostic evaluation shows an abnormality (either new or present on the screening exam), and a definitive procedure is provided that could make the conclusive diagnosis in two to three months after the window for data collection closes. In this situation it is <u>not</u> appropriate to record "No malignancy, condition not listed above," but rather to record "Further follow-up required." The reason for further follow-up should be recorded in Item D.18 (Comments). The SC must continue to collect medical records and update the DE form when information becomes available.

- It is the SC's responsibility to encourage timely follow-up of positive screens. If, despite SC efforts, the participant does not initiate follow-up of a positive screen for

several months, the SC must still adhere to the timeline set forth above for acquisition of medical records.

- All staging information related to the initial diagnosis of primary invasive lung cancer should be collected (the staging procedures that resulted in the TNM or stage of disease classifications recorded in Part C of the DE form). Staging information on lung cancer recurrence or cancer progression should not be collected.

- If multiple primary invasive lung cancers are diagnosed at the same time (i.e., as part of the same diagnostic evaluation process and prior to the first definitive treatment), it is necessary to complete a separate DE for each primary. "Multiple DE # ___" in the Administrative Section of the DE allows the SC Coordinator to indicate to which multiple primary invasive lung cancer the DE refers.

- Primary cancers of the trachea are classified as primary lung cancers for medical record abstraction purposes. In the event of a diagnosis of primary cancer of the trachea, Item A.5, Result of Diagnostic Evaluation for Primary Invasive Lung Cancer, should be recorded as primary invasive lung malignancy. The ICD-O-3 code for cancer of the trachea should be recorded in Part C. Since there is no TNM staging schema for cancers of the trachea, only summary staging information should be recorded.

- In the event of a T_3 DE form being completed because of a T_2 screening exam comparison read result of "A" for which there was no definitive diagnosis recorded on the T_2 DE form, the SC Abstractor should use the following guidelines:

  - The abstractor should contact the participant approximately six months after the completion of the T_2 DE form. If the T_2 DE form was completed early in the T_2 study year so that six months later, the participant has not yet entered his/her T_3 study year, the abstractor should wait to contact the participant when the T_3 study year opens. Abstractors should contact these participants to obtain information about further follow-up but should not encourage such follow-up.

  - In the instance that follow-up occurred beyond what was recorded on the T_2 DE form, the abstractor should collect all available information until a diagnosis is made or until 24 months after the T_2 screening exam date, whichever occurs first.

  - In the instance that follow-up did not occur beyond what was recorded on the T_2 DE form because the participant's health care provider deemed it unnecessary, even if this decision occurred during the T_2 study year, the abstractor should make a note in the participant's folder and continue to follow up with the participant in six month intervals until the T_3 DE form is due (24 months after the date of the T_2 screening exam). If, at the end of this time period, no additional follow-up occurred, the abstractor should complete the T_3 DE form and should mark Item A.1 "No, physician report" if medical records or communications with the physician confirms the advice, or "No, participant self-report" if the participant relayed the physician's advice but no direct proof is provided.

A definitive diagnosis on the T_2 DE form is represented by all responses except "No malignancy, determined by clinical evaluation only – no pathologic proof," "Further follow-up required," or "No information available."

Specifications for completing each item of the form are as follows:

Administrative Section:

Participant ID Label: Affix a PID label in the box provided at the top of the form.

Please mark the box if another DE form(s) has been submitted to the CC for this participant.

Date Abstracted: Record the date the medical record was abstracted. This is the date the form was completed. Zero fill month and day, if necessary, and record the last two digits of the year (e.g., 02/07/2002).

Abstractor ID: Record the four-digit staff ID number assigned to the individual who is abstracting the medical record and completing the DE form. If more than one abstractor completes the DE form, the SC Coordinator should determine which abstractor is responsible for the content of the form – it is this abstractor's ID number that should be recorded here. If this abstract is for QA ("re-abstract for QA"), this should be the QA abstractor's ID number.

- The nosologist and CTR or CTR-eligible individual should not record his/her staff ID number in this item. There is space for the nosologist and CTR or CTR-eligible individual to record his/her staff ID number for the specific items which s/he completes in Items B.6a, b; B.7a, b, c; C.11a, b, and C.14 through C.17.

Screening Center ID: Record the two-digit SC ID number.

Study Year: Indicate the study year the participant was in when s/he received the positive screening exam being followed-up or enter the study year the participant was in when the lung cancer was reported. In the case of a T_3 DE form being completed for a T_2 positive screen with a comparison result "A," the study year should be entered as T_3.

Please mark box if T_3 completion is due to T_2 positive screen: Check this box if the T_3 DE form is being completed because the result of the T_2 screening exam was positive (suspicious for lung cancer).

Date of Screening Exam or CDF Completion Date: Indicate the date of the screening exam done in the study year described above. In the case of a T_3 DE form being completed for a T_2 positive screen with a comparison result "A," the date of the T_2 screening exam should be entered in this space. If the cancer was reported via the ASU or a CNF, then the date the CDF was completed should be entered in the space provided. If the cancer reported on the ASU or CNF was the result of a work-up for a positive screen enter either the date that the CDF was completed or the date of the positive screen, which ever occurred first. Zero fill month and day, if necessary, and record the last two digits of the year (e.g., 02/07/2002).

Purpose of Abstract: This form may be used for either the initial abstracting of medical record information, or for repeat abstraction of the medical record for quality assurance. Mark the box corresponding to the purpose of the abstract as follows:

- **Initial abstract:** Medical record information is being abstracted for the first time to follow up a positive screen.

- **Re-abstract for QA:** Medical record information which has already been abstracted to follow up a positive screen is being re-abstracted for the purpose of quality assurance. (This will not apply to the SC MRAs.)

Multiple DE #: The purpose of this item is to link information arising from additional primary invasive lung cancers diagnosed simultaneously with or subsequent to the first primary invasive lung cancer within the same study year. Synchronous primary invasive lung cancers (diagnosed simultaneously) may have different histologies or be located in different parts of the lung and each should be recorded on a separate DE form. A second primary invasive lung cancer diagnosed within the same study year also should be recorded on a separate DE. Indicate the sequence number for the DE form as it relates to the primary cancer. The first DE form completed is always sequence number "1" and should be abstracted on a separate DE form. If this primary cancer is the second primary diagnosed (in chronological date order), enter number "2" entered for the multiple DE #. If it is the third, enter "3," etc. DEs in the subsequent study years also should start with the number "1".

NOTE: Cases in which no primary invasive lung cancer or only one primary invasive lung cancer was diagnosed, should be coded as "1."

Part A: Diagnostic Evaluation and Staging:

This section refers to the diagnostic evaluation. Abstracting these data will require careful review of the participant's medical records from one or more hospitals, clinics, or physicians' offices.

If this form is being completed for a positive screen, do not include information from any physician/hospital visits or procedures that took place prior to the participant's screening examination, even if these visits or procedures are related to a diagnosis that was made after the participant was screened. If the DE is being competed for a diagnosis of primary invasive lung cancer and this is unrelated to a screening exam, the abstractor will collect information once there is a suspicion for primary invasive lung cancer.

1. **Did participant undergo diagnostic procedures?** The purpose of this item is to document whether diagnostic procedures were performed. Mark the box corresponding to the most appropriate response. If the DE form is being completed to document a lung cancer confirmed on a Cancer Diagnosis Form, this question must be marked "Yes."

   Yes: The record indicates that diagnostic procedures were performed. This includes situations when diagnostic procedures were performed to follow up a positive screening examination (chest x-ray or spiral CT scan). In the latter situation, the internal review should be recorded as the first Diagnostic/Staging procedure.

   No, Physician Report: The medical record indicated or the health care provider reported to the SC that based on review of the NLST/LSS screening examination results, and possibly any medical history prior to the screening examination, no follow-up of the positive screening exam was deemed necessary. The health care provider's decision is not based on a visit with the participant. Mark "No malignancy, determined by clinical evaluation only – no pathologic proof" for Item A.5 (Result of Diagnostic Evaluation for Primary Invasive Lung Cancer) and complete Item D.18 (Comments) and Part E (Health

Care Provider/Hospital Location Information). The reason provided by the physician and the date should be recorded in D.18 (Comments). This category can only be used when the decision that follow-up is unnecessary is made without any additional information from the participant. If the information is obtained verbally from the health care provider or his/her office, document this on a telephone log or a memo with SC letterhead and place in the participant's folder.

In the event of a T_3 DE form being completed for a T_2 screening exam comparison read result (Item E.3a) of "A" for which there was no definitive diagnosis recorded on the T_2 DE form, the decision to not follow up the positive screening exam can be applied to the T_3 DE form, even if the decision was made during the T_2 study year.

No, Participant Self-Report: The participant reported that the physician reviewed the NLST/LSS screening examination results, and possibly other medical history prior to the screening examination, and deemed no additional follow-up was necessary. Mark "No malignancy, determined by clinical evaluation only – no pathologic proof" for Item A.5 (Result of Diagnostic Evaluation for Primary Invasive Lung Cancer) and complete Item D.18 (Comments) and Part E (Health Care Provider/Hospital Location Information). The reason the physician gave the participant why additional follow-up was unnecessary and the date should be recorded in D.18 (Comments).

In the event of a T_3 DE form being completed for a T_2 screening exam comparison read result (Item E.3a) of "A" for which there was no definitive diagnosis recorded on the T_2 DE form, the decision to not follow up the positive screening exam can be applied to the T_3 DE form, even if the decision was made during the T_2 study year.

- *Before accepting a participant self-report, the SC should first attempt to obtain written documentation from the participant's physician. If written documentation cannot be obtained from the physician, the SC should then attempt to obtain verbal confirmation from the physician's office that the physician did not recommend additional follow-up of the positive screening examination. In cases where <u>only</u> the participant's report of the physician's recommendation can be obtained, this box should be marked. Information from the participant's report should be documented on a telephone log or memo with SC letterhead and placed in the participant's file.*

2. **Reason for Initial Visit for Diagnostic Evaluation:** The purpose of this item is to identify the participant's motivation for seeking clinical evaluation. In the absence of evidence stating otherwise, it is assumed that if a participant seeks medical care within twelve months of a positive screen, it is for the purpose of follow-up of that positive screen. If medical care is sought more than twelve months after a positive screen, the NCI assumes that it is not for follow-up to a positive screen. Mark the boxes corresponding to all reasons that apply as follows:

   - **Symptomatic:** The record indicates that the participant went for a clinical evaluation because s/he was experiencing symptoms that are suspicious for possible lung cancer. This should be checked if the medical records note that symptoms worrisome for lung cancer motivated the participant to seek an initial evaluation.

   - **Follow-up of positive NLST screen:** The record indicates that the participant went for an initial clinical evaluation to follow up on a positive NLST screen, *within twelve months* of the positive screen.

- **Other (SPECIFY):** If the record indicates that the participant went for a clinical evaluation for a reason other than those listed, specify the reason in the space provided. This includes instances where the participant went for an initial clinical evaluation to follow up on a non-positive (Result code C or D) NLST screen.

3. **Diagnostic Evaluations:** The following are general guidelines for identifying diagnostic and staging procedures in the medical record:

   - Only procedures involved in diagnostic evaluation or staging and that are clearly stated in the record (including outpatient records, discharge summaries, and operative reports) should be recorded. If the operative report and/or discharge summary is missing, procedures noted in doctor's notes or a history taken *after* the procedure may be used to record a diagnostic/staging procedure. For example, if a chest CT report is missing but a clinician confirms in a subsequent note that it was done it should be recorded. Do not record those procedures that are planned but no report or documentation that it was carried out can be found. Every attempt should be made to obtain the appropriate documentation. *Please call the CC if there is any uncertainty about recording diagnostic/staging procedures.*

   - Following a positive screening examination (chest x-ray or spiral CT scan) at T_0 or T_1, the SC should collect information on all diagnostic and staging procedures until a conclusive diagnosis is made, the next screening exam is completed, or twelve months from the date of the positive screen, whichever comes first. For the time frame for DE's collected at T_2 see Chapter 7, Section 7.2. If the DE form is being completed to document a lung cancer confirmed on a Cancer Diagnosis Form, the SC should collect information on all diagnostic and initial staging procedures. (The abstractor should not collect diagnostic procedures related to the investigation of a potential complication, cancer progression or cancer recurrence.) If information about additional diagnostic procedures is found after the DE form has been completed and entered into IDEAS, the DE form should be modified.

   For each diagnostic/staging procedure performed, complete the following items:

   Procedure #: Enter the information regarding each procedure on a separate row.

   Date of Procedure: Record the month, day, and year that the diagnostic/staging procedure was performed. If it is not clear from the record the date that the diagnostic/staging procedure was performed, year and month can usually be assessed, even if the exact date cannot be determined. In this situation, record the exact month and year and the day as "99." Zero fill month and day, and record the last two digits of the year (e.g., 02/07/2002).

   Type of Procedure: Enter the number corresponding to the type of diagnostic/staging procedure performed. Refer to the Procedure Codes for the list of diagnostic and staging procedures for primary invasive lung cancer. When the procedure on the Procedure Code list indicates "SPECIFY," describe the body site or the actual procedure, as appropriate, in the space next to the code. The following are guidelines for coding type of procedure:

   - **Laboratory Tests**: Pulmonary function tests (PFTs) and cytology (sputum, bronchial washing/brushing) reports are the only laboratory tests to be recorded. All PFTs performed prior to the date of the lung cancer diagnosis or a conclusion that there is no lung cancer should be recorded. If primary invasive lung cancer

can not be confirmed within the window of data collection then all PFTs performed should be recorded.

- **Clinical Evaluation**: A clinical evaluation (clinical assessment) by a health care provider should be recorded in this section if there is a reference to either the NLST screening exam or follow-up to a screening for cancer. A clinical evaluation is defined as a visit to a health care provider for medical care and may include a history and physical examination of the lungs, or may include a history about the positive screening examination only. A telephone conversation with a health care provider is not considered a clinical evaluation. A subsequent clinical evaluation that only serves to repeat or confirm previous findings as in a follow-up medical appointment should not be recorded. The following examples illustrate how the form should be completed to document a clinical evaluation:

  - If a visit to a health care provider includes a history with some reference to the NLST screening exam as well as a physical examination of the lungs, this is considered a clinical evaluation. Document this clinical evaluation using procedure code 14 = Clinical evaluation. For subsequent examinations, to include consultations, record only those that give additional history, a new physical exam finding, or a new/different assessment or plan.

  - If a visit to a health care provider includes *only* a history and not a physical examination of the lungs, this is also considered a clinical evaluation. Record this procedure using 14 = Clinical evaluation. Again, only those visits to a health care provider that result in additional or new information should be recorded. Do not record subsequent clinical evaluations unless the evaluation contributes to the confirmation of or ruling out of cancer. While a subsequent referral to a consultant can result in a very detailed clinical evaluation, if there is no new information that helps to rule out cancer, it should not be recorded. (Generally, only the initial clinical evaluation will be recorded.)

- **Telephone Conversation:** When the decision not to have further follow-up of an abnormality from the NLST/LSS screening exam occurs in a phone conversation after some evaluation has occurred, document this using procedure code 36 = Other (SPECIFY), and specify "telephone conversation." This would be the only example for which a telephone conversation would be recorded as a procedure.

- **Chest Radiographs:**

  - 13 = Radiograph – chest should be used to code a diagnostic chest x-ray. Use this code when a diagnostic chest x-ray is in the record, regardless of whether a particular view is specified such as PA, lateral, bucky, kyphotic, or lordotic. Record the first chest x-ray in the record but do not record subsequent ones unless new information to rule in or to rule out lung cancer is noted.

  - 15 = Comparison with historical images should be coded in the instance of an internal referral or other review of multiple scans. Use this code only to note when a film is reviewed, compared, and interpreted at a different time from the original reading of the film. This code may also be used when a clinician is reviewing films at a later date to determine the significance of the abnormal finding. (This would be equivalent to rendering a second opinion.) Do not record the comparison with the prior screen performed at the NLST screening exam. Also do not include the comparison of films done as a component to

the interpretation of radiographic film if the comparison is noted prior to rendering the final impression of the film.

- **Biopsy and Cytology Procedures:**

  - Needle Aspiration Biopsy: There are several codes for a fine needle aspiration of the lung as described below:

    - Use code 58 if a cytology is obtained from bronchoscopic needle aspiration.

    - Use code 59 if a cytology is obtained through percutaneous transthoracic aspiration is specified.

    - Use code 60 if cytology was obtained but the method was not specified.

  - 08 = Biopsy - Other (SPECIFY): Record the site of the biopsy next to the code, not the method of biopsy. Use this code to record both incisional and excisional biopsies of organs other than the lung if the biopsy type does not match one of the existing codes.

- **Surgical Approaches:** Record the surgical approach documented in the medical record separately from related diagnostic and staging procedures, e.g. thoracotomy, thoracoscopy (to include video assisted thorascopic surgery), mediastinoscopy, or mediastinotomy.

- **Lymph Node Procedures**:

  - If lymph node sampling and lymph node dissection are both performed, this should be considered as one procedure and recorded only once as 29 = Lymphadenectomy/lymph node sampling.

  - Lymph node removal accompanying surgical resection should be coded as a separate procedure. Code both procedures separately under the appropriate codes.

- **Resection:** While a lobectomy and pneumonectomy are treatments for lung cancer, record 43 = Resection if a wedge resection, lobectomy, or pneumonectomy provides diagnostic/staging information. If done during the same procedure/ operation, then consider the surgical removal collectively as one resection. An exception is when a procedure involves an interruption to allow for an intraoperative pathology review for diagnosis. If cancer is confirmed, the surgery continues with an additional excision that would not have been done had cancer not been confirmed. For example, if cancer is not previously confirmed and a diagnostic wedge resection of the lung nodule is done and upon intraoperative pathology review, cancer is confirmed so a lobectomy is now performed, these procedures should be recorded separately. The diagnostic wedge resection should be recorded as an open surgical biopsy and the lobectomy as a resection. (On the TI form they will be recorded separately as well but as a wedge resection and lobectomy, respectively.) The type of resection may be specified on the TI form. If surgical resections are done during different procedures/operations, record separately using "43 = Resection" for each procedure.

- **CT Scans**: If CT procedures for multiple locations appear in the record as a combined procedure, they should be recorded as a single procedure with one date (e.g. code 17 = CT - Abdomen and pelvis, code 71 = CT - Chest and abdomen, and code 72 = CT - Chest, abdomen, and pelvis). If these procedures are performed on the same date and appear in the record as separate procedures, the abstractor should record them separately. Record what is ordered for the CT scan. For example, if a CT of the chest is ordered, and some of the cuts include organs in the upper abdomen, record as CT of the chest and not CT of the chest/upper abdomen combined.

- **"**CT – Chest, diagnostic" (code 57) includes any routine chest CT, either spiral or non-spiral, and either with or without contrast. Include with code 57 those chest CT scans that are a thin section of the entire chest (i.e., not limited thin section) and those spiral CT scans that are at not low dose. Special studies that are limited to a portion of the chest, such as a limited thin section CT of the nodule (code 23), a limited thin section CT of the entire lung (code 70), contrast enhanced densitometry (code 56), and low dose spiral CT (code 69) are recorded separately.

- **"**CT- Chest, low dose spiral" (code 69) includes CT exams performed as part of follow-up that are at doses similar or identical to those used in NLST.

The following is a list of many of the diagnostic and staging procedures that are named on the DE form. The procedures are listed in numerical order. A definition or explanation is provided for each of the procedures and for some procedures an example is given. Examples, when provided, directly follow the definition or explanation and are in italics.

01 **Biopsy – Endobronchial:** Biopsy obtained from within the bronchial tubes by bronchoscopy. An endobronchial lesion is usually visualized and then biopsied.

Bronchoscopy report: The Olympus fiberoptic bronchoscope was introduced transnasally. The cords and larynx were visualized and were normal. The bronchoscope was passed through the cords without difficulty into the trachea which was visualized and was normal. It was passed from the trachea down to the carina which was visualized and was normal. It was passed from the carina into the left side of the tracheobronchial tree. It was passed down into the left mainstem to the secondary carina. The left lower lobe bronchus was visualized. There were tumor implants extending up both the medial and lateral walls. Washings, brushings, and biopsies were done here. There was minimal bleeding which stopped with dilute epinephrine lavage. The left upper lobe and lingular bronchi were visualized and there were tumor implants there as well which extended back up into the left mainstem.

02 **Biopsy - Percutaneous liver:** A biopsy done by inserting a long needle through the skin between two of the right lower ribs into the liver to remove a sample of liver tissue.

03 **Biopsy – Lymph Node, other (Specify):** A biopsy in which a lymph node or a piece of a lymph node is removed for examination under a microscope. Use this if only one lymph node is removed. Specify the type of lymph node such as cervical, mediastinal, hilar, etc. Do not use if multiple lymph nodes are obtained, instead for multiple lymph nodes biopsies use lymphadenectomy or lymph node sampling.

04 **Biopsy – Lymph node, scalene (supraclavicular) nodes:** Biopsy of the supraclavicular lymph nodes above the clavicle or collar bone.

08 **Biopsy – Other (Specify):** Other biopsies not otherwise specified by a procedure code. The line next to the procedure code should be used to record the site of the biopsy, not the method of the biopsy.

09 **Biopsy – Open surgical:** Tissue obtained during surgery, typically through a thoractomy incision. For NLST, when a wedge resection is done prior to lobectomy for diagnostic purposes, this is to be coded as an open surgical biopsy.

10 **Biopsy – Transbronchial:** Utilized to obtain tissue from a pulmonary lesion too peripheral to be visualized directly from the bronchoscope. Biopsy forceps/ needle passed into the lesion using radiographic (fluoroscopic) guidance.

Bronchoscopy report: The bronchoscope was advanced into the left mainstem bronchus and subsequently into the left upper lobe, lingual, and left lower lobe bronchi. No endobronchial obstructing lesions were identified but there was mild chronic bronchitis. The bronchoscope was then withdrawn to the trachea and then advanced into the right mainstem bronchus and subsequently into the right upper lobe, right intermediate bronchus, right middle lobe, and right lower lobe bronchi. No endobronchial obstructing lesions were visualized, but there was moderate chronic bronchitis. Bronchial brushings were obtained for cytology and cultures from the right upper lobe. Multiple transbronchial lung biopsies were obtained from the right upper lobe, right middle lobe, and right lower lobe to evaluate for infiltrating bronchogenic carcinoma.

11 **Radiograph – Bone:** Radiographic (x-ray) examination of the bones.

13 **Radiograph – Chest:** X-ray of the chest cavity for the evaluation of the lungs and thoracic bones. This may also be referred to as CXR, PA, PA and Lateral CXR. Record only those chest x-rays that are screening/diagnostic for cancer, and not those to check for complications post procedures.

14 **Clinical Evaluation:** A clinical evaluation is defined as a visit to a health care provider for medical care and may include a history and physical examination of the lungs, or may include a history about the positive screening examination only. Record the clinical evaluation if there is a reference to either the NLST screening exam or follow-up to a screening for cancer. A telephone conversation is not considered a clinical evaluation. Generally, only the initial clinical evaluation will be recorded. Subsequent clinical evaluations that only serve to repeat or confirm previous findings should not be recorded. Subsequent clinical evaluations may be recorded if they contribute substantially to the confirmation of or ruling out of cancer, provide new and/or additional history, or provide new and/or different assessment or plan.

15 **Radiograph – Comparison with historical images:** Should be coded in the instance of an internal referral or other review of multiple scans. Use this code only to note when a film is reviewed, compared, or interpreted at a different time from the original reading of the film. This code may also be used when a

clinician is reviewing a film at a later date to determine the significance of the abnormal reading – e.g. rendering a second opinion.

Physician's notes: CT scan of the chest (04/23/03). It was not compared to the prior CT scans that were done with the Radiology Screening Research Protocol. It does not demonstrate the right-sided nodules that were seen before. There is the left lower lobe superior segment lesion that is essentially unchanged from that of four months ago. On this particular scan, it continues into the abdomen, and there is a nodular appearance in the adrenal gland. There are also some scattered small lymph nodes that were not mentioned in the screening scan, but all less than a centimeter. Additionally, there is a questionable lesion in the liver, and there are prior old fractures noted of his left ribs.

17 **CT – Abdomen and pelvis:** Computed Tomography or Computed Transaxial Tomography. Procedure wherein a computerized tomography scanner is used to scan and produce an axial image of an organ or area of the body. An abdominal and pelvis CT combined is one CT scan of the abdomen which is extended to include the pelvic region as one procedure, rather than viewing the abdomen and pelvis as two separate CT scans.

18 **CT – Brain:** Computed Tomography or Computed Transaxial Tomography of the brain. Procedure wherein a computerized tomography scanner is used to scan and produce an axial image of an organ or area of the body. May be used to evaluate known or suspected primary or secondary neoplasm, cystic lesions, seizure disorders, etc.

22 **CT – Other (Specify):** Other CT scans not otherwise specified by a procedure code. The line next to the procedure code should be used to record the type of CT scan done.

23 **CT – Chest, limited thin section of nodule:** Computed Tomography or Computed Transaxial Tomography utilizing thin sections of a nodule or a limited section of the lung.

Technique: Multiple noncontrast axial images were obtained through the chest using a 5 mm. slice thickness. In addition, multiple thin section 1.25 mm. slice thickness axial images were obtained through multiple pulmonary nodules.

Technique: Noncontrast CT images were obtained through the chest and upper abdomen. 1 mm. slices were obtained through the nodule in question.

Technique: Unenhanced helical images of the chest were made. In addition, thin section images were made of a nodule in the left upper lobe.

25 **Cytology – Sputum:** The study of the anatomy, physiology, pathology, and chemistry of cells obtained from sputum. Sputum is material, especially mucus or mucopurulent material, that is expelled by coughing and then spitting out what came up with the cough.

27 **Fluoroscopy:** An imaging technique commonly used to obtain real-time images of the internal structures of a patient through the use of a fluoroscope. In its

simplest form, a fluoroscope consists of an x-ray source and fluorescent screen between which a patient is placed. However, modern fluoroscopes couple the screen to an x-ray image intensifier and CCD video camera allowing the images to be played and recorded on a monitor.

29 **Lymphadenectomy/Lymph node sampling:** Lymphadenectomy consists of the surgical removal of one or more groups of lymph nodes. It is almost always performed as part of the surgical management of cancer.

30 **Mediastinoscopy/Mediastinotomy:** A surgical procedure used to view areas of the mediastinum, the cavity behind the breastbone that lies between the lungs. The organs in the mediastinum include the heart and its vessels, the lymph nodes, trachea, esophagus, and thymus. Mediastinoscopy is most commonly used to detect or stage cancer. It is also ordered to detect infection and to confirm diagnosis of certain conditions and diseases of the respiratory organs. A mediastinoscope is passed through a suprasternal notch incision, allowing access to some carinal and hilar nodes, to peribronchial and paratracheal nodes, and to the superior posterior mediastinum.

31 **MRI – Bone:** Magnetic Resonance Imaging of the bone. Procedure in which the patient is placed in a strong magnetic field and radiofrequency pulses are transmitted into the patient in an extremely controlled and defined manner. An MRI provides 3-D images of the body's interior, delineating muscle, bone, blood vessel, nerve, organ, and tumor tissue.

32 **MRI – Brain:** Magnetic Resonance Imaging of the brain. Procedure in which the patient is placed in a strong magnetic field and radiofrequency pulses are transmitted into the patient in an extremely controlled and defined manner. An MRI provides 3-D images of the body's interior, delineating muscle, bone, blood vessel, nerve, organ, and tumor tissue.

33 **MRI – Chest:** Magnetic Resonance Imaging of the chest. Procedure in which the patient is placed in a strong magnetic field and radiofrequency pulses are transmitted into the patient in an extremely controlled and defined manner. An MRI provides 3-D images of the body's interior, delineating muscle, bone, blood vessel, nerve, organ, and tumor tissue.

35 **MRI – Other (Specify):** Other MRI not otherwise specified by a procedure code. The line next to the procedure code should be used to record the site of the MRI.

36 **Other (Specify):** A diagnostic or staging procedure other than those listed in the procedure codes.

37 **Radiograph – Other (Specify):** Includes any type of x-ray film study other than those listed in the procedure codes. The line next to the procedure code should be used to record the site of the x-ray.

39 **Pulmonary function tests/spirometry:** Spirometry (meaning *the measuring of breath*) is the most common of the Pulmonary Function Tests (PFTs), measuring lung function, specifically the measurement of the amount (volume) and/or speed

(flow) of air that can be inhaled and exhaled. Spirometry is an important tool used for assessing conditions such as asthma, cystic fibrosis, and COPD. The following is a list of the components of a PFT.

- **TLC**: Total lung capacity is the volume of air in the lungs after maximal inspiration.
- **VC**: Vital capacity is the maximum volume of air exhaled from the point of maximum inspiration.
- **FVC**: Forced vital capacity is the vital capacity measured during a maximally forced expiratory effort.
- **FRC**: Functional residual capacity is the volume of air remaining in the lungs at the end-expiratory position.
- **RV**: Residual volume is that volume of air remaining in the lungs after maximal exhalation.
- **IC, ERV**: Dividing the vital capacity into portions above and below the functional residual capacity defines the inspiratory capacity and expiratory reserve volume.
- **VT**: Tidal volume is the volume exhaled during normal breathing, and may increase, during exercise, to a large fraction of vital capacity.
- **FEV1**: Forced expiratory volume in 1 second is the volume of air exhaled in the first second of the forced vital capacity.
- **FEV1/FVC%**: The FEV1-to-FVC ratio, expressed as a percentage.
- **FEF75**: Instantaneous forced expiratory flow after 75% of the FVC has been exhaled.
- **MVV**: Maximal voluntary ventilation. The volume of air expired in a specified period during repetitive maximal respiratory effort, expressed as L/min.
- **PO2, PCO2**: Partial pressure of the indicated gas in air, blood, or other liquid, expressed in the same units as barometric pressure (mm Hg or kP).
- **FIO2**: Fractional inspired oxygen concentration, e.g., the FIO2 of air is 0.21.

40 **Radionuclide scan – Bone:** A nuclear medicine study to detect bone abnormalities. The patient is injected with a small amount of radioactive material and then scanned with a Gamma camera, a device sensitive to the radiation emitted by the injected material. About half of the radioactive material is localized by the bones. The more active the bone turnover, the more radioactive material will be seen. Some tumors, fractures, and infections show up as areas of increased uptake. Others can cause decreased uptake of radioactive material.

41 **Radionuclide scan – Brain:** A nuclear medicine study utilizing radiopharmaceutical agents to visual the brain. Also known as brain scintigraphy, Ceretec brain scan, and Spectamine brain scan.

42 **Radionuclide scan – Liver:** A nuclear medicine study utilizing radiopharmaceutical agents to visual the liver. Also known as liver scintigraphy, liver and spleen scan, radioisotope hepatic scan, and spleen scan.

43 **Resection:** While lobectomy and pneumonectomy are treatments for lung cancer, record 43-Resection if a wedge resection, lobectomy, or pneumonectomy provides diagnostic/staging information. If done during the same procedure/ operation, then consider the surgical removal collectively as one resection. The exception is when a procedure involves an interruption to allow for an intraoperative pathology review for diagnosis. For example, if cancer is not previously confirmed, and a diagnostic wedge resection of the lung nodule is done and upon intraoperative pathology review, cancer is confirmed so a lobectomy is now performed, these procedures should be recorded separately. The diagnostic wedge resection should be recorded as an open surgical biopsy and the lobectomy as a resection.

- Wedge Resection (segmentectomy) – the surgical removal of a segment or wedge-shaped piece of the lung.
- Lobectomy – the surgical removal of one lobe of the lung.
- Bi-lobectomy – the surgical removal of two lobes of the lung.
- Pneumonectomy – the surgical removal of an entire lung.

46 **Thoracotomy:** A surgical incision into the chest. It is performed to gain access to the thoracic organs, most commonly the heart, the lungs, the esophagus, or thoracic aorta, or for access to the anterior spine. Thoracotomy is a major surgical maneuver – the first step in thoracic surgery, which involves major procedures such as coronary artery bypass surgery and pneumonectomy for lung cancer. There are many different approaches to thoracotomy. The most common modalities of thoracotomy follow.

- Median thoracotomy provides wide access to the mediastinum and is the incision of choice for most open-heart surgery.
- Posterolateral thoracotomy is a common approach for operations on the lungs or mediastinum, including the esophagus. When performed over the fifth intercostal space, it allows optimal access to the pulmonary hilum (pulmonary artery and pulmonary vein) and therefore is considered the approach of choice for pulmonary resection (pneumonectomy and pulmonary lobectomy).
- Anterolateral thoracotomy is performed upon the anterior chest wall.
- Bilateral anterolateral thoracotomy combined with tranverse sternotomy results in the "clamshell" incision, the largest incision commonly used in thoracic surgery.

47 **Thoracentesis:** The insertion of a hollow trocar or needle with a cannula into the pleural cavity or lung space to remove fluid from the lung. A diagnostic thoracentesis is most frequently performed to determine the etiology of a pleural effusion. Pleural fluid analysis is important in the diagnosis and staging of a suspected or known malignancy. A therapeutic thoracentesis is performed to relieve respiratory insufficiency caused by a large pleural effusion. It can be used to introduce sclerosing or antineoplastic agents into the pleural space after removing pleural fluid.

48 **Ultrasound (Specify):** Medical ultrasonography (sonography) is an ultrasound-based diagnostic imaging technique used to visualize muscles and internal organs, their size, structure, and any pathological lesions, making them useful for scanning the organs. Ultrasonography (sonography) is widely utilized in

medicine. It is possible to perform diagnosis or therapeutic procedures with the guidance of ultrasonography (for instance biopsies or drainage of fluid collections). Typically uses a hand-held probe (often called a scan head or transducer) that is placed directly on and moved over the patient: a water-based gel ensures good coupling between the patient and scan head. The line next to the procedure code should be used to specify the site of the ultrasound.

49 **Thoracoscopy:** The insertion of an endoscope, a narrow-diameter tube with a viewing mirror or camera attachment, through a very small incision (cut) in the chest wall. Thoracoscopy makes it possible to examine the lungs or other structures in the chest cavity, without making a large incision. It is an alternative to thoracotomy (opening the chest cavity with a large incision). Many surgical procedures, especially taking tissue samples (biopsies), can also be accomplished with thoracoscopy.

50 **Biopsy – Thoracoscopic:** Biopsy performed via thoracoscopy.

52 **Biopsy – Percutaneous adrenal:** A biopsy procedure whereby a needle or trocar is inserted through the skin (percutaneous) into the adrenal gland. Cells and tissue fragments are recovered for histologic or cytologic analysis.

53 **Biopsy – Percutaneous transthoracic yielding histology:** A biopsy procedure whereby a needle or trocar is inserted through the skin (percutaneous) into the chest and tissue fragments are recovered for histologic analysis.

54 **Bronchoscopy without biopsy or cytology:** Bronchoscopy (either flexible fiberoptic bronchoscope or a rigid bronchoscope) allows direct visual examination of the upper airway and tracheobronchial tree, sampling of respiratory tract secretions and cells, and biopsy of airway, lung, and mediastinal structures.

55 **CT – Abdomen (or liver):** Computed Tomography or Computed Transaxial Tomography of the abdomen or liver. Procedure wherein a computerized tomography scanner is used to scan and produce an axial image of an organ or area of the body. An abdominal CT scan may include the liver, spleen, kidneys, pancreas, aorta, retroperitoneum, gastrointestinal tract, and pelvis for the purposes of diagnosis and/or evaluation of cysts, tumors, masses, aneurysms, metastases, abscesses, and trauma.

56 **CT – Chest, plus contrast-enhanced nodule densitometry:** CT densitometry measures the attenuation coefficients of a particular lesion to determine its density. The results are expressed in Hounsfield units (HU).

57 **CT – Chest, diagnostic:** Computed Tomography or Computed Transaxial Tomography of the chest. Procedure wherein a computerized tomography scanner is used to scan and produce an axial image of an organ or area of the body. Includes any routine chest CT, either spiral or non-spiral, and either with or without contrast.

58 **Cytology – Bronchoscopic:** Cytology acquired during bronchoscopy.

59 **Cytology – Percutaneous transthoracic:** A procedure whereby a needle or trocar is inserted through the skin (percutaneous) into the chest. This procedure is used to obtain cytologic specimens from lung and mediastinal lesions, especially peripheral nodules in the lung parenchyma and pleural space. Less frequently, it is used to obtain specimens from infected areas of the lung for direct smear and culture for identification of specific pathogens.

60 **Cytology – Other (Specify):** Other cytology not otherwise specified by a procedure code. The line next to the procedure code should be used to record the site from where the cytology was collected.

61 **Echocardiography:** The echocardiogram is an ultrasound of the heart. Using standard ultrasound techniques, two-dimensional slices of the heart can be imaged. The latest ultrasound systems now employ 3-D real-time imaging. The standard echocardiogram is also known as a transthoracic echocardiogram, or TTE. In this case, the echocardiography transducer (or probe) is placed on the chest wall (or thorax) of the subject, and images are taken through the chest wall. This is a non-invasive, highly accurate and quick assessment of the overall health of the heart. A cardiologist can quickly assess a patient's heart valves and degree of heart muscle contraction (an indicator of the ejection fraction). The TTE is a popular test which keeps improving with more and more advances in the field. Another method to perform an echocardiogram is to insert a specialised scope containing an echocardiography transducer (TEE probe) into the patient's esophagus, and record pictures from there. This is known as a transesophageal echocardiogram, or TEE. The advantages of TEE over TTE are clearer images, since the transducer is closer to the heart. Some structures are better imaged with the TEE. These structures include the aorta, the pulmonary artery, the valves of the heart, and the left and right atria. While TTE can be performed easily and without pain for the patient, TEE may require light sedation and a local anesthetic lubricant for the esophagus. Unlike the TTE, the TEE is considered an invasive procedure. In addition to creating two-dimensional pictures of the cardiovascular system, the echocardiogram can also produce accurate assessment of the velocity of blood and cardiac tissue at any arbitrary point using Pulsed or Continuous wave Doppler ultrasound. This allows assessment of cardiac valve areas and function, any abnormal communications between the left and right side of the heart, any leaking of blood through the valves (valvular regurgitation), and calculation of the cardiac output as well as the ejection fraction.

62 **MRI – Abdomen (or liver):** Magnetic Resonance Imaging of the abdomen or liver. Procedure in which the patient is placed in a strong magnetic field and radiofrequency pulses are transmitted into the patient in an extremely controlled and defined manner. An MRI provides 3-D images of the body's interior, delineating muscle, bone, blood vessel, nerve, organ, and tumor tissue.

63 **Radionuclide scan – FDG-PET scan:** A nuclear medicine medical imaging technique which produces a three dimensional image or map of functional processes in the body. A short-lived radioactive tracer isotope which decays by emitting a positron, chemically incorporated into a metabolically active molecule, is injected into the blood circulation. There is a waiting period while the metabolically active molecule (usually a sugar) becomes concentrated in tissues of interest, then the subject is placed in the imaging scanner. The short-

lived isotope decays, emitting a positron. After travelling up to a few millimeters the positron annihilates with an electron, producing a pair of annihilation photons (similar to gamma rays) moving in opposite directions. These are detected when they reach a scintillator material in the scanning device, creating a burst of light which is detected by photomultiplier tubes. PET scanning with the tracer (^{18}F) fluorodeoxyglucose (FDG, FDG-PET) is widely used in clinical oncology. This tracer is a glucose analog and is taken up by cells, phosphorylated by hexokinase (whose mitochondrial form is greatly elevated in rapidly-growing malignant tumors), and retained by tissues with high metabolic activity, such as the brain, the liver, and most types of malignant tumors. As a result FDG-PET can be used for diagnosis, staging, and monitoring treatment of cancers, particularly in Hodgkin's disease, non Hodgkin's lymphoma, and lung cancer.

64 **Radionuclide scan – Gallium:** A procedure to detect areas of the body where cells are dividing rapidly. It is used to locate cancer cells or areas of inflammation. A very small amount of radioactive gallium is injected into a vein and travels through the bloodstream. The gallium is taken up by rapidly dividing cells in the bones, tissues, and organs and is detected by a scanner.

65 **Radionuclide scan – Somatostatin receptor:** A type of radionuclide scan used to find carcinoid tumors, also called Somatostatin receptor scintigraphy (SRS). In SRS, radioactive octreotide, a drug similar to somatostatin, is injected into a vein and travels through the bloodstream. The radioactive octreotide attaches to carcinoid tumor cells that have somatostatin receptors. A radiation-measuring device detects the radioactive material, showing where the carcinoid tumor cells are in the body. This procedure is also called an octreotide scan.

66 **Radionuclide scan – Ventilation/perfusion scan:** A diagnostic test for pulmonary embolism in which an x-ray of the lung records the distribution and perfusion of a radionuclide that is inhaled and a second radionuclide that is administered intravenously.

67 **Radionuclide scan – Other (Specify):** Other radionuclide scans not otherwise specified by a procedure code. The line next to the procedure code should be used to record the site of the scan.

68 **Radionuclide scan – Fusion PET/CT scan:** Fusion PET/CT scan offers the electronic fusion of CT and PET images on the same scanner. This technology allows for direct visual comparison of two different data sets. In other words, it shows how the organs look and how they are working. Traditional CT scans show the physical structure of the body in great detail, while a PET scan examines the body's chemistry, giving information about how the body is functioning.

Dosage: 13.34 mCi 18-FDG administered intravenously. After an uptake period of approximately 60 minutes, a PET/CT scan was performed from the skull base to the mid-thighs. Attenuated and non-attenuated PET images were reconstructed. The PET images, CT images, and the fused PET/CT images were reviewed on a 3-D workstation.

Technique: The PET images were acquired with F-18 fluorodeoxyglucose in the amount of 12 mCi. The CT images were acquired with oral contrast but no intravenous contrast. Imaging was performed from the base of the brain to the proximal thighs. Orthogonal tomograms of the PET, CT, and coregistered images were reconstructed.

Technique: Noncontrast CT from the skull base to upper legs was performed on the 16-slice helical scanner. One hour after intravenous injection of 16 mCi of F18-FDG (fluoroxyglucose), tomographic emission images were acquired over the same anatomy using the nuclear medicine PET scanner, reviewed in multiple planes. Data from the CT and PET scans were co-registered and the fusion images were reviewed at the workstation.

69 **CT – Chest, low dose spiral:** Computed Tomography or Computed Transaxial Tomography of the chest that utilizes a spiral and low dose technique. Includes CT exams performed as part of follow-up that are at doses similar or identical to those used in NLST.

70 **CT – Chest, limited thin section of entire lung:** Computed Tomography or Computed Transaxial Tomography of the chest that evaluates the entire lung area with thin sections.

Technique: 2.5 mm images performed through the chest without intravenous contrast.

Technique: Initially, unenhanced multidetector helical CT images were obtained through the mid-upper lung zones. Subsequently, following the uncomplicated intravenous administration of 150 ml of Omnipaque 300, multidetector helical CT scan was obtained from the thoracic inlet interior to the upper abdomen and reformatted at 2.5 mm slices through the chest and photographed in soft tissue, lung, and liver windows.

Technique: Helical axial T-2 scanning of the chest is performed at 5 mm increments without intravenous contrast. Additional thin section 1 mm scans were then reconstructed through the entire chest.

71 **CT – Chest and abdomen:** Computed Tomography or Computed Transaxial Tomography of the chest and abdomen. Procedure wherein a computerized tomography scanner is used to scan and produce an axial image of an organ or area of the body. A chest and abdomen CT, combined may extend from the lung apices to the abdominal area as one procedure. It evaluates not only the chest contents but also the parts of the abdomen, particularly lymph node abnormalities as well as the liver and spleen.

72 **CT – Chest, abdomen and pelvis:** Computed Tomography or Computed Transaxial Tomography of the chest abdomen and pelvis. Procedure wherein a computerized tomography scanner is used to scan and produce an axial image of an organ or area of the body.

4. Medical Complications: The only medical complications to be collected are the medical complications that are currently listed on the DE form under Complication Codes. General

guidelines for identifying these selected medical complications in the medical record are given below:

– Only those selected medical complications that were a result of the diagnostic evaluation or staging procedures *and that required medical attention* should be recorded.

– Information on medical complications can usually be found in the discharge summary, or the doctor's or nurse's notes within the medical record.

– Medical complications that occur up to six months after the date of diagnosis for primary invasive lung cancer should be collected. Medical complications that occur up to twelve months after the date diagnostic evaluation began should be collected for other diagnoses including non cancer diagnoses.

– Medical complications that are the result of treatment for cancer should not be recorded.

After review of the medical records to determine whether medical complications from diagnostic or staging procedures occurred, mark your response.

- **No:** If the review of the medical record indicates that none of the selected medical complications occurred, mark the box labeled "No", and go to A.5.

- **Yes:** If the record states or indicates that one or more of the selected medical complications listed on page 2 of the DE form resulted from a diagnostic or staging procedure, enter the date and the code for the complication(s) in the table. Record all complications occurring on a given date on the same line.

  The following are guidelines for coding some of the medical complications:

  01 = Acute respiratory failure: The record indicates that the participant experienced acute respiratory failure, which is sudden insufficient oxygenation that can result from a variety of causes and requires intervention. ARDs would be included here.

  02 = Allergic reaction: The record indicates that the participant experienced an allergic reaction, including swelling, itching, or rash (with or without local redness and warmth) that required treatment as a result of a diagnostic or staging procedure.

  03 = Anaphylaxis: The record indicates that the participant experienced anaphylaxis, a severe allergic reaction with a dramatic drop in blood pressure, severe wheezing, or dramatic swelling and requiring treatment with supplemental oxygen, intubation, or intravenous fluids as a result of a diagnostic or staging procedure.

  14 = Fever requiring antibiotics: The record indicates that the participant had a fever as a result of a diagnostic or staging procedure which necessitated the use of antibiotics (e.g., a fever resulting from an infection following a diagnostic or staging

procedure). Infections that are not accompanied by a fever but are treated with antibiotics should not be recorded as a medical complication.

17 = **Hospitalization post procedure**: Use only if reason for hospitalization is not another selected complication.

23 = **Pneumothorax requiring tube placement**: A pneumothorax is an accumulation of air or gas in the pleural cavity. The record indicates that the participant developed a pneumothorax, as a result of a diagnostic or staging procedure and medical intervention, specifically tube placement, was required. Often a small pneumothorax is seen after a chest procedure, but for this study, only those that required tube placement should be recorded. However, do not record the placement of a chest tube that is routinely done post-operatively from an open chest surgery. Rather record a pneumothorax as a complication if after the post-operative chest tube is removed it has to be re-inserted.

25 = **Respiratory arrest:** The record indicates that the participant experienced a respiratory arrest or cessation of breathing.

37 = **Infection requiring antibiotics:** The record indicates that the participant had an infection without fever attributable to a diagnostic or staging procedure and required antibiotics. For example, if after a bronchoscopy a participant develops pneumonia requiring antibiotics but does not have a fever because of steroid or NSAID use. This code should not be used if the antibiotics are prescribed prophylactically for a possible infection that is attributable to a diagnostic or staging procedure.

99 = **Unknown:** If you do not have all of the medical records or you cannot reliably determine complications, mark the box labeled "Unknown." Enter nines for the date of complication (e.g., 99/99/9999). Enter the appropriate complication code.

5. Result of Diagnostic Evaluation for Primary Invasive Lung Cancer: The purpose of this item is to record the overall results of the diagnostic evaluation for primary invasive lung cancer. This information should be found in the impression/conclusion sections of the various diagnostic and staging reports. Only one response should be recorded.

When multiple diagnoses are made, such as a cancer and a non-cancer diagnosis, only the most serious diagnosis should be recorded. If a primary lung malignancy is confirmed, this should always be recorded. If a primary lung malignancy is not confirmed, but another malignancy is confirmed, this should be recorded. If there is no malignancy, but one of the specific lung diagnoses is confirmed, this should be recorded.

Record the result of the diagnostic evaluation for primary invasive lung cancer as follows:

- **No malignancy, confirmed by histology or cytology:** The record indicates that no malignancy was found following diagnostic evaluation that included histology or

cytology. Mark the box, and complete Part B: Diagnosis Information for Any Condition Other Than Primary Invasive Lung Cancer, Items B.6 and B.7. Do not complete Part C: Primary Invasive Lung Cancer Diagnosis Information.

- **No malignancy, determined by clinical evaluation only – no pathologic proof:** The record indicates that no malignancy was found following diagnostic evaluation that included only a clinical evaluation, not histology or cytology. Mark the box, and complete Part B: Diagnosis Information for Any Condition Other Than Primary Invasive Lung Cancer, Items B.6 and B.7. Do not complete Part C: Primary Invasive Lung Cancer Diagnosis Information.

  A result of "No malignancy, determined by clinical evaluation only – no pathologic proof" should also be coded in the following situations:

  - When diagnostic follow-up data have been abstracted for twelve months following a positive screening examination or until the next screening examination, and the diagnosis was not conclusively malignant. Complete Part B.

  - When no diagnostic procedures are performed following a positive screening examination – (i.e., when Item A.1: Did participant undergo diagnostic procedures? is coded "No, physician report," or "No, participant self-report").

  - When the record clearly indicates that follow-up by a health care provider, or "active surveillance," is scheduled on a regular basis, such as every six months, to ensure stability of an abnormality.

- **Primary invasive lung malignancy confirmed histologically:** The record indicates that the participant has been diagnosed with primary invasive lung cancer, confirmed by histologic examination (study of tissue). Diagnosis of Carcinoid of the lung should be included here. Diagnosis of extranodal lymphoma of the lung, sarcoma of the lung, and neoplasm of uncertain behavior *should not* be included here as primary lung malignancies. Histologic information may come from a biopsy, and can be found on the pathology report, sometimes called a histopathology report. Mark the box and complete Part B: Diagnosis Information for Any Condition Other Than Primary Invasive Lung Cancer and Part C: Primary Invasive Lung Cancer Diagnosis Information.

- **Primary invasive lung malignancy confirmed cytologically:** The record indicates that the participant has been diagnosed with primary invasive lung cancer, confirmed by cytologic examination (study of cells). Diagnosis of Carcinoid of the lung should be included here. Diagnosis of extranodal lymphoma of the lung, sarcoma of the lung, and neoplasm of uncertain behavior *should not* be included here as primary lung malignancies. Diagnosis from cytologic information may come from a bronchial brushing or washing, or a fine-needle aspiration, and can be found on the cytology report, sometimes called a cytopathology report. Mark the box and complete Part B: Diagnosis Information for Any Condition Other Than Primary Invasive Lung Cancer and Part C: Primary Invasive Lung Cancer Diagnosis Information.

  NOTE: If the lung malignancy was confirmed by both histologic and cytologic examination, information from histologic confirmation takes precedence over

cytologic confirmation, and is the basis to answer Item A.5. If both histologic and cytologic examinations are present yet yield inconclusive results (e.g., "suspicious" for malignancy, but not confirmed) then Item A.5 must be recorded as "Primary lung malignancy diagnosed by clinical examination only – no pathologic proof."

- **Primary invasive lung malignancy diagnosed by clinical examination only – no pathologic proof**: The record indicates that the participant has been diagnosed with primary invasive lung cancer by clinical examination and the diagnosis has not been confirmed by histologic examination (study of tissue) or cytologic examination (study of cells) prior to disease modifying treatment (except for neoadjuvent treatment). It is an extremely rare event for a malignancy to be confirmed only by clinical examination and not histologically or cytologically. Mark the box and complete Part B: Diagnosis Information for Any Condition Other Than Primary Invasive Lung Cancer and Part C: Primary Invasive Lung Cancer Diagnosis Information. In the case of a clinically diagnosed lung cancer, Items C.14a and C.14b should be left blank; however, if treatment is given and then there is subsequent histologic or cytologic confirmation then this should be documented in C.14a and C.14b with an explanation in Item D.18 (Comments). In those cases where there is no cytologic or histologic confirmation of cancer prior to treatment, the results of the diagnostic evaluation remains "diagnosed by clinical evaluation only – no pathologic proof."

- **Malignancy other than primary invasive lung cancer, with or without lung metastasis, confirmed by histology or cytology:** The diagnosis of a malignancy other than primary invasive lung cancer was confirmed by histologic examination (study of tissue) or cytologic examination (study of cells). Histologic information can be found on the histology report, sometimes called the histopathology report, and cytologic information can be found on the cytology report, sometimes referred to as a cytopathology report. Mark the box and complete Part B: Diagnosis Information for Any Condition Other Than Primary Invasive Lung Cancer. Do not complete Part C: Primary Invasive Lung Cancer Diagnosis Information.

  - This answer category should also be coded if the diagnostic evaluation for primary invasive lung cancer reveals a malignancy (including a lung malignancy) that is a *metastasis* from a primary cancer site other than the lung. In this situation, the *primary* cancer site should be recorded in Part B: Diagnosis Information for Any Condition Other Than Primary Invasive Lung Cancer.

- **Malignancy other than primary invasive lung cancer, with or without lung metastasis, diagnosed by clinical evaluation only – no pathologic proof:** The diagnosis of a malignancy other than primary invasive lung cancer was confirmed by clinical evaluation only without documented pathological proof (histology or cytology). The MRA should make every attempt to determine if pathological proof is available prior to accepting the clinical evaluation as the only diagnosis. Mark the box and complete Part B: Diagnosis Information for Any Condition Other Than Primary Invasive Lung Cancer. Do not complete Part C: Primary Invasive Lung Cancer Diagnosis Information.

  - This answer category should also be coded if the clinical evaluation for primary invasive lung cancer reveals a malignancy (including a lung malignancy) that is a *metastasis* from a primary cancer site other than the lung. In this situation,

the *primary* cancer site should be recorded in Part B: Diagnosis Information for Any Condition Other Than Primary Invasive Lung Cancer.

- **Diffuse idiopathic pulmonary neuroendocrine hyperplasia:** The record indicates that the participant has been diagnosed with diffuse idiopathic pulmonary neuroendocrine hyperplasia. Mark the box, and complete Part B: Diagnosis Information for Any Condition Other Than Primary Invasive Lung Cancer, code the ICD-O-3 code (Item B.7a) and date of diagnosis (Item B.7b). Do not complete Part C: Primary Invasive Lung Cancer Diagnosis Information.

- **Carcinoma in situ:** The record indicates that the participant has been diagnosed with carcinoma in situ, confirmed by histologic examination. Carcinoma in situ is defined as malignant cell changes in the epithelial tissue that have not extended beyond the basement membrane of the mucosa. In situ may also be expressed as intraepithelial, non-infiltrating, non-invasive, pre-invasive, or no stromal invasion. Mark the box, and complete Part B, Diagnosis Information for Any Condition Other Than Primary Invasive Lung Cancer, code the ICD-O-3 code (Item B.7a) and date of diagnosis (Item B.7b). Do not complete Part C: Primary Invasive Lung Cancer Diagnosis Information.

- **Neoplasm of uncertain behavior:** The record indicates that the participant has been diagnosed with neoplasm of uncertain behavior, confirmed by histologic examination. A neoplasm of uncertain behavior is defined as a tumor that is no longer consistent with a benign neoplasm, but also does not have characteristics consistent with a malignancy. Neoplasms of uncertain behavior are certain histomorphologically well-defined neoplasms, the subsequent behavior of which can not be predicted from the present appearance. These are not, however, a malignancy at the time of diagnosis. Mark the box, and complete Part B, Diagnosis Information for Any Condition Other Than Primary Invasive Lung Cancer, code the ICD-O-3 code (Item B.7a) and date of diagnosis (Item B.7b). Do not complete Part C: Primary Invasive Lung Cancer Diagnosis Information.

- **Squamous dysplasia:** The record indicates that the participant has been diagnosed with squamous dysplasia. Mark the box, and complete Part B: Diagnosis Information for Any Condition Other Than Primary Invasive Lung Cancer, code the ICD-O-3 code (Item B.7a) and date of diagnosis (Item B.7b). Do not complete Part C: Primary Invasive Lung Cancer Diagnosis Information.

- **Atypical adenomatous hyperplasia – Lung:** The record indicates that the participant has been diagnosed with atypical adenomatous hyperplasia. Mark the box, and complete Part B: Diagnosis Information for Any Condition Other Than Primary Invasive Lung Cancer, code the ICD-O-3 code (Item B.7a) and date of diagnosis (Item B.7b). Do not complete Part C: Primary Invasive Lung Cancer Diagnosis Information.

- **Further follow-up required:** The record indicates that an abnormality was identified and no conclusive diagnosis was made. The health care provider indicates that it is necessary to re-evaluate the abnormality with a procedure that might provide conclusive diagnosis two to three months after the regular window of data collection has ended for that study year. This code should not be used when the record clearly indicates that follow-up, or "active surveillance," is scheduled on a regular basis, such

as every six months, to ensure stability of an abnormality. For "Further follow-up required" there must be a heightened suspicion for the possibility of primary invasive lung cancer, but the evaluation was not quite done prior to the close of the data collection window. Mark the box and go to Item D.18 (Comments), to record the reason for further follow-up. Do not complete Part B: Diagnosis Information for Any Condition Other Than Primary Invasive Lung Cancer or Part C: Primary Invasive Lung Cancer Diagnosis Information.

The SC must continue to collect medical records and update the DE form when more information becomes available. A DE form with a result of "Further follow-up required" must be updated before the close of the next study year window (i.e., a T_1 DE form with "Further follow-up required" must be updated before the end of the T_2 study year.)

- **No information available:** There is equivocal or no information available in the record regarding the result of the diagnostic evaluation for primary invasive lung cancer. Mark the box and go to Item D.18 (Comments), and record the reasons that a diagnosis could not be recorded. Do not complete Part B: Diagnosis Information for Any Condition Other Than Primary Invasive Lung Cancer or Part C: Primary Invasive Lung Cancer Diagnosis Information.

  - "No information available" should also be coded in the situation when diagnostic evaluation procedures are discontinued by the participant, and it cannot be determined conclusively whether the participant had no malignancy or had a lung or other malignancy.

*Note: When the participant has both a primary invasive lung cancer and an other (cancer or non-cancer) diagnosis, the MRA should complete only **one** DE form. The MRA will complete A.5, Result of Diagnostic Evaluation for Primary Invasive Lung Cancer, by selecting the appropriate box for lung cancer, and will complete Part B: Diagnosis Information for Any Condition Other Than Primary Invasive Lung Cancer and Part C: Primary Invasive Lung Cancer Diagnosis Information.*

Part B: Diagnosis Information for Any Condition Other Than Primary Invasive Lung Cancer:

Only diagnoses resulting from the diagnostic evaluation that have not been indicated in Item A.5 will be documented in this section. Many participants have multiple medical problems, include here medical problems identified through the diagnostic evaluation process which could include such things as any cancer other than lung; any pre-invasive neoplasm of uncertain behavior that is from a site other than the lung; and other non-cancer lung diagnoses such as emphysema, to name a few. The diagnosis of the other medical problems should be recorded from documents in the medical record that are prefaced with "Diagnosis/Impression/Conclusion/Assessment." These should be obtained directly from the participant's health care provider when the SC contacts him/her during follow-up of a positive screening examination. Depending on the extent of the information available and the health care provider's preference, the requested information may be obtained either by phone or written documentation. The diagnosis can be from a source other than the original diagnosing physician as long as the source states the original diagnosis. One example is a progress note. A pathology report documenting a benign condition is also an appropriate source.

Multiple Diagnoses: If the result of the diagnostic evaluation was a cancer other than the lung **and** a selected medical condition, record the selected medical condition in the space for

the ICD-9-CM code in B.6a & B6.b, and record the cancer in B.7a, B7b.and B.7c. [Only cancers other than primary invasive lung cancers should be recorded in B.7.]

For example, if the result of diagnostic evaluation is granuloma as well as a metastatic renal cancer, record the specified code for granuloma in B.6 and record the renal cancer B.7.

If more than one condition or cancer other than lung results from the diagnostic evaluation, the corresponding ICD-9-CM codes, ICD-O-3 codes, and dates of diagnosis should be recorded in Item D.18 (Comments). Begin your statement in Comments with the verbatim as recorded in the following example:

Item D.18 (Comments):

Item #	Comments
B.6	Additional Conditions are: ICD-9-CM code(s) – Date(s) of diagnosis -

AND/OR

Item #	Comments
B.7	Additional Other Cancer Diagnosis are: ICD-O-3 code(s) – Date(s) of diagnosis -

6a. **Non-Cancer Diagnosis:** This item is to be used to record all diagnoses other than cancer. If a condition other than cancer has been recorded in A.5, mark the box for "Yes" and complete the ICD-9-CM Classification, Date of Diagnosis, and Nosologist/Abstractor ID #. If a condition other than cancer has not been diagnosed, mark the box for "No" and go to Item D.18 (Comments) (Item B.6b will be left blank). Item B.7a is only completed if a malignancy other than primary invasive lung cancer was diagnosed.

ICD-9-CM Classification: Any non-cancer diagnosis must be classified according to ICD-9-CM (International Classification of Diseases, 9th Revision, Clinical Modification). ICD-9-CM coding for the NLST/LSS must be consistent with the national ICD-9-CM coding standards and should not be influenced by specific institutional coding philosophies.

6b. **Date of Diagnosis:** Record the date of diagnostic determination for the condition recorded in Item B.6a. Operative reports are generally more accurate for date of procedure than surgical pathology reports, so in the case of a discrepancy, record the date of procedure from the operative report as the date of diagnosis.

If the exact date of diagnosis cannot be determined from the record, year and month can usually be assessed. In this situation, record the exact month and year and the day as "99." Zero fill month and day, and record the last two digits of the year (e.g., 02/07/2002). For any portion of the date that is unknown, record "9's."

Nosologist/Abstractor ID#: Record the staff ID number for the nosologist/abstractor who completed the ICD-9-CM Classification.

7a. Cancer Diagnosis, Site other than primary invasive lung: This item is used to record all cancer diagnoses other than primary invasive lung cancer. If a cancer other than primary invasive lung cancer has been diagnosed, mark the box for "Yes" and complete the ICD-O-3 Cancer Classification, Date of Diagnosis, and CTR ID#. If a cancer other than primary invasive lung cancer has not been diagnosed, mark the box for "No." Remember to record only primary cancer from sites other than the lung, not the metastic site of the cancer, in Part B. The cancer that is recorded should be a result of the diagnostic evaluation and not an incidental finding from review of the medical record or other work up. Those cancers documented in Part B do not need to be documented on the CNF. Include here extranodal lymphoma of the lung and primary sarcoma of the lung. Also record lung carcinoma in situ; neoplasm of uncertain behavior; diffuse idiopathic pulmonary neuroendocrine hyperplasia; squamous dysplasia; and atypical adenomatus hyperplasia in this section.

ICD-O-3 Cancer Classification: This is the ICD-O-3 coding for cancer or neoplasms of uncertain behavior, with the origin other than lung. This item must be completed by a CTR who should enter the ten-digit ICD-O-3 classification code in the space provided. When the diagnosis of the cancer is from metastatic tissue (such as a lymph node) and not from the primary cancer site, record the ICD-O-3 grade as 9 (unknown). Place an asterisk by B.7a and record the grade of the metastatic tissue, if known, in Item D.18 (Comments).

7b. Date of Diagnosis: Record the date of diagnostic determination for the cancer recorded in the ICD-O-3 Cancer Classification. This is the date the abnormality is determined to be another (non-lung) cancer, and <u>not</u> the original date of diagnosis of the primary cancer, should the findings represent metastasis to the lung. For example, if the participant has a history of breast cancer diagnosed in 1992, and has a positive screen in 2002 that represents metastatic disease to the lung from breast cancer, record the date when the abnormality is determined to be a metastasis from the breast. Operative reports are generally more accurate for date of procedure than surgical pathology reports, so in the case of a discrepancy, record the date of procedure from the operative report as the date of diagnosis.

If the exact date of diagnosis cannot be determined from the record, year and month can usually be assessed. In this situation, record the exact month and year and the day as "99." Zero fill month and day, and record the last two digits of the year (e.g., 02/07/<u>20</u>02). For any portion of the date that is unknown, record "9's."

CTR ID#: Record the staff ID number for the CTR or CTR-eligible individual who completed the ICD-O-3 Cancer Classification.

7c. Is this Cancer Metastatic to Lung? Mark the box to indicate whether or not the cancer in B.7a has metastasized to the lung.

<u>Part C: Primary Invasive Lung Cancer Diagnosis Information:</u>

This section documents all relevant information pertaining to a primary invasive lung cancer diagnosis. If the participant was diagnosed with more than one primary invasive lung cancer, record information about the first (i.e., chronologically by date of diagnosis) primary in Part C. For all subsequent primaries use another DE form (refer to instructions for multiple primary invasive lung cancer in the Administrative Section of these specifications). If more than one primary was diagnosed on the first date of diagnosis, record information about the most advanced cancer diagnosed on that day in Part C, and use additional DE forms for any other cancers diagnosed on that day.

8. Date of Primary Invasive Lung Cancer Diagnosis: Record the month, day, and year of the primary invasive lung cancer diagnosis. The date recorded should be the earliest result of the diagnostic evaluation, determined by clinical evaluation, cytology, or histopathology that ***initially*** prompted a decision to treat the primary invasive lung cancer. If there are multiple reports that confirmed the primary cancer, record the earliest date available.

If the date corresponds to a histology/histopathology or cytology/cytopathology report, then record the date that the actual procedure (biopsy, surgery, aspiration of cells, etc.) was performed that confirmed this primary invasive lung cancer diagnosis. Operative reports are generally more accurate for date of procedure than surgical pathology reports, so in the case of a discrepancy, record the date of procedure from the operative report.

In the rare situation in which primary invasive lung cancer was diagnosed by clinical examination only and not histologically or cytologically, the date of first lung cancer diagnosis is the date of the clinical examination that diagnosed the cancer prior to the initiation of treatment.

Zero fill month and day, and record the last two digits of the year (e.g., 02/07/2002) of the date of diagnosis of primary invasive lung cancer. If confirmed histologically or cytologically, this date will correspond to the date of a procedure in Item A.3. If clinically confirmed, this date will correspond to another procedure in Item A.3. An exact date is expected.

9. Photocopy of Report Confirming Primary Invasive Lung Cancer: The purpose of this item is to document that the clinical examination record, the histology/histopathology report, or the cytology/cytopathology report that confirmed the primary invasive lung cancer has been photocopied and placed in the participant's study file.

- If there are multiple pathology reports confirming this primary invasive lung cancer, the photocopy should be of the first histology or cytology report which was the source for the date of the primary invasive lung cancer diagnosis recorded in Item C.8, and the ICD-O-3 code recorded in Item C.11. If the Date of Primary Invasive Lung Cancer Diagnosis and the ICD-O-3 Cancer Classification came from different reports, keep copies of both reports.

- A situation may arise in which an institution does not allow the photocopying of records. Every reasonable attempt should be made to obtain permission to photocopy the histology or cytology report since it captures critical information. If special permission or approval is required, the abstractor should work with the SC Coordinator/Principal Investigator to obtain the necessary approval. If this item cannot be completed in a timely manner, mark "Report exists but cannot be obtained."

Mark the box to indicate whether a photocopy of the histology or cytology report is available as follows:

- **No Report/Clinical Examination:** There is no histology or cytology report in the medical record. This is the rare occasion where primary invasive lung cancer was diagnosed by clinical examination, and not histologically or cytologically confirmed. In this situation, Item C.10, Verbatim Description of Primary Invasive Lung Cancer Diagnosis, must be completed.

- **Histology/Histopathology:** The histology report is available and a photocopy has been obtained and placed in the participant's study file. The photocopy should be labeled with the PID, titled "medical record abstract/histology report," and inserted into the participant's folder.

- **Cytology/Cytopathology:** The cytology report is available and a photocopy has been obtained and placed in the participant's study file. The photocopy should be labeled with the PID, titled "medical record abstract/cytology report," and inserted into the participant's folder.

- **Report exists but cannot be obtained:** The histology or cytology report exists in the medical record, but a photocopy cannot be obtained. Place an asterisk by Item C.9, and provide a detailed explanation in the Comments section (Item D.18) of why the pathology report cannot be obtained. In this situation, Item C.10, Verbatim Description of Primary Invasive Lung Cancer Diagnosis, must be completed. Begin your statement in Comments with the verbatim as recorded in the following example:

Item D.18 (Comments):

Item #	Comments
C.9	Histology or cytology report cannot be obtained because:

10. Verbatim Description of Primary Invasive Lung Cancer Diagnosis: This item is concerned with the actual physician diagnosis of primary invasive lung cancer. This item is optional except in the following situations:

- The diagnosis is based on clinical examination only and not histology/cytology; or

- The SC is unable to obtain a copy of the histology or cytology report that corresponds to the ICD-O-3 code in Item C.11.

Record the verbatim description of the primary invasive lung cancer diagnosis from the histology/histopathology report (or cytology/cytopathology report if a pathology report is not available). The verbatim description should come from the diagnosis section of the *earliest* (chronological) histology report (or cytology report if the histology report is not available) that had an adequate specimen and that confirms the cancer diagnosis.

- Occasionally, the diagnosis section will say "see above" or "see microscopic." In this situation record verbatim all of the information from the appropriate section of the report that pertains to the cancer diagnosis.

- Do not record any information about metastases or recurrent cancer.

- Do not record any information about benign conditions listed in the diagnosis section of the histology or cytology report.

11a. ICD-O-3 Cancer Classification: This item is for classifying the physician diagnosis of the primary invasive lung cancer according to ICD-O-3 (International Classification of Diseases for Oncology, Third edition, 2000) and should be based on histology, if available.

NOTE: This item is to be completed by a Tumor Registrar who is a CTR or CTR-eligible individual.

The CTR or CTR-eligible individual should code the ten digit ICD-O-3 classification in the space provided above "Topography," "Morphology," "Behavior," and "Grade." The CTR or CTR-eligible individual should also record his/her four-digit staff ID number in the space provided.

- The ICD-O-3 code should be based on the earliest histology specimen that confirms the diagnosis. This may not be the earliest confirmation of the cancer (i.e., clinical evaluation or cytological confirmation) as reflected in C.8 – Date of Primary Invasive Lung Cancer Diagnosis.

- If the record clearly indicates that primary invasive lung cancer was confirmed by a histology or cytology report but the report is not available, code the diagnosis from other available documents, (i.e. physician's notes, progress reports, etc.) that reference the earliest procedure from an adequate specimen. Indicate the source used to derive the ICD-O-3 code in Item C.11b. If the histology and cytology report are unavailable, and another source was used then place an asterisk by Item C.11b, and indicate in the Comments section the source of the diagnosis. Begin your statement in Comments with the verbatim as recorded in the following example:

Item D.18 (Comments):

Item #	Comments
C.11b	Histology or cytology report not available. Source of diagnosis is:

- When the diagnosis of the cancer is from metastatic tissue (such as a lymph node) and not from the primary cancer site, record the ICD-O-3 grade as 9 (unknown), place an asterisk by C.11a, and record the grade of the metastatic tissue obtained, if known, in Comments, D.18.

- If the primary invasive lung cancer was diagnosed by clinical examination only, code the diagnosis using the report from the clinical examination that diagnosed the cancer. Using the clinical examination report, complete as much of C.11 as is known.

- The ICD-O-3 cancer classification should be entered by the CTR or CTR-eligible individual regardless of whether the ICD-O-3 code is available in the medical record.

11b. Source: This item is for classifying the source used for coding the ICD-O-3 code. In most cases the source will be histology, but in some instances cytology can be used when supporting histology documentation is not present. The most complete information on the tumor should be coded even if it requires using information from different sources.

Occasionally both histology and cytology documentation will be used to derive the ICD-O-3 code describing the type of primary invasive lung cancer. In this instance, indicate that both were used and complete the comments in Item D.18 indicating why both types of supporting documentation were necessary to derive the ICD-O-3 code. If there is an unknown component of an ICD-O-3 code from the initial biopsy that confirmed the cancer, and a later specimen is obtained that provides the missing information, then the CTR should use the information form both histological and cytological samples to have the ICD-O-3

code be as complete as possible. An example of when a combined source would be used is if the diagnosis is confirmed from cytology from a pleural effusion but there is tissue obtained from an additional procedure. The confirmation from the cytology would provide information for all but the grade of the primary tumor (as the grade of a metastatic site cannot be attributed to the primary tumor). Rather than record "9" to indicate that the information regarding grade is missing based on the cytological specimen, record the actual grade from the histological sample obtained from the subsequent procedure.

Mark the box to indicate whether the histology, cytology, combined cytology and histology, or clinical examination results were used to derive the ICD-O-3 code as follows:

- **Histology:** The histology report is available and was used to derive the ICD-O-3 code regardless of whether a photocopy of the documentation was obtained for the participant's folder.

- **Cytology:** The cytology report is available and was used to derive the ICD-O-3 code regardless of whether a photocopy of the documentation was obtained for the participant's study folder.

- **Combined (Cytology and Histology):** The histology and cytology reports are available and were both used to derive the ICD-O-3 code regardless of whether a photocopy of the documentation was obtained for the participant's study folder. Provide a detailed explanation of why both types of reports were used to derive the ICD-O-3 code in the Comments section (Item D.18).

- **Clinical:** The ICD-O-3 code was derived based on clinical examination only (no pathological proof). Provide a detailed explanation of why the results of the clinical examination were used to derive the ICD-O-3 code in the Comments section (Item D.18).

12. **Primary Tumor Location:** This item is to document the site of origin of the malignant lung tumor, as determined by a surgical report, pathology report, or radiology report. Mark all boxes that correspond to the site of origin. If the primary tumor location is unknown or not mentioned in the record, mark the box next to "Unknown." For example, if the primary tumor is in the right upper lobe and the satellite metastasis is noted in the right middle lobe, then only the right upper lobe would be recorded. If the primary tumor is overlapping the right upper and middle lobes, then both would be marked. Note that generally the topography code in C.11 should match the location indicated in C.12. (Note in the Comments section if there is a reason for the difference.)

13. **Pathology Lesion Size:** This item documents the size of the tumor (lesion) at its maximum dimension in millimeters. This information can be determined from the pathology report (preferable), operative report, or radiology report. If the size of the lesion cannot be determined, or if the information is unknown or not recorded, the "999" should be entered. The boxes should be zero filled as necessary.

14a. **Pathologic Type for Primary Invasive Lung Cancer:** This item is to be completed only by a CTR or CTR-eligible individual. This refers to the ICD-O-3 morphology code and behavior for the type of cell composing the tumor, usually determined by the pathologist from a tissue specimen. This information can be obtained from the histology or cytology report. If there are multiple reports that confirmed the primary invasive lung cancer, use information from the report that collected the most tissue. If there is no histology report (no tissue obtained), but there is cytological confirmation, then cytology can be used. If neither

a histology report nor a cytology report is available, this information may be found in the discharge summary, or an operative report. If the histopathologic type is obtained from a source other than the pathology report, place an asterisk by C.14, and record the source of the information in Comments (Item D.18). Begin your statement in Comments with the verbatim as recorded in the following example:

Item D.18 (Comments):

Item #	Comments
C.14	Source of histopathologic type of lesion is:

- If the cancer was diagnosed by clinical evaluation only – no pathologic proof, this item should be left blank. If pathologic information becomes available after treatment, this information should be updated and an explanation provided in Item D.18 (Comments).

- If the cancer has two different histopathologic types, the diagnosis is usually based on the predominant type. This should be stated in the pathology report. In this situation, record the predominant histopathologic type. If the pathology report does not indicate a predominant type, record the first type in Item C.14, place an asterisk by Item C.14, and record the other type(s) in the Comments section. Begin your statement in Comments with the verbatim as recorded in the following example:

Item D.18 (Comments):

Item #	Comments
C.14	Additional histopathologic type of lesion is:

- If the histopathologic type is unknown or not available, the appropriate general ICD-O-3 code such as 8000/3 or 8000/1 in the spaces provided. An example of when to use this is if the lung cancer diagnosis is confirmed in the absence of pathologic proof and the tissue is obtained post treatment. Record "9's" for the date indicating unknown or not applicable.

- Note that if a specific histopathologic type is recorded for the ICD-O-3 in C.11, this question cannot be completed with a nonspecific morphology code and unknown date.

- While the morphology that is recorded in C.14a may not exactly match what is recorded in C.11, there should be some similarity. For example, if on the biopsy that confirms a squamous cell carcinoma, NOS is noted, in C.11 the morphology code would be 8070/3. However, in a subsequent lobectomy, the pathology is reported to be squamous cell carcinoma, large cell, nonkeratinizing, NOS, in C.14a the morphology code would be 8072/3. This is a reasonable change. What would not be expected is a combination of squamous cell carcinoma from a biopsy (8070/3), and small cell carcinoma (8043/3) from a wedge resection. If such a difference in morphology of the primary tumor is noted from a biopsy to a later resection, record a note in the comments section that the difference was verified.

14b. Date of Pathologic Confirmation: This is the date that corresponds to the response in Item C.14a. Record the date that the actual procedure (biopsy, surgery, aspiration of cells, etc.)

was performed that collected the most tissue and confirmed this primary invasive lung cancer diagnosis. Operative reports are generally more accurate for date of procedure than surgical pathology reports, so in the case of a discrepancy, record the date of procedure from the operative report. In the event of a clinically diagnosed lung cancer, this item should be left blank, but may be updated if pathologic information becomes available post-treatment. An explanation of the source of the information should be provided in Item D.18 (Comments).

If the exact date of histopathologic confirmation cannot be determined from the record, year and month can usually be assessed. In this situation, record the exact month and year and the day as "99." Zero fill month and day, and record the last two digits of the year (e.g., 02/07/2002). For any portion of the date that is unknown, record "9's."

15. Grade of Primary Invasive Lung Cancer: This item is to be completed only by a CTR or CTR-eligible individual. Grade refers to a system of classifying certain characteristics of the cell. This information can be obtained directly from the histology report that collected the most tissue, a cytology report, a TNM form, a staging classification form, the discharge summary, or from doctor's notes.

- If the medical record states two types of histopathologic grades or a range of grades, record the most severe type. "Well differentiated" is the least severe type and "Undifferentiated" is the most severe type. The most severe grade should be recorded from the primary site. The grade from the metastatic site should not be recorded here, even if it is more severe.

Mark the box for "Unknown" when there is no indication in the record of the histopathologic grade.

16. TNM Staging for Primary Invasive Lung Cancer: This item refers to the TNM or AJCC (American Joint Committee on Cancer) staging system and is to be completed by a CTR or CTR-eligible individual. S/he should use all relevant information from the patient's medical record to assign the TNM stage.

TNM staging describes the anatomic extent of disease based on three components:

(1) The extent of the primary tumor (T),

(2) The absence or presence and extent of regional lymph node metastases (N), and

(3) The absence or presence of distant metastases (M).

In each of these components, the accompanying number indicates the extent of the malignant disease, thus showing progressive increase in tumor size or involvement.

- If the participant receives neoadjuvant therapy prior to staging, the abstractor should mark the box for "Yes" to indicate that the participant received neoadjuvant therapy prior to surgical resection. Mark the box for "No" to indicate that the participant did not receive neoadjuvant therapy prior to surgical resection.

The AJCC Manual for Staging of Cancer provides the minimum requirements for clinical and pathological staging. A list of relevant documentation, based on those requirements can be found below.

Note: The 6th Edition of the AJCC Cancer Staging Manual should be used to code the staging of all NLST lung cancers.

General Guidelines for N_X vs. N_0 and M_X vs. M_0:

The X category should be used when involvement of regional lymph nodes or distant metastatic sites was not evaluated or could not be evaluated. It is not sufficient to assume that an evaluation would have been negative (or positive). If there is a statement in the record documenting the physician's assessment of regional lymph nodes and/or metastatic sites as negative or not involved, without physical examination, imaging or other diagnostic procedures, this may be used to assign 0 rather than X. The use of category 0, as in N_0 or M_0, means that no involvement was found after some type of evaluation including appropriate work-up and/or the physician's clinical impression.

(NOTE: SCs should photocopy any documents from medical records that are used for TNM staging, and keep these with the participant's file.)

16a. TNM Clinical Staging (To be completed only by a CTR or CTR-eligible individual.)

Clinical staging is based on the assessment of the anatomic extent of disease. All information available prior to the first definitive treatment of primary invasive lung cancer may be used for TNM clinical staging. Relevant documentation that is suggested to assign clinical staging includes:

- Physical examination and medical history;
- Imaging procedures;
- Endoscopy, including bronchoscopy, esophagoscopy, mediastinoscopy, thoracentesis, and thoracoscopy, and
- Other tests designed to demonstrate extrathoracic metastasis and regional extension.

After review of the records; mark whether or not TNM Clinical Staging is available.

- **YES:** Mark yes if any part of the TNM Clinical Staging can be completed. Mark the boxes corresponding to the Primary Tumor (T) code, the Nodal Involvement (N) code, and the Distant Metastases (M) code.
- **NO:** Mark no if none of the TNM Clinical Staging is available. If any part of the TNM Clinical Staging is missing, skip to C.16b, TNM Pathological Staging.

16b. TNM Pathological Staging (To be completed only by a CTR or CTR-eligible individual.)

If both clinical and pathological staging are available, both should be recorded. Relevant documentation which is necessary to assign pathologic staging includes:

- Any data for clinical staging; and
- Examination of the resected specimen, including lymph nodes.

After review of the records, mark whether or not TNM Pathological Staging is available.

- **YES:** Mark yes if any part of the TNM Pathological Staging can be completed. Mark the boxes corresponding to the Primary Tumor (T) code, the Nodal Involvement (N) code, and the Distant Metastases (M) code.

- **NO:** Mark no if none of the TNM Pathological Staging is available. If any part of the TNM Pathological Staging is missing, skip to C.17, Record Stage.

17. Record Stage: Complete only if any part of the TNM Pathological Staging is x, (Tx, Nx, or Mx), unknown, or unavailable. This item is to document the stage of disease for primary invasive lung cancer using a system other than TNM. There are three stage classifications provided for lung cancer: "Stage Only," "VALSCG" (Veterans Administration Lung Cancer Study Group) for small cell lung cancer only, and "Summary Staging."

- If information about one or more of the stage classifications is not available in the medical record, it is not necessary to try to obtain it from another source.

- For small cell lung cancer, the VALSCG stage should be recorded, even if pathologic TNM stage is complete.

- If stage of disease is not available for any of these classification, but a different stage of classification is available in the record, place an asterisk beside Item C.17, and record in the Comments section the staging information found in the record. Begin your statement in Comments with the verbatim as recorded in the following example:

Item D.18 (Comments):

Item #	Comments
C.17	Other Stage of Classification is _____. Stage = _____.

If "Stage Only," "VALCSG," and/or "Summary Staging" is available, mark the boxes corresponding to the code for each. If stage of disease is not available for any particular classification, mark the box next to "Not available" in the appropriate column. If no stage of disease information is available, it is not necessary for the abstractor to obtain it from another source.

- For carcinoids (of the lung) that are malignant, "Summary Stage" should be completed.

Part D: Comments:

18. Comments: Use this section to record notes, comments and any overflow information while abstracting from the participant's medical record. Discrepant information should not be recorded in Comments. If an item being abstracted has conflicting or discrepant information, the SC Lead Abstractor, SC Coordinator, and/or Principal Investigator should review the discrepant information for the appropriate coding decision prior to contacting the CC MRA Coordinator.

If there are no additional comments, mark the box next to "No." If there are additional comments, mark the box next to "Yes," then record the comments as follows:

- Any additional diagnostic or staging procedure that is listed in Comments should be entered into IDEAS under Item A.3.

- Enter the item number to which the comments are related and record the comments in the space provided to the right of the item number.

- Throughout these specifications, standard phrases are given to preface comments so they will be easier to locate during analysis. *Please use these phrases at the beginning of the comments, if applicable.*

- Place an asterisk next to the item number being referenced in the main body of the DE form.

Part E: Health Care Provider/Hospital Location Information:

In this section, record health care provider and hospital location information, where the participant received diagnostic evaluation for lung cancer. Items E.19 and E.20 are not required, but it is recommended they be completed to facilitate collection of additional medical record data.

19. Health Care Provider for Diagnostic Evaluation: Record the name, address, and telephone number of the health care provider who performed diagnostic evaluation for lung cancer. Space has been allotted for entry of two health care providers. Record the health care provider's office address, if available. Record the participant's medical record or chart number for each health care provider location.

20. Hospital or Clinic for Diagnostic Evaluation: Record the name, address, and telephone number of the hospital or clinic at which the participant underwent diagnostic evaluation for lung cancer. Space has been allotted for entry of two hospitals or clinics. Record the participant's medical record or chart number for each hospital or clinic location.

After completing the form:

- The form should be checked to make sure it is accurate, legible, and complete.

- The SC staff member who completed the form should write his/her initials in the space labeled "Initials Complete" in the box at the top of the first page.

- The SC staff member who checked the form for completion should write his/her initials in the space labeled "Initials QC" in the box at the top of the first page. This should not be the same SC staff member who completed the form.

- Enter the form into IDEAS.

- File the form in the participant's study file.

National Lung Screening Trial / Lung Screening Study (NLST/LSS)

MEDICAL RECORD ABSTRACT TREATMENT INFORMATION FORM (TI)

Administrative Section

Date Abstracted: |__|__| / |__|__| / |2|0|__|__|

Abstractor ID: |__|__|__|__|

Screening Center ID: |__|__|

Study Year: T|__|

Purpose of Abstract:

- ☐ Initial Abstract
- ☐ Re-abstract for QA

Multiple DE #_____

Initials Complete: _____

Initials QC: _____

TI

Participant ID Label

PART A: INITIAL TREATMENT FOR PRIMARY INVASIVE LUNG CANCER

1. Radiation Treatment For Primary Invasive Lung Cancer:

- ☐ No (GO TO A.2)
- ☐ Yes
- ☐ Unknown (GO TO A.2)

1a. Sequence of Radiation Treatment:
(CHECK ALL THAT APPLY)

- ☐ Pre-operative
- ☐ Post-operative
- ☐ Definitive
- ☐ Unknown

1b. Details of Radiotherapy Treatment:

Radiotherapy Site	Start Date (mm/dd/yyyy)	End Date (mm/dd/yyyy)
Primary Chest Tumor and/or Regional Nodes	|__|__| / |__|__| / |2|0|__|__|	|__|__| / |__|__| / |2|0|__|__|
Prophylactic Brain	|__|__| / |__|__| / |2|0|__|__|	|__|__| / |__|__| / |2|0|__|__|
Other (Specify) _____	|__|__| / |__|__| / |2|0|__|__|	|__|__| / |__|__| / |2|0|__|__|
Unknown	|__|__| / |__|__| / |2|0|__|__|	|__|__| / |__|__| / |2|0|__|__|

2. Surgical Treatment for Primary Invasive Lung Cancer:

☐ No (GO TO A.4)
☐ Yes (IF YES, COMPLETE CHART BELOW USING SURGICAL PROCEDURE CODES LISTED)
☐ Unknown (GO TO A.4)

Surgical Procedure Code	Date of Procedure (mm-dd-yyyy)
|__|__| _____	|__|__|-|__|__|-|2|0|__|__|
|__|__| _____	|__|__|-|__|__|-|2|0|__|__|
|__|__| _____	|__|__|-|__|__|-|2|0|__|__|
|__|__| _____	|__|__|-|__|__|-|2|0|__|__|
|__|__| _____	|__|__|-|__|__|-|2|0|__|__|

SURGICAL PROCEDURE CODES

01 – Exploratory thoracotomy without resection
02 = Median sternotomy
03 = Lobectomy
04 = Bilobectomy
05 = Pneumonectomy
06 = Wedge resection
07 = Segmental resection
08 = Lymphadenectomy/lymph node sampling
09 = Chest wall resection
10 = Thoracentesis
11 = Partial pleurectomy
12 = Multiple wedge resections
13 = Multiple segmental resections
88 = Other (SPECIFY)
99 = Unknown

3. Any Local or Regional Residual Disease After Surgery:..... (TO BE COMPLETED BY CTR OR CTR-ELIGIBLE STAFF)

CTR ID # |___|___|___|___|

☐ No
☐ Yes – Microscopic
☐ Yes – Gross Tumor
☐ Unknown

4. Systemic Chemotherapy for Primary Invasive Lung Cancer:

☐ No (GO TO A.5)
☐ Yes (IF YES, COMPLETE DATE CHEMOTHERAPY BEGAN)
☐ Unknown (GO TO A.5)

Date Course of Chemotherapy Began:

|___|___| - |___|___| - |2|0|__|__|
MO DAY YEAR

5. Other Type of Treatment for Primary Invasive Lung Cancer:

☐ No (GO TO B.6)
☐ Yes (IF YES, COMPLETE TABLE BELOW SPECIFYING TYPE OF TREATMENT AND START DATE)
☐ Unknown (GO TO B.6)

Type of Treatment 01 Immune Therapy 02 Radiofrequency Ablation 03 Thermal Ablation 04 Chemical Ablation 05 Other (specify) 99 Unknown treatment	Treatment Start Date (mm-dd-yyyy)
_____	__-__-2___
_____	__-__-2___
_____	__-__-2___
_____	__-__-2___
_____	__-__-2___

PART B: COMMENTS

6. Comments:

☐ No
☐ Yes (IF YES, PLEASE SPECIFY)

ITEM	COMMENTS

PART C: HEALTH CARE PROVIDER/HOSPITAL LOCATION INFORMATION

7. HEALTH CARE PROVIDER FOR TREATMENT:

a. NAME: MR./MRS./MISS/MS./DR. | FIRST | MIDDLE | LAST | (JR., SR., etc.)

STREET ADDRESS 1 | STREET ADDRESS 2 | SUITE OR OFFICE NO.

CITY | STATE | ZIP

TELEPHONE 1	TELEPHONE 2	FAX NUMBER
( )	( )	( )

MEDICAL RECORD / CHART NUMBER:

b. NAME: MR./MRS./MISS/MS./DR. | FIRST | MIDDLE | LAST | (JR., SR., etc.)

STREET ADDRESS 1 | STREET ADDRESS 2 | SUITE OR OFFICE NO.

CITY | STATE | ZIP

TELEPHONE 1	TELEPHONE 2	FAX NUMBER
( )	( )	( )

MEDICAL RECORD / CHART NUMBER:

8. HOSPITAL OR CLINIC FOR TREATMENT:

a. NAME OF HOSPITAL OR CLINIC:

STREET ADDRESS 1 | STREET ADDRESS 2 | SUITE OR OFFICE NO.

CITY | STATE | ZIP

TELEPHONE 1	TELEPHONE 2	FAX NUMBER
( )	( )	( )

MEDICAL RECORD / CHART NUMBER:

b. NAME OF HOSPITAL OR CLINIC:

STREET ADDRESS 1 | STREET ADDRESS 2 | SUITE OR OFFICE NO.

CITY | STATE | ZIP

TELEPHONE 1	TELEPHONE 2	FAX NUMBER
( )	( )	( )

MEDICAL RECORD / CHART NUMBER:

National Lung Screening Trial (NLST)

Specifications for Completion of the Medical Record Abstract Treatment Information Form (TI)

This form should be completed by the SC Coordinator, the Medical Record Abstractor, and the CTR or CTR-eligible individual. The SC Coordinator should complete the Administrative Section. The SC MRA and CTR should complete the remainder of the form, although only the CTR should complete Item A.3 (Any Local or Regional Residual Disease After Surgery). This form should be completed in black or blue ink.

Some key guidelines for abstracting treatment information are presented below:

- The TI form is only expected after a DE form is completed with a result of the diagnostic evaluation of primary invasive lung cancer. Each DE form with a result of primary invasive lung cancer will set an expectation for a separate TI form.
- Primary cancers of the trachea are classified as primary invasive lung cancers for the purposes of medical record abstraction; therefore, a TI form is required following completion of the DE form.
- When abstracting date information for items with multiple treatments, record the dates in the order in which they are found in the medical record.
- Sources of information for abstracting the variable items on the form should be used in priority order by best source. The preferred sources of information are a health care provider, hospital, or tumor registry. If the treatment is considered to be a non-traditional therapy that would not usually be mentioned in a medical record, it is acceptable to take the participant's self-report. In all other cases, the SC should attempt to obtain information from a clinic or health care provider before accepting a report from the participant only.
- Information about treatment procedures should be collected for the initial, or first, course of treatment. Initial treatment usually begins within six months of the cancer diagnosis; however, if an initial treatment begins more than six months after diagnosis, it should still be recorded. The maximum time period for which medical records should be collected for treatment information is one year from the date of a cancer diagnosis.
- This form includes items that require that data be entered verbatim, such as recording "Other (Specify)," and recording comments. The MRA should be sure to use clear language and legible handwriting when completing these items.
- If additional space is needed to record treatment information, use the Comments section. Record the same type of data as requested in the initial treatment information section.
- If any item has unclear, discrepant, or conflicting information, review this information with the SC Lead Abstractor, SC Coordinator, or the Principal Investigator prior to contacting the CC MRA Coordinator.

Specifications for completing each item of the form are given on the following pages.

Appendix 7-5 Specifications for Completion of the Medical Record Abstract Treatment Information Form (TI)

Administrative Section:

Participant ID: Affix a PID label in the box provided at the top of the form.

Date Abstracted: Record the date the medical record was abstracted. This is the date the form was completed. Zero fill the month and day and record the last two digits of the year (e.g., 05/05/2002).

Abstractor ID: Record the four-digit staff ID number assigned to the individual who is abstracting the medical record and completing the TI form.

Screening Center ID: Record the two-digit SC ID number.

Study Year: Record the study year the participant was in when s/he received the positive screening exam for which follow-up revealed a primary lung cancer, or if the cancer diagnosis is not the result of a positive screening exam, enter the study year the participant was in when the lung cancer was reported. If the cancer diagnosis originated from a T_3 DE form completed following a T_2 screening exam with a result code "A," enter T_3 as the study year for the TI form.

Purpose of Abstract: This form may be used for either the initial abstracting of medical record information, or for repeat abstraction of the medical record for quality assurance. Mark the box corresponding to the purpose of the abstract as follows:

Initial abstract: Medical record information is being abstracted for the "first" time to confirm the treatment of lung cancer.

Re-abstract for QA: Medical record information that has already been abstracted to confirm the treatment of lung cancer is being re-abstracted for the purpose of quality assurance. (This will not apply to the SC MRA.)

Multiple DE #: The purpose of this item is to indicate whether this form is being used to abstract information about an additional primary invasive lung cancer that was diagnosed simultaneously with or subsequent to the first primary invasive lung cancer within the same study year. The sequence number used here should match the number used on the DE form that describes the same particular primary invasive lung cancer. The MRA will determine the correct DE form by comparing the diagnostic information given in Part C of the DE form (histology, cytology, staging, date of diagnosis) with the description of the cancer that is part of the treatment information provided in the medical record.

NOTE: Cases in which no primary invasive lung cancer or only one primary invasive lung cancer was diagnosed, should be coded as "1."

Part A: Initial Treatment Information for Primary Invasive Lung Cancer:

In this section, record all treatments that make up the initial, or first course of, treatment the participant received for primary invasive lung cancer. Do not record treatments for metastases to the lung from other primary cancers.

- Initial treatment, in general, is treatment that is received within six months of the diagnosis.

- If the treatment is intended as initial treatment, it should be recorded, even if it occurs more than six months after diagnosis.

- Time Period Rules for First Course of Treatment (in order of precedence):

  (1) If there is a documented first course of treatment, record treatments that occur through the end of this course, regardless of its duration.

  (2) If the patient is treated according to a facility's standards of practice, first course ends according to the facility's standards of practice.

  (3) If there is no documentation of a first course of treatment or standards of practice, *first course of treatment includes all treatment received before disease progression or treatment failure*. If it is undocumented whether there is disease progression/treatment failure and the treatment in question begins more than one year after diagnosis, assume that the treatment is not part of the first course.

  (4) If a patient refuses all treatment modalities and does not change his/her mind within one year, or if the health care provider opts not to treat the patient, record that there was no treatment in the first course.

All modalities of treatment should be included, regardless of their sequence or the degree of completion.

- If there is a significant treatment that is not in the first course of treatment and the abstractor and the SC Principal Investigator feel it should be recorded, the relevant medical records should be copied (identifiers deleted) and sent to the CC MRA Coordinator with a memo describing the situation.

  - Combination Treatments: If multiple treatments of the same type are given in combination, enter the date of the first treatment for the combination treatments. If a treatment is added to or removed from the combination, the new combination should be recorded as a new treatment with a new start date.

1. Radiation Treatment for Primary Invasive Lung Cancer: This item asks for the radiation treatment the participant received for lung cancer. Radiation treatment most commonly consists of either external photon beam therapy or brachytherapy (interbronchial implant). More rarely, radiation treatment may consist of either neutron or proton external beam therapy. Note that this item is concerned with radiation treatment and **not** diagnostic x-rays such as a CT scan.

External photon beam therapy is delivered by a machine which generates x-rays or contains a large amount of a radioactive isotope, such as cobalt, or is delivered by a linear accelerator. External beam treatments are given in one or more "series" or "courses." Each course of radiation is administered over a period of days or weeks in small daily doses.

Brachytherapy is a method of radiotherapy in which radioactive sources are applied to the external surface of the patient, implanted in tissue, or inserted into body cavities. Brachytherapy procedures usually are performed in an operating room since they require anesthesia. Although the brachytherapy treatment may be performed in a surgical suite and

recorded in surgical notes, it is radiotherapy and should be recorded as such for purposes of describing the participant's treatment.

Some institutions may have the capability to deliver neutron beam therapy, via a hospital based high-energy cyclotron, or proton beam therapy via a hospital-based synchrotron. Treatment via these modalities is usually administered in "courses" or "series" over a period of time. Hyperfractionated therapy refers to treatment with more than one fraction of radiation a day.

Mark the box corresponding to whether the participant received radiation treatment as follows:

- **No:** The record clearly states that the participant did not receive radiation treatment, or there is no mention of radiation treatment (planned or given) in the records. Mark the box for "No" and go to Item A.2.

- **Yes:** The record indicates that the participant received radiation treatment. Mark the box for "Yes" and complete Item A.1a.

- **Unknown:** The record states that a radiation treatment is planned but provides no mention of whether or not it was actually given. This code should also be used if the record clearly states that this information is unknown. Mark the box for "Unknown" and go to Item A.2.

1a. Sequence of Radiation Treatment (CHECK ALL THAT APPLY): This item asks for specification as to the timing of the radiation treatment received in relation to surgical resection. Mark the boxes corresponding to whether the radiation treatment was pre-operative, post-operative, definitive, or unknown. Check all that apply.

- **Pre-operative:** Mark this box if the radiation treatment was received prior to surgical resection.

- **Post-operative:** Mark this box if the radiation treatment was received following surgical resection.

- **Definitive:** Mark this box if the radiation treatment was received without a therapeutic surgical resection. Treatments other than surgical resection, such as chemotherapy, may have been utilized, though.

- **Unknown:** Mark this box if the sequence of radiation treatment in relation to other treatments is unknown.

1b. Details of Radiotherapy Treatment: This item asks for the radiotherapy site, and the start and end dates for treatment. The options for radiotherapy site are Primary Chest Tumor and/or Regional Nodes, Prophylactic Brain, Other, and Unknown. For start and end dates, record the month, day, and year that the radiation treatment was begun and ended for a particular course next to the appropriate site. If the first course of radiation treatment is given to the same site as an initial component and then a boost, record the overall dates. If radiotherapy treatment was given both pre-operatively and post-operatively, complete Item A.1b using the dates of the pre-operative therapy, and then record the dates of the post-operative therapy in Item B.6, Comments. Zero fill month and day, and record the last two digits for the year (e.g., 02/07/2002). If the date is not clear, year and month can usually be assessed, even if

the exact date cannot be determined. In this situation, record the exact month and year. Record the day as "99"

2. **Surgical Treatment for Primary Invasive Lung Cancer:** This item asks for the surgical treatment that the participant received for lung cancer. Mark the box corresponding to whether the participant received surgical treatment as follows:

   - **No:** The record clearly states that the participant did not receive surgical treatment, or there is no mention of surgical treatment (planned or given) in the records. Mark the box for "No" and go to Item A.4.

   - **Yes:** The record indicates that the participant received surgical treatment. Mark the box for "Yes" and record the appropriate surgical code(s) and the date(s) surgical treatment(s) began. Refer to the Surgical Procedure Codes listed for the list of common surgical procedures for lung cancer. If the participant had a surgical procedure other than those listed, mark the box for "Other (SPECIFY)" and record the surgical procedure performed on the line provided. Record the month, day, and year that the surgical procedure was performed. If the date is not clear, year and month can usually be assessed, even if the exact date cannot be determined. In this situation, record the exact month and year and the day as "99." Zero fill month and day, and record the last two digits for the year (e.g., 02/07/2002). Record information for up to five surgical procedures.

     Type of Surgical Procedure: Complete the table. Record the two digit procedure code in the spaces provided, then write the type of procedure in the space provided, and record the date the procedure was performed using the month, day, year format. Refer to the Surgical Procedure Codes listed for the common surgical procedures for lung cancer. If the participant has a surgical procedure other than those listed, record "88" for "other" and write the type of procedure in the space provided.

     - If surgical resection with removal of lymph nodes was performed, this should be coded as two separate procedures using the appropriate code for surgical resection and code "08" for the lymph node removal.

     - Mediastinoscopy is not a treatment for lung cancer and should not be documented as a procedure.

     - If an open surgical biopsy (diagnostic wedge resection) and a surgical resection were performed, these should be coded as two separate procedures using the appropriate code for surgical resection and code "06" for the wedge resection.

If more space is needed to record additional surgical procedures, use the Comments section (B.6) to record those procedures. In Comments, record A.2 and date(s) of surgical procedures.

   - **Unknown:** The record states that a surgical treatment is planned but then there is no mention of whether it occurred. This code should also be used if the record clearly states that this information is unknown. Mark the box for "Unknown" and go to Item A.4.

3. **Any Local or Regional Residual Disease After Surgery:** This item should be completed only by a CTR or CTR-eligible individual. The individual who completes the form should

enter their CTR staff ID number in the space provided. This item documents whether the participant had any local or regional residual disease after surgery. Record information for this item for any attempted surgical procedure *even if the procedure was not completed.* Surgery is defined as any of the surgical procedures listed in Item A.2. If there are multiple surgeries, use the last surgery in the first course of treatment. Regional residual disease is defined as a cancer that remains after surgery and is related to the original site by direct extension. It does not apply to metastases. If neither pathology nor operative reports are available, a discharge summary or health care provider's note with treatment plan may be used to record this item. Mark the box corresponding to whether the participant had any local or regional residual disease left after surgery as follows:

- **No:** The record indicates that the participant had no local or regional residual disease left after surgery. Mark the box for "No" and go to Item A.4.

- **Yes - Microscopic:** The record indicates that the participant had local or regional residual disease left after surgery which was microscopic (of minute size and cannot be visualized with the naked eye). For example, if the pathology report states "tumor to surgical margin" mark the box for "Yes – Microscopic" and go to Item A.4.

- **Yes – Gross Tumor:** The record indicates that the participant had local or regional residual disease left after surgery which was macroscopic (can be visualized with the naked eye). Mark the box for "Yes – Gross Tumor" and go to Item A.4.

- **Unknown:** The record does not mention if the participant had local or regional residual disease after surgery, or the record clearly states that this information is unknown. Mark the box for "Unknown" and go to Item A.4.

4. Systemic Chemotherapy for Primary Invasive Lung Cancer: This item asks for any systemic chemo-therapy the participant received for primary invasive lung cancer. Chemotherapy is the use of drugs as treatment for cancer. Chemotherapy may be the primary treatment prescribed in cases of advanced cancer, or may be an adjuvant treatment, given in addition to surgery or radiation.

The participant's medical record may not contain chemotherapy data. Unlike surgery and radiation, which must be performed at a hospital or clinic, chemotherapy may be administered at a health care provider's office. In addition, it may be self-administered under the supervision of a health care provider. It is therefore especially important that the abstractor carefully review the record and, if necessary, contact the health care provider for information on chemotherapy.

A course of chemotherapy is typically divided into discrete components called cycles. Each cycle has a set of medications given in a prescribed sequence for a set duration. Examples of chemotherapeutic medications include vindesine, cisplatin, cyclophosphamide, doxyrubicin, vinblastine, etoposide (VP-16), and mitomycin. Often the combinations are part of a protocol. For a given course of chemotherapy, a predetermined number of cycles are given – for example, a participant may be on his first course of chemotherapy that has six cycles. In such a cycle, drug 1 may be given day one for a six-hour infusion. Drug 2 may be given days one through seven for an hour infusion each day. A third drug may be given day ten. The cycle may be 28 days long with the 29th day being day one of the next cycle, and the regimen is repeated. In such a case, six cycles would require 24 weeks, and would be considered one course of chemotherapy. The start of the three drug regimen (day one, cycle one) would be the date of the first course of chemotherapy. The entire treatment of six cycles is considered one course of chemotherapy.

Mark the box corresponding to whether the participant received chemotherapy treatment as follows:

- **No:** The record clearly states that the participant did not receive chemotherapy or there is no mention of chemotherapy (planned or given) in the records. Mark the box for "No" and go to Item A.5.

- **Yes:** The record indicates that the participant received chemotherapy, including the instance where a participant is enrolled in a chemotherapy randomized controlled trial with no placebo arm (e.g. one chemotherapy regimen versus another chemotherapy regimen). Mark the box for "Yes" and record the date chemotherapy began: Record the month, day, and year that the chemotherapy was begun for a particular course. If the date is not clear, year and month can usually be assessed, even if the exact date cannot be determined. In this situation, record the exact month and year and the day as "99." Zero fill month and day, and record the last two digits for the year (e.g., 02/07/2002).

  If more space is needed to record additional chemotherapy treatments, use the Comments section (B.6) to record the same type of data. In Comments, record A.4 and date(s) chemotherapy began.

- **Unknown:** The record states that a chemotherapy treatment is planned but provides no mention of whether it was given. This code should also be used if the record clearly states that this information is unknown. Mark the box for "Unknown" and go to Item A.5.

  If the participant is enrolled in a chemotherapy randomized controlled trial with a placebo arm and the randomization assignment is blinded and thus unknown, mark the box for "Unknown" and provide a comment in Part B. If the participant's treatment arm becomes known in the future, update the TI form and IDEAS to indicate the correct Yes or No response.

5. Other Type of Treatment for Primary Invasive Lung Cancer: This item asks for any treatment other than surgery, radiation, and chemotherapy treatment, which the participant received for primary invasive lung cancer. Other types of treatment might include immune therapy, radiofrequency ablation, thermal ablation, or chemical ablation. *(Note: Pleurodesis is not considered an "Other Type of Treatment for Primary Invasive Lung Cancer" as it treats a problem related to the cancer, not the lung cancer itself.)*

Mark the box corresponding to whether the participant received some other type of treatment as follows:

- **No:** The record clearly states that the participant did not receive any other type of treatment, or there is no mention of other treatments (planned or given) in the records. Mark the box for "No" and go to Item B.6.

- **Yes:** The record indicates that the participant received some other type of treatment. Mark the box for "Yes" and record the type of treatment and date(s) other treatment began. Record the month, day, and year that the other type of therapy began. Specify the type of treatment by noting the appropriate treatment code in the boxes next to the date. If the participant had a treatment other than those listed, mark the box for "Other (SPECIFY)" and record the treatment on the line provided. Record information for up to five "other" treatments in this section of the form. If the date is

not clear, year and month can usually be assessed, even if the exact date cannot be determined. In this situation, record the exact month and year and the day as "99." Zero fill month and day, and record the last two digits for the year (e.g., 02/07/2002).

If more space is needed to record other type of treatments for lung cancer, use the Comments section (B.6) to record the same type of data. In Comments, record A.5 and date(s) other treatment(s) began.

- **Unknown:** The record states that an "other" treatment is planned but provides no mention of whether or not it was given. This code should also be used if the record clearly states that this information is unknown. Mark the box for "Unknown" and go to Item B.6.

Part B: Comments:

6. Comments: Use this section to record notes, comments, and any overflow information. Discrepant information should not be recorded in Comments. If an item being abstracted provides conflicting or discrepant information, the SC Lead Abstractor, SC Coordinator, and/or Principal Investigator should review the discrepant information for the appropriate coding decision prior to contacting the CC MRA Coordinator.

If there are no additional comments, mark the box next to "No." If there are additional comments, mark the box next to "Yes," then record the comments as follows. Enter the item number to which the comments are related, record the comments in the space provided to the right of the item number. Place an asterisk next to the item number being referenced in the main body of the TI form.

Part C: Health Care Provider/Hospital Location Information:

In this section, record health care provider location information, where the participant received treatment for lung cancer. Items C.7 and C.8 are not required, but it is recommended they be completed to facilitate collection of additional medical record data.

7. Health Care Provider for Treatment: Record the name, address, and telephone number of the health care provider who provided care during the participant's treatment for lung cancer and/or the health care provider who provided or administered the treatment. Space has been allotted for entry of two health care providers. Record the health care provider's office address, if available. Record the participant's medical record or chart number for each health care provider location.

8. Hospital or Clinic for Treatment: Record the name, address, and telephone number of the hospital or clinic at which the participant underwent treatment for lung cancer. Space has been allotted for entry of two hospitals or clinics. Record the participant's medical record or chart number for each hospital or clinic location.

After completing the form:

- The form should be checked to make sure it is accurate, legible, and complete.
- The SC staff member who completed the form should write his/her initials in the space labeled "Initials Complete" in the box at the top right corner of the first page.

- The SC staff member who checked the form for completion should write his/her initials in the space labeled "Initials QC" in the box at the top right corner of the first page. This should not be the same SC staff member who completed the form.
- Enter the form into IDEAS.
- File the form in the participant's study file.

National Lung Screening Trial / Lung Screening Study (NLST/LSS)

MEDICAL RECORD ABSTRACT
CANCER PROGRESSION FORM (CP)

Administrative Section	
Date Completed: |_|_|/|_|_|/|2|0|_|_|	Initials Complete:_____ Initials QC: _____ CP
Abstractor ID: |_|_|_|_|	
Screening Center ID: |_|_|	
Study Year: T|_|	Participant ID Label
Purpose of Abstract: ☐ Initial Abstract ☐ Re-abstract for QA	

Part A. Progressive Disease Following Treatment of First Primary Invasive Lung Cancer

1. Did the participant develop progressive disease (progression of primary site, metastatic disease, recurrence) following treatment for lung cancer?

☐ No (Go to B.4)

☐ Yes

☐ Unknown (Go to B.4)

2. Date of the first documentation of progressive lung cancer: \|_\|_\|-\|_\|_\|-\|2\|0\|_\|_\|

3. Site(s) of progression (record all that apply):

a. \|_\|_\|
b. \|_\|_\|
c. \|_\|_\|
d. \|_\|_\|
e. \|_\|_\|

01 Original lung site
02 Other lung site
03 Pleura
04 Mediastinum
05 Brain
06 Bone
07 Liver
08 Adrenal
09 Other, specify_____
99 Unknown site

Part B. Development of Second Primary Invasive Lung Cancer

4. Did the participant develop a second primary invasive lung cancer after treatment for the first lung cancer during the trial?

- ☐ No (Go to B. 6)
- ☐ Yes
- ☐ Unknown (Go to B. 6)

5. Date of diagnosis of second primary invasive lung cancer: |_|_|-|_|_|-|2|0|_|_|

6. Comments: ____________________

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Medical Chart Abstractor

National Lung Screening Trial (NLST)

Specifications for Completion of the Cancer Progression Form (CP)

This form is to be completed yearly following completion of the DE and TI forms, through 2009~~,~~ by the MRA for each participant with confirmed lung cancer. Some key guidelines for abstracting cancer progression information are presented below:

- The CP form should be completed within the first two months of the study year following the study year in which the TI is completed. However, IDEAS will not set an expectation for the CP form until the TI form has been entered. For example, if the date of a positive T_0 screen is 02/01/03, the DE is completed on 10/15/03, and the TI is completed on 03/01/04 (T_1 study year), then the CP will be expected during the T_2 study year. The CP form is to be completed within the first 2 months of the study year in which it is due.

- The purpose of the form is to document the progression of lung cancer. The progression of the lung cancer documented on this form will only be for the participant's current study year. If the participant has already had a progression of his/her lung cancer that was recorded on a previous CP, that information should not be repeated.

- Each CP is identifying new or further progression of disease. The MRA will request medical records for the interim (previous study year) at the beginning of each new study year following the confirmation of the lung cancer. The form will be used initially the study year after the TI was receipted. Expectations will be set to receive the form on an annual basis once the DE is entered in IDEAS.

- Primary cancers of the trachea are classified as primary invasive lung cancers for the purposes of medical record abstraction; therefore, a CP form is required in the study year following completion of the DE and TI forms.

- If there is an expectation in IDEAS for a CP form and the participant is deceased, the CP form should be completed with information about disease progression since the time of completion of the TI form or the most recent CP form.

Administrative Section

Participant ID Label: Affix a PID label in the box provided at the top of the form.

Date Completed: Record the date the CP form was completed. Zero fill month and day, if necessary, and record the last two digits of the year (e.g., 02/07/2002).

Abstractor ID: Record the four-digit staff ID number assigned to the individual who is abstracting the medical record and completing the DE form. If more than one abstractor completes the DE form, the SC Coordinator should determine which abstractor is responsible for the content of the form – it is this abstractor's ID number that should be recorded here.

Screening Center ID: Record the two-digit SC ID number.

Study Year: Indicate the study year the participant is currently in when the CP is being completed.

Appendix 7-7 Specifications for Completion of the Cancer Progression Form (CP)

Purpose of Abstract: This form may be used for either the initial abstracting of medical record information, or for repeat abstraction of the medical record for quality assurance. Mark the box corresponding to the purpose of the abstract as follows:

Initial abstract: Medical record information is being abstracted for the first time to document the progression of lung cancer.

Re-abstract for QA: Medical record information that has already been abstracted to document the progression of lung cancer is being re-abstracted for the purpose of quality assurance. (This will not apply to the SC MRA.)

Part A. Progressive Disease Following Treatment of First Primary Invasive Lung Cancer

1. Progressive Disease:

- **No,** the participant did not develop progressive disease following treatment for lung cancer. If No is recorded then the MRA should skip to Item B.4 and leave Items A.2 and A.3 blank.

- **Yes,** the participant did develop progressive disease following treatment of lung cancer. Progressive disease is defined as enlargement of the original tumor, new metastasis to lymph nodes or other organ site not included in the original tumor staging, or disease recurrence. Death is not considered disease progression.

- **Unknown**, it is unknown whether the participant developed progressive disease following treatment for lung cancer. If Unknown is recorded then the MRA should skip to Item B.4 and leave Items A.2 and A.3 blank.

2. Date of the First Documentation of Progressive Lung Cancer: Record the date progressive lung cancer was first documented in the medical record. Zero fill month and day, if necessary, and record the last two digits of the year (e.g., 02/07/2002).

3. Site(s) of Progression: Record the site where progression has been identified. More than one site may be recorded. If the site is not listed, then record 09 = Other, specify and record the site in the space provided. If the site of progression is unknown, record 99.

Part B. Development of Second Primary Invasive Lung Cancer

4. Development of Second Primary Invasive Lung Cancer: Indicate whether the participant developed a second primary invasive lung cancer after treatment for the first lung cancer during the trial.

5. Date of Diagnosis of Second Primary Invasive Lung Cancer: Record the date a second primary invasive lung cancer was first documented in the medical record. Zero fill month and day, if necessary, and record the last two digits of the year (e.g., 02/07/2002). If a second cancer is identified the SC should check to see that a CNF was completed.

6. Comments: Document any comments in the space provided.

Medical Chart Abstractor: The MRA completing the form should sign this form when completed.

After completing the form:

- The form should be checked to make sure it is accurate, legible, and complete.
- The SC staff member who completed the form should write his/her initials in the space labeled "Initials Complete" in the box at the top right corner of the first page.
- The SC staff member who checked the form for completion should write his/her initials in the space labeled "Initials QC" in the box at the top right corner of the first page. This should not be the same SC staff member who completed the form.
- Enter the form into IDEAS.
- File the form in the participant's study file.

National Lung Screening Trial (NLST)

Medical Records Abstraction Quality Assurance Plan

It is the responsibility of the Coordinating Center (CC) to ensure the quality of medical records abstraction at each SC. The CC MRA Coordinator will monitor the QA process at each SC and provide input for resolution of medical record abstraction issues. To achieve this, the CC MRA Coordinator will implement the following medical records quality assurance plan. The primary goals of the plan are to:

- Ensure that the SC MRAs utilize standard abstracting procedures;
- Ensure a high level of accuracy for data elements;
- Evaluate the quality of data recorded on the Diagnostic Evaluation, Treatment Information, and Cancer Progression Forms, and
- Improve the quality of data abstracted by providing feedback to the SC MRAs in areas where problems are identified.

The CC will re-abstract a portion of cases to assess accuracy and completeness of MRA form completion, as well as to provide feedback to the SCs. All SCs will be asked to submit to the CC a copy of the medical records for the first ten primary invasive lung cancer cases and the first ten non-cancer cases abstracted. The QA process will continue for all SCs and the proportion of forms selected for re-abstraction may change over time, depending on MRA performance and after consultation with the SC. Currently, the selection process is as follows:

- Diagnostic Evaluation (DE) Form: The CC will perform a monthly selection of forms for QA review from all DE forms entered into IDEAS within the past month. The selection will include one hundred percent (100%) of DE forms with a diagnosis of primary invasive lung cancer and a random sample of five percent (5%) of all non-lung cancer cases.
- Treatment Information (TI) Form: The CC will perform a yearly selection of forms for QA review from all TI forms received within a specified one-year time period. The case selection will include 45 forms from each screening arm and will represent a pre-determined number of early and late stage lung cancer cases.
- Cancer Progression (CP) Form: The CC will perform an initial selection of five CP forms per SC for review. Following the initial review period, the CC will perform a yearly selection of forms for QA review from all CP forms received within a specified one-year time period. The cases selection will include 45 forms from each screening arm and will represent a pre-determined number of early and late stage lung cancer cases.

The SCs will follow the usual process of requesting records and supporting documents that are needed for abstraction, removing all identifiers for those sent to the CC for re-abstraction. The CC and the SCs will follow these procedures for the Quality Assurance of Medical Records Abstraction:

- The CC will identify the PIDs for the forms selected for re-abstraction according to the previously described criteria;

- The CC will record the PID numbers from those forms identified;
- The CC will request that the SCs provide copies of all medical records documenting information abstracted on the DE, TI, or CP form for the identified PIDs;
- The SC MRAs will copy the requested medical records, removing all personal identifiers from the medical records, and submit these to the CC with a Forms Transmittal Log (Appendix 11-14) within two weeks of the initial request for medical records;
- Qualified CC MRAs will re-abstract these medical records on appropriate forms (DE, TI, or CP);
- The CC will compare the CC re-abstracted form to the original form from the SC for each identified PID;
- The CC will perform adjudication of any discrepancies identified during the comparison;
- The CC will provide feedback regarding the review to the SCs on a regular basis;
- The SCs will make necessary revisions to the IDEAS database based upon feedback from the CC;
- The CC will provide the SC with quarterly QA reports for review, and
- The CC will provide the NCI with monthly QA reports for review.

The SCs are encouraged to contact the CC MRA Coordinator with any questions or issues that arise on any aspect of the medical record abstraction process. The CC MRA Coordinator will provide a prompt response.

8. ASCERTAINMENT OF CANCER STATUS

8.1 Overview

Each SC will implement procedures to ascertain cancer status through December 31, 2009 for all randomized individuals. Ascertainment of cancer status will include procedures to investigate and confirm diagnoses for all primary invasive lung cancers identified among randomized individuals. In addition, SCs will investigate and confirm diagnoses for all reported cancers and for all cancers identified as part of the Endpoint Verification Process. (See Chapter 9 for information regarding the Endpoint Verification Process.) Ascertainment of cancer diagnosis can occur either as a result of follow-up of a positive screening examination or from reports of cancer from other sources, such as the participant, the participant's family members or physician, or a Death Certificate. Chapter 7 provides detailed information regarding the ascertainment of cancer resulting from the follow-up of a positive screen, including information regarding completion of the Diagnostic Evaluation (DE), Treatment Information (TI), and Cancer Progression (CP) forms. Any cancer recorded on a DE form, including the non-lung primary cancers that are the result of the diagnostic evaluation, does not need to be documented on a Cancer Notification Form (CNF). Chapter 8 provides information regarding the ascertainment of cancer from other sources, such as the participant, the participant's family members or physician, or a Death Certificate.

All reports of cancer will be documented and investigated according to protocol. Cancers reported to have been diagnosed on or before December 31, 2009 will be investigated for verification of the diagnosis. Cancers reported to have been diagnosed after December 31, 2009 will be documented, but not investigated. For these cancers, only the diagnosis and estimated diagnosis date will be collected. For every case of confirmed primary invasive lung cancer diagnosed on or before December 31, 2009, information on diagnostic evaluation, cancer diagnosis, initial treatment, and cancer progression (if necessary) will be collected. For every case of confirmed non-lung cancer diagnosed on or before December 31, 2009, information on the cancer diagnosis will be collected. The information collected will be abstracted onto the appropriate medical record abstract forms. The main steps for cancer ascertainment are as follows:

1. Ascertain each participant's cancer status through sources such as the ASU, the participant, the participant's family members or physician, or the Death Certificate.

2. For all cancers reported outside of the ASU or DE form, complete a Cancer Notification Form (CNF, Appendix 8-1). The Specifications for Completion of the CNF are found in Appendix 8-2.

3. For all cancers documented on an ASU or CNF with a diagnosis date on or before December 31, 2009, collect medical records to confirm the diagnosis.

4. For all reported cancers documented on an ASU or CNF, complete a Cancer Diagnosis Form (CDF, Appendix 8-3) to confirm the diagnosis. If the cancer was reported to have been diagnosed after December 31, 2009, only the diagnosis and estimated diagnosis date should be recorded on the CDF. The Specifications for Completion of the CDF are found in Appendix 8-4. If a cancer was erroneously reported, this should be recorded on the CDF.

5. If the CDF confirms a primary invasive lung cancer that has not previously been reported, complete a Diagnostic Evaluation (DE) form, Treatment Information (TI) form, and Cancer Progression (CP) form, if necessary (See Chapter 7). Attach a copy of the pathology report that supports the diagnosis.

6. Upon completion of the appropriate medical record abstract form(s), or MDF(s), enter the form(s) into IDEAS.

7. Monitor the cancer ascertainment process through use of the Expected Forms Report (Appendix 11-18).

The cancer ascertainment and documentation procedures listed above are presented in a flowchart, Exhibit 8-1.

8.2 Sources for Ascertaining Cancer Status

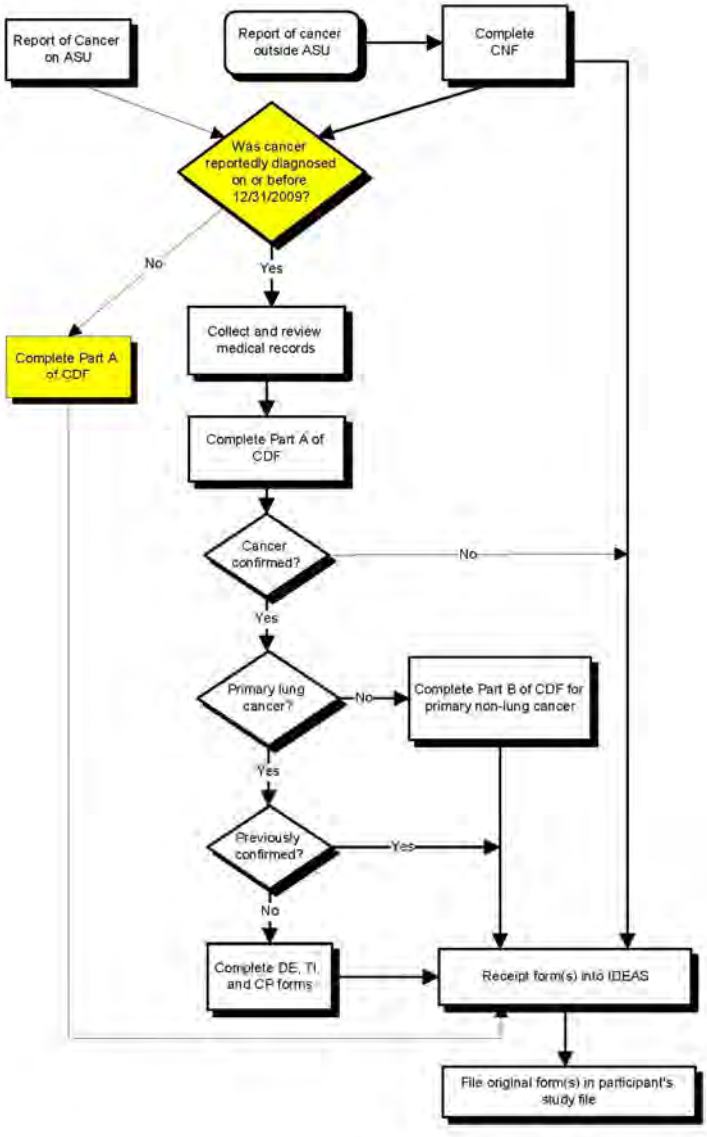
The SC should attempt to ascertain cancer status for all participants. This will be accomplished primarily through two types of sources: notification by the participant on the Annual Study Update (ASU, Appendix 3-11) and notification by sources outside the ASU. These may include notification by the participant other than on the ASU, notification by a participant's family member or health care provider, or notification by the participant's Death Certificate.

8.2.1 Notification of Cancer on the Annual Study Update (ASU)

The ASU will be administered to all randomized participants each year of the study after the baseline year with the final ASU administered on an accelerated schedule in 2010. The ASU is the

primary method of identifying potential cancers among participants who have refused to schedule screening examinations and for participants who have completed all years of screening. The ASU asks if a participant has been newly diagnosed with any type of cancer and collects the type of cancer and the date of diagnosis. The identification of a cancer on the ASU will set an expectation for a CDF. If the reported cancer was diagnosed outside of the time period covered by the ASU and the cancer was previously reported on an ASU or CNF, the participant's response can be edited and the cancer does not need to be investigated. If the reported cancer was diagnosed within the time period covered by the ASU, even if the cancer was previously reported, the cancer must be investigated and documented on a CDF. If a cancer is reported on an ASU, it does not need to be reported on a CNF.

Exhibit 8-1 NLST/LSS
Cancer Ascertainment Process



8.2.2 Notification of Cancer Outside of the Annual Study Update (ASU)

An SC can be notified of a potential cancer through many sources other than the ASU. The primary sources will be the participant, the participant's family members or health care provider, and the participant's Death Certificate. All reports of cancer outside the ASU must be documented on a CNF, which will set an expectation for a CDF.

8.2.2.1 Notification from the Participant, a Family Member, or Health Care Provider

A variety of people could notify the SC of a cancer diagnosis. The SC should implement a system, such as a telephone log, to record such information when it is received. All reports of cancer outside the ASU should be recorded on a CNF. Only one CNF should be completed per participant, per study year. The CNF should be updated if there are subsequent reports of cancer. Once completed, this form should be entered into IDEAS, which will set an expectation for a CDF.

8.2.2.2 Notification from the Participant's Death Certificate

The SCs will be responsible for collecting Death Certificates for participants who are reported to be deceased if the date of death was on or before December 31, 2009. On a monthly basis, the SCs will ship Death Certificates to the CC for cause of death coding. If, prior to shipping the Death Certificate to the CC, the SC discovers a cancer that has not previously been reported, a CNF must be completed and entered into IDEAS. In addition, as part of the EVP, the CC will ask the SC to document cancers that are reported on the Death Certificate but have not yet been investigated. These cancers will be identified with a "Cancer Suspicion" (CS) status on the EVP Algorithm Report (see Section 9.8.2). As necessary, the CC MRA Coordinator will provide guidance to the SC Abstractors for completing the required abstraction forms when a CS status is assigned. The SC must complete a CNF for all newly reported cancers and enter it into IDEAS, which will generate an expectation for a CDF.

8.3 Confirmation of Cancer

A separate CDF should be completed for each cancer reported, even if multiple cancers are reported on the same ASU or CNF. The primary method for confirming reports of cancer is the collection and review of medical records. Cancers diagnosed after December 31, 2009 should be documented on a CDF with the estimated date of diagnosis; however, medical records should not be collected to confirm the diagnosis.

8.3.1 Collection of Medical Records

The process of confirming the diagnosis of cancer includes collecting participant medical records. The nature and quantity of medical records to be collected can vary depending on the type of the suspected cancer (lung or non-lung cancer).

The SC must contact the participant's health care provider or obtain medical records to determine whether cancer was diagnosed. In addition to obtaining information from the participant's medical records, the SC may use the tumor registry information to help obtain additional source documents, but the SC should not complete NLST/LSS abstracts on the basis of a tumor registry abstract alone.

Sufficient medical records must be collected to enable the abstractor to record the result of the investigation (lung primary, metastasis, non-lung primary, etc.), the date of diagnosis for the primary cancer, and the ICD-O-3 code for the primary cancer.

In some cases, the SC may be charged fees for obtaining copies of medical records. Since the NLST is a federally-funded research study, the SC may attempt to obtain a waiver of fees from each institution from which they obtain medical records. Medical Record Release Authorization Forms (Appendix 3-4) generally are required for collection of records as described in Section 3.2.1.4.

Once copies of the medical records have been obtained, they should be carefully reviewed to confirm that they pertain to the correct participant. The records should then be organized chronologically. A PID label should be affixed to each page of the medical record. Each document should be reviewed for legibility and completeness. Consistency of information between documents should be compared and, if

necessary, the health care provider should be contacted to resolve any problems. In addition, if the records are not complete, the diagnosing health care provider may need to be contacted for additional information.

8.3.1.1 Acquisition of the Histopathology/Cytopathology Report

For each case of lung and non-lung cancer diagnosed histologically or cytologically on or before December 31, 2009, the SC will obtain a photocopy of the histology or cytology report that confirms the initial cancer diagnosis. Information from the histology or cytology report will also be abstracted onto the CDF or DE forms. If the cancer was diagnosed both histologically and cytologically, information should be abstracted from the earliest histology procedure with an adequate specimen that gives a definitive diagnosis of cancer. If no adequate histology specimen is available, but a cytology specimen is available, the cytology report should be used. A copy of the corresponding histopathology or cytopathology report that supports the diagnosis of cancer on the DE form or the CDF must be maintained in the participant's study file.

8.4 Completion of the Cancer Diagnosis Form (CDF)

The outcome of the cancer ascertainment process will be documented on Part A of the CDF. If the result of the investigation is a primary invasive lung cancer that has not previously been reported, a DE form and a TI form must be completed to document the diagnostic evaluation, staging, and initial treatment of the primary invasive lung cancer. A CP form will be required during the first two months of each subsequent study year through 2009. Detailed instructions for completing these forms are provided in Chapter 7. If the result of the investigation is a primary non-lung cancer, the diagnosis information will be recorded on Part B of the CDF. The SC should make every attempt to investigate and complete the CDF within one to two months.

If a cancer is reported but the diagnosis cannot be verified after a review of the medical record, the SC should consider the report of cancer to be erroneous. The SC should complete the CDF with a result of "erroneous report of cancer."

If a cancer is reported with a diagnosis date after December 31, 2009, the diagnosis and estimated diagnosis date should be recorded on the CDF. No additional documentation is necessary.

If the result of the investigation is a primary invasive lung cancer or a metastasis to the lung from a non-lung primary cancer, expectations for future screening exams will be turned off.

8.5 Documenting Non-response for Cancer Confirmation

In some cases, the SC will not be able to complete a CDF for the participant. The following are the conditions under which an MDF should be completed for a CDF:

- When the SC is unable to locate the participant to obtain consent to collect medical records, code 02 (Can't locate) should be recorded on the MDF for the CDF;
- When the participant sought follow-up attention but has subsequently died and the SC is unable to contact the participant's family for consent to obtain medical records, or the participant's family is contacted, but refuses to consent to the release of the participant's medical records, code 22 (Family refuses to release medical records) should be recorded on the MDF;
- When the medical records necessary for the completion of the CDF are not available because the records cannot be located, code 25 (Medical records lost) should be recorded on the MDF;
- When the medical records necessary for the completion of the CDF are not available because of institutional refusal, or foreign or non-local institution, code 23 (Health care provider refuses to release medical records) or code 24 (Health care provider does not respond to record requests) should be recorded on the MDF, and
- When a participant refuses to sign a Medical Record Release Authorization Form for the SC to obtain medical records to document diagnostic follow-up procedures, code 21 (Participant refuses to release medical records) should be recorded on the MDF.

8.6 Tracking, Reporting, and Monitoring Medical Record Abstraction Activities

A detailed discussion on the process of reporting and monitoring medical record abstraction can be found in Chapter 7, Section 7.8.

8.7 Quality Assurance for Cancer Confirmation

At each SC, a trained and approved medical record abstractor will abstract information regarding diagnostic evaluation, cancer confirmation, initial treatment, and cancer progression. A certified nosologist (medical coder) is required for coding cancer and non-cancer diagnoses. A certified tumor registrar is required for coding cancer information. (Refer to Chapter 7, Section 7.7.1 for qualifications and certification requirements for the medical record abstractor and the study nosologist.)

The MRA Coordinator at the CC will facilitate regular communication between the SCs and the NCI regarding medical record abstraction issues and problem resolution and will coordinate training. This process is discussed in detail in Chapter 7, Section 7.7.2. The lead abstractor at each SC will assist the CC MRA Coordinator in monitoring internal quality assurance at their SC and provide input for medical record abstraction issue resolution.

Appendices for Chapter 8

Appendix 8-1 Cancer Notification Form (CNF)

National Lung Screening Trial / Lung Screening Study (NLST/LSS)

CANCER NOTIFICATION FORM (CNF)

ADMINISTRATIVE SECTION

Screening Center ID: |___|___|

Screening Center Staff ID: |___|___|___|___|

Study Year: T |__|

Initials Complete:_____

Initials QC: _____

CNF

Participant ID Label

PART A. CANCER INFORMATION

1. TYPE/SITE OF CANCER	2. DATE REPORTED	3. SOURCE OF INFORMATION
A. _____	A. |_|_|-|_|_|-|2|0|_|_|	A. 1 2 3 4 5 6 _____ (Specify)
B. _____	B. |_|_|-|_|_|-|2|0|_|_|	B. 1 2 3 4 5 6 _____ (Specify)
C. _____	C. |_|_|-|_|_|-|2|0|_|_|	C. 1 2 3 4 5 6 _____ (Specify)

SOURCE CODES

1. Participant
2. Relative, spouse, or friend
3. Health care provider
4. Medical records
5. Death certificate
6. Other (SPECIFY)

National Lung Screening Trial (NLST)

Specifications for the Completion of the Cancer Notification Form (CNF)

The purpose of the Cancer Notification Form (CNF) is to document the type, date reported, and source of information for a cancer reported from sources other than the ASU and not as the result of a positive screen. These sources include the participant; the participant's relative, spouse, or friend; health care provider; medical records; or Death Certificate. The CNF should not be completed to document cancers that are identified as a result of follow-up from a positive screen, including non-lung primary cancer. The completion of the form triggers an expectation for a Cancer Diagnosis Form (CDF).

This form should be completed for every report of cancer outside of the ASU and not as the result of a positive screen, except for basal-cell and squamous-cell skin cancers, which should not be reported. Multiple cancers reported in the same study year should be reported on one form. Only one CNF should be completed per participant, per study year. If another cancer of the same type is reported at a later time within the same study year, the original CNF must be updated on the form and in IDEAS. The same applies to multiple reports of the same cancer, which would be recorded on one line only of the CNF, but additional information such as other sources can be added. The CNF is edited via completion of the SC Edit Form (Appendix 11-7). The Specifications for Completion of the SC Edit Form can be found in Appendix 11-8.

Administrative Section:

Participant ID Label: Affix a PID label to the space provided in the upper right-hand corner of the form. DO NOT write the PID in this space.

Screening Center ID: Record the two-digit SC ID number.

Screening Center Staff ID: Record the four-digit SC staff ID number of the person completing the form.

Study Year: Record the study year that the participant was in when the cancer was reported.

Part A. Cancer Information

1. **Type/Site of Cancer:** Write in the type/site of cancer reported. If more than one cancer was reported, it should be documented on the same CNF. List each cancer reported on a different line.

2. **Date Reported:** Record the date the cancer was reported. Zero fill month and day, if necessary, and record the last two digits of the year (e.g., 02/07/2002).

3. **Source of Information:** Circle the number corresponding to the source from which the SC learned the participant had cancer. Refer to the Source Codes printed at the bottom of the

CNF for the list of possible sources of information. If the SC learned of the cancer from the ASU, the CNF should not be completed. If a cancer was reported from more than one source, multiple sources can be recorded on the same line. The same cancer should not be recorded on separate lines.

After completing the form:

- The form should be checked to make sure it is accurate, legible, and complete.
- The SC staff member who completed the form should write his/her initials in the space labeled "Initials Complete" in the box at the top of the form.
- The SC staff member who checked the form for completion should write his/her initials in the space labeled "Initials QC" in the box at the top of the form. This should not be the same SC staff member who completed the form.
- Enter the form into IDEAS.
- File the form in the participant's study file.

Appendix 8-3 Cancer Diagnosis Form (CDF)

National Lung Screening Trial / Lung Screening Study (NLST/LSS)

CANCER DIAGNOSIS FORM (CDF)

ADMINISTRATIVE SECTION

Completion Date: |__|__| / |__|__| / |_2_|_0_|___|___|
Month Day Year

Date Cancer Suspicion Reported: |__|__| / |__|__| / |_2_|_0_|___|___|
Month Day Year

Screening Center ID: |___|___|

Screening Center Staff ID: |___|___|___|___|

Study Year: T |___|

Initials Complete: _____

Initials QC: _____

CDF

Participant ID Label

PART A. RESULT OF INVESTIGATION OF REPORTED CANCER

1. Reported Cancer: _____

2. Source of Cancer Suspicion Information:

	FORM	LINE		
☐	ASU	☐ A	☐ B	☐ C
☐	CNF	☐ A	☐ B	☐ C

3. Results of Confirmation of Reported Cancer: (**MARK ONLY ONE**)

- ☐ Primary cancer – lung (Must complete DE if not already completed for this cancer.)
- ☐ Primary cancer – site other than lung
- ☐ Metastases to lung from non-lung primary cancer
- ☐ Metastases to lung from unknown primary cancer
- ☐ Metastases to other site from primary invasive lung cancer (Must complete DE if not already completed for this cancer.)
- ☐ Metastases to other site from non-lung primary cancer
- ☐ Metastases to other site from unknown primary cancer
- ☐ Cancer diagnosed prior to randomization (Complete PHVF if participant randomized ineligible.)
- ☐ Erroneous report of cancer (GO TO PART C)
- ☐ Cancer reportedly diagnosed on or after January 1, 2010. Estimated diagnosis date: _____ (GO TO PART C)

3a. Has this cancer been previously confirmed?
- ☐ Yes (GO TO PART C)
- ☐ No (COMPLETE PART B IF NON-LUNG PRIMARY. GO TO PART C IF LUNG PRIMARY.)

Appendix 8-3 Cancer Diagnosis Form (CDF)

PART B. PRIMARY NON-LUNG CANCER DIAGNOSIS INFORMATION

4. Date of Primary Cancer Diagnosis:

|___|___| / |___|___| / |2 |0 |___|___|

5. ICD-O-3 Cancer Classification of Primary Cancer:

C: |___|___|___| |___|___|___|___| |___| |___| CTR ID #: |___|___|___|___|

TOPOGRAPHY MORPHOLOGY BEHAVIOR GRADE

PART C. COMMENTS

6. Comments: _____

☐ continued

National Lung Screening Trial / Lung Screening Study (NLST/LSS)

Specifications for Completion of the Cancer Diagnosis Form (CDF)

The purpose of the Cancer Diagnosis Form (CDF) is to document the SC investigation of cancer(s) reported on the Annual Study Update (ASU), or Cancer Notification Form (CNF). Cancer diagnosis information such as the ICD-O-3 code will be recorded on this form for reported primary cancers other than lung cancer and for primary cancers when reported cancers are determined to be metastatic sites. The CDF also documents an erroneous report of cancer if the cancer is not confirmed by a health care provider's documentation and documents cancer site and estimated diagnosis date for cancers diagnosed after December 31, 2009. This form should be completed for each report of a different cancer from a source other than follow-up of a positive screen. Subsequent reports of the same cancer will require a CDF to be completed. Only one suspected cancer should be reported on a form. If more than one cancer is reported on the ASU or CNF, a separate CDF should be completed for each cancer.

The SC MRA and a tumor (or cancer) registrar who is a certified tumor registrar (CTR) or CTR-eligible should complete the CDF. Specifically, the MRA will complete all non-administrative items on the form, with the exception of medical coding. The medical coding Item B.5, ICD-O-3 Cancer Classification of Primary Cancer is to be completed by the CTR. The MRA may complete all items if s/he is also a CTR or CTR-eligible. This form should be completed in black or blue ink.

For guidelines on general abstracting techniques, refer to Chapter 7 (see Section 7.5). Some key guidelines are presented below.

- This form includes items that require that data be entered verbatim, such as recording the cancer diagnosis and recording comments. The abstractor should be sure to use clear and legible handwriting when completing these items.

- If the medical record contains unclear or conflicting information for any item, the SC Lead Abstractor, SC Coordinator, and/or Principal Investigator should first be consulted for a resolution and an appropriate coding decision, prior to contacting the CC MRA Coordinator.

- Tumor registry information may be used to help obtain additional source documents, but CDFs should not be completed on the basis of a tumor registry abstract.

Below are some specific guidelines for the collection of information about "other cancer" using this form:

- The SCs should consult the ICD-9-CM coding manual to determine whether reported conditions are cancer or not. All conditions that are coded in ICD-9-CM as a primary malignant neoplasm (140-195, 200-208), carcinoma in-situ (230-234), or neoplasms of uncertain behavior, including carcinoids (235-238), should be reported.

- This form should be completed for cancer diagnosed both *before* and *after* the participant is enrolled in the study. If the primary cancer that was diagnosed before randomization is lung cancer, a Protocol and HIPAA Violation Form (PHVF) should also be completed to document the participant as a randomized ineligible (see Section 11.5.2.1). Primary lung cancers diagnosed prior to randomization should be recorded in Item A.3 as a "Cancer diagnosed prior to randomization," rather than a "Primary cancer – lung."

- The SC should document diagnosis information on the CDF about non-lung primary cancers only. Date of diagnosis and ICD-O-3 code should be collected for all non-lung primary cancers. The SC's responsibility is to document the result of the investigation of each report of "cancer." When a participant, relative, etc., reports a cancer, the SC must first investigate whether it is primary, metastatic, or an erroneous report. It is possible that the participant may report several "cancers" but upon investigation, it is determined that one or more of them is actually a metastatic site, not a primary cancer.

- When an ASU is completed with a "yes" for cancer or when a CNF is completed, an expectation is set for the CDF. If an ASU is completed with more than one report of cancer, expectations will be set for that number of cancers. The expectation for a CDF should first trigger an investigation by the SC. The results of the investigation should be recorded on the CDF.

- A separate CDF should be completed for each report of cancer.

- If a reported cancer has been previously confirmed, this should be documented on the CDF.

- For multiple reports of a cancer that have been confirmed as a metastatic site in a previous study year, the SC will be required to determine (via a method chosen by the SC such as a review of diagnosis dates, contact with the participant, review of medical records) whether it is the same metastasis or a new primary, and to properly document it on the CDF.

- If, upon review of the medical record to confirm a reported "cancer," there was found to be no cancer, it should be properly noted on the CDF.

- If the primary cancer site is identified to be lung, Part B should not be completed. If this cancer has not previously been confirmed, a DE form must be completed.

- Primary cancers of the trachea are classified as primary lung cancers for medical record abstraction purposes. In the event that a reported cancer is confirmed as a primary cancer of the trachea, Item A.3, Results of Confirmation of Reported Cancer, should be recorded as "primary cancer – lung" and Part B should not be completed. If this cancer has not previously been confirmed, a DE form must be completed.

- Once the SC is notified of a cancer, every attempt should be made to investigate and complete the CDF within one to two months.

- If the cancer is confirmed by both a histology and a cytology report, information from the earliest procedure with adequate histology should be abstracted onto the CDF. A copy of the report should be kept in the participant's file. Histology provides a more definitive diagnosis; therefore, every attempt should be made to determine if one exists. If multiple procedures with histology were performed and the earliest does not have a confirming histology report, a later procedure with a confirming histology report should be used to code the ICD-O-3 cancer diagnosis, if necessary. Other items must be coded from the earliest procedure, using other documentation, such as health care provider notes or progress reports. If the cancer is confirmed by cytologic diagnosis alone, then information should be taken from the earliest procedures with cytology. If the cancer is confirmed by clinical examination and diagnostic tests such as radiology, information may be taken from the earliest report if no histology or cytology report exists. For the date of diagnosis, the SC should record the date of the earliest procedure with histology that gave a definitive

diagnosis of cancer and the most complete picture of the cancer. The earliest procedure with adequate histology is determined by date, whereas the most complete picture of cancer is determined through a confirming histology report.

- Medical records should not be collected to confirm cancers reported to have been diagnosed after December 31, 2009. For these cancers, Part A of the CDF should be completed to document the diagnosis and the estimated diagnosis date. The ICD-O-3 code should not be recorded in Part B and no further documentation is required.

Specifications for completion of the form are given below.

Administrative Section:

Participant ID Label: Affix a PID label to the space provided in the upper right-hand corner of the form. DO NOT write the PID in this space.

Completion Date: Record the date that the entire CDF was completed. Month and day should be zero filled, and the last two digits of the year should be recorded (e.g., 02/07/2002).

Date Cancer Suspicion Reported: Record the date that the most recent ASU was completed or the date the cancer was reported on the CNF. Month and day should be zero filled, and the last two digits of the year should be recorded (e.g., 02/07/2002).

Screening Center ID: Record the two-digit SC ID number.

Screening Center Staff ID: Record the four-digit SC staff ID number.

Study Year: Record the study year that the participant was in when the cancer was reported.

Part A: Result of Investigation of Reported Cancer:

1. **Reported Cancer:** Write the type of cancer reported on the ASU or CNF.

   For each cancer listed on the ASU or CNF, a separate CDF should be completed. Reports of cancers are designated on the ASU and CNF by letter (A, B, etc.). Complete and attach additional forms if necessary.

2. **Source of Cancer Suspicion Information:** Use this section to mark from what source the SC learned that the participant had cancer.

   - **ASU:** Mark this box if the first documentation of the specified cancer was from the ASU.

     A: Mark this box if the cancer for which the CDF is being completed was recorded under "A" on the ASU.

     B: Mark this box if the cancer for which the CDF is being completed was recorded under "B" on the ASU.

C: Mark this box if the cancer for which the CDF is being completed was recorded under "C" on the ASU.

- **CNF:** Mark this box if the first documentation of the specified cancer was from the CNF.

  A: Mark this box if the cancer for which the CDF is being completed was recorded under "A" on the CNF.

  B: Mark this box if the cancer for which the CDF is being completed was recorded under "B" on the CNF.

  C: Mark this box if the cancer for which the CDF is being completed was recorded under "C" on the CNF.

3. Results of Confirmation of Reported Cancer: This item should be completed after the SC has investigated the reported cancer(s) and determined the primary cancer. Mark only one box to record category of cancer. The result chosen should reflect the result of the investigation for the **reported** cancer. The result categories are described below.

- **Primary cancer – lung:**

  - Mark this box if the reported cancer is primary invasive lung cancer. If this is a newly reported primary invasive lung cancer, completion of this item and receipt of the CDF will set an expectation for a DE form. Part B of the CDF should not be completed since this information will be recorded on the DE form.

  - If the primary lung cancer was diagnosed prior to randomization, it should be recorded as a "Cancer diagnosed prior to randomization," rather than a "Primary cancer – lung." A PHVF must also be completed.

- **Primary cancer – site other than lung:**

  - Mark this box if the investigation of the reported cancer reveals a primary non-lung cancer confirmed by histologic examination (study of tissue), cytologic examination (study of cells), clinical examination only, or clinical investigation (such as radiography, immunologic or biologic tests, exploratory surgery, etc.).

  - If the primary cancer was confirmed by both histologic and cytologic examination, information should be abstracted only from the earliest histology report with an adequate sample, even if it has a later date than the cytology report. As the histology report is more definitive, every attempt should be made to determine if one exists before using the cytology report for diagnosis. Other documents such as health care provider notes or progress reports may be used as confirmation of histologic diagnosis. If the primary cancer was confirmed by cytologic examination alone, then cancer diagnosis information should be taken from the cytology report.

- **Metastases to lung from non-lung primary cancer:**

- Mark this box if the investigation of the reported cancer reveals a primary non-lung cancer with metastasis to the lung confirmed by histologic examination (study of tissue), cytologic examination (study of cells), clinical examination only, or clinical investigation (such as radiography, immunologic or biologic tests, exploratory surgery, etc.).

- If the primary cancer was confirmed by both histologic and cytologic examination, information should be abstracted only from the earliest histology report with an adequate sample, even if it has a later date than the cytology report. As the histology report is more definitive, every attempt should be made to determine if one exists before using the cytology report for diagnosis. Other documents such as health care provider notes or progress reports may be used as confirmation of histologic diagnosis. If the primary cancer was confirmed by cytologic examination alone, then cancer diagnosis information should be taken from the cytology report.

■ **Metastases to lung from unknown primary cancer:**

- Mark this box if the investigation of the reported cancer reveals that it is actually a metastasis from a primary cancer that could not be identified.

■ **Metastases to other site from primary invasive lung cancer:**

- Mark this box if the investigation of the reported cancer reveals that it is actually a metastasis from a primary invasive lung cancer. If this is a newly reported primary invasive lung cancer, completion of this item and receipt of the CDF will set the expectations for confirmation of the lung cancer and receipt and completion of a DE form. Part B of the CDF should not be completed since this information will be recorded on the DE form.

■ **Metastases to other site from non-lung primary cancer:**

- Mark this box if the investigation of the reported cancer reveals that it is actually a metastasis from a non-lung primary cancer.

■ **Metastases to other site from unknown primary cancer:**

- Mark this box when the investigation of the reported cancer reveals that it was actually a metastasis to a different site, other than the site reported, from a primary cancer that could not be identified.

■ **Cancer diagnosed prior to randomization:**

- Mark this box when the investigation of the reported cancer reveals that the primary cancer was diagnosed prior to the randomization date.

- Mark this box in instances where a primary tumor associated with a recent recurrence was initially diagnosed prior to NLST enrollment. If the initial diagnosis was at least five years prior to eligibility determination (and randomization), a PHVF (Chapter 11, Section 11.5.2) is not necessary since the participant is not a randomized ineligible. However, if the initial cancer was

diagnosed within five years of the eligibility determination, the participant should have been randomized ineligible, a PHVF should be completed.

- If the reported cancer is primary lung, a PHVF should be completed to document the participant as randomized ineligible.

- The investigation of reported cancer reveals a primary cancer confirmed by histologic examination (study of tissue), cytologic examination (study of cells), clinical examination only, or clinical investigation (such as radiography, immunologic or biologic tests, exploratory surgery, etc.).

■ **Erroneous report of cancer:**

- Mark this box when the investigation of the reported cancer reveals it is not a cancer. Part B of the form should be skipped.

■ **Cancer diagnosed on or after January 1, 2010:**

- Mark this box when the cancer was reported to have been diagnosed after December 31, 2009. Record the reported diagnosis date from the ASU or CNF in the space provided. Part B of the form should be skipped.

3a. Has this cancer been previously confirmed? Mark the box corresponding to whether this cancer has previously been confirmed. If the cancer has previously been confirmed, Part B of the CDF should be skipped and Part C should be completed. If the cancer has not previously been confirmed AND it is a non-lung primary cancer, Part B of the form should be completed. Part B should NOT be completed for a primary invasive lung cancer. This question refers to the diagnosis of the primary cancer, and not the metastasis. For example, if breast cancer is reported in 2003 on an ASU and a CDF is completed with the confirmation of the breast cancer diagnosis, and in 2004 bone metastasis are reported related to the breast cancer then the answer to this question would be "Yes" as the breast cancer is previously diagnosed and documented in IDEAS.

Part B. Primary Non-Lung Cancer Diagnosis Information:

4. Date of Primary Cancer Diagnosis: Record the month, day, and year of a newly diagnosed primary non-lung cancer diagnosis that is confirmed by histology or cytology report. This is the date that the actual procedure was performed that confirmed this cancer diagnosis. If there are multiple reports that confirmed this cancer, record the earliest date available. If the primary cancer is known, this should be the date the primary cancer was first diagnosed. If the primary cancer is unknown, this should be the first date of diagnosis for the unknown primary.

Documentation of the cancer diagnosis should be maintained in the participant's file. This documentation should include copies of histology or cytology reports that report the participant's cancer. If no diagnostic reports are available, but cancer is documented in the other sources, these sources should be photocopied or recorded verbatim. All confirmation material should be attached to the CDF and maintained in the participant's file.

- This item should not be completed when the reported cancer is a primary invasive lung cancer or is found to be a metastatic site from a primary invasive lung cancer.

- If the reported cancer is a metastasis from a recently or newly diagnosed non-lung or unknown primary, this item should be completed with information regarding the primary cancer, not the metastatic site. If the report of cancer is a metastasis from a previously diagnosed primary cancer that was diagnosed prior to enrollment in the study, the date of diagnosis is the date that the metastasis is diagnosed. For example, bone metastasis is noted in 12/03 from breast cancer that was originally diagnosed in 1990. The date should reflect the date of diagnostic determination that the metastasis was from the breast cancer, and not the date of the original breast cancer diagnosis. In the comments (Part C, Item 6) note the date of the original diagnosis of the primary cancer.

- If both histology and cytology reports are available confirming the cancer diagnosis, use the earliest histology report with an adequate specimen that provides definitive information for a cancer diagnosis. In most instances, the histology report should be used as the source for recording information, even if the histology report has a later date than the cytology report. If only a cytology report is available, then record the date from that report. If only a radiographic report or a report from some other diagnostic examination is available, record the date from the available report.

- If a report that confirms date of cancer diagnosis is unavailable, another source from the medical record can be used to complete this item. Other sources include health care provider notes, admission notes, history and physical, discharge summary, or surgical pathology report with a reference to the prior slide from the biopsy (with date of collection).

- In the rare occasion where the cancer is diagnosed by clinical examination only and not histologically or cytologically, the date of the cancer diagnosis is the date of the clinical examination during which the cancer was diagnosed.

- Zero fill month and day, and record two digits for the year. Month and year of primary cancer diagnosis must be known, however, if the day is unknown, record "99."

5. ICD-O-3 Cancer Classification of Primary Cancer: This item is for classifying the diagnosis of the primary cancer according to ICD-O-3 (International Classification of Diseases for Oncology, Third edition, 2000).

- This item should not be completed when the reported cancer is a primary invasive lung cancer or is found to be a metastatic site from a primary invasive lung cancer.

- If the reported cancer is a metastasis from a non-lung or unknown primary, this item should be completed with information regarding the primary cancer, not the metastatic site.

- This item is to be completed by a tumor registrar who is a CTR or is CTR-eligible. The CTR should code the ten digit ICD-O-3 classification in the space provided. The CTR should also record his/her four-digit staff ID number in the space provided for "CTR ID."

- The ICD-O-3 code should reflect the diagnosis from the *earliest* (chronological) histology report (or cytology report if the histology report is not available) with the initial definitive diagnosis. This item *must* be coded from the histology report on an adequate tissue specimen. If multiple procedures with histology were completed, and the earliest does not have a confirming histology report, a later procedure with histology and a confirming histology report should be used to code this item. Other sources, i.e. cytology report, health care provider notes, admission notes, history and physical, discharge summary, or surgical pathology report with reference to the prior slide from the biopsy (with date of collection), may not be used to code this item. The source used to code this item might not be the same source used to code the date of diagnosis in Item B.4.

- If the primary cancer is unknown, the topography section of the ICD-O-3 code should be C809.

- The ICD-O-3 cancer classification should be coded by the CTR, if the required documents are available in the medical record.

Part C. Comments

6. Comments: Use this section to record any overflow information or discrepant information while abstracting from the participant's medical records.

- If an abstracted item has conflicting or discrepant information, the SC Lead Abstractor, SC Coordinator, or, if necessary, the Principal Investigator should review the discrepant information prior to submission to the CC MRA Coordinator.

- In the Comments Section, first enter the item number indicating the item to which the comments are related, record the comments in the space provided, and then record your initials and the date.

- Place an asterisk on the form next to the item number being referenced in Comments.

After completing the form:

- The form should be checked to make sure it is accurate, legible, and complete.

- The SC staff member who completed the form should write his/her initials in the space labeled "Initials Complete" in the box at the top of the first page.

- The SC staff member who checked the form for completion should write his/her initials in the space labeled "Initials QC" in the box at the top of the first page. This should not be the same SC staff member who completed the form.

- Enter the form into IDEAS.

- File the form in the participant's study file.

9. VITAL STATUS ASCERTAINMENT AND THE ENDPOINT VERIFICATION PROCESS

9.1 Introduction

9.1.1 Background

The SCs, the CC, and the NLST Endpoint Verification Team (EVT) will participate in activities to implement a review of cause of death for all participants who die during the course of the study. The purpose of the Endpoint Verification Process (EVP) is to minimize error and bias in assignment of cause of death for study participants, and therefore, ensure a more accurate assessment of the ability of the spiral CT and chest x-ray screening exams to affect lung cancer mortality.

Participants randomized to receive a spiral CT examination may be diagnosed with lung cancer earlier in its natural history than those receiving a chest x-ray examination. Moreover, since these participants undergo a potentially more sensitive screening test, it is possible that a cancer may be diagnosed that would never have presented in that individual's lifetime. Therefore, during each year of follow-up in this study, the incidence of lung cancer in the spiral CT arm is likely to be higher than that in the x-ray arm. This may affect mortality data, since it has been shown that cancer diagnoses influence assignment of cause of death on Death Certificates. This effect, known as "sticking diagnosis bias," may lead to an over-reporting of lung cancer as cause of death among spiral CT arm participants. Further investigation of medical records may reveal that some of these deaths were not actually due to lung cancer.

Certain ICD-10 and ICD-O-3 codes may represent a misreported lung cancer diagnosis or death. Examples include causes of death which suggest uncertainty of the diagnosis of cancer. Further investigation of medical records may reveal that some of these deaths were due to lung cancer.

Concern over another bias that might affect screening trials has recently been expressed (Black et al., 2002). The "slippery linkage bias" has been described as follows, "Many subjects in the screened group may undergo invasive testing for a suspicious screening result, and many others may be treated for early disease. These interventions may lead to deaths that are difficult to trace back to screening."

Because the EVP will involve a review of deaths occurring among persons diagnosed with lung cancer, deaths with mention on the Death Certificate of lung cancer, certain medical misadventures or other causes possibly masking death due to lung cancer, as well as deaths occurring within close proximity to certain diagnostic evaluation procedures, the process will minimize error associated with over- and underreporting of lung cancer as the Death Certificate cause of death. This process will further ensure that ascertainment of the fact of death is equally applied to the spiral CT and chest x-ray arm participants.

9.1.2 Overview of the Endpoint Verification Process

The following is a brief overview of the activities to be completed by the SCs, the CC, and the EVT to implement the EVP. Details of the actual EVP review process are found in a separate document entitled *NLST Endpoint Verification Process Summary and Supporting Documents*, which can be obtained from the CC after permission for release is granted by NCI. Another manual, *Endpoint Verification Process Manual – Coordinating Center Procedures*, documents CC-specific tasks.

- **Ascertainment of the Fact of Death:** Each SC is responsible for implementing procedures to follow up all study participants for vital status ascertainment during the course of the study. For participants who are reported deceased, the SC is responsible for confirmation of death through procurement of the Death Certificate. The SC is responsible for shipping Death Certificates to the CC on a monthly basis.

- **Cancer Ascertainment:** Each SC will determine cancer diagnoses for study participants during the course of the study as described in Chapters 7 and 8. Each SC will collect medical records to abstract diagnostic evaluation for all positive screens and reported lung cancers, as well as treatment information and cancer progression information for all confirmed lung cancers.

- **Identification of Deaths for Review by the EVT:** The CC will be responsible for identifying deaths to be submitted to the EVT for review. The CC will code causes of death and significant conditions listed on the SC-supplied Death Certificates, including the NCHS Derived Underlying Cause of Death. This information will be entered into the central EVICT database, and a computer algorithm will be applied at least monthly to select deaths that meet criteria for EVT review. For those deaths that do not meet the criteria of the selection algorithm, the death will be deemed "Certified" and no additional action is required. Deaths lacking sufficient information for processing will be rejected by the algorithm and re-processed once information is provided by the SC.

- **Collection of Medical Records for Endpoint Verification:** The SC will be responsible for collecting all necessary documentation for deaths requiring EVT

review. All records will be carefully reviewed by the SC, and any portion of the record that identifies personal information, randomization assignment, whether a lung cancer was screen- or symptom-detected, or makes mention of the NLST/LSS, will be deleted. When record collection is complete, the SC will prepare a folder with all requested EVP documentation, batch it with other completed EVP folders, and forward them to the CC. The CC will verify that documents are present and properly edited before forwarding the information to the EVT Chair for review.

- **Review by the Endpoint Verification Team:** The EVT is composed of five physicians who are not affiliated with the NLST or any of its SCs. The review process will determine whether a death was due to lung cancer and will result in collection of data concerning the impact of diagnostic evaluation or treatment of a confirmed or suspected lung cancer on a participant's death. In addition, data will be collected concerning the impact on the participant's death of diagnostic evaluation or treatment of a clinically significant finding identified on an NLST screening exam.

  All deaths selected for EVT review are first reviewed by the Chair. The Chair's cause of death assignment is compared to the NCHS Derived Underlying Cause of Death, which is ascertained from information on the Death Certificate. Some Chair-reviewed deaths also will be reviewed by an additional EVT member and some deaths reviewed by the Chair and an additional member also will be reviewed by a panel of EVT members. The need for review beyond the Chair-level depends, in most instances, on whether there exists disagreement between two sources (Chair versus Death Certificate or additional member versus Chair) on lung cancer as cause of death. Once agreement is reached as to whether a death was due to lung cancer or diagnostic evaluation or treatment of a suspected lung cancer, that death is certified and the EVT-determined cause of death is recorded. All results will be reported monthly to the SCs.

The remainder of this chapter will describe in detail the SC procedures and review activities to be completed for ascertaining and confirming participant deaths, providing Death Certificates to the CC, identifying cases for submission to the EVT, and obtaining, editing, and processing all medical record documentation to be submitted to the EVT. Activities performed by the CC, including central Death Certificate coding, data processing, coordination procedures, and procedures to be completed by the EVT will be documented in the *Endpoint Verification Process Manual – Coordinating Center Procedures.* Details of the review process are found in the *NLST Endpoint Verification Process Summary and Supporting Documents.*

9.2 Vital Status Ascertainment Activities

9.2.1 Introduction

The SC will determine the vital status of all participants during the course of the study and obtain Death Certificates for those participants reported to be deceased. Tracing procedures will be implemented for all participants who are considered lost to follow-up in order to ascertain their vital status.

9.2.2 Vital Status Ascertainment

Ascertainment of vital status is the first step in the EVP. The primary method for identifying possible deaths is the Annual Study Update (ASU) (Appendix 3-11), which is to be completed by all participants on an annual basis. Participants who do not respond to the ASU will require follow-up tracing activities to determine whether they are alive or deceased. In some cases, the participant's relatives or friends may complete and return the ASU indicating that the participant has died, or the ASU mailing may prompt the participant's relatives or friends to call and report the death. If a participant is reported deceased on an ASU or by a relative, friend, or obituary, the SC Coordinator must complete a Non-Response Form (NRF) (Appendix 11-3). If the SC learns of a potential death through post office returned mail, the SC Coordinator should investigate the report of death prior to completing the NRF and should only complete the NRF if the report is confirmed through another source (such as a relative or friend.) Once an NRF is completed, the participant's vital status will then be updated to "presumed deceased." For presumed deaths occurring on or before December 31, 2009, the SC Coordinator should initiate procedures to confirm the death. The SC Coordinator will need to obtain the date of death and state of death in order to obtain the Death Certificate from the appropriate state Vital Statistics Bureau. The SC Coordinator will determine the most appropriate strategy to obtain this information. For presumed deaths occurring after December 31, 2009, confirmation of the death is not required.

When participants are considered lost to follow-up because of failure to return the ASU or to keep an appointment for a screening visit, relatives, friends, and/or physicians/health care providers may be contacted for information. The Participant Contact Form (PCF) (Appendix 3-1) and the Participant Contact Update Form (Appendix 3-7) collect contact information on the participant's relatives, friends, and current physicians/health care providers. If the participant was identified as having a positive

screening examination and/or lung cancer at some time during the study, Part E of the Diagnostic Evaluation (DE) form (Appendix 7-2) will provide additional information about health care providers, hospitals, or clinics where the participant was seen. In the absence of contact within 18 months, tracing procedures should be initiated (Section 9.2.3). The 18-month period begins on the date of the very last verbal or written contact with a participant or participant's spokesperson. Tracing procedures may include a search for fact of death with the Social Security Death Index (SSDI), tumor registries, Departments of Motor Vehicle Administration, and Vital Statistics Bureaus.

Critical identifying information, essential for making submission requests for vital status determination and for tracing participants, will be maintained by the SC. This information is collected on the Eligibility Verification Form (EVF) (Appendix 2-10) and the PCF and/or PCUF. It includes:

- Name: first, middle, and last;
- Sex;
- Date of Birth: month, day, and year;
- Social Security Number, and
- Last known address and date last known address was ascertained.

9.2.3 Tracing Lost Participants

When participant contact is attempted for any follow-up activity, it may be determined that the participant can no longer be reached at the last known address and/or phone number. In this situation, tracing activities must be initiated. The information collected on the PCF/PCUF should greatly facilitate the tracing process. It is suggested that this information be used initially to try to locate the participant. In subsequent years of the study, outside sources such as the Department of Motor Vehicles, the Social Security Administration, National Death Index, Post Office checks, cancer registries, credit bureaus, etc., may be utilized. Every effort must be made to minimize the number of participants lost to follow-up during the course of the study.

Each SC is responsible for tracking tracing efforts for all participants lost to follow-up. Tracking may be done manually or using an automated system. The SC Coordinator will determine the tracking method.

9.2.3.1 Centers for Medicare and Medicaid Services (CMS)

The Centers for Medicare and Medicaid Services (CMS) are a good resource for determining the vital status of participants who are lost to follow-up. CMS is the government agency that administers the programs. For individuals who received benefits, the CMS files can provide date and state of death. Prior approval is required by CMS for all submissions for record searches. An application and instructions can be obtained by contacting CMS at the address below.

Centers for Medicare and Medicaid Services
Bureau of Data Management and Strategy
6325 Security Boulevard
Baltimore, MD 21207

CMS files can be searched either by Social Security Number or by name. Submission requirements include a valid Social Security Number for the Social Security Number search, or the first and last name and full date of birth for the name search. The Social Security Number match is strongly recommended over the name search because of the quality of information provided. Once a submission is made, the response time is quick and the information provided is accurate.

9.2.3.2 Social Security Death Index

The Social Security Death Index (SSDI) is an online search index of deceased individuals whose Social Security benefits have been paid out. It provides the last and first name; the Social Security Number; birth and death dates; city, county, state, and zip code of the last residence, and city, county, state, and zip code to which the final lump sum payment was made. It is useful for verifying a death or completing information about a death prior to submission to the state vital statistics office. The SSDI is updated monthly. The main disadvantages to using this system are that it includes only those individuals assigned a Social Security Number and who have had Social Security benefits paid out and the accuracy of the information is not guaranteed.

The SSDI may be accessed on the Internet at http://ssdi.genealogy.rootsweb.com/ or http://www.ancestry.com/search/rectype/vital/ssdi/main.htm. Both of these Web sites provide information about using the SSDI.

9.2.3.3 Other Sources for Vital Status Determination

It is expected that most deaths will be ascertained through the methods described above. Other tracing resources that may be useful for locating lost to follow-up participants and for determining vital status include: National Death Index, cancer registries, Departments of Motor Vehicle Administration, and Vital Statistics Bureaus. These sources may be most useful in subsequent years of the study when there has been an increase in the number of participants who are lost to follow-up. The SC Coordinator will be responsible for establishing the tracing methodologies to be used and for conducting all searches.

9.2.4 Searching the National Death Index Database

The National Death Index (NDI), a product of the National Center for Health Statistics (NCHS), is a computerized database that contains death record information from all 50 states, the District of Columbia, the Virgin Islands, and Puerto Rico. The NDI was developed to facilitate health research efforts and covers deaths that occurred from 1979 forward. An NDI-Plus search, which provides coded causes of death (using the International Classification of Diseases, ICD-10), is available for a particular calendar year approximately 14 to 16 months after the close of that year. For example, NDI-Plus will provide nearly complete coverage for deaths that occurred through 2004 by April 2006. All proposed search requests must be accompanied by a formal application and must be approved by the NDI Board.

The NLST will utilize NDI to obtain vital status and cause of death information for participants with whom the SCs have lost contact. The CC prepared and submitted the NDI application for the request on behalf of the NLST/LSS SCs. For each search, the SCs will prepare and submit a data file directly to the NDI, and results will be returned to the SC, generally within one week. The NCI has established an interagency agreement with the NCHS that provides payment for the cost of the search.

Prior to each file submission, the SCs will receive additional information from the CC regarding preparation of data files using IDEAS and interpretation of NDI results. A copy of *NDI User's Manual and NDI Plus: Coded Causes of Death, Supplement to the User's Manual* also will be provided

to all SC Coordinators. The SCs are responsible for retrieving the returned NDI output and for determining appropriate matches.

9.2.4.1 Submission of Files to NDI

In May 2006, the SCs began annual NDI-Plus searches in order to determine vital status and to obtain coded causes of death for participants who are lost to follow-up, or those known to be deceased but for whom the SC has been unable to obtain a Death Certificate. Any SC not planning to perform an annual NDI search must provide written justification to the NCI. The NDI Website, http://www.cdc.gov/nchs/ndi.htm, describes the NDI database, outlines the procedures for submitting data files, and provides contact information for NDI staff. It is recommended that the SC Coordinator maintain a system for storing NDI documents by creating an NDI folder for each year the search is completed. The NDI folder should include NDI search queries, submission files, NDI return files, and NDI Results Forms.

The SC Coordinator will utilize IDEAS to facilitate the NDI searches by generating a query to identify potential NDI candidates. The SC Coordinator can locate the program in IDEAS through the NDI module. The "NDI Submission" option will enable the SC to perform an initial query to identify all potential candidates. The query will identify participants who have an NRF with a reason of "lost contact," "refusals" (hard refusals only), "medical condition," or "deceased" (with no Death Certificate on file) through December of the year in which the NDI database is current. It is important to note that participants who reportedly died within the past calendar year will not be included because NDI will not yet have a record of their death. The IDEAS query will incorporate the necessary identifying information from the randomization database, MHQ, and PCF/PCUF for each PID. Each record will contain the following information, if available:

First name, last name, middle initial
Date of birth
Social Security Number
Sex
State of residence

These data elements are included in the search to enable as close a match as possible with NDI records. In order to be eligible for an NDI search each record must contain at least one of the three following combinations of data elements:

First and Last Name and Social Security Number;
First and Last Name and Month and Year of Birth, or
Social Security Number and Date of Birth and Sex.

The IDEAS NDI submission program has been designed to identify participants whose information is insufficient to perform a search. Upon attempting to select the record for inclusion in the submission file, the program will automatically check for the above three combinations, and will display an error message when participants do not have at least one of the three. The program will prevent these participants from being selected for the final submission file. The SC staff should review the participant files for any information that is lacking and add missing data by editing the PCF/PCUF or entering the missing data items into a new PCF/PCUF. The updated information will be picked up by re-running the query, after which it will show up in the initial query results grid in IDEAS.

After reviewing the output from the initial query to determine if the information available is complete, the SC Coordinator will select participants to be included in the submission file. For instance, the SC staff may be aware of information about a participant that would lead them to exclude him/her from the NDI search, such as knowledge that the participant is no longer in the United States. A participant may be excluded from the submission file by simply not selecting him/her.

Once the SC staff have reviewed the candidates and selected all records to be included in the submission file, they will click on the Create File button. At this time, the system will generate either one or two submission files, depending on the type of candidates selected, and will replace the NLST PID with a unique NDI identification number. One file will contain records for participants who are known to be deceased (NRF with reason code 5, but no Death Certificate) and the other will contain records for participants with NRF reason codes 1, 2, or 4, participants whose status is unknown. This distinction will determine fees for the search.

The user will be able to view and print the participant records included in the submission file. The SC should print a copy and save it in the NDI folder. IDEAS will save the submission file on the SC server. The file should be copied onto a CD-ROM or standard 3.5-inch diskette. The NDI

recommends that the submission file be password protected prior to mailing. The CC will forward to the SCs information regarding their assigned NDI numbers, which is to be included in the submission file name and also recorded on the outside of the CD or diskette

A transmittal form will be provided to each SC and must accompany each file submitted for an NDI search. The CC will provide the transmittal form, the specifications for completing that form, and a fee worksheet prior to the expected submission. The transmittal form, fee worksheet, and CD or diskette that contains the files should be sent by express mail on the designated dates for all SCs (in order to have all NLST/LSS files arrive at NDI on approximately the same day) to:

National Death Index
National Center for Health Statistics
3311 Toledo Road, Room 7318
Hyattsville, MD 20782
Phone: 301-458-4444

SCs should e-mail NDI (ndi@cdc.gov) in order for NDI to anticipate receipt of a submission file from that center. The SC also should send a copy of the e-mail to the CC NDI Coordinator.

9.2.4.2 NDI Reports

Approximately one week after NCHS receives the data file, a CD-ROM containing the NDI output will be returned directly to each SC for review and determination of matches. This output will contain ten different output files; one of which will be the NDI Retrieval Report. Whenever a participant record matches with NDI records, it will appear on this report. The other reports provide information on the records that were submitted, coded causes of death, and a file for forms to request Death Certificates from states' vital statistics offices. For a list and brief description of the NDI Retrieval Reports, see Appendix 9-17.

9.2.4.3 Determining NDI Matches

When evaluating each NDI match, it is important to realize that many submitted records will either have false matches, or will not have a match at all. Specific matching criteria have been developed

that should be applied to the NDI record matches to assist in correctly identifying a particular participant. The NDI Retrieval Report is the main report to use when determining matches. On the NDI Retrieval Report, the results of each match are ranked according to the number of NDI data items that are in agreement with data items belonging to the participant. When all items submitted by the SC match exactly with an NDI record, the NDI record will have an asterisk next to the state of death. The NDI-Plus search provides cause of death codes for matches that are ranked first or achieve a high enough "probabilistic score" (please refer to Appendix A of the *NDI-Plus User's Manual* for a discussion of probabilistic scoring). For NLST purposes, the terms "Exact" and "Probable" will be based upon the definitions below.

Exact Match: If the following data items match exactly, the NDI record is an Exact Match to the PID:

- First and Last Names, and Middle Initial
- Social Security Number
- Date of birth
- Sex

Probable Match: Possible matches appear on the NDI Retrieval Report ranked based on the number of data items that are in agreement with the data items of the participant. For NLST purposes, a record is a Probable Match when some of the data items do not match exactly, but there is indication that they are close. Sex code must always match. However, if other data items do not match exactly, they must at least meet the following criteria:

- Under "Name" in the Retrieval Report, if F (for first name) has an NDI code of "I," this indicates that the first initial of the first name matches.
- Under "Name" in the Retrieval Report, if L (for last name) has an NDI code of "N," this indicates that the name matched only on NYSIIS (New York State Identification and Intelligence System) phonetic codes.
- At least the last four digits of the Social Security Number match. If the Social Security Number is not provided, then the DOB should match exactly, i.e., month, day, and year.
- Month of birth within one month before or after the participant's date of birth.
- Year of birth within ten years before or after the participant's date of birth.

The submission file also includes state of residence to help determine the suitability of a match. If a record does not meet the criteria for an Exact Match or Probable Match, then they fall into one of the two following categories:

No Match:

- The participant record was not involved in an Exact or Probable Match with NDI records.

Rejected:

- No information was returned from NDI for this participant because the record failed to satisfy the basic criteria of the NDI edit program and was rejected prior to the search. These participants can be easily identified using the Rejected User Records report.

9.2.4.4 Entering the Results of the NDI Search into IDEAS

Results from the NDI search should be entered into IDEAS using the National Death Index Results (NDIR) Form. After the submission files have been created, the SC staff will need to generate NDI Results Forms for each participant record submitted. These forms can be generated immediately following the creation of the submission file or at any time before the results are returned, but it is recommended that they be printed soon after the file has been created. IDEAS will generate one form for each participant. The forms will be preprinted with the participant's NLST PID and their assigned unique NDI identification number for this particular submission. Since the NLST PID will not be sent to the NDI, the results from the search will need to be matched with the participant's unique NDI identification number. The NDIR form will collect data on the type of match that resulted from the search, whether a Death Certificate will be requested for a probable match as well as the underlying cause of death (ICD-10), and year of death. Please refer to Appendices 9-18 and 9-19 for the NDIR form and specifications.

Once the NDI results have been reviewed and the NDIR form has been completed, the form should be entered into IDEAS. Data entry will occur within the NDI module under "NDI Results."

Following entry of the NDIR forms into the IDEAS database, copies should be filed in the participant's NLST folder as well as the NDI results folder.

9.2.4.5 Requesting Death Certificates

The Death Certificate should be requested for all Exact Matches, and for Probable Matches that appear to correctly identify a participant. If a participant has an Exact Match and Probable Matches, the SC Coordinator should request a Death Certificate only for the Exact Match. In general, only one Death Certificate will be requested per PID. However, in the event that several Probable Matches appear to identify a participant equally well, the SC Coordinator can request these Death Certificates. Upon receipt of the Death Certificates, the SC Coordinator must compare the information on the Death Certificates with the information in the participant folder. Additional data in the folder such as race, occupation, and marital status may lead to identifying the correct Death Certificate for the participant. Death Certificate(s) that are determined not to correctly identify the participant should be shredded immediately.

With the return of the results of the NDI search, the SC also will receive a document entitled Obtaining State Death Certificates. This document contains the most recent available information on each state's requirements and charges for the release of copies of Death Certificates. The document also includes the name, address, and phone number of a contact person in each state's vital statistics office, as well as the specific Death Certificate release policy and charge.

When requesting copies of Death Certificates from a vital statistics office, the SCs are strongly encouraged to use NDI's Death Certificate Request Form, which comes with the NDI search reports (Appendix 9-20). The Death Certificate Request Form lists the NDI record matches for each state sorted first by year of death and then by Death Certificate number. Selected information from each matching record is also presented. This information assists the vital statistics office in releasing the correct Death Certificate. The request form for certain states is several pages long. For such a form, the SC should eliminate all pages (other than the first page) that do not contain requests for certificates.

Steps in requesting Death Certificates identified through NDI are as follows:

1. Place a check mark in the left margin of the Death Certificate Request Form for those Death Certificates that are being requested.

2. Always complete the first page of a state's Death Certificate Request Form. Eliminate all other pages that do not contain requests for Death Certificates.

3. Contact vital statistics offices to determine their fees, how to make payment, and what additional information is needed in order to allow the office to release copies of the Death Certificates.

4. Mail the forms along with payment to the appropriate state office.

5. Upon receipt of the Death Certificate, the SC staff should verify that the information on the Death Certificate matches with information in the participant's file.

9.3 Death Certificate Acquisition

Death Certificates must be obtained for all deceased participants with a reported date of death on or before December 31, 2009. The death is not considered confirmed until the Death Certificate is obtained. The SC will be responsible for the procurement and processing of all Death Certificates. The process of requesting and receiving Death Certificates at the SC is documented on the Death Certificate Tracking Form (DCTF) (Appendix 9-15). The DCTF is expected for all participants with an NRF participant status of "deceased" and a reported date of death on or before December 31, 2009. Specifications for Completion of the DCTF are found in Appendix 9-16. A certified copy of the Death Certificate is not required for the EVP; the SC may obtain a photocopy of the Death Certificate. Copies of all Death Certificates will be edited to delete identifying information and shipped monthly to the CC for cause of death coding. A new folder will be prepared to store the Death Certificate, as well as the medical record information relating to the EVP (see Section 9.6). This documentation is in addition to the documentation collected for medical record abstraction that is used for the cancer ascertainment process.

Some state Vital Statistics Bureaus have begun to release electronic Death Certificates. Electronic Death Certificates typically do not include all of the pertinent information needed for the NLST. If an SC receives notification that a Death Certificate will be released electronically, the SC Coordinator should request a hard copy. In this situation, the NCI can provide a letter for the SC to submit to the state Vital Statistics Bureau with justification for the request. If necessary, the SC should contact the CC to obtain such a letter.

A brief description follows of the various activities associated with Death Certificate acquisition and processing:

- Prepare and submit all necessary application forms to the various state Vital Statistics Bureaus for approval to obtain Death Certificates.
- Once approval has been received, prepare and submit Death Certificate requests to the state Vital Statistics Bureaus.
- Receive and review results of the Death Certificate acquisition efforts.
- Determine which Death Certificates are likely to represent the participant under investigation based on comparisons with the data submitted to the state.
- Conduct quality assurance by ensuring the Death Certificate matches the participant for whom the request was made, by checking Death Certificates for legibility and accuracy, and, if necessary, follow back to the Vital Statistics Bureau for clarification.
- Verify that the Death Certificate contains date of death, date of birth, race, occupation, and cause of death information. (Some states, such as Florida, have two versions of the Death Certificate, one with the cause of death, and one without.)
- Place a PID label where it does not obscure any information, preferably in the upper right hand corner of the Death Certificate. DO NOT write in the PID.

It is expected that Death Certificates can be obtained for all deaths occurring in the United States. For deaths occurring outside the U.S., every attempt should be made to obtain the Death Certificate from the country in which the participant died or through the State Department. In extremely rare circumstances, SC efforts to obtain a Death Certificate may not be successful. In theses instances, the SC must contact the CC to obtain a blank Documentation for a Missing Death Certificate (Appendix 9-22) to document the missing Death Certificate. Specifications for completing the Documentation for a Missing Death Certificate are found in Appendix 9-23. The CC and the NCI will review the completed form to determine whether all reasonable efforts have been exhausted. Upon NCI approval, the CC will turn off expectations for the Death Certificate and the SC must initiate medical record collection for the EVP.

9.4 Shipment of Death Certificates

Once a Death Certificate is received, it must be shipped to the CC. All Death Certificates must be photocopied and the copy edited to delete participant identifiers. Death Certificates will be shipped monthly to the CC following the procedures described below:

- Photocopy the Death Certificate and place the original in the participant's EVP folder (see Section 9.6).

- On the photocopy, delete the following identifying information: the deceased's name, Social Security Number, address, spouse or other relative names and addresses, and informant name and address. It is recommended that a black marker be used. The area should be blacked out on both sides of the document. Do NOT delete participant date of birth on the Death Certificate.
- Verify that the identifiers cannot be read.
- Prior to shipping, complete or generate from IDEAS a Death Certificate Transmittal Log (Appendix 9-1). The transmittal log should list the PID for each Death Certificate included in the shipment.
- Assemble the Death Certificates in the order in which they appear on the transmittal log. Verify that all Death Certificates are present. If any Death Certificates cannot be located or are not ready to be shipped, cross off the corresponding PID on the transmittal log.
- Include one copy of the Death Certificate Transmittal Log with the package of Death Certificates sent to the CC. Fax a copy of the Death Certificate Transmittal Log to:

  Ellen Martinusen
  GA 26A
  301/963-5455

- Keep one copy of the Death Certificate Transmittal Log for the SC files.
- Package the Death Certificates in a Tyvek envelope and send to:

  Ellen Martinusen
  9274 Gaither Road, GA 26A
  Gaithersburg, MD 20877

- Send the Death Certificates to the CC using Federal Express, UPS, or another certified mail carrier. Keep a record of the package number.
- Any month that the SC will not be shipping Death Certificates, the SC must notify Ellen Martinusen (EllenMartinusen@westat.com) with this information.

The CC will receive and verify all shipments of Death Certificates from the SC. Upon receipt of a shipment, the CC will check the Death Certificate Transmittal Log. If there is a discrepancy between the transmittal log and the contents of the shipment, or if any of the certificates are incorrect or illegible, the CC Data Manager (Ellen Martinusen) will contact the SC Coordinator by telephone, fax, or e-mail to resolve the discrepancy.

9.5 Destruction of Identifiable NDI Data and Death Certificates from NDI Searches

In 2007, the NDI formalized recommendations for destruction of "identifying or identifiable death record information" with a request for studies approved prior to April 2007 to develop a plan for destroying this information at the end of the study. The completed NDI Data Destruction Form, signed by the NLST/LSS Project Officer and approved by the NDI, is considered current by NDI until June 2012, and is described in the next paragraph.

SCs and the CC must destroy all original and photocopied Death Certificates three years after the completion of final data analysis and published final results for the study. In addition, electronic files and/or printouts containing identifying information obtained from the NDI or death records must be destroyed within the same time period. If an individual state has more stringent requirements for destruction of Death Certificates, the SC is responsible for tracking this information, reporting the requirements to the CC, and destroying the Death Certificates as required by the state. Acceptable methods for destruction of hard copy materials include shredding or incineration.

9.6 Folder Preparation and the Death Documentation Sheet (DDS)

Once a death has been confirmed through acquisition of the Death Certificate, a new folder should be prepared for the participant's file. The folder should be a color or type unique to the EVP and it should be labeled with the PID number. All documentation relating to the EVP, including a copy of the Death Certificate, should be placed in the EVP folder to facilitate access and review. An EVP folder should be created for all deceased participants, regardless of whether or not they are selected for review by the EVT.

In addition to the Death Certificate, each EVP folder should contain a Death Documentation Sheet (DDS) (Appendix 9-2). The DDS is a manual tracking record to document and monitor completion of each step of the EVP. It should be used to indicate completion of cancer ascertainment, ongoing medical record collection and editing, and shipment of EVP materials. The SC may wish to develop an addendum to the DDS to meet SC specific procedures for requesting and obtaining medical record documentation. The Specifications for Completion of the DDS are provided in Appendix 9-3.

9.7 Cancer Status Determination and Confirmation

Once a participant's vital status has been confirmed through collection of the Death Certificate, the cancer confirmation process must begin. Cancer confirmation in preparation for EVP includes the following major steps:

- Identify and document on a CNF all previously unreported cancers from outside the ASU, including the Death Certificate;
- Administer the History of Malignancy form (HOM) (Appendix 9-4) for those participants whose Death Certificates list the cause of death as "natural causes;"
- Complete and process the CDF for all suspected cancers, and
- Close out the DE forms for all positive screening exams, and DE and TI forms for all confirmed lung cancers.

These steps are described in detail in the following sections.

9.7.1 Cancer Reports from ASU and Other Sources

Cancer in participants may be reported by the participant on the ASU or the SC may be notified by a participant, relative, physician, health care provider, or health care clinic, etc. that a cancer has been diagnosed. The SC may also incidentally find a primary cancer diagnosis upon review of the participant's medical record or a previously unreported cancer may be reported on the participant's Death Certificate. The SC is responsible for documenting all reports of cancer outside the ASU on a CNF. The SC is responsible for following up cancer suspicions from the ASU and CNF and documenting the results of the investigation on a CDF.

9.7.2 Death Certificates with Causes of Death – "Natural Causes"

The cause of death on Death Certificates is occasionally listed as "natural causes." In such cases, additional information needs to be collected for the EVT in order to determine a more specific cause of death. In addition, the EVT needs to confirm that there was no lung cancer.

To obtain this information, the History of Malignancy (HOM) form (Appendix 9-4) should be sent to the deceased participant's physician/health care provider or health care clinic. The Specifications for Completion of the HOM are found in Appendix 9-5. The SC should send the HOM to the physician/health care provider or health care clinic with a cover letter. A sample cover letter is provided in Appendix 9-6. The HOM should be sent only for those individuals who died of "natural causes."

9.7.3 Completion of the CDF for Suspected Cancers

Cancer ascertainment and confirmation is not considered complete until a CDF has been completed for all cancers reported on an ASU or CNF. Further details regarding cancer ascertainment and confirmation are provided in Chapter 8.

9.7.4 Completion of DE and TI Forms for Positive Screening Exams and Confirmed Lung Cancers

The SC must complete a DE form for all positive screening exams, and for all confirmed lung cancers documented on a CDF and diagnosed on or before December 31, 2009. The SC must complete a TI form for all confirmed lung cancers documented on a DE form. The SC must complete a CP form for all confirmed lung cancers each year through 2009 beginning in the study year following the completion of the TI form. Further details regarding completion of the DE, TI, and CP forms are provided in Chapter 7.

9.8 Determining Eligibility for EVT Review

All participant deaths will be reviewed by a computer algorithm at the CC that examines the causes of death and significant conditions listed on the participant's Death Certificate as well as other participant data to determine eligibility for EVT review. The algorithm will reject deaths that have incomplete information following pre-processing, identify deaths with outstanding cancer suspicions, select deaths requiring EVT review, and certify deaths with complete information that do not require EVT review and therefore require no additional action.

The procedures to determine the eligibility of a death for EVT review are described below.

9.8.1 CC Cause of Death Coding

On a monthly basis, the CC will review the recent shipment of Death Certificates for proper editing and legibility. The SC Coordinator will be notified if there is a problem with a Death Certificate. Two CC nosologists will code all causes of death, including the NCHS Derived Underlying Cause of Death, using a Death Certificate Coding Form (DCCF), as documented in the *Endpoint Verification Process Manual – Coordinating Center Procedures.* Any discrepancies in coding will be arbitrated by a third CC nosologist as necessary.

9.8.2 The EVP Algorithm

At least once a month, certain deaths (those with newly coded Death Certificate information or those that need to be re-processed) will be run through the CC EVP selection algorithm. The algorithm will perform an initial pre-processing step to identify those deaths that are missing an NRF or have an IDEAS expectation for, but no receipt of, medical record abstract forms (CDF or DE). Deaths that are missing an NRF, DE form, or CDF are rejected by the algorithm and assigned a status of "RJ" for "Rejected." SCs will be required to complete the outstanding information before the death can continue through the algorithm.

Deaths that are not rejected during the pre-processing phase will continue through the selection algorithm to determine whether there is a need for review by the EVT. Deaths selected by the algorithm for EVT review will be assigned a status of "AR" for "Additional Review." Deaths that do not meet any of the criteria for additional review will be assigned a status of "AC" for "Achieved Certification." Deaths that have mention of a previously undocumented cancer on the Death Certificate are assigned a status of "CS" for "Cancer Suspicion."

A designated user at each SC will be able to access the Endpoint Verification Internal Computerized Tracking (EVICT) system to view the current status of the algorithm results in the algorithm reports. The algorithm report consists of four separate sub-reports, one for each status (RJ, AR,

AC, and CS), which will list all deceased participants by report run date and PID. See Appendix 9-7 for examples of the EVP Algorithm Reports.

All deaths designated "AC" are certified and require no additional action. All deaths designated "AR" require review by the EVT; therefore, the SC should begin record collection as described in Section 9.9. All deaths designated "RJ" or "CS" will need to be investigated by the SC and outstanding study forms and/or incomplete information will need to be provided before the death can continue processing through the selection algorithm. For example, an "RJ" status may be assigned if there is a positive screening exam for which a DE form has not been completed. The SC will be asked to complete the DE form to document follow-up of the positive screen. A "CS" status may be assigned if a cancer that was initially reported on the Death Certificate has not been confirmed by a CDF or DE. If the cancer was not reported on an ASU or CNF, the SC will be asked to complete a CNF to document the report of cancer and generate an expectation for a CDF. The SC must complete the CDF and any resulting DE expectations must be closed out. Deaths initially assigned a status of "RJ" or "CS" will continue to be included in the monthly algorithm run until either an "AR" or "AC" status is assigned.

9.9 Collection and Preparation of Documents for the EVT

The SC will be responsible for preparing all documentation for the EVT. All documentation collected for the EVP should be placed in the participant's EVP folder. Documentation should be collected, reviewed, and edited by a trained medical record abstractor with at least two years experience abstracting medical records, and a demonstrated knowledge of medical record terminology, anatomy, physiology, and concepts of disease. The SC should attempt to collect the same types of information for all participants selected for endpoint verification. Obtaining all relevant documentation is critical for the determination of the underlying cause of death. If the SC is experiencing problems obtaining information from a physician/health care provider's office, hospital, or health care clinic, assistance from the Principal Investigator may be necessary. Procedures for collection and preparation of documents for the EVT review are given in the following sections.

9.9.1 Document Collection

Any participant with an EVP status code of "AR," as designated by the selection algorithm, requires review by the EVT. The EVT will require all in/outpatient medical records including:

- Diagnosis documents;
- Treatment documents;
- Outpatient notes;
- Hospital admission history/physical;
- Operative procedures reports;
- Pathology reports;
- Chemotherapy notes;
- Radiotherapy notes;
- Hospital discharge abstracts;
- Hospital discharge summary;
- Diagnostic procedure reports;
- Diagnostic imaging reports;
- Autopsy reports;
- Clinical laboratory data;
- Consultation reports, and
- Emergency medicine documents.

The EVT will also require any notes regarding the management of co-existing cancers and terminal events.

Diagnostic documents will differ depending on the type of cancer. The Medical Documentation Section (Part B) of the DDS should be updated as each document is collected.

For each case, SCs must exercise informed judgment regarding the appropriate time frame for medical record collection. The required medical records will vary in amount and nature according to each individual case, but generally there should be sufficient records to determine the cause of death as well as the contributing factors that led up to death. The time frame should be long enough to enable adequate characterization of cancer status at the time of death, and in general will encompass the last several weeks or months of life.

The EVT should also be given information on cancers diagnosed prior to randomization. This information will simply be the fact that a cancer was diagnosed, based on participant self-report on the Medical History Questionnaire (MHQ) (Appendix 3-5). Any cancers listed on the MHQ should be reported to the EVT by photocopying Item 26 from the MHQ and including it with the EVP folder.

In some cases, the physician/health care provider's office, hospital, or health care clinic may not accept the NLST/LSS consent form as sufficient for release of medical records. Additional authorization may need to be requested from the participant's next of kin. A sample Medical Records Release Authorization Form that may serve this purpose is provided in Appendix 3-4; however, some hospitals or insurance plans may require a release in a specific format. A template letter to be signed by the SC Principal Investigator is provided in Appendix 9-21 and may be helpful for collecting medical records in difficult cases. If necessary, a letter from the NLST/LSS Project Officer can also be obtained by contacting the CC.

9.9.2 Document Review

Once the SC Coordinator determines that all available information has been collected, all documents should be reviewed and edited. Documentation should be evaluated for completeness, placed in chronological order, and each of the following questions should be answered:

- Does each hospital discharge summary have a corresponding admission history and physical? (Exceptions may occur, if initial diagnosis and treatment were outpatient.)
- Is there an operative and pathology report for all surgical procedures related to a malignancy or suspected malignancy?
- Is there a report for each diagnostic procedure performed?

If the answer to any of these questions is "no," then additional information should be collected. If the SC has attempted and is unable to obtain certain documentation, this should be documented in Part B of the DDS. Copies of any call logs that include documentation of these efforts also should be attached to the DDS.

9.9.3 Document Editing

Participant identifiers, including date of birth, should be deleted from all medical records to maintain participant confidentiality. EVT members will be blinded as to participant randomization arm (spiral CT or chest x-ray), and as to whether a cancer was screen-detected or symptom-detected. Therefore, medical records submitted to the EVT should be edited to remove mention of the NLST/LSS, participation in research (e.g. clinical trials), involvement in special lung cancer detection programs, and the method of cancer detection.

Medical records should be edited using the following guidelines:

- Editing should only be performed on a copy of the medical record. Original medical records should be photocopied and returned to the participant file or hospital (if on loan). **The SC should keep an unedited copy of the medical records in the file.**
- All participant identifiers, including date of birth, should be crossed out with a black marker or White Out.
- Any mention of the NLST/LSS should be crossed out with a black marker or White Out.
- Any reference to the participant's randomization arm should be removed.
- Any indication as to whether the cancer was screen-detected or symptom-detected should be deleted.
- Incorrect grammar and spelling should not be changed.
- When in doubt, do NOT white it out. The CC and EVT Chair will help provide examples of information that should be deleted from the record. The CC EVP Coordinator will provide feedback to the SCs regarding information that should have been deleted.
- Edits should not be initialed, dated, or highlighted in any way.
- Each page of documentation should be labeled with a PID number (PID label or stamp, do NOT hand write). The PID should be placed anywhere on the front of the page (so that it will appear on the photocopies). This step is important in case a folder becomes disassembled at some point during the Endpoint Verification Process.
- All documentation that is required by the EVT should be included in the EVP folder, and if it is not available, this should be documented on the DDS.

After all documentation has been gathered and is complete, the DDS should be updated to indicate that medical record collection and editing is complete and the folder is ready for shipment (Part C).

9.10 EVP Material Shipment

EVP materials should be shipped to the CC as folders are completed. Once the SC Coordinator has verified that a participant's documentation is complete, one copy of the participant's EVP folder should be made. Completed folders should then be batched and shipped to the CC as follows:

- Verify that the DDS is included in the folder.
- Photocopy all documents in the participant's EVP folder; do NOT staple the documents together.
- Identify each document and folder with the appropriate PID.
- Include a copy of the Death Certificate that was previously sent to the CC.
- Include one full page of extra PID labels for each participant.
- Place a rubber band around each folder to ensure that all materials stay together.
- Batch receipt the DDS into IDEAS for each PID being sent to the CC.
- Prepare and print a batch transmittal log (See Appendix 9-8, EVP Material Transmittal Log) of PIDs included in the shipment using IDEAS.
- Compare the log against the actual hard copy material. If any folders cannot be located or are not ready to be shipped, they should not be included on the transmittal log. Delete any PIDs for which EVP materials are not being included in the shipment.
- Keep one copy of the transmittal log for SC files.

- Assemble the folders in the order they appear on the transmittal log. Package the folders and a copy of the batch transmittal log in a box and send to the CC using Federal Express, UPS, or another certified mail carrier. Keep a record of the package number. Send the package to Kristen Keating at the following location:

  Kristen Keating
  Westat
  1500 Research Blvd., TB 320
  Rockville, MD 20850

9.11 CC Preparation of Materials for the EVT

The CC will receive and verify all shipments of documentation from the SC. Upon receipt of a shipment, the CC will check the transmittal log. If there is a discrepancy between the transmittal log and the contents of the shipment, the CC EVP Coordinator will contact the SC Coordinator by telephone or e-mail to resolve the discrepancy.

Once the contents of the shipment have been verified, the CC will review all of the material to ascertain that proper editing has occurred. When the CC review is complete, the EVT review process will commence with initial review of folders by the EVT Chair.

9.12 Requests for Additional Information from the SC

The CC, EVT Chair, and other members of the EVT participating in the review process will evaluate the adequacy of the information provided. If more information is needed, an Additional Documentation Request (ADR) form (Appendix 9-9) will be completed. Specifications for Completion of the ADR are provided in Appendix 9-10. The EVT Chair and/or members will complete the ADR and fax or e-mail it to the CC EVP Coordinator. The CC EVP Coordinator will forward the request to the SC. The ADR will document the specific additional information that is needed. The SC will collect these documents, delete identifiers and any other information as stated above, and send a photocopy to the CC in the same manner as the original EVP documentation, using the EVP Material Transmittal Log. Should the SC be unable to obtain requested information, the reason should be documented in the transmittal log. Upon receipt, the information will be reviewed at the CC to ensure proper editing. Once the review is complete, the CC EVP Coordinator will forward the documentation to the requestor. The SC should keep a copy of all information that is sent to the CC.

Since the clinical record may contain conflicting or ambiguous information regarding the cancer diagnosis, EVT members may request acquisition and an external review of pathology slides by two NLST-designated pathologists and/or review of diagnostic images by external radiologists. A Pathology/Radiology Review Request (PRR) form (Appendix 9-11) will be used to document this request. The Specifications for Completion of the PRR are provided in Appendix 9-12. The SC Coordinator will complete the Pathology/Radiology Review Request Transmittal Log (Appendix 9-13) when sending slides or images to the CC. The Specifications for Completion of the PRR Transmittal Log are provided in Appendix 9-14.

Appendices for Chapter 9

9-1	Death Certificate Transmittal Log
9-2	Death Documentation Sheet (DDS)
9-3	Specifications for Completion of the Death Documentation Sheet
9-4	History of Malignancy Form (HOM)
9-5	Specifications for Completion of the History of Malignancy Form
9-6	History of Malignancy Cover Letter
9-7	Algorithm Reports
9-8	Endpoint Verification Process Material Transmittal Log
9-9	Additional Documentation Request Form (ADR)
9-10	Specifications for Completion of the Additional Documentation Request Form
9-11	Pathology/Radiology Review Request Form (PRR)
9-12	Specifications for Completion of the Pathology/Radiology Review Request Form
9-13	Pathology/Radiology Review Request Transmittal Log
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9-15	Death Certificate Tracking Form (DCTF)
9-16	Specifications for Completion of the Death Certificate Tracking Form
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9-19	Specifications for Completion of the National Death Index Results Form
9-20	National Death Index Death Certificate Request Form
9-21	Template PI Letter for EVP Medical Record Collection
9-22	Documentation for a Missing Death Certificate
9-23	Specifications for Completion of the Documentation for a Missing Death Certificate

National Lung Screening Trial (NLST)

DEATH CERTIFICATE TRANSMITTAL LOG

Please complete this transmittal for the Death Certificates which are currently being shipped (one copy for each PID). Keep a copy of this log at the SC for your records and fax a copy to Ellen Martinusen at 301/963-5455. Please ship transmittal and Death Certificates to:

Ellen Martinusen
GA 26A
9274 Gaither Drive
Gaithersburg, MD 20877

SC: _____ Date Sent to Westat: _____

PID
1.
2.
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18.

Appendix 9-2 Death Documentation Sheet (DDS)

National Lung Screening Trial (NLST)

DEATH DOCUMENTATION SHEET (DDS)

Screening Center _____

Participant's Date of Death _____/_____/_____

Initials Complete: _____
Initials QC: _____

DDS

Participant ID Label

PART A: CANCER CONFIRMATION

Check each step as it is completed:

- ☐ All ASUs receipted.
- ☐ All outside reports of cancer documented on CNF.
- ☐ All suspected cancers confirmed on CDF.
- ☐ Follow-up of all positive screens documented on DE forms.
- ☐ All confirmed lung cancers documented on DE forms.

Was this case selected for review? ☐ YES (COMPLETE PARTS B AND C) ☐ NO (END)

PART B: MEDICAL DOCUMENTATION

Complete the following chart as documents are collected for endpoint verification.

Document Type	Requested (√)	Received (√)	N/A (√)	Comments
Terminal events				
Hospital admission history/physical				
Operative procedures reports				
Pathology reports				
Chemotherapy notes				
Radiotherapy notes				
Management of co-existing cancers				
Hospital discharge abstracts				
Hospital discharge summary				
Diagnostic procedure reports				
Diagnostic imaging reports				
Outpatient notes				
Autopsy Reports				
Clinical Laboratory Data				

Appendix 9-2 Death Documentation Sheet (DDS)

Document Type (ctd.)	Requested (√)	Received (√)	N/A (√)	Comments
Consultation Reports				
Emergency Medicine Documents				
Other diagnosis documents				

Specify:

Other treatment documents				

Specify:

PART C: EDITING AND SHIPPING EVP DOCUMENTS

Check each step as it is completed:

Editing of Documentation:

- ☐ Identifiers removed
- ☐ References to NLST/LSS removed or not applicable
- ☐ References to participant allocation (SCT or XRY) removed or not applicable
- ☐ Method of cancer detection removed or not applicable
- ☐ Each page labeled with PID

Medical Record Documentation Complete? ☐ Yes ☐ No

Shipping of Materials:

- ☐ One copy of EVP folder
- ☐ One copy of death certificate
- ☐ One copy of MHQ Question 26 only
- ☐ One full page of extra PID labels
- ☐ Folders organized
- ☐ EVP Material Transmittal completed

Date Materials Posted to CC: / /

Additional Comments:

National Lung Screening Trial (NLST)

Specifications for Completion of the Death Documentation Sheet (DDS)

The Death Documentation Sheet (DDS) is a manual tracking record to document and monitor completion of each step of the Endpoint Verification Process (EVP). It should be initiated when the Death Certificate is received by the SC and should be used as a checklist to indicate completion of cancer ascertainment, ongoing medical record collection and editing, and shipment of EVP materials.

Specifications for completing each item of the form are given below:

Administrative Section:

Participant ID: Affix a PID label to the space provided in the upper right section of the form. DO NOT write in the PID.

Screening Center: Enter the two-digit Screening Center ID.

Participant's Date of Death: Record the participant's date of death.

Part A: Cancer Confirmation: This section documents the cancer confirmation activities that must take place prior to submission of the case to be evaluated for endpoint verification (the algorithm run at the CC). In this section, the SC staff member should check off each task as it is completed. The tasks are described below.

All ASUs receipted: The SC has receipted an ASU or an MDF for an ASU for each study year in which it is expected for the participant.

All outside reports of cancer documented on CNF: The SC has completed and receipted a CNF for all reports of cancer outside the ASU, including any searches of cancer registries and hospital records that the SC routinely performs for cancer identification.

All suspected cancers confirmed on CDF: The SC has completed all medical record abstracting for all cancers reported on an ASU or CNF, and there are no open expectations for any CDFs.

Follow-up of all positive screens documented on DE forms: The SC has completed and receipted all medical record abstracting for diagnostic evaluation information following all positive screening examinations.

All confirmed lung cancers documented on DE forms: The SC has completed and receipted all medical record abstracting for diagnostic evaluation information for all lung cancers confirmed on a CDF.

Was this case selected for review? This item indicates whether or not this death was selected for review by the endpoint verification algorithm (run by the CC).

Yes: Check this item if the case was classified by the algorithm as "AR" (Review).

No: Check this item if the algorithm determined that the case does not need review and classified it as "AC" (Certified). If this item is checked, the EVP is considered completed for this participant.

Part B: Medical Documentation: The purpose of this section is to document the medical record collection process. The chart will serve as a checklist to help the SC ensure complete records collection and will help the EVT assess the scope and success of the medical records collection task.

Document Type: This is the type of document that may be collected for endpoint verification. Not all document types will be collected for a single case.

Requested: Place a check mark in this column if all applicable documents of this type were requested.

Received: Place a check mark in this column if all applicable documents of this type were received.

N/A (Not Applicable): Place a check mark in this column if this type of document is not applicable to this case.

Comments: Use this space to record any comments related to why this document could not be obtained, including the number of attempts made to obtain it. Attach copies of any call logs that document these efforts.

Part C: Editing and Shipping EVP Documents: The purpose of this section is to document the editing of the medical records for the EVT and the shipping of the one copy to the CC for distribution to the team.

Editing of Documentation:

Identifiers Removed – all participant and relative names and participant medical record number or Social Security Number and date of birth removed.

References to NLST/LSS removed or not applicable – If there were references to NLST/LSS or to lung cancer screening in the record, they have been removed.

Reference to participant allocation (SCT or XRY) removed or not applicable – If there were references to the participant's randomization arm, they were removed.

Method of cancer detection removed or not applicable – If there were references to whether the cancer was detected as a result of a screening examination, they were removed.

Each page labeled with PID – Each page has been labeled with a PID label. DO NOT write the PID.

When the SC considers the editing to be complete, all boxes should be checked.

Medical Record Documentation Complete? Check the appropriate response as follows:

Yes – All available records have been collected.

No – All available records have not been collected. The SC did attempt to obtain some records that may have been appropriate for the EVP but were not available. Details should be provided in the appropriate Comments section.

Shipping of Materials

One copy of EVP folder – Check this item when a photocopy of the EVP folder (including the DDS) has been made. Ensure that the photocopy is readable before shipping to the CC.

One copy of Death Certificate – Check this item when a photocopy of the Death Certificate has been made. Ensure that the photocopy is readable before shipping to the CC.

One copy of MHQ Question 26 only – Check this item when a photocopy of MHQ question 26 has been made. This is necessary only if the participant reported a cancer on question 26 of the MHQ. Ensure that the photocopy is readable before shipping to the CC. If cancer was not reported on question 26 of the MHQ, write "N/A" for "Not Applicable" next to the check box.

One full page of extra PID labels – Check this item when the full page of extra PID labels have been enclosed in the EVP folder.

Folders organized – Check this item when the folders are organized in the order they appear on the transmittal and secured with rubber bands to prevent documents from falling out of the folders. Do not staple the documents.

EVP Material Transmittal completed – Check this item when the EVP Material Transmittal is completed and checked against the folders.

After completing the form:

- The form should be checked to make sure it is accurate, legible, and complete.
- The SC staff member who completed the form should write his/her initials in the space labeled "Initials Complete" in the box at the top right corner of the first page.
- The SC staff member who checked the form for completion should write his/her initials in the space labeled "Initials QC" in the box at the top right corner of the first page. This should not be the same SC staff member who completed the form.

Initials edit: _____

FOR OFFICE USE

National Lung Screening Trial (NLST)

HISTORY OF MALIGNANCY FORM (HOM)

To Dr. _____ Date: _____/_____/_____

Re: _____ Patient's Address: _____

Date of Birth: _____/_____/_____ _____

Date of Death: _____/_____/_____ SSN: _____-_____-_____

Please answer the following questions. Check only one box, unless instructed otherwise.

1. On what date did you last see this patient? _____/_____/_____

2. During which years was this patient seen at your facility? _____ to _____

3. Have you ever diagnosed cancer in this patient? □ No (Go to 4)
   □ Yes

   a. On what date did you first make the diagnosis? _____/_____/_____

   b. At what institution(s) were the diagnostic tests performed?

      1. Hospital/Clinic/Physician Office: _____

         Address: _____

      2. Hospital/Clinic/Physician Office: _____

         Address: _____

   c. Was it possible to determine the organ within which the tumor arose (primary site)?
      □ No
      □ Yes (Site: _____)

4. If you have not diagnosed a malignancy in this patient, are you aware of a diagnosis of cancer made by another physician caring for your patient?
   □ No
   □ Yes (Site and type of cancer _____)

   Diagnosing physician's name and address:

   Name: _____

   Address: _____

Form completed by: Signature: _____

Print name: _____ Date Completed: _____/_____/_____

National Lung Screening Trial (NLST)

Specifications for Completion of the History of Malignancy Form (HOM)

The History of Malignancy Form (HOM) is to be administered to the physician/health care provider or health care clinic for deceased NLST/LSS participants whose cause of death is listed as "Natural Causes." SC staff should identify the appropriate physician/health care provider or health care clinics and complete the top administrative section of the form. The HOM should be sent to the physician/health care provider or health care clinic with a cover letter.

Specifications for completing each item of the form are given below:

Administrative Section:

This section should be completed by the SC staff prior to sending the HOM to each physician/health care provider or health care clinic. The PID should not be written on the form, nor should a PID label be applied to the form prior to mailing, since this would provide a link between the participant's name and the PID and could compromise participant confidentiality.

To Dr.: Record the name of the physician/health care provider or health care clinic.

Date: Record today's date.

Re: Record the name of the participant.

Address: Record the last known address of the participant.

Date of Birth: Record the participant's date of birth.

Date of Death: Record the participant's date of death.

SSN: Record the participant's Social Security Number, if available.

Question 1: On what date did you last see this patient?

The physician/health care provider or health care clinic should record date of the most recent office visit or examination by the physician/health care provider or health care clinic.

Question 2: During which years was this patient seen at your facility?

The physician/health care provider or health care clinic should record the year of the first encounter between the participant and himself/herself, and the year of the last encounter between them, even if there was a gap of several years between encounters. The year of the last encounter should correspond with the date of the last visit in Question 1.

Question 3: Have you ever diagnosed cancer in this patient?

The physician/health care provider or health care clinic should record "Yes" if s/he diagnosed cancer in the patient. If there were several cancers diagnosed, the physician/health care provider or health care clinic should record the information for one cancer in Items 3a – 3c and the same information for additional cancers on a separate sheet or on the back of the form.

a. On what date did you first make the diagnosis?

The physician/health care provider or health care clinic should record the date of the first diagnosis of cancer in this participant.

b. At what institution(s) were the diagnostic tests performed?

The physician/health care provider or health care clinic should record up to two hospitals, clinics, or physician's offices in which the main diagnostic procedures were performed.

c. Was it possible to determine the organ within which the tumor arose (primary site)?

The physician/health care provider or health care clinic should indicate whether it was possible to determine the primary site of the cancer. If "Yes" is recorded, the physician/health care provider or health care clinic should write in the site in the space provided.

Question 4: If you have not diagnosed a malignancy in this patient, are you aware of a diagnosis of cancer made by another physician caring for your patient?

The physician/health care provider or health care clinic should indicate whether s/he is aware of a cancer diagnosed by another physician caring for the patient. If "Yes" is recorded, the physician/health care provider or health care clinic should write the site and type of cancer in the space provided, and record the name and address of the physician who diagnosed the cancer in the lines provided.

Form completed by: The physician/health care provider or health care clinic staff member should sign his/her full name, and print his/her full name.

Date Completed: The physician/health care provider or health care clinic staff member should record the date on which s/he completed this form.

<u>After completing the form</u>:

- If another physician was listed in Question 4, the SC should follow-up with this physician to obtain information concerning the cancer diagnosis.
- If a cancer was reported on the HOM, the SC should complete a CNF and CDF as appropriate.

Appendix 9-5 Specifications for Completion of the History of Malignancy Form

- The form should be checked to make sure it is accurate, legible, and complete.
- The person who checks the form for completion should write their initials in the designated space in the box at the top right corner of the first page.
- The HOM form should be filed in the participant's EVP folder.

National Lung Screening Trial (NLST)

HISTORY OF MALIGNANCY COVER LETTER

(*Date*)

(*Physician Name*)
(*Physician Address*)
(*City, State, Zip Code*)

Dear (*Physician Name*):

(*Participant Name*) was a participant in the National Lung Screening Trial (NLST) at (*Screening Center*) and our records indicate that you were involved in his/her medical care.

The National Cancer Institute (NCI) and *(Screening Center)* are sponsoring this nationwide study of older Americans with a history of long-term or heavy smoking. The purpose of the study is to compare screening with spiral CT and screening with chest x-ray for effectiveness in reducing the number of deaths due to lung cancer.

(In the past, you provided us with information about participant's _____ cancer. Thank you for that information. We would now like to confirm whether or not there were any additional cancer diagnoses in participant). We would appreciate your cooperation in completing the enclosed questionnaire. Also enclosed is an authorization for release of information signed by (*Participant*)'s (*relationship, e.g., brother, wife, etc.*). Please return the questionnaire to:

(*Study Coordinators name and address*)

By completing this questionnaire, you will be making an important contribution to this project. We have enclosed a self-addressed, stamped envelope for your convenience. If you have any questions, please contact me at (*PI phone number*). Thank you for your help.

Sincerely,

(Name of Investigator)
Principal Investigator

National Lung Screening Trial (NLST)

NLST ENDPOINT VERIFICATION PROCESS ALGORITHM REPORT - AC

The following Participant IDs have achieved certification and require no additional action.

Date Printed: Executed By:

Batch No	Participant ID	Report Status	ReportRunDate

National Lung Screening Trial (NLST)

NLST ENDPOINT VERIFICATION PROCESS ALGORITHM REPORT- AR

The following Participant IDs have been assigned to the EVP Coordinator for additional review.

Date Printed: Executed By:

Batch No	Participant ID	Report Status	ReportRunDate

National Lung Screening Trial (NLST)

NLST ENDPOINT VERIFICATION PROCESS ALGORITHM REPORT- REJECTION REPORT

The following Participant IDs require Screening Center resolution. They have a current status of Rejected.

Date Printed: Executed By:

Batch No	Participant ID	Report Status	ReportRunDate

Appendix 9-8 Endpoint Verification Process Material Transmittal Log

National Lung Screening Trial (NLST)

ENDPOINT VERIFICATION PROCESS MATERIAL TRANSMITTAL LOG

Please complete this transmittal for the EVP folders which are currently being shipped (one copy for each PID). Please print out and keep a copy of this log at the SC for your records, and include a copy of the log in the package of EVP folders to be shipped to:

Kristen Keating
Westat
1500 Research Blvd., TB 320
Rockville, MD 20850

SC: _____ Date Sent to Westat: _____

PID	DATE OF BIRTH
1.	
2.	
3.	
4.	
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10.	
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12.	
13.	
14.	
15.	

National Lung Screening Trial (NLST)

ADDITIONAL DOCUMENTATION REQUEST FORM (ADR)

Screening Center ID |__|__|

Participant's Date of Death |__|__|-|__|__|-|2|0|__|__|

Requested by:
☐ CC
☐ EVT Reviewer Name: _____

Date Requested |__|__|-|__|__|-|2|0|__|__|

Participant ID: _____

Document Type	Date
1	
2	
3	
4	
5	
6	
7	
8	

National Lung Screening Trial (NLST)

Specifications for Completion of the Additional Documentation Request Form (ADR)

The Additional Documentation Request (ADR) form for the Endpoint Verification Process (EVP) is used by the CC and the Endpoint Verification Team (EVT) to request additional medical record documents from the SC to support the EVP.

Specifications for completing each item of the form are given below:

Administrative Section:

Participant ID: This will be generated electronically.

Screening Center: Record the two digit SC ID number.

Participant's Date of Death: Record the month day and year of the participant's death. Record the last two digits of the year (e.g., 02/07/2002).

Requested by: Check a box to indicate whether the request is from the CC EVP Coordinator or a member of the EVT. If the request is from the EVT, record the name of the reviewer.

Date Requested: Record the date of the CC or EVT member's request for additional documentation.

Document Request Section:

This section is used to request documents. The requestor should describe the missing document(s) (e.g., pathology report, urinalysis, etc.) and record the approximate or exact date(s) of the document(s). This will help the SC to determine the source from which the document(s) should be requested (hospital or physician office).

After this form is completed: EVT requestors should submit the form via fax or electronically to the EVP Coordinator. The CC EVP Coordinator will track the request and send an e-mail to the SC Coordinator requesting the material. Copies of the ADR or e-mail notification should be kept with the EVP folder both at the SC and the CC.

National Lung Screening Trial (NLST)

PATHOLOGY/RADIOLOGY REVIEW REQUEST FORM (PRR)

SC ID: _____

DATE OF DEATH: _____

DATE REQUESTED: _____

EVT Member(s): _____

PID_____

NO.	INSTITUTION	ANATOMIC LOCATION	PATHOLOGY ACCESSION NUMBER	RADIOLOGY CASE NUMBER	IMAGE TYPE	DATE
1						
2						
3						
4						
5						

Comments:

_____

_____

_____

_____

_____

National Lung Screening Trial (NLST)

Specifications for Completion of the Pathology/Radiology Review Request Form (PRR)

The Pathology/Radiology Review Request Form (PRR) for the Endpoint Verification Process (EVP) is used by the Endpoint Verification Team (EVT) to request review of pathology slides by external pathologists, and/or review of images by external radiologists. The form is completed electronically in the Endpoint Verification Internal Computerized Tracking system (EVICT). Specifications for completing each item of the form are given below:

Administrative Section:

Participant ID: The EVT member will enter the PID in the space provided in EVICT.

Screening Center ID: The two-digit SC ID number will be pre-filled electronically in EVICT.

Date of Death: The participant's date of death will be pre-filled electronically in EVICT.

Date Requested: The EVT member will enter the date that the request is made in the space provided in EVICT.

EVT Member(s): The EVT member(s) will enter his (their) name(s) in the space provided in EVICT.

Slide/Radiology Request Section: This section is used to request the slide or image to be reviewed. This information should be ascertained from the participant's medical records and will help the SC to determine the source from which the slide/image should be requested. There is also space for additional comments.

For Pathology Requests:

Institution: Enter the name of the institution where the tissue sample was obtained.

Anatomic Location: Enter the organ site where the tissue sample was obtained.

Pathology Accession Number: Enter the pathology accession number for the tissue sample being requested.

Date: Enter the date the tissue sample was obtained.

For Radiology Requests:

Institution: Enter the name of the institution where the image was obtained.

Anatomic Location: Enter the organ site or anatomic location that was imaged.

Appendix 9-12 Specifications for Completion of the Pathology/Radiology Review Request Form (PRR)

Radiology Case Number: Enter the radiology case number for the image being requested.

Image type: Enter the type of image being requested. (e.g.: CT, X-ray, or FDG-PET scan).

Date: Enter the date that the image was obtained.

After this form is completed: The EVT reviewer submits the form electronically in EVICT.

National Lung Screening Trial (NLST)

PATHOLOGY/RADIOLOGY REVIEW REQUEST TRANSMITTAL LOG

SC ID: _____

SC Staff ID #: _____

DATE PRR RECEIVED FROM CC: _____

DATE SLIDES/IMAGES SENT: _____

Participant ID

PATHOLOGY

NO.	INSTITUTION	ANATOMIC LOCATION	PATHOLOGY ACCESSION NUMBER	SLIDE NUMBER	RETURN REQUESTED (Yes/No)
1					
2					
3					
4					
5					

Total number of slides sent:

Comments:

_____

_____

RADIOLOGY

NO.	INSTITUTION	ANATOMIC LOCATION	RADIOLOGY CASE NUMBER	IMAGE TYPE / NUMBER OF IMAGES	RETURN REQUESTED (Yes/No)
1					
2					
3					
4					
5					

Total number of images sent:

Comments:

_____

_____

National Lung Screening Trial (NLST)

Specifications for Completion of the Pathology/Radiology Review Request Transmittal Log

A Pathology/Radiology Review Request Transmittal Log must be completed for each shipment of pathology slides or radiological images to the CC. This log is to be completed by the SC staff member who is responsible for shipping the pathology slides or images to the CC. Complete only the portion of the log that applies to the type of material being sent. If slides or images from more than one PID are being sent, use a separate transmittal log for each PID. Specifications for completing each item of the form are given below:

Administrative Section:

Participant ID Label: Affix a Participant ID label in the space provided.

SC ID: Enter the two-digit screening center ID.

SC Staff ID #: The SC staff member who prepared the transmittal should record his/her SC staff ID number.

Date PRR Received from the CC: Record the date that the PRR containing the request for the materials that are being sent was received from the CC.

Date Slides/Images Sent: Record the month, day, and year the slides or images are sent to the CC.

Log for Pathology Slides:

Institution: Record the institution name where the pathology was carried out.

Anatomic Location: Record the location (i.e. the organ site) from which the tissue was removed for the pathology slide.

Pathology Accession Number: Record the pathology accession number for the tissue sample being sent. If there are multiple slides for the same tissue sample, this number only needs to be listed once.

Slide Number: Record the slide number for each slide on a separate line.

Return Requested (yes/no): Indicate whether or not the slide needs to be returned to the SC.

Total Number of Slides Sent: Record the total number of slides sent to the CC.

Comments: This space can be used by the SC staff member to record any information s/he would like to communicate to the CC regarding the pathology slides.

Log for Radiological Images:

Institution: Record the institution name where the image was obtained.

Anatomic Location: Record the organ site or anatomic location that was imaged.

Radiology Case Number: Record the radiology case number for the image being sent.

Image Type: Record the type of image being sent (e.g.: CT, X-ray, or FDG-PET scan).

Return Requested (yes/no): Indicate whether or not the image needs to be returned to the SC.

Total Number of Images Sent: Record the total number of images sent to the CC.

Comments: This space can be used by the SC staff member to record any information s/he would like to communicate to the CC regarding the radiological images.

After the transmittal log is completed:

- The form should be checked to make sure it is accurate, legible, and complete.
- The SC should fax the transmittal log to:

  Kristen Keating
  TB 320
  301/294-2092

- The SC should ship the transmittal log and materials to:

  Kristen Keating
  Westat
  1500 Research Blvd, TB 320
  Rockville, MD 20850

National Lung Screening Trial (NLST)

DEATH CERTIFICATE TRACKING FORM (DCTF)

Participant ID Label

Initials Complete: _____

Initials QC: _____

1. Date SC learned of participant's death: |___|___| / |___|___| / |2|0|___|___|
   Month Day Year

2. Date Death Certificate requested: |___|___| / |___|___| / |2|0|___|___|
   Month Day Year

3. Was Death Certificate received? ☐ Yes ☐ No (Go to Item 4)

   3a. If yes, date received: |___|___| / |___|___| / |2|0|___|___|
   Month Day Year

4. Comments:

National Lung Screening Trial (NLST)

Specifications for Completion of the Death Certificate Tracking Form (DCTF)

The purpose of the Death Certificate Tracking Form (DCTF) is to document the SC's efforts to obtain a Death Certificate for each deceased participant. Expectations will be set to receive the form once a Non-Response Form (NRF) has been completed indicating that the participant is deceased. The DCTF will not be expected for deaths occuring after December 31, 2009. The DCTF is to be kept in the participant's study file. The form should be completed by the SC Coordinator or his/her designee. The DCTF can either be completed as the information becomes available or once the process is completed using information from the participant's study file.

The data from the completed form will be entered into IDEAS when the Death Certificate is sent to the CC or when all reasonable attempts to obtain the Death Certificate have failed.

Specifications for completion of the form are given below.

Participant ID Label: Affix a PID label in the space provided. DO NOT write the participant ID in this space.

1. **Date SC learned of participant's death:** Record the date that the SC learned of the participant's death from any source including NDI. Month and day should be zero filled and the last two digits of year should be recorded (e.g., 02/07/2003).

2. **Date Death Certificate requested:** Record the date that the SC initially requested the Death Certificate. If more than one request was made, the dates for each additional request should be recorded in the Comments section. Month and day should be zero filled, and the last two digits of the year should be recorded (e.g., 02/09/2003).

3. **Was Death Certificate received?** Mark the box corresponding to whether the Death Certificate has been received.

Yes: The Death Certificate was received.

No: This box should only be marked when all reasonable attempts to obtain the Death Certificate have failed. The information regarding the effort made to obtain the Death Certificate, including dates of contact, must be recorded in the Comments section. If No is recorded, skip to Item 4 and leave Item 3a blank.

3a. **If yes, date received:** Record the date that the SC received a copy of the Death Certificate. Month and day should be zero filled, and the last two digits of year should be recorded (e.g., 02/09/2003).

4. **Comments:** Use this space to record information regarding the effort made to obtain the Death Certificate. This includes but is not limited to the dates of any additional requests for the Death Certificate following the initial request.

After completing the form:

- The form should be checked to make sure it is accurate, legible, and complete.
- The SC staff member who completed the form should write his/her initials in the space labeled "Initials Complete" in the box at the top of the page.
- The SC staff member who checked the form for completion should write his/her initials in the space labeled "Initials QC" in the box at the top of the page. This should not be the same SC staff member who completed the form.
- Enter the form into IDEAS.
- File the form in the participant's study file.

NDI Retrieval Reports

A standard NDI search will generate Files 1-8. An NDI-Plus search will generate all ten.

File 1 **Summary Retrieval Statistics** (page 37 of the *NDI User's Manual*) -- This file contains a three page report, which provides summary information about the NDI search. The information includes the SC Coordinator's name and address, years of death searched, number of NDI records involved in possible record matches, and other statistics related to the NDI search.

File 2 **NDI Retrieval Report** (page 41 of the *NDI User's Manual*) -- The NDI Retrieval Report indicates which participant records matched with the NDI records.

File 3 **Compressed NDI Retrieval Report** (page 45 of the *NDI User's Manual*) – This report contains the same information as the NDI retrieval report, but without the column and headings and spacing to reduce the amount of paper generated when printing this report.

File 4 **Death Certificate Request Form** (page 46 of the *NDI User's Manual*) – This report lists all the possible NDI matches grouped by the states in which the deaths occurred. A separate form is generated for each state that had at least one NDI match.

File 5 **Combined File** (page 49 of the *NDI User's Manual*) – This file combines the participant record with the matching NDI records. A separate Combined Record is created for each NDI record match. The file is intended for users who receive a large number of matches and would like to write a computer program to assess the quality of these matches.

File 6 **Matching User Records** (page 52 of the *NDI User's Manual*) – This file only contains those records submitted by the SC that were involved in possible matches with one or more NDI records.

File 7 **Non-Matching User Records** (page 52 of the *NDI User's Manual*) – This file only contains those records submitted by the SC that were not involved in matches with any NDI records.

File 8 **Rejected User Records** (page 52 of the *NDI User's Manual*) – This file contains the records that did not satisfy the basic criteria of the NDI edit program and were thus rejected prior to the search of the NDI file. Records are rejected if they did not contain the participant's social security number, date of birth, and sex code.

File 9 **Cause of Death File** (page 9 of the *NDI-Plus: Coded Causes of Death*) – This file begins with the same record format as the Combined File, but includes the coded causes of death (positions 180-438). Prior to using this file, true and questionable NDI record matches should be determined.

File 10 **Cause of Death Report** (page 20 of the *NDI-Plus: Coded Causes of Death*) – This report is meant to be an easy-to-read printout of the same coded causes of death included in the Cause of Death File. This report is intended primarily for NDI users who submit a small number of records for an NDI-Plus search.

NATIONAL DEATH INDEX RESULTS FORM (NDIR)

ADMINISTRATIVE SECTION		
		Initials Complete: _____ Initials QC: _____
Screening Center ID: |__|__| Screening Center Staff ID: |__|__|__|__| Submission Year: <Insert Year>	<Insert NDI ID>	<Insert Participant ID>

1. Indicate the results of the NDI search for this participant. Select the best match for this participant:

   ☐ Exact match
   ☐ Probable match
   ☐ No match (END)
   ☐ Rejected (END)

2. Will you be requesting a Death Certificate for this match?

   ☐ Yes
   ☐ No

3. Record results of NDI search:

   Underlying cause of death: ICD-10 |____|____|____|____|

   Year of death: |____|____|____|____|

Specifications for Completion of the National Death Index Results Form

The SC Coordinator should complete the National Death Index Results Form to document the outcome of the search of the National Death Index database.

Specifications for the completion of each item of the form are given below:

Administrative Section:

Screening Center ID: Record the two-digit SC ID number.

Screening Center Staff ID: Record the four-digit SC staff ID.

Submission Year: Enter the four-digit calendar year in which the PID was sent to the NDI search.

NDI ID: IDEAS generates a unique NDI identification number that will automatically appear in the space provided.

Participant ID: IDEAS will automatically print the PID label in the space provided.

NDI Results Section:

Question 1. Indicate the results of the NDI search for this participant:

For this question, the SC Coordinator will have to review the files from the NDI results.

Exact Match: Exact matches are indicated on the NDI Retrieval Report with an asterisk next to the State of Death. If the following data items match exactly, the NDI record is an Exact Match to the PID:

- First and Last Names, and Middle Initial
- Social Security Number
- Date of birth
- Sex code

Probable Match: Possible matches appear on the NDI Retrieval Report ranked based on the number of NDI data items that are in agreement with the data items of the participant. For NLST purposes, a record should be considered a Probable Match when some of the data items do not match exactly. Sex code must always match. Other data items need to match exactly or meet the following criteria:

- Under "Name" in the Retrieval Report, if F (for first name) has an NDI code of "I," this indicates that the first initial of the first name matches.
- Under "Name" in the Retrieval Report, if L (for last name) has an NDI code of "N," this indicates that the name matched only on NYSIIS (New York State Identification and Intelligence System) phonetic codes.

- At least the last four digits of the Social Security Number match. If the Social Security Number is not provided, then the DOB should match exactly, i.e., month, day, and year.
- Month of birth within one month before or after the participant's date of birth.
- Year of birth within ten years before or after the participant's date of birth.

The submission file also included state of residence to help determine the suitability of a match. If a record does not meet the criteria for an Exact Match or Probable Match, then one of the two following codes may be assigned:

No match (END)

- Select this box if the participant record was not involved in an Exact or Probable Match with NDI records.

Rejected (END)

- Select this box if no information was returned from NDI for this participant. These participants can be easily identified using the Rejected User Records report.

Question 2. Will you be requesting a Death Certificate for this match?

- **Yes** If the search resulted in an Exact Match, the SC Coordinator should request the Death Certificate and this box should be checked. If the search did not result in an Exact Match, but resulted in a Probable Match that the SC Coordinator considers as correctly identifying a participant, than the Death Certificate should be requested and this box should be checked.

- **No** If the results ended in a Probable Match that does not match well enough with information identifying the participant, and the SC Coordinator decides against requesting a Death Certificate, this box should be checked.

Question 3. Record results of the NDI search:

Underlying cause of death: ICD-10. To locate the correct response to this question, the SC staff should refer to the National Death Index Plus: Cause of Death Report. This report lists coded causes of death for the PIDs that are ranked first or have a high "probabilistic score" (for a description of probabilistic scores, please refer to Appendix A of the *NDI-Plus User's Manual*). The control number (fourth field in the first line of the output for each record) refers to the unique NDI identification number generated by IDEAS. After the correct unique NDI ID has been identified, then the SC Coordinator can identify the underlying cause of death. The underlying cause code occupies the sixth field on the first line of the output for each record, and specifies the International Classification of Diseases 10 code. It should be entered here as it appears in the Cause of Death report: alpha-number-number (if it is a two-digit number, leave the first space blank) or alpha-number-number-number.

Year of death. Year of death occupies the first field on the first line of the output for each record. Enter all four digits.

Appendix 9-20 National Death Index Death Certificate Request Form

UNITED STATES DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
CENTERS FOR DISEASE CONTROL
NATIONAL CENTER FOR HEALTH STATISTICS

RUN DATE: 07/17/90

N A T I O N A L   D E A T H   I N D E X

D E A T H   C E R T I F I C A T E   R E Q U E S T   F O R M S

NDI APPLICATION NUMBER: 900099

REQUESTOR: ROBERT BILGRAD
N. C. H. S.
DEMONSTRATION RUN
PRESIDENTIAL
6525 BELCREST ROAD
HYATTSVILLE MD 20782
PHONE: 301-436-8951

ALL OF THE POSSIBLE NDI RECORD MATCHES ARE GROUPED ON THE ATTACHED FORMS BASED ON THE REGISTRATION AREAS IN WHICH THE DEATHS OCCURRED. WITHIN A GIVEN REGISTRATION AREA, THE RECORDS ARE SORTED FIRST BY YEAR OF DEATH AND THEN BY DEATH CERTIFICATE NUMBER.

YOU ARE ENCOURAGED TO USE THESE FORMS TO REQUEST COPIES OF DEATH CERTIFICATES FROM THE REGISTRATION AREA OFFICES. AFTER YOU EVALUATE EACH NDI RECORD MATCH LISTED IN YOUR NDI RETRIEVAL REPORT, YOU CAN USE THESE FORMS TO CHECK OFF ONLY THOSE DEATH CERTIFICATES YOU WOULD LIKE TO OBTAIN FROM EACH OFFICE. BEFORE MAILING THESE FORMS TO THE REGISTRATION AREA OFFICES, REFER TO THE DOCUMENT ENTITLED "OBTAINING STATE DEATH CERTIFICATES" FOR INFORMATION ON STATE FEES, REQUIREMENTS FOR THE RELEASE OF CERTIFICATES, AND PERSONS TO CONTACT FOR ADDITIONAL INFORMATION.

* * * * NOTE: DATA IN THIS SAMPLE REPORT ARE PURELY HYPOTHETICAL. * * * *

Appendix 9-20 National Death Index Death Certificate Request Form

NATIONAL DEATH INDEX: DEATH CERTIFICATE REQUEST FORM

PAGE 1

RUN DATE: 07/17/90

REGISTRATION AREA: CALIFORNIA

NDI APPLICATION NO: 900099

WE ARE REQUESTING COPIES OF ONLY THOSE DEATH CERTIFICATES WHICH WE HAVE CHECKED IN THE LEFT MARGIN. PLEASE SEND COPIES TO:

TOTAL NDI RECORD MATCHES: 7

NO. OF CERTIFICATES REQUESTED: ....

STATE CHARGE PER CERTIFICATE: $..............

TOTAL STATE CHARGE (ATTACHED): $..............

QUESTIONS SHOULD BE DIRECTED TO:

NAME:........................

TELEPHONE:(...)..............

TO BE COMPLETED BY REGISTRATION AREA: NUMBER OF CERTIFICATES FURNISHED........ NOT FURNISHED........

PLEASE RETURN THIS FORM WITH COPIES OF THE REQUESTED CERTIFICATES. IF YOU ARE UNABLE TO FURNISH A PARTICULAR CERTIFICATE, PLEASE PLACE AN "X" IN THE LEFT MARGIN AND PROVIDE A BRIEF EXPLANATION IN THE SPACE BELOW THE RECORD.

	NDI RECORD		USER RECORD INFORMATION							SEQ NO
	CERT NUMBER	DATE OF DEATH	NAME OF STUDY SUBJECT	FATHERS SURNAME	SOC SEC NO	BIRTH DATE	CONTROL NO/DATA			
....	066571	04-27-81	JOHN C. WILLIAMS	WILLIAMS	444-55-6666	09-16-14	NCHS	15	85	00001
....	110809	08-13-82	MARY B. JONES	SMITH	987-65-4321	03-30-19	NCHS	13	79	00002
....	051447	03-11-84	JOHN C. WILLIAMS	WILLIAMS	444-55-6666	09-16-14	NCHS	15	85	00003
....	126195	08-02-84	MARY B. JONES	(N)SMITH	987-65-4321	03-30-19	NCHS	13	79	00004
....	159867	10-24-86	(N)RICHARD D. DOE	DOE	678-90-1234	05-21-30	NCHS	21	82	00005
....	144084	08-07-87	JOHN C. WILLIAMS	WILLIAMS	444-55-6666	09-16-14	NCHS	15	85	00006
....	192015	11-11-87	JOHN C. WILLIAMS	WILLIAMS	444-55-6666	09-16-14	NCHS	15	85	00007

(A)=ALIAS RECORD (N)=NYSIIS PHONETIC MATCH ON NAME(S)

Appendix 9-21 Template PI Letter for EVP Medical Record Collection

National Lung Screening Trial / Lung Screening Study (NLST/LSS)

(Date)

(Health Care Provider/Clinic/Hospital Name)
(Health Care Provide/Clinic/Hospital Address)
(City, State, Zip Code)
Attention Medical Records Department

RE: (*Participant Name)*
(*Date of Birth)*

Dear Director of Medical Records Correspondence:

We would like to request copies of medical records for the above named patient who, prior to *(his/her)* death, was a participant in the National Lung Screening Trial (NLST). This is a long-term study being conducted by the National Cancer Institute (NCI) and *(Screening Center Name)* to determine if screening is effective in reducing the number of deaths from lung cancer. In order to complete the research file we would appreciate receiving copies of medical records as indicated below.

- □ Physician/clinic/outpatient notes
- □ Hospital admission history/physical
- □ Operative procedure reports
- □ Pathology reports
- □ Radiology reports
- □ Chemotherapy notes
- □ Hospital discharge abstracts/summary
- □ Diagnostic procedure reports
- □ Diagnostic imaging reports
- □ Autopsy reports
- □ Clinical laboratory results
- □ Consultation reports
- □ Emergency Medicine documents
- □ Other documents: _____

In accordance with the Health Insurance Portability and Accountability Act (HIPAA), 45 CFR, 164.512(i)(1)(iii) you are allowed to release this protected health information (PHI) to NLST without a separate authorization other than the one signed by the participant, as the participant is deceased and use of the PHI is solely for research purposes. The requested PHI is absolutely essential to the outcome of the trial and I assure you that the PHI will be used only as directed in the informed consent.

If you have any questions, please contact *(SC Coordinator's Name)* at the number listed below.

Sincerely yours,

(Principal Investigator's Name)
Principal Investigator
National Lung Screening Trial

Appendix 9-22 Documentation for a Missing Death Certificate

National Lung Screening Trial / Lung Screening Study (NLST/LSS)

DOCUMENTATION FOR A MISSING DEATH CERTIFICATE

Administrative Section

Date Completed: __ __/__ __/2 0__ __

Screening Center ID: __ __

SC Staff Member: _____

Participant ID Label

SC Documentation

1. How did the SC first learn of this death? _____

_____

_____

2. Source for confirmation of death:

☐ Death Transcript ☐ Medical Records

☐ NDI (If not exact match, specify match criteria) _____

☐ SSDI (specify match criteria) _____

☐ Other (specify) _____

3. Describe measures taken to obtain the death certificate and reasons why it could not be obtained. Attach any supporting documentation.

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

For CC Use Only

Date sent to NCI: __ __/__ __/2 0__ __

Date approved by NCI: __ __/__ __/2 0__ __

Date DCCF entered: __ __/__ __/2 0__ __

Date selected for EVP: __ __/__ __/2 0__ __

National Lung Screening Trial / Lung Screening Study (NLST/LSS)

Specifications for Completion of the Documentation for a Missing Death Certificate

An SC staff member should complete the Documentation for a Missing Death Certificate to document instances when a death certificate cannot be obtained for a death that occurred on or before December 31, 2009. The form should be completed only after all efforts to obtain the death certificate have been exhausted. The completed form should be sent to the CC for processing, including NCI approval, close-out of expectations for a death certificate, and selection for EVP review.

Specifications for completing each item of the form are given below:

Administrative Section:

Participant ID Label: Affix a PID label to the space provided in the upper right portion of the form. Do not write the participant ID in this space.

Date Completed: Record the date the form was completed. Month and day should be zero filled, and the last two digits should be recorded for the year (e.g., 02/07/2002).

Screening Center ID: Record the two-digit SC ID number.

SC Staff Member: Record the name of the SC staff member completing the form.

SC Documentation Section:

1. **How did the SC first learn of this death?:** Briefly describe how the SC first learned of the participant's death. This may include a report by a family member or friend, returned mail from the post office, or obituary.

2. **Source for confirmation of death:** Check the box next to the official source used by the SC to confirm the participant's death.

   Death Transcript: Check this box if the SC was able to obtain an official death transcript to confirm the death.

   Medical Records: Check this box if the participant's death was documented in medical records.

   NDI: Check this box if the participant's death was confirmed through an NDI search. If the NDI search yielded a probable match for the participant, specify the match criteria.

   SSDI: Check this box if the participant's death was confirmed through a search of the Social Security Death Index (SSDI). Specify the match criteria.

   Other (specify): Check this box if the SC confirmed the participant's death using an official source other than those listed. Specify the source.

3. **Describe measures taken to obtain the death certificate and reasons why it could not be obtained:** Describe the measures taken by the SC to obtain the death certificate and the reason(s) why the death certificate could not be obtained. Attach copies of any supporting documentation, such as Call Logs.

After completing the form:

- The form should be checked to make sure it is accurate, legible, and complete.
- Send a copy of the completed form to the CC Coordinator for NCI approval and CC processing.
- File the form in the participant's study file.

10. PROCEDURES TO ASSESS CONTAMINATION

10.1 Overview

As part of the NLST/LSS, a sample of participants having a negative result with no significant abnormalities on their most recent screening examination will be recontacted to estimate the extent to which participants receive screening examinations outside of this study. Contamination will be measured by the Health Assessment Questionnaire (HAQ, Appendix 10-1). Participants who are beyond their baseline (T_0) study year will be randomly selected on an annual basis to complete the HAQ. The HAQ will assess the extent to which study participants received either spiral CT examinations (for participants randomized to the chest x-ray arm) or chest x-ray examinations (for participants randomized to the spiral CT arm) outside of those screens administered through the NLST/LSS. The NCI will provide additional criteria for selection. The CC will designate the participants who are to complete the HAQ and the SCs will have one month to collect contamination information from the designated participants. The NCI may also request additional sampling from other categories of negative results to ascertain screening behavior.

10.2 Timeframe

Contamination assessment will occur annually according to the following timetable.

- **February-March** - The NCI determines the number and criteria for contamination assessment.
- **March** - The CC will randomly select participants for the sample.
- **April** - The CC will send HAQs pre-printed with the PID number, participant study year, and SC name and address to the appropriate SC. The sample from each SC will consist of participants who had a negative chest x-ray screening examination with no significant abnormalities at their most recent screening examination and participants who had a negative spiral CT screening examination with no significant abnormalities at their most recent screening examination.
- **May** - The SCs will mail packets containing the pre-printed HAQs along with a cover letter and postage-paid return envelope to selected participants. Three weeks after the mailing, the SCs will contact non-responding participants by telephone to administer the HAQ.

- **June -** The SCs will forward the last completed HAQs or completed MDFs to the CC. All attempts to contact non-respondents and all data retrieval will be completed.

10.3 Methods for Administration of the Health Assessment Questionnaire (HAQ)

The CC and each SC share the responsibilities for completing tasks associated with contamination assessment. Due to the short period of time allotted for this activity, it is important that the CC and SCs have staff and materials available to meet the stated deadlines. The responsibilities of the CC and SCs are described in the sections that follow.

10.3.1 CC Responsibilities

The NCI will provide the criteria for selection of participants. To initiate contamination assessment, a sample of participants from each SC and each study arm stratified by study year, will be randomly selected to complete an HAQ. The CC is responsible for the random selection of the participants from those with negative screening examination results with no significant abnormalities on their most recent NLST/LSS screening examination. The selection will be completed in March of each year. At that time, the CC will prepare each HAQ with the PID number, participant study year, and the SC mailing address. The CC will send the HAQs to the SCs approximately two weeks prior to the SC mailing date. The CC will also send blank HAQs to the SCs for use for telephone follow-up.

10.3.2 SC Responsibilities

The SC is responsible for mailing the HAQs to selected participants. Upon receiving the pre-printed HAQs, the SC will assemble the packets and prepare the packets for mailing. The SC will include the following items in each packet:

- An HAQ pre-printed with PID number, participant study year, and SC mailing address;
- A cover letter on SC letterhead, and
- A postage-paid return envelope with first-class postage.

The HAQ packets will be mailed from the SCs to the selected participants with a cover letter explaining the purpose and the one month timeframe for completion of the HAQ. These packets should be sent by first-class mail.

The HAQ should be completed and returned by mail to the SC. The SCs will have one month to obtain completed HAQ information on all randomly selected participants. Participants not responding to the mailed HAQ within three weeks of mailing (non-respondents) will be called in an attempt to administer the HAQ by telephone. It will be the responsibility of the SC staff to attach a PID label and record the participant study year on the CC-supplied blank HAQ used for telephone administration. Specifications for Completion of the HAQ are provided in Appendix 10-2. The SC is responsible for shipping completed forms to the CC.

A sample cover letter for the HAQ is provided in Appendix 10-3. If the SC wishes to use a letter that differs from the sample, it must be submitted to the CC and approved by the NCI prior to use.

10.4 Editing and Data Retrieval for the HAQ

SCs should attempt to obtain completed HAQs for one hundred percent (100%) of the selected participants to ensure an unbiased estimation of contamination. The SC is responsible for shipping completed HAQ forms to the CC. Items 4, 6, 7, 8, 9, and 10 on the HAQ are **critical data items** and data retrieval must be performed as necessary.

When a completed HAQ is received by mail, SC staff will review it for legibility, completeness, and consistency. Participant identifiers and any personal notes should be removed from the HAQ. If the SC receives a HAQ with any missing or unclear critical data items, the participant should be contacted by telephone to obtain the information.

In cases where the SC must contact the participant by phone to complete the HAQ, at a minimum, follow-up efforts as described in section 3.9.1 should be made.

The SC may wish to use a participant call record for the HAQ to track SC efforts in telephone data collection. A Sample Call Record is provided in Appendix 11-13.

10.5 Documenting Non-Response to the HAQ

If an HAQ was not completed for a selected participant during the designated time period, the SC will complete an MDF in place of the HAQ (see Section 11.5.1). It is expected that an HAQ or an MDF will be on file at the SC for each participant who was sent an HAQ at the end of the designated collection period.

10.6 Tracking, Reporting, and Monitoring HAQ Collection Activities

Each SC will track the collection of HAQs in order to document whether all expected HAQs have been collected. Each SC will have a system, manual or automated, for tracking the steps involved in the collection and transmittal of HAQs. This system will include, at a minimum, a tracking record for each participant randomly selected for the contamination assessment. The SC will track the date the HAQ was sent to the participant, the date of receipt of the HAQ from the participant, and the date the HAQ is sent to the CC after receipt from the participant. The SC will track the progress of the contamination assessment process using the Expected Forms Report (Appendix 11-18). This report will allow for the monitoring of missing HAQs by the SC and the CC during the contamination assessment period. SC staff should use this report to ensure that CC records for the collection of HAQs match the SC records.

10.7 Transmittal of the HAQ to the CC

In preparation for shipping completed forms to the CC, the SC should photocopy the HAQs. Participant identifiers and any personal notes should be removed from the HAQs. The HAQs should be mailed to the CC each week. A Transmittal Log (Appendix 11-14) should accompany each shipment of HAQs.

Appendices for Chapter 10

10-1 Health Assessment Questionnaire (HAQ)

10-2 Specifications for Completion of the Health Assessment Questionnaire

10-3 Sample Cover Letter for the Health Assessment Questionnaire

National Lung Screening Trial / Lung Screening Study (NLST/LSS)

HEALTH ASSESSMENT QUESTIONNAIRE (HAQ)

For Office Use Only	
Screening Center ID: |___|___|	Initials Complete:_____ Initials QC:_____ HAQ
Screening Center Staff ID: |___|___|___|___|___|	Participant ID Label
Sample Year 20_____	

Instructions: *Please complete each question by placing a check (✔) in the box next to the answer that best fits your situation.* ***Mark only one answer for each question.***

Since April of 200__, have you had any of the following physical examinations or medical tests?

1 A blood pressure check? 1☐ Yes → 2☐ No (GO TO ITEM 2) 8☐ Don't Know (GO TO ITEM 2)	1a. If yes, what was the main reason you had this blood pressure check? 1☐ Because of a specific health problem 2☐ Follow-up to a previous health problem 3☐ Part of a routine physical examination or as a screening exam*
2. A test to check your blood cholesterol level? 1☐ Yes → 2☐ No (GO TO ITEM 3) 8☐ Don't Know (GO TO ITEM 3)	2a. If yes, what was the main reason you had this test to check your blood cholesterol level? 1☐ Because of a specific health problem 2☐ Follow-up to a previous health problem 3☐ Part of a routine physical examination or as a screening exam*

* A screening examination is a medical test used to detect a disease before symptoms have occurred.

Instructions: *Please complete each question by placing a check (✓) in the box next to the answer that best fits your situation.* ***Mark only one answer for each question.***

Since April of 200__, have you had any of the following physical examinations or medical tests?

3. A test to examine your eyes for glaucoma or cataracts? 1☐ Yes → 2☐ No (GO TO ITEM 4) 8☐ Don't Know (GO TO ITEM 4)	3a. If yes, what was the main reason you had this eye examination? 1☐ Because of a specific health problem 2☐ Follow-up to a previous health problem 3☐ Part of a routine eye examination or as a screening exam*
4. A spiral CT exam of your chest or lungs, not including any spiral CT exam(s) you may have had for the National Lung Screening Trial? 1☐ Yes → 2☐ No (GO TO ITEM 5) 8☐ Don't Know (GO TO ITEM 5)	4a. If yes, what was the main reason you had this spiral CT examination? 1☐ Because of a specific health problem 2☐ Follow-up to a previous health problem 3☐ Part of a routine physical examination or as a screening exam*
5. An examination of your colon or rectum? 1☐ Yes → 2☐ No (GO TO ITEM 6) 8☐ Don't Know (GO TO ITEM 6)	5a. If yes, what was the main reason you had this examination of your colon or rectum? 1☐ Because of a specific health problem 2☐ Follow-up to a previous health problem 3☐ Part of a routine physical examination or as a screening exam*
6. An FDG-PET scan of your chest or lungs? 1☐ Yes → 2☐ No (GO TO ITEM 7) 8☐ Don't Know (GO TO ITEM 7)	6a. If yes, what was the main reason you had this FDG-PET scan? 1☐ Because of a specific health problem 2☐ Follow-up to a previous health problem 3☐ Part of a routine physical examination or as a screening exam*

* A screening examination is a medical test used to detect a disease before symptoms have occurred.

Instructions: *Please complete each question by placing a check (✓) in the box next to the answer that best fits your situation.* ***Mark only one answer for each question.***

Since April of 200__, have you had any of the following physical examinations or medical tests?

7. An MRI scan of your chest or lungs?

1 ☐ Yes → 7a. If yes, what was the main reason you had this MRI scan?
2 ☐ No (GO TO ITEM 8)
8 ☐ Don't Know (GO TO ITEM 8)

1 ☐ Because of a specific health problem
2 ☐ Follow-up to a previous health problem
3 ☐ Part of a routine physical examination or as a screening exam*

8. A chest x-ray, not including any chest x-ray(s) you may have had for the National Lung Screening Trial?

1 ☐ Yes → 8a. If yes, what was the main reason you had this chest x-ray?
2 ☐ No (GO TO ITEM 9)
8 ☐ Don't Know (GO TO ITEM 9)

1 ☐ Because of a specific health problem
2 ☐ Follow-up to a previous health problem
3 ☐ Part of a routine physical examination or as a screening exam*

9. What is your date of birth? |__|__| / |__|__| / |1|9|__|__| (MO / DAY / YEAR)

10. Today's date: |__|__| / |__|__| / |2|0|__|__| (MO / DAY / YEAR)

* A screening examination is a medical test used to detect a disease before symptoms have occurred.

Thank you for completing this questionnaire. Please return this form to:

(SC Name)

(Address)

National Lung Screening Trial / Lung Screening Study (NLST/LSS)

Specifications for Completion of the Health Assessment Questionnaire (HAQ)

This form is designed to be self-administered by all participants selected to complete the HAQ. However, if the participant has difficulty completing the HAQ, the SC staff member may assist the participant (by telephone). If the participant does not return a completed HAQ within three weeks of the initial mailing, the SC staff member should administer the HAQ by telephone. These specifications provide guidelines for the completion of each question on the HAQ. An asterisk (*) in these specifications indicates a critical data item. These consist of whether the participant has had a spiral CT exam (Item # 4), an FDG-PET scan (Item # 6), an MRI (Item # 7), or chest x-ray (Item # 8), the participant's date of birth (Item # 9), and the date of completion (Item # 10). The SC should perform data retrieval on all critical data items. Data retrieval is not necessary for the other items on the form. Specifications for each item on the HAQ are given below:

Participant ID Number, Study Year, SC Name and Address: The CC will print the PID on the HAQ in both numeric and barcode formats. The CC will insert the participant study year on the HAQ and will also print the SC name and address after the last question on the form.

If the SC uses blank forms for non-respondents or data retrieval, it is the responsibility of SC staff to affix the appropriate PID label and record the participant study year on each HAQ.

The HAQ concerns the participant's physical exams or medical tests since April of the previous calendar year. For each examination or medical test, the participant is asked if s/he had the examination or test since April of the previous calendar year, and the reason for the examination or test. The participant should mark only one response for each question. The text of the base question for all questions on the form is listed at the top of each page. The wording of that text is as follows:

Since April of 200___, have you had any of the following **physical examinations or medical tests**?

1. A blood pressure check?

Mark the appropriate response. If "Yes," complete 1a. If "No" or "Don't Know," skip to 2.

1a. What was the main reason you had this blood pressure check?

Mark the box indicating the appropriate reason for the blood pressure check. The possible reasons include the following:

- *Because of a specific health problem*: The participant had his/her blood pressure checked due to a particular health problem. It was not done as part of a regular or routine physical examination and not as part of a follow-up examination for a pre-existing or past health problem for which s/he has previously had an exam.

- *Follow-up to a previous health problem*: The participant had his/her blood pressure checked due to a previous health problem and for follow-up purposes only. The examination was not due to a new health problem or part of a regular or routine physical exam.

- *Part of a routine physical examination or as a screening exam*: The participant had his/her blood pressure checked during the course of and as part of a regular physical examination or as a screening examination. The examination was not performed as a result of a specific health problem or as a follow-up examination due to a specific health problem, but as one of many routine checks during the participant's regular office visit. An insurance physical is considered a routine physical exam.

2. A test to check your blood cholesterol level?

Mark the appropriate response. If "Yes," complete 2a. If "No" or "Don't Know," skip to 3.

2a. What was the main reason you had this test to check your blood cholesterol level?

Mark the box indicating the appropriate reason for the blood cholesterol test. The possible reasons include the following:

- *Because of a specific health problem*: The participant had a blood cholesterol test due to a particular health problem. It was not done as part of a regular or routine physical examination and not as part of a follow-up examination for a pre-existing or past health problem for which s/he has previously had an exam.

- *Follow-up to a previous health problem*: The participant had a blood cholesterol test due to a previous health problem and for follow-up purposes only. The examination was not due to a new health problem or part of a regular or routine physical exam.

- *Part of a routine physical examination or as a screening exam*: The participant had a blood cholesterol test during the course of and as part of a regular physical examination or as a screening examination. The examination was not performed as a result of a specific health problem or as a follow-up examination due to a specific health problem, but as one of many routine checks during the participant's regular office visit. An insurance physical is considered a routine physical exam.

3. A test to examine your eyes for glaucoma or cataracts?

Mark the appropriate response. If "Yes," complete 3a. If "No" or "Don't Know," skip to 4.

3a. What was the main reason you had this eye examination?

Mark the box indicating the appropriate reason for the glaucoma or cataracts test. The possible reasons include the following:

- *Because of a specific health problem*: The participant had a glaucoma or cataracts test due to a particular health problem. It was not done as part of a regular or routine eye

examination and not as part of a follow-up examination for a pre-existing or past health problem for which s/he has previously had an exam.

- *Follow-up to a previous health problem*: The participant had a glaucoma or cataracts test due to a previous health problem and for follow-up purposes only. The examination was not due to a new health problem or part of a regular or routine eye exam.

- *Part of a routine eye examination or as a screening exam*: The participant had a glaucoma or cataracts test during the course of and as part of a regular eye examination or as a screening examination. The examination was not performed as a result of a specific health problem or as a follow-up examination due to a specific health problem, but as one of many routine checks during the participant's regular office visit. An insurance physical is considered a routine physical exam.

4.* A "whole body" CT examination or a CT examination of your chest or lungs, not including any CT examination(s) you may have had for the National Lung Screening Trial?

This does not include any spiral CT screening examination received as part of the National Lung Screening Trial.

Mark the appropriate response. If "Yes," complete 4a. If "No" or "Don't Know," skip to 5.

This question is a critical data item. If it is incomplete or not answered, data retrieval must be attempted. If data retrieval is successful, make any changes in a different color ink, and record your initials and the date of data retrieval in the white space next to the question. If data retrieval is unsuccessful, write "D.R. attempted," your initials, and the date of the data retrieval attempt in the white space next to the question.

4a. What was the main reason you had this CT examination?

Mark the box for the appropriate reason for the spiral CT exam. The possible reasons include the following:

- *Because of a specific health problem*: The participant had a spiral CT due to a particular health problem. It was not done as part of a regular or routine physical examination and not as part of a follow-up examination for a pre-existing or past health problem for which s/he has previously had an exam.

- *Follow-up to a previous health problem*: The participant had a spiral CT due to a previous health problem and for follow-up purposes only. The examination was not due to a new health problem or part of a regular or routine physical exam.

- *Part of a routine physical examination or as a screening exam*: The participant had a spiral CT during the course of and as part of a regular physical examination or a screening examination. The examination was not performed as a result of a specific chest problem or as a follow-up examination due to a specific chest problem, but as

one of many routine checks during the participant's regular office visit. An insurance physical is considered a routine physical exam.

5. An examination of your colon or rectum?

An examination of the colon or rectum could include a barium enema, flexible sigmoidoscopy, or colonoscopy. If a participant asks for descriptions of these exams, the SC should read the following:

- A barium enema involves giving an enema containing barium, a white, chalky liquid, and taking x-rays of the colon and rectum.
- A flexible sigmoidoscopy examination involves the insertion of a thin, lighted viewing instrument into the rectum to look at the rectum and partial length of the colon.
- A colonoscopy is a procedure in which a doctor or health care provider inserts a long, flexible viewing tube into the rectum to inspect the rectum and the entire length of the colon.

Mark the appropriate response. If "Yes," complete 5a. If "No" or "Don't Know," skip to 6.

5a. What was the main reason you had this examination of your colon or rectum?

Mark the box indicating the appropriate reason for the examination of the colon or rectum. The possible reasons include the following:

- *Because of a specific health problem*: The participant had an examination of the colon or rectum due to a particular health problem. It was not done as part of a regular or routine physical examination and not as part of a follow-up examination for a pre-existing or past health problem for which s/he has previously had an exam.
- *Follow-up to a previous health problem*: The participant had an examination of the colon or rectum due to a previous health problem and for follow-up purposes only. The examination was not due to a new health problem or a regular or routine physical exam.
- *Part of a routine physical examination or as a screening exam*: The participant had an examination of the colon or rectum during the course of and as part of a regular physical examination or screening examination. The examination was not performed as a result of a specific health problem or as a follow-up examination due to a specific health problem, but as one of many routine checks during the participant's regular office visit. An insurance physical is considered a routine physical exam.

6.* An FDG-PET scan of your chest or lungs?

If a participant asks for descriptions of an FDG-PET scan, the SC should read the following:

- An FDG-PET scan, or fluorodeoxyglucose positron emission tomography, involves injecting an individual with a solution known as a glucose tracer, and then using a powerful computerized camera, or scanner to take pictures of the body.

Mark the appropriate response. If "Yes," complete 6a. If "No" or "Don't Know," skip to 7.

This question is a critical data item. If it is incomplete or not answered, data retrieval must be attempted. If data retrieval is successful, make any changes in a different color ink, and record your initials and the date of data retrieval in the white space next to the question. If data retrieval is unsuccessful, write "D.R. attempted," your initials, and the date of the data retrieval attempt in the white space next to the question.

6a. What was the main reason you had this FDG-PET scan?

Mark the box indicating the appropriate reason for the FDG-PET scan. The possible reasons include the following:

- *Because of a specific health problem*: The participant had an FDG-PET scan due to a particular health problem. It was not done as part of a regular or routine physical examination and not as part of a follow-up examination for a pre-existing or past health problem for which s/he has previously had an exam.

- *Follow-up to a previous health problem*: The participant had an FDG-PET scan due to a previous health problem and for follow-up purposes only. The examination was not due to a new health problem or a regular or routine physical exam.

- *Part of a routine physical examination or as a screening exam*: The participant had an FDG-PET scan during the course of and as part of a regular physical examination or screening examination. The examination was not performed as a result of a specific health problem or as a follow-up examination due to a specific health problem, but as one of many routine checks during the participant's regular office visit. An insurance physical is considered a routine physical exam.

7.* An MRI scan of your chest or lungs?

If a participant asks for descriptions of an MRI scan, the SC should read the following:

- An MRI, or magnetic resonance imaging, uses a strong magnetic field, radio waves, and computers to look inside an individual's body. An MRI usually requires an individual to lie on his/her back and then be slid into a horizontal tube, or a scanner with open sides. Once the body part to be scanned is in the exact center of the magnetic field, the scan begins. Sometimes an individual is injected with a dye before the scan begins to enhance the image obtained.

Mark the appropriate response. If "Yes," complete 7a. If "No" or "Don't Know," skip to 8.

This question is a critical data item. If it is incomplete or not answered, data retrieval must be attempted. If data retrieval is successful, make any changes in a different color ink, and record your initials and the date of data retrieval in the white space next to the question. If data retrieval is unsuccessful, write "D.R. attempted," your initials, and the date of the data retrieval attempt in the white space next to the question.

7a. What was the main reason you had this MRI scan?

Mark the box indicating the appropriate reason for the MRI scan. The possible reasons include the following:

- *Because of a specific health problem*: The participant had an MRI scan due to a particular health problem. It was not done as part of a regular or routine physical examination and not as part of a follow-up examination for a pre-existing or past health problem for which s/he has previously had an exam.

- *Follow-up to a previous health problem*: The participant had an MRI scan due to a previous health problem and for follow-up purposes only. The examination was not due to a new health problem or a regular or routine physical exam.

- *Part of a routine physical examination or as a screening exam*: The participant had an MRI scan during the course of and as part of a regular physical examination or screening examination. The examination was not performed as a result of a specific health problem or as a follow-up examination due to a specific health problem, but as one of many routine checks during the participant's regular office visit. An insurance physical is considered a routine physical exam.

8.* A chest x-ray not including any chest x-ray(s) you may have had for the National Lung Screening Trial?

This does not include any chest x-ray the participant may have had as part of the National Lung Screening Trial.

Mark the appropriate response. If "Yes," complete 8a. If "No" or "Don't Know," skip to 9.

This question is a critical data item. If it is incomplete or not answered, data retrieval must be attempted. If data retrieval is successful, make any changes in a different color ink, and record your initials and the date of data retrieval in the white space next to the question. If data retrieval is unsuccessful, write "D.R. attempted," your initials, and the date of the data retrieval attempt in the white space next to the question.

8a. What was the main reason you had this chest x-ray?

Mark the box for the appropriate reason for the chest x-ray. The possible reasons include the following:

- *Because of a specific health problem*: The participant had a chest x-ray due to a particular health problem. It was not done as part of a regular or routine physical

examination and not as part of a follow-up examination for a pre-existing or past health problem for which s/he has previously had an exam.

- *Follow-up to a previous health problem*: The participant had a chest x-ray due to a previous health problem and for follow-up purposes only. The examination was not due to a new health problem or a regular or routine physical exam.

- *Part of a routine physical examination or as a screening exam*: The participant had a chest x-ray during the course of and as part of a regular physical examination or a screening examination. The examination was not performed as a result of a specific chest problem or as a follow-up examination due to a specific chest problem, but as one of many routine checks during the participant's regular office visit. An insurance physical is considered a routine physical exam.

9.* Date of Birth: Instruct the participant to enter the month, day, and year s/he was born.

This question is a critical data item. If it is incomplete or not answered, data retrieval must be attempted. If data retrieval is successful, make any changes in a different color ink, and record your initials and the date of data retrieval in the white space next to the question. If data retrieval is unsuccessful, write "D.R. attempted," your initials, and the date of the data retrieval attempt in the white space next to the question.

10.* Today's Date: This is the date the form is completed. Instruct the participant to enter the month, day, and year. Month and day should be zero filled, if applicable. For the year the last two digits should be filled in.

This item is a critical data item. If this item is incomplete or not answered, use the date of receipt of the form as the date of completion. Complete this information according to the following guidelines:

1. *If the participant left all parts of the date blank (month, day, and year), replace the blanks with the full receipt date (month, day, and year). Record this date in another color ink in the space provided. Note on the form that the date recorded is the date the form was received at the SC.*

2. *If the participant wrote a partial date (e.g., month, day only) or a partially incorrect date (e.g., month and day fall prior to date questionnaire was sent to him/her), replace what the participant wrote with the full receipt date (month, day, and year). Record this date in another color ink in the white space near the participant's response. Do not replace part(s) of the completion date with part(s) of the receipt date.*

After completing the form:

- The form should be checked to make sure it is accurate, legible, and complete.

- If administered by telephone, the SC staff member who completed the form should write his/her initials in the space labeled "Initials Complete" in the box at the top right corner of the first page.
- If self-administered by the participant, the SC staff member who checked the form for completion should write his/her initials in the space labeled "Initials QC" in the box at the top right corner of the first page.
- Copy the form.
- Send the original form to the CC.
- File a copy of the form in the participant's study file.

Appendix 10-3 Sample Cover Letter for the Health Assessment Questionnaire (HAQ)

National Lung Screening Trial/Lung Screening Study (NLST/LSS)

(Date)

(Participant Name)
(Participant Address)
(City, State, Zip Code)

Dear *(Participant Name)*:

On *(date of screening exam)*, you received a *(Chest x-ray/Spiral CT)* as part of the National Lung Screening Trial. We thank you for your participation. We would like to receive some additional information about your recent health care. We are interested in the time since April 200__. Enclosed is a questionnaire that we are asking you to complete.

The questionnaire is very brief and will take about five minutes to fill out. Instructions for completing the questionnaire can be found on the form itself. We would appreciate it if you would complete the questionnaire and return it in the enclosed postage-paid envelope as soon as possible, preferably within the next week. If you are unable to complete the questionnaire or if you have any questions while completing the questionnaire, please contact the study office.

Please be assured that all information you provide will be kept strictly confidential. Your name or other identifying information will not appear on any study report – all results from the National Lung Screening Trial will be reported as statistical summaries only.

Do not hesitate to call the study office at *(Telephone Number)* if you have any questions or concerns about the questionnaire or any aspect of the National Lung Screening Trial. Your participation represents a valuable contribution to medical research, and we thank you again for your cooperation.

Sincerely yours,

(Name of SC PI or Coordinator)
(Title)

11. ADMINISTRATIVE PROCEDURES

11.1 Overview

The Screening Center (SC) Coordinator has overall responsibility for the management of the Screening Center. These management tasks include staffing and training, scheduling and documenting data collection activities, record keeping, requesting information, completing data collection forms, entering data into IDEAS, shipping Medical History Questionnaires (MHQ) and Health Assessment Questionnaires (HAQ) forms to the Coordinating Center (CC), transmitting data to the CC, monitoring SC activities, and quality assurance. This chapter describes the SC management activities and the tools provided to perform these activities.

11.2 Software and Communications Support

The CC has provided the SCs with computer systems support for randomization pre-processing, data entry, monitoring and reporting participant status in the NLST/LSS, data cleaning, and the Endpoint Verification Process (EVP). The CC also has provided computer systems support for the NLST/LSS Publications, Presentations, and Associated Studies (PPA) process and the NLST Publications and Presentations Committee (PPC) process. The major systems functions that are provided include the following.

Randomization pre-processing. This is a program located on the hard drive of the PC. It identifies as ineligible, potential participants who are participating in PLCO or the NLST/LSS. (See the *NLST/LSS IDEAS User's Guide* for additional information.)

Integrated Data Entry and Administration System. The CC provides an Integrated Data Entry and Administration System (IDEAS) that is used by both the SC and the CC for study management. The desktop PCs are configured with IDEAS. IDEAS provides reports, through both pre-programmed queries and a query builder, to identify forms and activities that are upcoming and delinquent. Using the data from all SCs, the CC produces monthly progress and monitoring reports for CC discussions with the NCI. (See the *NLST/LSS IDEAS User's Guide* for additional information.)

Data Cleaning System. The CC developed a Web-based system for managing data cleaning tasks. The CC will use this system to program new logic checks, run edit checks against NLST/LSS study data, review edit failures, and post data cleaning tasks on a monthly basis. The system will be available to the SCs for viewing edit

failures, printing CC Edit Forms, requesting overrides, and tracking the status of data cleaning tasks.

Endpoint Verification Internal Computerized Tracking System. The CC developed the Web-based Endpoint Verification Internal Computerized Tracking (EVICT) system to support the EVP. EVICT is available to the SCs for viewing the status of participants in the EVP and is available to the Endpoint Verification Team (EVT) to complete required forms for cases selected for review. The CC uses EVICT to manage and track the progress of the EVP.

NLST/LSS Study Tracking and Review System (STARS). The CC developed NLST/LSS STARS, a Web-based system, to facilitate the submission and review process for all associated study proposals, as well as publications, presentations, and abstracts utilizing NLST/LSS data. Refer to Section 1.6.3 for more information.

NLST Joint ACRIN/LSS STARS. The CC developed a second STARS Web-based system to facilitate the submission and review process for all associated study proposals, as well as publications, presentations, and abstracts utilizing NLST joint ACRIN/LSS data. Refer to Section 1.6.3 for more information.

Basic office automation software. The desktop PCs are configured to include various software packages to support basic office automation. This package will include Microsoft Office.

Telecommunications. The CC has configured each PC to import and export data to and from the CC securely and reliably. The SC is prohibited from loading additional software, including utilities like screen savers, or upgrading any software, such as browsers, that is not provided by the CC without express permission prior to the activity. User Support will assist SCs in ensuring compatibility of additional software before it is loaded and in handling any configuration issues.

The CC provided each SC with two PCs and a printer. SC requests for additional equipment must be submitted through the CC and approved by the NCI. The SCs will provide one dedicated phone line, unless otherwise agreed with the CC and NCI. The telephone line must be of data quality and not a "shared" or "rollover" line. Licenses for all software provided by the CC are held by the CC. The SC is responsible for acquiring software licenses for any individual software (approved by the CC) that the SC may wish to use in addition to what is provided by the CC.

11.3 Interactive Voice Response System

During randomization the CC provided an interactive telephone-based randomization system for SC use. The SCs used existing telephone lines to call the centralized randomization system and enter

required data elements using the telephone keypad. The system was configured for access by a toll-free number and was available 24 hours a day, seven days a week. The toll free number to access the system was (800) 955-2342. A separate User Support Hotline provided assistance to the SCs and could be reached by dialing (800) 509-5559; User Support was also reached by fax at (713) 529-4924. The SCs provided a designated e-mail address for use in receiving confirmation reports related to the randomization process. Confirmations were sent to this designated e-mail address only, so it was critical that it be accessed regularly to check for confirmation reports. (See Appendix 2-12, *NLST\LSS WesTrax™ Users Guide*.)

11.4 Training and Registration of SC Staff by CC

The CC is responsible for training the SC Coordinators in the protocol and procedures for conducting the study. The primary reason for training the SC Coordinator is to ensure that the protocol is clearly understood and to ensure that standard procedures are followed across all SCs. Central training sessions conducted by the CC offer the opportunity for introduction to and discussion of procedures and hands-on practice with reference materials and data collection instruments. SC Coordinators attended training sessions in August 2000 prior to randomization of LSS feasibility study participants, in October 2001 prior to the extension of the LSS feasibility study, and in April and September 2002 prior to the start of NLST. The CC also has conducted periodic workshops for Medical Record Abstractors, and conducted a central training for Pathology Tissue Collection in November 2008. The CC will conduct further training sessions for SC Coordinators as needed. The purpose of the training is to familiarize the SC Coordinators with requirements, protocols, timeline, and tools of the study in subsequent study years. In addition, the CC distributes information using Decision Logs and annual updates to the Manual of Operations and Procedures are discussed during the Steering Committee Meeting which is held twice a year.

11.4.1 Training of SC Staff by SC Coordinator

The SC Coordinator has ongoing responsibility for training all staff on forms completion and administrative procedures. It is the SC Coordinator's responsibility to ensure that study forms are completed accurately. When training SC staff, the SC Coordinator should emphasize the following key items:

The PID label for the appropriate participant should be placed on all participant study forms. The CC will define label specifications and the SC will have the ability to print PID labels as needed. The PID label should be affixed in the designated location. The PID should never be hand written in this section of the form.

The specifications for completing each study form should be reviewed prior to completion. It is important to follow the form specifications to ensure accurate completion of each study form.

The study form should be reviewed to make sure the handwriting is legible and that all of the requested information is given.

The "Administrative Section" or the "For Office Use Only" section should be completed in advance of the participant's study visit or should be completed prior to mailing the form to the participant. The remainder of the form should not be pre-filled prior to the participant's visit or mailing to him/her.

A Missing Data Form (MDF, Appendix 11-1), should be completed when a participant is unable or unwilling to complete a study activity. The Specifications for Completion of the MDF appear in Appendix 11-2.

The confidentiality of study forms should be maintained at all times. Any information linking the PID to the participant's name should be removed or blacked out prior to the shipment of the forms to the CC.

11.4.2 Certification and Registration of Staff

For each staff member, the SC Coordinator must document the individual's qualifications for the NLST/LSS on a Record of Experience, Credentials, and Training (ECT, Appendix 11-5). Training/ certification requirements for examiners are described in Chapters 4 and 5. Training/certification requirements for medical record abstractors and nosologists are described in Chapter 7. The ECT must be transmitted to the Credentialing Coordinator at the CC before the staff member performs any NLST/LSS tasks, including screening examinations. Additionally, the ECT must be approved by the NCI before a staff member may perform duties for the NLST/LSS. Specifications for Completion of the ECT are

provided in Appendix 11-6. In addition, the SC Coordinator must assign a staff ID number to each person performing NLST/LSS tasks. If an individual is currently a registered staff member for PLCO, a new ECT must be completed for the NLST/LSS; however, the SC Coordinator should assign that person the same staff ID number as his/her PLCO staff ID number.

Updates to the credentials for previously submitted ECTs will be requested on an annual basis throughout the screening phase by the CC for radiologic technologists, radiologists, and medical physicists. ECTs for radiologic technologists must be submitted with current ARRT certifications or proof that the individual is board eligible. The ECT for medical physicists must be accompanied by a state license. Radiologists must be board eligible or have a current ARRT certificate and a state license. Please refer to Sections 4.5.4 and 5.5.4 for specifications on submitting annual updates.

11.5 Additional Study Documentation

For each participant, data collection activities will take place at baseline (T_0) and annually through December 2009 with an accelerated effort to complete final ASUs in 2010 (See Section 3.6.1). Additional data collection will take place for participants who are diagnosed with lung cancer or who die during the course of the study.

Additional documentation is necessary when study activities cannot be completed, are not completed according to the NLST/LSS protocol, or are associated with participant complications. The following sections provide an overview of the procedures for documenting missing data activities, documenting and resolving protocol and HIPAA violations, reporting adverse events, and documenting withdrawal from the study.

11.5.1 Documenting Missing Data Activities and Non-Response

The SC Coordinator will complete a Missing Data Form (MDF, Appendix 11-1) when a participant is unable or unwilling to complete a study activity for a given study year. This may be due to a variety of reasons such as participant refusal or inability to locate the participant. The MDF should be used only when all efforts to obtain data have been unsuccessful and it is believed the data for that study year will never be obtained.

Specifications for Completion of the MDF are included in Appendix 11-2. After the form has been completed, it should be reviewed to ensure that it has been filled out completely. The form should be entered into IDEAS and then filed in the participant's study file.

If an MDF has been completed for a study form that is later found or able to be completed, the SC should delete the MDF from IDEAS, and then enter the study form into IDEAS. The deleted MDF should be attached to the study form that replaced it and then filed in the participant's study folder.

If the SC Coordinator considers the participant's inactive status to be permanent, a Non-Response Form (NRF, Appendix 11-3) should be completed. The participant's permanent inactive status may be due to a variety of reasons such as inability to locate the participant, participant refusal, an incapacitating medical condition, or death of the participant. Presumed and confirmed deaths should be documented on an NRF, although an MDF for the study year in which the participant's death was discovered also should be completed.

Once the NRF is completed and entered into IDEAS, no further MDFs for any form will be necessary or expected for future study years; however, MDFs for all forms expected during the study year in which the NRF was completed are still required to be submitted into IDEAS. For example, Participant A has complete T_0 information and dies midway through T_1. An NRF is completed during the T_1 study year and forms are closed out for T_2 –T_7, however an MDF must still be completed for all outstanding T_1 forms. The NRF also will allow for the reactivation of a participant's status should circumstances change.

Specifications for Completion of the NRF are included in Appendix 11-4. Only the SC Coordinator or IDEAS Administrator should complete an NRF. After the form has been completed, it should be reviewed to ensure that it has been filled out completely. The form should be entered into IDEAS and then filed in the participant's study file.

11.5.1.1 Data Collection Involving Living Non-responders

While most non-response is due to participant death, some living participants will refuse participation in certain or all study activities. These participants are classified by their degree of

unwillingness to participate. Data collection activities vary by type of refusal. There are three categories of refusal: soft, hard, and absolute.

Participants who no longer wish to be screened but are willing to participate in all other study activities are classified as soft refusals. An NRF is not completed on soft refusals, and all study forms for all remaining study years remain expected. An MDF is to be completed for the current screening exam. MDFs should not be completed for future screening exams on the off-chance that the participant wishes to return to screening. Medical records are to be collected on soft refusals in the instance of a lung cancer diagnosis or selection for EVP. In the event of death, a Death Certificate should be collected as well.

Participants who state verbally that they are no longer interested in participating in any aspect of the study, including screening exams and completion of study questionnaires, are classified as hard refusals. An NRF is completed for all hard refusals. Additionally, MDFs should be completed for outstanding expected forms for the study year in which the NRF is completed. If the participant has signed a Medical Records Release Authorization Form that is likely to be honored by medical facilities, the SC may, but is not required to, attempt to collect medical records in the instance of a lung cancer diagnosis or selection for EVP. The SC should exercise caution in making the decision to collect medical records for hard refusals, especially in the instance of an irate participant. A Death Certificate is to be collected for hard refusals, however. If at all possible, the SC should inform all hard refusals that their data will remain in the study database unless a written request to exclude it is received. If it is not possible to collect medical records, a note should be placed in the EVP folder describing the circumstances that are responsible for the lack of documentation.

Participants who in writing withdraw their consent, request that their data be removed from study, or request that study forms be returned to him or her are classified as absolute refusals. For each instance of an absolute refusal, the SC should provide documentation to the CC, who will discuss the case with the NCI. After receiving approval from the CC and NCI, the SC should complete an NRF. Additionally, MDFs should be completed for outstanding expected forms for the study year in which the NRF is completed. No additional data collection is to be attempted for absolute refusals, even if a signed Medical Records Release Authorization Form is available and likely to be honored by a medical facility. Furthermore, a Death Certificate should not be obtained in the case of death. Following completion of the NRF, the SC should provide a written confirmation to the participant that his/her data will be removed or returned. The SC should forward a copy of the NRF and written confirmation that was sent to the participant to the CC. The SC will be responsible for removing all hard copy documents from NLST files

as dictated by the SC IRB, but should maintain a copy of these documents, including the signed informed consent, in a location separate from active NLST files in case litigation ensues. If requested, the SC should return to the participant all study documents completed by the participant (including but not limited to informed consents, PCFs, ASUs, MHQs), but should not return study documents never seen by the participant (such as screening exam forms or DE forms). The SC must also delete participant information from all SC-maintained electronic databases. Upon receipt of the completed NRF and written confirmation, the CC will initiate procedures to delete participant information from NLST data files. Any hard copy forms and/or images stored at the CC will be retrieved and returned to the SC. Electronic data pertaining to the participant will be deleted from all applicable sources, including IDEAS, EVICT, and any other data collection repositories. In addition, the CC will coordinate the removal of all participant data from external locations, including IMS and the CTIL. The CC will provide a written report to the SC Coordinator when this process has been completed.

11.5.2 Documenting and Resolving Protocol and HIPAA Violations

All investigators are expected to adhere to the procedures set out in the NLST/LSS protocol. Instances where SC staff perform activities that deviate from established study protocol are considered protocol violations. All protocol violations must be documented on a Protocol and HIPAA Violation Form (PHVF, Appendix 11-9). Only one protocol violation per participant should be reported on each PHVF.

If a participant's protected health information (PHI) is released in a manner that is inconsistent with confidentiality assurances in the study consent forms, this is considered a violation of the Health Insurance Portability and Accountability Act (HIPAA). Although the event may not be considered a protocol violation, all HIPAA violations must be reported on the Protocol and HIPAA Violation Form (PHVF). (See Appendix 11-10, Specifications for Completion of the Protocol and HIPAA Violation Form.) It may be necessary for the SC to consult their institutional IRB or HIPAA expert to determine if a violation has occurred. Reporting the results of a screening exam to the wrong participant is both a protocol violation and a HIPAA violation. Sharing PHI with an outside institution or agency without permission from the participant is an example of a HIPAA violation.

The original PHVF should be sent to the CC and a copy of the PHVF should be placed in the participant's study file. The PHVF should be checked for completeness and entered into IDEAS.

Protocol and HIPAA violations should be reported to the CC in the SC's weekly report to the CC. The CC will use PHVF reports to report violations to the appropriate entities (e.g. NCI, DSMB). All HIPAA violations must be reported to the NCI. Some common examples of protocol violations are:

Randomizing ineligible participants;

Randomizing the same individual more than once;

Screening a participant without a signed consent form;

Screening a participant with lung cancer;

Performing the screening exam to which the participant was not randomized;

Reporting erroneous results to participants or health care providers;

Performing a duplicate screening exam, and

Using incorrect technical parameters for the screening examination.

The following sections discuss the documentation of some of the examples of protocol violations.

11.5.2.1 Randomized Ineligibles

If the SC becomes aware that a randomized participant was ineligible at the time of randomization, the participant should be documented as "ineligible participant randomized" on the PHVF. The following information should be recorded on the PHVF:

Date the SC discovered that the ineligible individual was randomized;

Date the protocol violation occurred, which is the date the individual was randomized;

Reason the individual was not eligible for the study at the time of randomization, and

Method of discovery.

Randomization errors may involve the following:

Individuals who were randomized in error (i.e., the participant provided information to the SC indicating his/her ineligibility, but the SC failed to exclude him/her from the study), and

Individuals who were randomized appropriately based on information provided at the time of randomization, but for whom it was discovered after randomization that the information provided had been incorrect.

It is important to document on the PHVF the specifics of the situation so that the above situations can be distinguished.

The CC will use PHVF reports to determine the number of randomized ineligible protocol violations that have occurred for each SC within a given timeframe.

All participants discovered to have been ineligible after randomization (with the exception of those who did not sign a consent form) will continue to be study participants regardless of the method of discovery. Randomized ineligible participants should be offered screening exams and followed for all study activities. If the participant refuses screening, an MDF should be completed for all screening forms.

11.5.2.2 Duplicate Randomization

If a participant is randomized more than once, the first assignment, both PID and study arm, should be used.* A PHVF should be completed regardless of whether the two randomizations resulted in assignment to the same arm or different arms. The duplicate randomization PID label should be affixed to the upper right hand corner of the form and the original PID should be written in the proper field adjacent to the violation type. In the highly unlikely instance of triplicate randomization, the third PID assignment should be documented on a new PHVF and the corresponding PID label affixed to the form. The CC and the participant should be informed of the error. The charts can be combined or left separate but complete documentation must be kept so that both PIDs are easily identified and the correct records can be traced if necessary.

* *Note: In the event that the participant has been randomized at both an NLST/LSS and ACRIN site, the site which first (earliest date) randomized the participant maintains the participant for the study. The site (NLST/LSS or ACRIN) that performed the second randomization must complete a PHVF according to study protocol and bear the responsibility of informing the participant of the correct study arm and study site. Additionally, the site with the second randomization will maintain a record of the protocol violation (duplicate randomization) but will not continue to track the participant as a randomized ineligible. A*

record of crossover duplicate randomizations should be maintained by the SCs and reported to the NLST Executive Committee.

11.5.2.3 Incorrect Screening Exam Performed

Instances in which an incorrect screening exam was performed (e.g., a chest x-ray for a participant who was randomized to the spiral CT arm or vice versa) should be documented on a PHVF. Results from the examination actually completed should be sent to the participant and his/her health care provider. The participant should not receive another screening examination for that study year. IDEAS will not allow the SC to enter a screening examination form for an erroneous screen. An MDF with a code of 88 (Other, specify) should be entered in lieu of the proper screening exam form. A DE form must be completed for an incorrect screening exam that yields a positive result. In this instance, the DE form should not be entered into IDEAS. The DE form should be filed in the participant's study file.

11.5.2.4 Erroneous Results Reported

If the results letter that was mailed to the participant and/or his/her health care provider were found to be erroneous (i.e., incorrect results were reported), this must be documented on a PHVF. In addition, the participant and his/her health care provider must be contacted and given the correct results.

11.5.2.5 Duplicate Screen Performed

If a participant is erroneously screened more than once in a study year, a PHVF should be completed. The earlier screening exam and the PHVF should be entered into IDEAS. The second screening exam should not be entered into IDEAS. A copy of both screening exam forms should be included when the PHVF is sent to the CC. Results for both screening exams should be sent to the participant and his/her health care provider. If the second screening exam results in a positive screen, a DE form must be completed. In this instance, the DE form should not be entered into IDEAS. The DE form should be filed in the participant's study file.

11.5.3 Reporting Adverse Events

SCs are responsible for reporting the occurrence of any adverse events that may be related to participation in the NLST/LSS. The SCs should document the following as adverse events:

Death;

Life-threatening event;

In-patient hospitalization;

Persistent or significant disability/incapacity;

Medical or surgical intervention to prevent one of the above outcomes, and

Other, Specify.

If medical complications occur at the SC during the screening visit procedure a member of the SC staff should complete a Report of Adverse Events for NIH-Sponsored Clinical Trials (RAE, Appendix 11-11). These complications should be documented in the Comments Section of the appropriate screening examination form (see Chapters 4 and 5) and submitted to the CC. If there are any questions regarding whether a medical complication is an adverse event, contact the CC.

If an adverse event occurs, the SC must notify its local IRB and complete an RAE. The adverse event should be thoroughly described on this report. Specifications for Completion of the RAE are provided in Appendix 11-12. The RAE should be kept in the participant's study file and appropriate follow-up with the participant and his/her health care provider should be conducted until the problem is resolved. When the problem is resolved, the RAE should be entered into IDEAS and filed in the participant's study file. The CC will use RAE reports to report the occurrence of adverse events to the appropriate entities (e.g., NCI, DSMB).

11.5.4 Documenting Withdrawal from the Study

If a participant decides to withdraw from the study, the SC should complete a Non-Response Form (NRF, Appendix 11-3). Specifications for the Completion of the Non-Response Form are found in Appendix 11-4.

11.6 Processing, Receipting, and Shipping of Study Data

All study forms should be entered into IDEAS, with the exception of the MHQ and HAQ, which will be copied and shipped to the CC. The following sections cover these activities.

11.6.1 Manual Editing of Study Forms

All forms should be manually edited twice prior to entry into IDEAS. The SC staff member who completes the form will perform the first edit and then write his/her initials in the space labeled "Initials Complete" in the box at the top of the page. If the form is completed at a screening visit, the edit should be completed before the participant departs the SC so that any corrections can be made immediately. The SC Coordinator or a designated staff member will perform the second edit and then write his/her initials in the space labeled "Initials QC" in the box at the top of the page. The second edit should be performed after the first edit is completed and before the forms are entered into IDEAS. **The SC staff member who performs the second edit should not be the same SC staff member who completed the form.** The manual editing process involves two main steps: (1) reviewing the form for completeness, legibility, consistency, and accuracy and (2) making changes to the form after the review or data retrieval. The following are guidelines for manual editing:

1. Review for completeness, legibility, consistency, and accuracy. Consult the form specifications during this review.

2. Make changes that do not require data retrieval. Initial and date all changes to individual items. Any erasure or change that has not been initialed and dated will be considered a participant or examiner change rather than an edit.

3. Perform data retrieval for critical data items.

    - Data retrieval may be performed in person if the participant is in the clinic.

    - If the participant is not in the clinic, attempts should be made to contact the participant to complete data items before forms are entered into IDEAS.

    - Five attempts should be made to contact the participant to complete critical data items. See Section 3.9.1 for guidelines on making follow-up telephone calls. If the data cannot be obtained, leave the item blank, and mark your initials and date near the question.

- Maintain a call record to document attempts to contact the participant. A Sample Call Record is given as Appendix 11-13. Call records to document forms completion should be stored in the participant's study file.

4. Annotate the form as follows to document data retrieval.

   - If the item in question was left blank and, upon data retrieval, the participant or examiner is unwilling or unable to supply the data, leave the item blank, and mark your initials and the date near the question.

   - If the item in question was left blank and, upon data retrieval, the participant or examiner supplies the data, complete the item and mark your initials and the date near the question. If the new data involve a verbatim response, record the data in another color ink or pencil (except red) from the participant's original response.

   - If the item in question was completed incorrectly (e.g., an incorrect examination result) or required clarification, and the participant or health care provider supplied different or additional data, make the changes and mark your initials and the date near the question. If the changes involve a verbatim response, using another color ink or pencil (except red), cross out the original verbatim response with one line and write the corrected response near it; original verbatim responses should never be erased.

If the SC Coordinator discovers an error after forms have been entered into IDEAS, the SC should make the appropriate change to the form and in the database. If the SC Coordinator discovers an error to the HAQ or MHQ after they have been sent to the CC, the SC Edit Form (Appendix 11-7) should be completed and sent by e-mail or by FedEx package to the CC. The SC Edit Form should document changes on only one data form. Each form that needs to be changed should have its own SC Edit Form. Specifications for Completion of the SC Edit Form are found in Appendix 11-8. A copy of the completed form that documents the change should be maintained in the participant's study file behind the first version of the form. Only one participant should be listed on a form. Once the form is submitted to the CC, a copy should be placed in the participant's study file.

11.6.2 Critical Data Items

Critical Data Items, referred to throughout the MOOP, are the specific items listed in form specifications that require data retrieval to ensure the item is completed.

11.6.3 Shipping Forms to the CC

The Medical History Questionnaire (MHQ), Health Assessment Questionnaire (HAQ), Protocol and HIPAA Violation Form (PHVF), the Report of Adverse Events for NIH-Sponsored Clinical Trials (RAE), and the SC Edit Form will be shipped to the CC. The forms, with an accompanying transmittal detailing the contents of the shipment, will be shipped by FedEx.

Forms should be copied prior to shipment to the CC. The copies should be filed in the participant study files at the SC. Original study forms should be shipped to the CC. All identifying or personal information should be removed or blacked out prior to shipment to the CC.

A Transmittal Log (Appendix 11-14) will accompany each form shipment. A transmittal log will be generated from IDEAS listing all forms included in the shipment. The SC Coordinator should locate the study forms that have been receipted since the last shipment and scan the PIDs into the transmittal listing. Forms should be placed in PID order within form type. For detailed information in generating a shipment transmittal refer to the *NLST/LSS IDEAS User's Guide*. The SC Coordinator should make a copy of the transmittal and copy all study forms for shipment that have not yet been copied. The original transmittal should be placed on top of the batched forms for shipment. A copy of the transmittal should be filed at the SC for reference.

The following **original study forms** should be processed and shipped to the CC as needed:

Medical History Questionnaire (MHQ)
Health Assessment Questionnaire (HAQ)
Protocol and HIPAA Violation Form (PHVF)
Report of Adverse Events for NIH-Sponsored Clinical Trials (RAE)
SC Edit Form

Study forms should only be sent when the form has been comprehensively edited and all data have been retrieved. The SC Coordinator is responsible for checking the forms prior to sending any materials to the CC.

The CC should <u>not</u> receive copies of any forms that contain identifying information from NLST/LSS participants or potential participants. The SC should <u>not</u> ship the following forms to the CC:

Consent Form

Screening Examination Results Letters (unless requested for QA purposes)

Eligibility Screener (ES)

Eligibility Verification Form (EVF)

Participant Contact Form (PCF)

Medical Record Release Authorization Form

Results Withheld Form

Cover page of MHQ

Call Records

11.7 Data Quality Assurance

The implementation of procedures designed to ensure the collection of quality data is critical to the success of a research study. The NLST/LSS employs various data quality assurance procedures at the SCs and CC to ensure that complete and accurate data are available for data analysis. The purpose of this section is to describe NLST/LSS data quality procedures currently being implemented and to outline recommended practices for the SCs and CC to promote the production of complete and accurate NLST/LSS study data.

11.7.1 Data QA Responsibilities of the SC

The SC will be responsible for developing and implementing data quality assurance procedures at their site. In addition, the SC is responsible for ensuring that all study staff are appropriately informed of all QA procedures for which they will be responsible. The SC will also be responsible for adhering to the data QA guidelines for data security, data processing, and data monitoring outlined in this section.

11.7.1.1 Data Security at the SC

Study documents and data may not be stored in the participant's regular medical record at any hospital or institution with which the SC may be affiliated. Copies of screening results, however, may eventually become part of a participant's regular medical record as a result of referral of the participant to a health care provider for follow-up of an abnormal screening result. Study documents should be kept for at least ten years after the end of the study and then destroyed. Study documents related to individuals that were never enrolled in the trial, such as Eligibility Screeners, Eligibility Verification Forms, and call records will be destroyed by the SCs at the direction of the NCI.

All study materials that carry identifying information such as name, address, and Social Security Number should be kept in a locked and secure area at the SC. The SC Coordinator will control access to this area. If the central file is computerized, the system must be protected from outside access (e.g., password control, locked system, or data encrypted). Similarly, all reports produced from the system that carry such data must have controlled distribution and be destroyed when no longer needed (e.g., shredded). Any computerized data management system that processes NLST/LSS study data, either in-house or provided by the CC (e.g., IDEAS) will be password protected and will have undergone validation checks to ensure data integrity. Additional guidelines for SC data security were set forth in a memo from the CC to the SCs and are provided in Appendix 11-15.

During the recruitment phase, mailing houses may have been contracted to recruit potential participants. Any SC wishing to release participant information to organizations for such a circumstance must first have obtained from the organization a written statement assuring that participant confidentiality would be maintained. A copy of the statement was to be submitted to the NCI and the CC. However, if the SC provided a list or file of names and addresses of potential participants without any data elements linking the potential participant to enrollment in the study, it was not necessary to obtain an assurance of confidentiality.

11.7.1.2 Data Processing at the SC

The SC will be responsible for maintaining standard data processing procedures for promoting the collection of good quality data. These data processing procedures will involve reviewing data for accuracy and completeness and identifying and resolving data discrepancies.

All study forms will be manually reviewed by study staff according to the guidelines provided in MOOP Chapter 11.6.1, Manual Editing of Study Forms, prior to data entry. Study forms that have passed the manual editing review will be single or double entered into IDEAS at the individual SCs by trained data entry staff. The SC staff member who performs the second entry should not be the same SC staff member who performed the first entry. Each SC will be responsible for developing a system for ensuring that forms are entered into IDEAS in a timely manner. The *NLST/LSS IDEAS User's Guide* provides a list of study forms requiring data entry into IDEAS and the method of entry appropriate for each form.

The IDEAS database is designed to assess the preliminary validity of data by placing certain restrictions on data at time of entry. These restrictions are implemented through the incorporation of edit checks that run on data entered during both Pass 1 and Pass 2. Section 11.7.2.2 provides details on the types of edit checks that have been incorporated into the IDEAS application.

The same basic edit checks are run on data entered during Pass 1 and Pass 2 but during Pass 2 the database also compares the data being keyed to the data that was entered during Pass 1. If the data differs, the Pass 2 operator receives a comparison failure alert either at the moment of entry or when attempting to save the record. The data entry operator then checks the form to determine which value is correct and makes the appropriate change to the data at that time. When the Pass 2 operator accepts or enters a new value, the edit checks will run again and if the error has been resolved the record will be saved to the final NLST/LSS database.

If the operator enters a data value that still does not pass the edit check, a discrepancy will remain and a printable error log will be generated. At this point the data entry process remains in the pending phase until the discrepancy can be resolved and the form successfully meets the edit check requirements of Pass 2 data entry.

11.7.1.3 Data Monitoring at the SC

The SC will be responsible for monitoring the quality of study data to identify missing and/or delinquent study forms. This can be accomplished through the use of data queries, manual review of participant charts, and the regular generation of data reports. The SCs will be able to run data queries and generate data reports using the IDEAS application. IDEAS queries and reports are essential data

quality tools for promoting the timely collection of complete and accurate data and for this reason, SCs are strongly encouraged to use these QA tools on a regular basis. See Section 11.7.3 Data Reports, for a list of the reports available in IDEAS.

11.7.2 Data QA Responsibilities of the CC

The CC will be responsible for the development and implementation of data quality procedures for the promotion of good quality data collection and maintenance of NLST/LSS study data. The CC will be responsible for implementing data quality procedures related to data security, data processing, and data monitoring. The CC is responsible for ensuring that all NLST/LSS staff have been informed of any data QA procedures for which they are responsible.

In addition to developing QA procedures for internal use, the CC is also responsible for developing various data quality assurance tools to assist sites in identifying and resolving inconsistencies in their study data. Examples of data QA tools that will be provided to the SCs include but are not limited to the following:

- Programmed validation edit checks in the IDEAS study database
- Data querying tools in IDEAS
- Data monitoring reports in IDEAS
- Data clarification requests as a result of discrepancies identified through QA procedures performed at the CC
- Web-based data cleaning system

11.7.2.1 Data Security at the CC

All NLST/LSS study forms at the CC will be kept stored in a locked cabinet in a secure environment. In addition, any documents or reports generated by the CC that contain results of PID-specific study data will be stored in a locked cabinet in a secure area.

Any computerized system developed or maintained by the CC for the purpose of processing or storing NLST/LSS study data will undergo systems validation testing and must be protected from outside access (e.g., password control, locked system, or data encrypted) to ensure data integrity. In addition, reports produced from the system that carry participant study data must have controlled distribution and be destroyed when no longer needed (e.g., shredded).

11.7.2.2 Data Processing at the CC

Once IDEAS study data have been transmitted to the CC or keyed into the IDEAS database by CC data entry staff, the CC will perform additional quality assurance checks on the study data on a regular basis. Data discrepancies identified during this process will be communicated to the SC by one of the following ways: the CC Edit Form (Appendix 11-16), e-mail, telephone, or the Web-based data cleaning system. The SC will be responsible for responding to any requests for data retrieval within the time specified, or a reasonable period of time should no deadline be given.

The CC is responsible for developing edit checks to assess the quality of data entered into the database. Prior to the transition to a distributed data entry system (IDEAS), double data entry was performed by CC data processing staff and edit checks were run on keyed data. Any discrepancies identified during the edit check run were distributed to each SC through the use of the CC Edit Form or by telephone or e-mail. This particular system of data entry is still utilized for the entry of HAQ forms, and this process applies to the data collected on this form.

For the majority of the NLST/LSS study forms, data processing and data entry occurs at each individual SC with data entered into the IDEAS database. The CC has incorporated the following pre-programmed edit checks into the IDEAS application:

- Data type errors (e.g., a character response entered into a numeric field or decimal response to a question that takes an integer);
- Length errors (e.g., the question was defined with a length of 4 and the value entered has a length of 3);
- Code list errors (the value entered is not a valid response);
- Date errors (e.g., only part of the date was entered when a whole date was expected, date entered is in the future);
- Mandatory response is missing;
- Range checks (e.g., technical parameter is not within the acceptable range of values);

- Comparison checks across data fields (e.g., date of screening exam is after the previous scan date of any comparison exam in Part E), and
- Cross-form checks (e.g., an attempt is being made to enter a DE form when there is no corresponding positive screening exam or CDF with a confirmed primary lung cancer, date of screening exam is prior to randomization date).

11.7.2.3 Data Monitoring at the CC

The CC will monitor data collection and the quality of study data through the use of data queries and the generation of data reports. During the screening phase of the trial, the CC will be responsible for generating monthly data reports regarding recruitment, retention, screening examination results, data collection, and other study-related activities for distribution to NCI. During the follow-up phase of the trial, the CC will generate pertinent reports for distribution to NCI on a quarterly basis. Data reports will be reviewed by CC staff members responsible for monitoring study activities at the SCs and will discuss issues with the SC as needed. The CC will continue to monitor study data and request clarification and/or resolution for identified errors throughout the study.

11.7.3 Data Reports

- SC Cumulative Recruitment Summary Report (Appendix 11-17): This report was used during the recruitment phase of the study to show summary totals for recruitment activities at each SC. The report was produced by the CC using information entered by the SC from the Cumulative Recruitment Summary Form.
- SC Receipt Activity Report (RAR, Appendix 11-18): This report displays the total number of forms that have been entered into IDEAS by form type and study year. The RAR generated in IDEAS at the SC will show only data for that particular site. The CC will be able to generate the RAR for each SC.
- Expected Forms Report (EFR, Appendix 11-19): For each participant, this report shows the data collection forms that are expected but have not yet been entered into IDEAS. These real-time reports will be generated in IDEAS at the SC with each center having the capability to view only its own report. For viewing ease, the report can be limited to form type and month of randomization, or month of expected receipt date, if desired. In addition, the report may be sorted by PID, randomization date, form type, or study arm. The form may be printed or exported as a data file from IDEAS. The CC will be able to generate the EFR for all SCs.

- Screening Exam Results Report (SERR, Appendix 11-20): This real time report, generated in IDEAS, will provide the SC with a list of participant exam results at its screening center. The report will show PID, study arm, study year, screening exam date, and screening result. This report will also show the date the results letter was sent and will indicate if results were sent late when result letter generation takes place in IDEAS. This report also identifies screens performed on ineligible participants and can be sorted by PID, study arm, screening date, or screening result. The CC will be able to generate the SERR for all screening centers.

- Participant Overview Report (POR, Appendix 11-21): This PID-specific report will provide the SC with a summary of study activities for the participant as well as provide participant status information. The report will be useful in assisting the SC with scheduling study activities and for follow-up related to positive screens. The CC will not be able to generate the POR since the report contains confidential privacy data.

- Study Progression Report (SPR, Appendix 11-22): This report shows the total number of participants randomized and the total number of participants in each study window at the time the report is run. The report also shows a breakdown of screening activities by window, including the number of participants eligible to be screened, the number of completed screens, the number MDFs for screening exams, the number of positive screens and DE form completion status. Reports generated by the SC will not contain summary data related to positive screens or DE form completion as a result of the DSMB decision to limit SC access to data on positivity rates. Unlike the SCs, the CC will be able to generate reports containing positivity data. The CC will also be able to choose to generate individual reports for each screening center or a summary report containing information on all sites.

- Medical Abstraction Report (MAR, Appendix 11-23): This report was designed to assist the SC in managing and tracking the completion of medical record abstraction activities. The various querying options available in the MAR enable the SC to view the status of all expected DE forms and CDFs based upon user selected criteria. This feature is especially useful in identifying PIDs for outstanding forms by number of months since the expectation was generated. Results of the report can be exported from IDEAS and merged with the SC's in-house study management system.

Appendices for Chapter 11

Appendix 11-1 Missing Data Form (MDF)

National Lung Screening Trial / Lung Screening Study (NLST/LSS)

MISSING DATA FORM (MDF)

Date Form Completed: |___|___|-|___|___|-|_2_|_0_|___|___|
MONTH DAY YEAR

Screening Center ID: |___|___|

Screening Center Staff ID: |___|___|___|___|

Study Year: T |__|

Initials Complete: _____

Initials QC: _____

MDF

Participant ID Label

STUDY FORM	CHECK BOX	REASON CODE (IF CODE = 88, SPECIFY REASON)	REASON FOR CODE = 88
1. Medical History Questionnaire (MHQ)	|___|	|___|___|	
2. Annual Study Update (ASU) or ASU-Post Screening (ASU-PS)	|___|	|___|___|	
3. Chest X-ray Screening Examination Form (XRY)	|___|	|___|___|	
4. Spiral CT Screening Examination Form (SCT)	|___|	|___|___|	
5. Diagnostic Evaluation Form (DE)	|___|	|___|___|	
6. Treatment Information Form (TI)	|___|	|___|___|	
7. Cancer Diagnosis Form (CDF) ☐ ASU or ASU-PS ☐A ☐B ☐C	|___|	|___|___|	
☐ CNF ☐A ☐B ☐C		|___|___|	
8. Cancer Progression Form (CP)	|___|	|___|___|	
9. Health Assessment Questionnaire (HAQ)	|___|	|___|___|	
10. Participant Contact Form (PCF)	|___|	|___|___|	

Reason Codes

02 = Can't locate
03 = Deceased
05 = No response
06 = Out of area
07 = No show for scheduled appointments
08 = Transportation problems
09 = Concerned about privacy
10 = Physical illness/cognitive impairment
11 = Family responsibilities
12 = Work demands
13 = Concerned about medical cost responsibility
14 = Concerned about health effects of participation
15 = Active surveillance
16 = Participating in other research study
17 = Loss of interest in study
18 = Dissatisfied with study
19 = No reason given
20 = Reported lung cancer
21 = Participant refuses to release medical records
22 = Family refuses to release medical records
23 = Health care provider refuses to release medical records
24 = Health care provider does not respond to record requests
25 = Medical records lost
26 = No perceived benefit
88 = Other (SPECIFY)

National Lung Screening Trial / Lung Screening Study (NLST/LSS)

Specifications for Completion of the Missing Data Form (MDF)

An SC staff member should complete a Missing Data Form (MDF) to document the absence of a study data collection form. This MDF will cancel expectations for the noted missing form(s) and any other related expectations. These missing data may be due to a variety of reasons such as participant refusal, inability to locate the participant, death of the participant, and inability to obtain medical records.

Specifications for completing each item of the form are given below:

Administrative Section:

Participant ID Label: Affix a PID label to the space provided in the upper right portion of the form. Do not write the participant ID in this space.

Date Form Completed: Record the date the MDF was completed. Month and day should be zero filled, and the last two digits should be recorded for the year (e.g., 02/07/2002).

Screening Center ID: Record the two-digit SC ID number.

Screening Center Staff ID: Record the four-digit SC staff ID number.

Study Year: Record the study year for the missing data collection form.

Missing Data Section:

Study Form: Mark the box next to the data collection form(s) that is/are missing, i.e., the form(s) that will not be completed by or for the participant, and therefore will not be receipted at the CC.

Since a Cancer Diagnosis Form (CDF), which is completed when there is a report of cancer, is expected from an ASU, ASU-PS, or a CNF and each of those can report up to three cancers, an MDF needs to be completed listing both the form and the cancer type, by marking the box that corresponds to the reported cancer. If the MDF is being used to close multiple reports of cancer, the box corresponding to each reported cancer to be closed must be marked.

For Cancer Diagnosis Form (CDF):

- ASU or ASU-PS: Mark this box if the first documentation of the specified cancer was from the ASU or ASU-PS.

  A. Mark this box if the cancer for which the MDF is being completed was recorded under "A" on the ASU or ASU-PS.

  B. Mark this box if the cancer for which the MDF is being completed was recorded under "B" on the ASU or ASU-PS.

C. Mark this box if the cancer for which the MDF is being completed was recorded under "C" on the ASU or ASU-PS.

- CNF: Mark this box if the first documentation of the specified cancer was from the CNF.

  A. Mark this box if the cancer for which the MDF is being completed was recorded under "A" on the CNF.

  B. Mark this box if the cancer for which the MDF is being completed was recorded under "B" on the CNF.

  C. Mark this box if the cancer for which the MDF is being completed was recorded under "C" on the CNF.

Reason Code: For each missing form, complete this item to document the reason the data collection form is missing. Refer to the Reason Codes printed at the bottom of the MDF for the list of possible reasons the data collection form is missing. If more than one reason applies, the primary reason should be determined. Enter the code corresponding to the reason the data collection form is missing as follows:

02 = Can't locate: The SC is unable to locate the participant during the study period, despite tracing efforts.

03 = Deceased: The participant has died. This reason code will "turn off" the expectations for study activities that require participant contact (such as exams and forms).

05 = No response: The participant is contacted but does not respond to SC requests to complete data collection forms or schedule study visits.

06 = Out of area: The participant is contacted but is unwilling or unable to schedule study visits or screening examinations because s/he is out of the area.

07 = No show for scheduled appointments: The SC has scheduled study visits with the participant but s/he repeatedly fails to show up for the visits.

08 = Transportation problems: The participant refuses to schedule a study visit because s/he does not have transportation to/from the screening center.

09 = Concerned about privacy: The participant refuses to complete data collection forms or schedule study visits because s/he is concerned about privacy.

10 = Physical illness/cognitive impairment: The participant refuses to complete data collection forms or schedule study visits because s/he has a physical illness or cognitive impairment. This code may also be selected if the participant's family member or health care provider reports that s/he is unable to participate in study activities due to a physical illness or cognitive impairment.

11 = Family responsibilities: The participant refuses to complete data collection forms or schedule study visits because s/he has family responsibilities that preclude participation in the study activities.

12 = Work demands: The participant refuses to complete data collection forms or schedule study visits because s/he has work demands that preclude participation in the study activities.

13 = Concerned about medical cost responsibility: The participant refuses to schedule a screening examination because s/he is concerned about medical costs that may arise as a result of the exam (i.e., follow-up procedures).

14 = Concerned about health effects of participation: The participant refuses to schedule a screening examination because s/he is concerned about negative health effects of participation.

15 = Active surveillance: The participant refuses to schedule a screening examination because s/he is under active surveillance for a lung condition by a health care provider. This code may also apply if the participant has been advised not to receive the exam by his/her health care provider because s/he is under active surveillance.

16 = Participating in other research study: The participant refuses to complete study activities because s/he is currently participating in another research study.

17 = Loss of interest in study: The participant refuses to complete study activities because s/he has lost interest in the study.

18 = Dissatisfied with study: The participant refuses to complete study activities because s/he is dissatisfied with the study.

19 = No reason given: The participant refuses to complete study activities but does not give a specific reason for his/her refusal.

20 = Reported lung cancer: The participant is not eligible to receive a screening examination because s/he is reported to have lung cancer. The report of lung cancer must be documented on the Annual Study Update (ASU), ASU-PS, or a Cancer Notification Form (CNF).

21 = Participant refuses to release medical records: The medical records necessary for completion of the CDF, DE, TI, or CP form cannot be obtained because the participant refuses to have the records released.

22 = Family refuses to release medical records: The medical records necessary for completion of the CDF, DE, TI, or CP form cannot be obtained because the participant's family refuses to have the records released.

23 = Health care provider refuses to release medical records: The medical records necessary for completion of the CDF, DE, TI, or CP form cannot be obtained because the participant's health care provider refuses to release the records.

24 = Health care provider does not respond to record requests: The medical records necessary for completion of the CDF, DE, TI, or CP form cannot be obtained because the participant's health care provider does not respond to SC requests for the records.

25 = Medical records lost: The participant's medical records were obtained but the CDF, DE, TI, or CP form cannot be completed because the SC lost the records.

26 = No perceived benefit: The participant does not see the utility in returning for his/her NLST screening examination, or does not follow up with his/her health care provider (HCP) via phone or in person following a screening exam. Also, the code may be used in other instances when the participant states that s/he does not see a benefit in completing a study activity, for example, not completing the ASU or ASU-PS.

88 = Other (SPECIFY): Please SPECIFY the reason for the missing data in the space provided.

Reason for Code = 88: If Reason Code 88 = Other (SPECIFY) is marked, please specify the reason for the missing data in the designated column.

After completing the form:

- The form should be checked to make sure it is accurate, legible, and complete.
- The SC staff member who completed the form should write his/her initials in the space labeled "Initials Complete" in the box at the top of the first page.
- The SC staff member who checked the form for completion should write his/her initials in the space labeled "Initials QC" in the box at the top of the first page. This should not be the same SC staff member who completed the form.
- Enter the form into IDEAS.
- File the form in the participant's study file.

Appendix 11-3 Non-Response Form (NRF)
National Lung Screening Study / Lung Screening Study (NLST/LSS)

NON-RESPONSE FORM (NRF)

ADMINISTRATIVE SECTION

Date Form Completed: |___|___|-|___|___|-|2|0|___|___|
MO DAY YEAR

Screening Center ID: |___|___|

Screening Center Staff ID: |___|___|___|___|

Study Year: T |__|

Date of Last Contact:

|___|___|-|___|___|-|2|0|___|___|
MO DAY YEAR

NRF

Participant ID Label

PARTICIPANT STATUS	CHECK ONLY ONE	COMMENTS
Lost Contact Can't locate – No active contact with participant	|___|	
Refusals Hard refusal – Refuses further participation in NLST; **OR** Absolute refusal – Participant withdraws consent	|___| |___|	
Medical Condition Physical illness or cognitive impairment	|___|	
Deceased Date of death |___|___|-|___|___|-|2|0|___|___| MO DAY YEAR	|___|	
Return to NLST	|___|	

National Lung Screening Trial / Lung Screening Study (NLST/LSS)

Specifications for Completion of the Non-Response Form

The SC Coordinator or IDEAS Administrator should complete a Non-Response Form (NRF) to document the cessation of data collection from an inactive participant. The NRF should be utilized when a participant's inactive status is considered permanent. The NRF form also will allow for the reactivation of a participant should circumstances change.

Changes can be made to the Administrative Section and date of death field in the participant's most recent NRF in IDEAS. A change in the participant's status will require completing a new NRF from and entering it into IDEAS. Any previous NRF forms completed for that participant can be viewed in IDEAS, but not updated. If the participant status on the original NRF is determined to have been incorrect (i.e. participant was presumed deceased, but later discovered to be alive), the NRF with the incorrect status should be deleted. If necessary, a new NRF with the correct status (e.g. lost contact) should be entered.

Once the NRF is completed and entered into IDEAS, no further MDFs for any form will be necessary or expected for future study years; however, MDFs for all forms expected during the study year in which the NRF was completed are still required to be submitted into IDEAS. For example, Participant A has complete T_0 information and dies midway through T_1. An NRF is completed during the T_1 study year and forms are closed out for $T_2 - T_7$, however an MDF must still be completed for all outstanding T_1 forms.

The participant's inactive status may be due to a variety of reasons such as inability to locate the participant, participant refusal, an incapacitating medical condition, or death of the participant. Specifications for completing each item of the form are given below:

Administrative Section:

Participant ID Label: Affix a PID label to the space provided in the upper right portion of the form. Do not write the participant ID in this space.

Date Form Completed: Record the date the NRF was completed. Month and day should be zero filled, and the last two digits should be recorded for the year (e.g., 02/07/2002).

Screening Center ID: Record the two-digit SC ID number.

Screening Center Staff ID: Record the four-digit SC staff ID number.

Study Year: Record the study year the participant is in when the Non-Response Form is completed. For example, if a participant dies during the T_2 study year; but the SC learns of the death during his/her T_4 study year, the study year for the NRF should be T_4.

Date of Last Contact: Record the date on which the SC last had any communication (verbal or written) with the participant, family member or known acquaintance of the participant. The definition of the "Date of Last Contact" is dependent on the reason for the

participant's status. Guidelines for recording the date of last contact are specified for each reason in the Participant Status Section below.

Month and day should be zero-filled and the last two digits should be recorded for the year (e.g., 02/07/2002).

Participant Status Section

Mark the box next to the reason for the participant's inactive status. Only one box may be checked for participant status, so if more than one reason applies, the primary reason should be documented. The code and the description of participant status will be displayed on the Participant Overview Report (POR) in IDEAS.

Lost Contact:

The purpose of this item is to document participant non-response because the participant has been lost to follow-up. This reason should only be entered as a last resort when there is no active contact with the participant, and the SC is unable to locate the participant during the study period, despite intensive tracing efforts over a reasonably long period of time. Tracing resources may include but are not limited to: the Department of Motor Vehicles, Social Security Administration, the National Death Index, and the US Postal Service. The SC should not complete this form if tracing efforts will continue or if the participant has simply relocated and may be willing to return to the SC for annual visits or to complete questionnaires by mail. Participant status on the POR is displayed as "Lost Contact." No further MDFs for any form will be necessary or expected for future study years; however, MDFs for all forms expected during the study year in which the NRF was completed are still required to be submitted into IDEAS. In the event of death, a Death Certificate should be collected. If the participant has signed a Medical Records Release Authorization Form that is likely to be honored by medical facilities, the SC should attempt to collect medical records in the instance of a lung cancer diagnosis or selection for EVP.

The "Date of Last Contact" is defined in this instance as the date the SC last had any verbal or written communication with the participant. This does *not* include any contact with the participant's family members or acquaintances. If the written contact was the receipt of a form at the SC, the date of last contact should be the date the participant completed the form, not the receipt date in IDEAS.

Refusals:

Hard refusal:
The purpose of this item is to document that the participant refuses further participation in NLST. The refusal may be for a variety of reasons which could include transportation problems, concern about privacy, family responsibilities, work demands, concern about medical cost that may arise as a result of the exam, concern about negative health effects of participation, active surveillance for a lung condition, participation in another research study, loss of interest in study, dissatisfaction with study, or no stated reason. No further MDFs for

any form will be necessary or expected for future study years; however, MDFs for all forms expected during the study year in which the NRF was completed are still required to be submitted into IDEAS. If the participant has signed a Medical Records Release Authorization Form that is likely to be honored by medical facilities, the SC may, but is not required to, attempt to collect medical records in the instance of a lung cancer diagnosis or selection for EVP. The SC should exercise caution in making the decision to collect medical records for hard refusals, especially in the instance of an irate participant. In the event of death, a Death Certificate is to be collected for hard refusals, however. If at all possible, the SC should inform all hard refusals that their data will remain in the study database unless a written request to exclude it is received.

The "Date of Last Contact" is defined in this instance as the date the SC last had any verbal or written communication with the participant regarding his/her withdrawal from the trial; or the date a relative/friend of the participant notified the SC (verbally or written) of the participant's withdrawal from the trial.

Absolute refusal:
The purpose of this item is to document that the participant withdraws consent to participate in the study or indicates that s/he no longer wants his/her name or records included as part of the study. The SC will need to obtain documentation of such a request in writing and the documentation should be forwarded to the CC for NCI approval prior to entering the NRF into IDEAS. Once the NRF is entered, no further MDFs for any form will be necessary or expected for future study years, however, MDFs for all forms expected during the study year in which the NRF was completed still require submission into IDEAS. In addition, all information regarding the participant is removed from NLST study files/tables after consultation with NCI. No additional data collection is to be attempted for absolute refusals, even if a signed Medical Record Release Authorization Form is available and likely to be honored by a medical facility. Furthermore, a Death Certificate should not be obtained in the case of death. The participant is unavailable for EVP.

The "Date of Last Contact" is defined in this instance as the date the SC last had any verbal or written communication with the participant regarding his/her withdrawal from the trial; or the date a relative/friend of the participant notified the SC (verbally or written) of the participant's withdrawal from the trial.

Medical Condition:

The purpose of this item is to document when the participant is unwilling or unable to complete data collection forms or schedule study visits because s/he has a physical illness or cognitive impairment. For example, this reason would be used in the situation where a participant diagnosed with lung cancer decides to no longer participate actively in the trial. This reason may also be selected if the participant's family member or health care provider reports that s/he is unable to participate in study activities due to a physical illness or cognitive impairment. No further MDFs for any form will be necessary or expected for future study years; however, MDFs for all forms expected during the study year in which the NRF was completed are still required to be submitted into IDEAS. The participant remains available for EVP, if necessary.

The "Date of Last Contact" is defined in this instance as the date the SC last had any verbal or written communication with the participant regarding his/her withdrawal from the trial; or the date a relative/friend of the participant notified the SC (verbally or written) of the participant's withdrawal from the trial.

Deceased:

The purpose of this item is to document when a participant is presumed or confirmed dead. No further MDFs for any form will be necessary or expected after the end of the study year in which the NRF was submitted, but MDFs for all forms expected during the study year in which the NRF was completed are still required to be submitted into IDEAS, and EVP will be instituted. The SC should not select this reason code if the death was reported through returned mail, unless the report has been confirmed through another source (such as a relative.)

Record the date of death in the spaces provided. Month and day should be zero filled, and the last two digits should be recorded for the year (e.g., 02/07/2002). If, upon receipt of the Death Certificate, it is determined that the date of death recorded on the NRF is not correct, the SC should write the correct date of death on the hard copy NRF and sign and initial the change. The date of death must also be updated in IDEAS.

The "Date of Last Contact" is defined in this instance as the date the SC last had any verbal or written communication with the participant regarding his/her withdrawal from the trial; or the date the SC last had any verbal or written communication with a relative/friend of the participant regarding the participant's status in the trial.

Return to NLST:

The purpose of this item is to document when the participant wishes to return to the trial after an NRF has been submitted for any of the above reasons, apart from death. The SC should complete a new NRF and check the box for "Return to NLST" under the Participant Status Section of the form. Expectations for all forms will be re-set for the study year in which the new NRF was receipted into IDEAS and for all future study years. It may be necessary to complete an MDF for any form expected in the study year the new NRF was receipted. MDFs generated by IDEAS for study years prior to the study year in which the new NRF is receipted will be retained in the IDEAS database. The participant status will then be displayed as "Active" in the POR.

This code should not be used for participants who were presumed deceased but were later determined to be alive. In this situation, the NRF with the "deceased" status should be deleted. If necessary, a new NRF with the appropriate status should be entered.

Comments: Further comments, if necessary, can be recorded in this section.

After completing the form:

- The form should be reviewed to make sure it is accurate, legible, and complete.
- Enter the form into IDEAS.
- File the form in the participant's study file.

RECORD OF EXPERIENCE, CREDENTIALS, AND TRAINING (ECT)
EXAMINER/INTERPRETER/QUALITY ASSURANCE EXAMINER/MEDICAL PHYSICIST/ MEDICAL RECORD ABSTRACTOR/NOSOLOGIST
REGISTRATION FORM

1. DATE FORM COMPLETED: |___|___|–|___|___|–|_2_|_0_|___|___|
   MONTH DAY YEAR

2. SCREENING CENTER ID: |___|___|

3. NAME OF STAFF MEMBER TO BE REGISTERED:_____
   Last First Middle Initial

4. **STAFF POSITION:** (Mark all that apply.)

XRY	SCT	ABSTRACTOR	NOSOLOGIST
☐ Examiner	☐ Examiner	☐ Medical Record Abstractor	☐ ICD-9-CM Coder
☐ Interpreter	☐ Interpreter		☐ ICD-O-3 Coder
☐ QA Examiner	☐ QA Examiner		☐ TNM Staging Coder
☐ Medical Physicist	☐ Medical Physicist		

5. DATE NLST/LSS TRAINING COMPLETED: |___|___|–|___|___|–|_2_|_0_|___|___|
   MONTH DAY YEAR

6. SCREENING CENTER STAFF ID OF THE PERSON COMPLETING FORM: |___|___|___|___|

Appendix 11-5 Record of Experience, Credentials, and Training (ECT)

7. **EXPERIENCE:** (Mark the experience that applies. For abstractors and nosologists, provide a specific number for what is asked.)

XRY: Technologist (Examiner)

☐ Meets current ACR guidelines

Radiologist (Interpreter/QA Examiner)

☐ Meets current ACR guidelines

Medical Physicist

☐ Meets current ACR guidelines

SCT: Technologist (Examiner)

☐ Meets current ACR guidelines

Radiologist (Interpreter/QA Examiner)

☐ Meets current ACR guidelines

Medical Physicist

☐ Meets current ACR guidelines

ABSTRACTOR: Medical Record Abstractor

____ Number of years of on-the-job experience abstracting medical records (Minimum of two years on-the-job experience. Attach documentation such as resume or letter of reference.)

NOSOLOGIST: ICD-9-CM coding/ICD-O-3 coding and TNM Staging

____ Number of years of on-the-job experience performing coding (Attach documentation such as resume or letter of reference.)

Appendix 11-5 Record of Experience, Credentials, and Training (ECT)

8. **CREDENTIALS**: (Mark the credentials that apply. Attach a photocopy of the documentation requested.)

XRY: Technologist (Examiner)

- ☐ Meets current ACR guidelines
- ☐ Other: _____ (Attach copy of qualifying documentation.)

Radiologist (Interpreter, QA Examiner)

- ☐ Meets current ACR guidelines
- ☐ Is licensed to practice in _____ (state) with license # _____
- ☐ Other: _____ (Attach copy of qualifying documentation.)

Medical Physicist

- ☐ Meets current ACR guidelines
- ☐ Other: _____ (Attach copy of qualifying documentation.)

SCT: Technologist (Examiner)

- ☐ Meets current ACR guidelines
- ☐ Other: _____ (Attach copy of qualifying documentation.)

Radiologist (Interpreter, QA Examiner)

- ☐ Meets current ACR guidelines
- ☐ Is licensed to practice in _____ (state) with license # _____
- ☐ Other: _____ (Attach copy of qualifying documentation.)

Medical Physicist

- ☐ Meets current ACR guidelines
- ☐ Other: _____ (Attach copy of qualifying documentation.)

ABSTRACTOR: Medical Record Abstractor

- ☐ Knowledge of medical record terminology, anatomy, physiology, and concepts of disease
- ☐ Basic medical coding education (Attach qualifying documentation.)

NOSOLOGIST: All Coders

- ☐ Knowledge of medical record terminology, anatomy, physiology, and concepts of disease
- ☐ Basic medical coding education (Attach qualifying documentation.)

ICD-9-CM Coder

- ☐ Certified Coding Specialist, CCS (Attach copy of certification.)
- ☐ Registered Health Information Technician, RHIT (Attach copy of certification.)
- ☐ Registered Health Information Administrator, RHIA (Attach copy of certification.)
- ☐ Other: _____ (Attach copy of qualifying documentation.)

ICD-O-3 and TNM Staging Coder

- ☐ Certified Tumor Registrar, CTR (Attach copy of certification.)
- ☐ Tumor Registrar, CTR-eligible.
- ☐ Other: _____ (Attach copy of qualifying documentation.)

Appendix 11-5 Record of Experience, Credentials, and Training (ECT)

9. **TRAINING:** (Complete for all that apply. Required training on protocols and forms must be documented for each Examiner, Interpreter, QA Examiner, and Medical Physicist (protocol only) position marked in Item 4

XRY:
- ☐ Protocol for Chest x-ray Exam
- ☐ XRY Form

SCT:
- ☐ Protocol for Spiral CT Exam
- ☐ SCT Form

ABSTRACTOR AND NOSOLOGIST:
- ☐ DE Form
- ☐ CDF
- ☐ TI Form
- ☐ CP Form

10. **REGISTRATION:** (To be completed by the NCI reviewer.)

This individual is qualified to perform as a National Lung Screening Trial: (Mark all that apply.)

XRY	SCT	ABSTRACTOR	NOSOLOGIST
☐ Examiner	☐ Examiner	☐ Medical Record Abstractor	☐ ICD-9-CM Coder
☐ Interpreter	☐ Interpreter		☐ ICD-O-3 Coder
☐ QA Examiner	☐ QA Examiner		☐ TNM Staging Coder
☐ Medical Physicist	☐ Medical Physicist		

Signature of NCI reviewer: _____

Date: _____

Comments:

_____

_____

_____

_____

STAFF ID# ASSIGNMENT: (To be completed by the Screening Center **following NCI approval**.)

Staff ID#: |___|___|___|___|

Date:_____

National Lung Screening Trial / Lung Screening Study (NLST/LSS)

Specifications for Completion of the Record of Experience, Credentials, and Training (ECT)

Examiner/Interpreter/Quality Assurance Examiner/Medical Physicist/ Medical Record Abstractor/Nosologist

Registration Form

This form is to be completed for all SC staff who are to perform or interpret screening examinations, serve as a medical physicist, or perform medical records abstraction or coding for the NLST/LSS. One form should be completed for each staff member, including those who are currently registered as staff members for PLCO. When the form is completed and approved by the NCI reviewer, it will be sent back to the SC for assignment of a staff ID number. No staff member may work on the NLST/LSS without a staff ID number. The form will be completed one time per staff member; however, annual updates to the information provided will be requested by the CC.

Items 1-9 are to be completed by SC staff. Specifications for completion of these items are given below.

1. **Date Form Completed:** Record the date the ECT was completed. Month and day should be zero filled, and the last two digits should be recorded for the year (e.g., 12/07/2000).

2. **Screening Center ID:** Enter the two-digit SC ID number.

3. **Name of Staff Member to be Registered:** Enter the full name (last, first, middle initial) of the staff member to be registered.

4. **Staff Position:** Place a mark in the box next to each position that this new staff member will assume. Mark all positions that apply.

5. **Date NLST/LSS Training Completed:** Record the date the staff member completed the NLST/LSS training required for their position.

6. **Screening Center Staff ID of Person Completing Form:** Enter the four-digit SC staff ID number of the person completing the form.

7. **Experience:** For each XRY or SCT position marked in Item 4, mark whether the new staff member meets current ACR guidelines. For abstractors, record the total years of on-the-job experience abstracting medical records (a minimum of two years) and attach documentation to substantiate experience (such as a resume or letter of reference). For nosologists, record the number of years of on-the-job coding experience, and attach documentation to substantiate experience (such as a resume or letter of reference).

8. Credentials: For each position marked in Item 4, place a mark next to the credential that qualifies the staff member for this position. Attach a photocopy of the qualifying documentation requested (such as certification, etc.). Please note that in the "NOSOLOGIST" section, the "All Coders" section must be filled out for ICD-9-CM coders and ICD-O-3 and TNM staging coders. In addition to the "All Coders" section, the "ICD-9-CM Coder" and "ICD-O-3 and TNM staging Coder" sections should be completed based on the staff person's coding position (ICD-9-CM and/or ICD-O-3 and TNM staging).

For each position, the minimum qualifications, as given in the current screening examination protocols, include:

Function	Position	Minimum Qualifications
XRY Exam	Technician	- Meets current ACR guidelines
	Interpreter/QA Examiner	- Meets current ACR guidelines - Licensed to practice in ___ (state) with license # _____ (for radiologist only)
	Medical Physicist	- Meets current ACR guidelines
SCT Exam	Technician	- Meets current ACR guidelines
	Interpreter/QA Examiner	- Meets current ACR guidelines - Licensed to practice in ___ (state) with license # _____ (for radiologist only)
	Medical Physicist	- Meets current ACR guidelines
Medical Records Abstraction	Abstractor	- Knowledge of medical record terminology, anatomy, physiology, and concepts of disease - Basic medical coding education - A minimum of two years on-the-job experience abstracting medical records
	Nosologist (All Coders)	- Knowledge of medical record terminology, anatomy, physiology, and concepts of disease - Basic medical coding education
	Nosologist (ICD-9-CM Coder only)	- One or more of the following credentials: Certified Coding Specialist (CCS) Registered Health Information Technician (RHIT) Registered Health Information Administrator (RHIA)
	Nosologist (ICD-O-3 Coder only) and TNM Staging Coder	- Certified Tumor Registrar (CTR or CTR-eligible)

If the staff member does not possess any of the credentials listed, but possesses some other credential that the SC feels qualifies him/her for this position, mark the box next to "Other" and record the type of credential being submitted. Attach a photocopy of the documentation of this credential.

9. Training: For each position marked in Item 4, place a mark next to each training activity completed by the staff member. All Examiners, Interpreters, QA Examiners, Medical Record Abstractors and Nosologists must undergo training on the appropriate examination protocol and

form completion. All Medical Physicists must undergo training on the appropriate examination protocol only.

Item 10 is to be completed by the NCI reviewer. Specifications for completion of this item are given below.

10. Registration: For each position marked in Item 4, review the experience (Item 7), credentials (Item 8), and training (Item 9) to determine whether or not the staff member is qualified to perform in that position for the NLST/LSS. If so, place a mark in the box for the appropriate position.

Sign the form and record the date of signature. In the Comments Section, record any additional comments regarding this staff member.

The following item is to be completed by the SC <u>following NCI approval</u>. Specifications for completion of this item are given below.

Staff ID# Assignment: Record the staff ID number and the date it was assigned in the space provided. If the staff member is a registered staff member for PLCO, the SC Coordinator should assign him/her the same staff ID number used for PLCO. Notify the Credentials Coordinator at the CC what staff ID number has been assigned.

<u>After completing the form:</u>

- The form should be checked to make sure it is accurate, legible, and complete.
- The original ECT form for all newly registered staff should be sent to the Credentials Coordinator at the CC when completed.
- A copy of the ECT should be kept on file at the SC.

Appendix 11-7 SC Edit Form

National Lung Screening Trial / Lung Screening Study (NLST/LSS)

SC EDIT FORM

Date Completed: |___|___|-|___|___|-|_2_|_0_|___|___|
Month Day Year

Screening Center ID: |___|__|

Screening Center Staff ID: |___|___|___|___|

Initials Complete: _____

Initials QC: _____

SC

Participant ID Label

INSTRUCTIONS: Complete PID, Form Type, Item Number, and correct data for each item to be updated.

Form Type	Item Number	Description of Change [SPECIFY CORRECT DATA]

SC staff member who completed the form _____

SC staff member telephone number _____

Send the original or e-mail version of the form to the CC. Retain a copy for participant files.

National Lung Screening Trial / Lung Screening Study (NLST/LSS)

Specifications for Completion of the SC Edit Form

This form is to be completed by an SC staff member to document changes to data after a data collection form has been sent to the CC.

Specifications for completing each item of the form are given below:

Administrative Section:

Participant ID Label: Affix a PID label to the space provided in the upper right corner of the form. **Do NOT** write the participant ID in this space. If the SC Edit Form is e-mailed, type in the PID.

Date Completed: Record the date the SC Edit Form was completed. Month and day should be zero-filled, and the last two digits of the year should be recorded (02/07/2002).

Screening Center ID: Record the two-digit SC ID number.

Screening Center Staff ID: Record the four-digit SC staff ID number of the person completing the form.

Data Update Section:

One SC Edit Form should be completed for each participant. For each form that has a data correction(s), complete the form type, the item number requiring the change, and the correct data. Multiple changes to one form can be listed. However, once the form has been submitted to the CC, subsequent edits should be noted on another SC Edit Form.

As an example of completing the SC Edit Form, suppose there is a change to the description of the second abnormality on the Spiral CT Screening Examination Form. It might be recorded as follows:

Form Type	Item Number	Description of Change [SPECIFY CORRECT DATA]
SCT	C.2.2.2	Code = 3

Note that Item C.2 on the SCT form is a grid. When dealing with grids, the row number should be given before the column number. In this example, the data to be changed is in Item C.2, row 2 (Abnormality), column 2 (Location of Epicenter).

After completing the form:

- The form should be checked to make sure it is accurate, legible, and complete.
- The SC staff member who completed the form should write his/her initials in the space labeled “Initials Complete” in the box at the top right corner of the page.
- The SC staff member who checked the form for completion should write his/her initials in the space labeled “Initials QC” in the box at the top right corner of the page. This should not be the same SC staff member who completed the form.
- Send the completed form to the CC via FedEx shipment, or an e-mail attachment,
- File a copy of the form in the participant’s study file.

PROTOCOL AND HIPAA VIOLATION FORM (PHVF)

Date Form Completed: |___|___|-|___|___|-|_2_|_0_|___|___|
Month Day Year

Screening Center ID: |___|___|

Screening Center Staff ID: |___|___|___|___|___|

Study Year: T |___|

Initials Complete: _____

Initials QC: _____

PHVF

Participant ID Label

INSTRUCTIONS: Please mark the type of protocol or HIPAA violation below. Depending on the type of violation, please provide the information requested on all pages. Attach additional sheets as necessary.

***PLEASE COMPLETE A SEPARATE FORM FOR EACH PARTICIPANT AND FOR EACH INSTANCE OF A PROTOCOL OR HIPAA VIOLATION.**

1. MARK THE TYPE OF PROTOCOL OR HIPAA VIOLATION BEING REPORTED

- ☐ Ineligible participant randomized
- ☐ Participant randomized more than once **(Original PID #|__|__|-|__|__|__|__|__|-|__|)**
- ☐ Participant completed study activity before signing consent form
- ☐ Screened eligible participant with a reported or confirmed lung cancer
- ☐ Chest x-ray screen administered to spiral CT arm participant
- ☐ Spiral CT screen administered to chest x-ray arm participant
- ☐ Erroneous results reported to participant or health care provider
- ☐ Duplicate screen administered
- ☐ Incorrect technical parameters used for screening examination
- ☐ Original hard copy or digital screening exam image can no longer be accessed and no backup exists
- ☐ Protected Health Information (PHI) revealed
- ☐ Other, Specify (In the space below, include any error not listed above.)

_____

_____

2a. Date Violation Discovered: |___|___|-|___|___|-|_2_|_0_|___|___|
Month Day Year

2b. Date Violation Occurred: |___|___|-|___|___|-|_2_|_0_|___|___|
Month Day Year

Appendix 11-9 Protocol and HIPAA Violation Form (PHVF)

THIS SECTION IS TO BE COMPLETED ONLY FOR PROTOCOL VIOLATION "INELIGIBLE PARTICIPANT RANDOMIZED"

3a. Reason for Ineligibility: (Mark all that apply.)

- ☐ 01 = Unwilling/Unable to provide consent
- ☐ 02 = Spiral CT screen in past 18 months
- ☐ 03 = Other Specify **(MARK ALL THAT APPLY)**
- ☐ 31 = Age < 55 yrs or > 74 years
- ☐ 32 = Non-smoker or quit smoking more than 15 yrs ago
- ☐ 33 = Less than 30 pack-years smoking history
- ☐ 34 = Participant in PLCO or other cancer screening study
- ☐ 35 = Participant in cancer prevention study other than smoking cessation
- ☐ 36 = Diagnosed with confirmed lung cancer **(Complete 3b)**
- ☐ 37 = Evidence of cancer, or in treatment for cancer other than non-melanoma skin cancer or carcinoma in situ (except transitional cell CIS, or bladder CIS) within the past five years
- ☐ 38 = Had a lung, or any portion of a lung surgically removed
- ☐ 40 = Unable to lie on back with arms raised over head
- ☐ 41 = Metallic implants in chest or back
- ☐ 42 = Home oxygen supplementation requirement
- ☐ 43 = Weight loss greater than 15 pounds in past 12 months or recent hemoptysis
- ☐ 44 = Pneumonia or respiratory infection requiring antibiotics in past 12 weeks

3b.* Date of Lung Cancer Diagnosis: |__|__|-|__|__|-|__|__|__|__| ☐ Estimated day
MO DAY YEAR

*only complete if 36 is coded in 3a.

4. Description of Protocol or HIPAA Violation:

Describe the violation by including the following elements: How was the violation discovered? How did the violation occur? What are the ramifications for the participant? What was done to clean up after this violation (include contacts with participants, systems changes, forms completed, etc.)? What steps have been taken to prevent future occurrences of this type of violation?

4. Description of Violation (continued):

National Lung Screening Trial / Lung Screening Study (NLST/LSS)

Specifications for Completion of the Protocol and HIPAA Violation Form (PHVF)

This form is to be completed by an SC staff member to document any violation of the requirements of the protocol for study enrollment or screening. This form is also used to document any violation of the Health Insurance Portability and Accountability Act (HIPAA).

Specifications for completing each item of the form are given below:

Administrative Section:

Participant ID Label: Affix a PID label in the box provided. DO NOT write the participant ID in this space.

Date Form Completed: Record the date the PHVF was completed. Month and day should be zero-filled, and the last two digits of the year should be recorded (e.g., 02/07/2002).

Screening Center ID: Enter the two-digit SC ID number.

Screening Center Staff ID: Enter the four-digit staff ID number of the person completing the form.

Study Year: Record the study year the participant was in when the violation was discovered.

Please do not include the participant's name or any identifying information. Use the PID to identify the participant. Please complete a separate form for each participant and for each instance of a violation.

Protocol or HIPAA Violation Information:

1. **Type of Violation:** Put a mark in the box to the left of the type of violation being reported.

- **Ineligible participant randomized:** Mark this box when it is discovered that an erroneous randomization occurred, that is, randomization of an individual who did not meet eligibility criteria at the time of randomization. **Do not use this code to report a duplicate randomization.**

- **Participant randomized more than once:** Mark this box when it is discovered that a participant was randomized more than once, regardless of whether the second randomization was to the same study arm or the opposite study arm. **Write the original PID number in the space provided. Place the new PID label in the space provided on the form.**

- **Participant completed study activity before signing consent form:** Mark this box when it is discovered that a participant completed any study activity before signing a consent form.

- **Screened eligible participant with a reported or confirmed lung cancer:** Mark this box when it is discovered that an eligible participant with a reported or confirmed lung cancer was inadvertently given a screening examination.

- **Chest x-ray screen administered to spiral CT arm participant:** This box is marked when a participant randomized to the spiral CT arm is screened with a chest x-ray instead of a spiral CT scan. A copy of the erroneous XRY Form and a completed MDF for the SCT should accompany the PHVF.

- **Spiral CT screen administered to chest x-ray arm participant:** This box is marked when a participant randomized to the chest x-ray arm is screened with a spiral CT scan instead of a chest x-ray. A copy of the erroneous SCT Form and a completed MDF for the XRY should accompany the PHVF.

- **Erroneous results reported to participant or health care provider**: Mark this box when it is discovered that the results letter sent to the participant or the participant's health care provider incorrectly reported the results of the screening examination.

- **Duplicate screen administered:** Mark this box when it is discovered that a participant was screened more than once during a study year.

- **Incorrect technical parameters used for screening examination:** Mark this box when it is discovered that one or more technical parameters used for the screening examination were outside the range specified in the protocol.

- **Original hard copy or digital screening exam image can no longer be accessed and no backup exists:** Mark this box when the original hard copy or digital screening examination image can no longer be accessed (due to loss, corruption, or irreversible modification such that the image can no longer be read according to study protocol) and no backup copy exists. For example, this box should be marked if the original spiral CT image was replaced with an image that utilized a filter that was not allowed by the protocol and no backup copy of the original image (with an allowable filter) exists.

- **Protected Health Information (PHI) revealed:** Mark this box when it is discovered that a participant's PHI has been released in a manner that is inconsistent with confidentiality assurances in the study consent forms.

- **Other, Specify:** Mark this box if there is a violation of the study protocol other than those listed above and indicate the nature of the violation in the space provided. If the comparison read was not performed at the T_1 or T_2 visit, mark this box and record the reason the comparison was not performed (e.g. T_0 image lost). Note that if the T_0 and/or T_1 images are available, the comparison read must be performed and a PHVF should not be completed.

2a. Date Violation Discovered: Record the date that the SC staff discovered the violation. For ineligible participant randomized, record the date that the ineligibility was discovered. Month and day should be zero-filled, and the last two digits of the year should be recorded (e.g., 02/07/2002).

2b. Date Violation Occurred: Record the date that the violation actually occurred. For ineligible participant randomized, record the date that the participant was randomized. Month and day should be zero-filled, and the last two digits of the year should be recorded (e.g., 02/07/2002).

Information Regarding Protocol Violation for a Randomized Ineligible Participant:

3a. Reason for Ineligibility: The reason for ineligibility is the criterion or criteria that should have made the participant ineligible at the time of randomization. Mark either box 01, 02, or 03 corresponding to the appropriate exclusion criterion. If box 03 "Other Specify" is marked, mark the subcategory under "Other Specify" that corresponds to the participant's situation. If the participant met more than one of the exclusion criteria, mark all that apply.

3b. Date of Lung Cancer Diagnosis: If Code 36 has been marked in 3a. complete 3b. Record the month, day, and year the cancer was diagnosed. If you have only the month and year, record "15" as an estimated day and mark the "Estimated Day" box. If you have only the year, record the year, and list "99" for month and day.

4. Description of Violation: Provide a detailed description of the violation and the resolution. The description should include the following elements:

- How the violation was discovered;
- How the violation occurred;
- Ramifications for the participant;
- What was done to "clean-up" after the violation (include contacts with participants, systems changes, forms completed, etc.), and
- The steps that have been taken to prevent future occurrences of this type of violation.

One of the purposes of the PHVF is to differentiate between types of "randomized ineligibles." If the violation being described is a randomized ineligible, the description should also include details that specify the type of randomized ineligible, as described below:

1. Participant was randomized in error (i.e., the participant provided information to the SC indicating his/her ineligibility, but the SC failed to exclude him/her from the trial);

2. Participant was randomized appropriately based on information provided at the time of randomization, but it was discovered after randomization that the information provided had been incorrect.

After completing the form:

- The form should be checked to make sure it is accurate, legible, and complete.

- The SC staff member who completed the form should write his/her initials in the space labeled "Initials Complete" in the box at the top right corner of the first page.

- The SC staff member who checked the form for completion should write his/her initials in the space labeled "Initials QC" in the box at the top right corner of the first page. This should not be the same SC staff member who completed the form.

- Enter the form into IDEAS.
- Copy the form.
- Send the original form to the CC.
- File a copy of the form in the participant's study file.

National Lung Screening Trial / Lung Screening Study (NLST/LSS)

Report of Adverse Events for NIH-Sponsored Clinical Trials (RAE)

Date of Associated Screening Exam: |___|___|-|___|___|-|_2_|_0_|___|___|
Month Day Year

Date of Adverse Event: |___|___|-|___|___|-|_2_|_0_|___|___|
Month Day Year

Screening Center ID: |___|___|

Screening Center Staff ID: |__|__|__|__|

Study Year: T |___|

Visit Number: |___|

Initials Complete: _____

Initials QC:

RAE

Participant ID Label

1. Category of event (Mark all that apply):

- ☐ Death
- ☐ Life threatening event
- ☐ In-patient hospitalization
- ☐ Persistent or significant disability/incapacity
- ☐ Medical or surgical intervention to prevent one of the above outcomes
- ☐ Other, Specify _____

2. Description of participant who experienced the adverse event, such as gender, age, etc. (no identifiers please):

_____
_____
_____
_____
_____

3. Brief description of the event:_____
_____
_____
_____
_____

4. Description of the outcome of the event:_____
_____
_____
_____
_____

☐ **(continued)**

5. Using your best judgement, do you believe that the adverse event was study related?

   ☐ Yes, study related
   ☐ Possibly study related
   ☐ Not study related
   ☐ Unknown

6. Do you feel revision to the consent form is necessary?

   ☐ Yes, revision of the consent form is necessary
   ☐ Revision of the consent form may be necessary
   ☐ No revision of the consent form is necessary
   ☐ Unknown

Investigator's Signature and Date: _____

Investigator's Printed Last Name and Initial: _____

(Please attach copies of any relevant examination forms or other documentation regarding the event.)

National Lung Screening Trial / Lung Screening Study (NLST/LSS)

Specifications for Completion of the Report of Adverse Events for NIH-Sponsored Clinical Trials (RAE)

The Report of Adverse Events for NIH-Sponsored Clinical Trials (RAE) is to be completed for all adverse events, regardless of their nature or severity that may occur as a result of screening procedures performed as part of the NLST/LSS. The following should be documented as adverse events:

- Death
- Life threatening event
- In-patient hospitalization
- Persistent or significant disability/incapacity
- Medical or surgical intervention to prevent one of the above outcomes
- Other, Specify

Complications that would not be included in the RAE would include, for example, problems that resulted from diagnostic evaluations for a positive screening exam such as a pneumothorax after a bronchoscopy. Complications such as this would be recorded in the medical complications section of the Diagnostic Evaluation forms and not on an RAE.

The RAE should be kept in the participant's study file and appropriate follow-up with the participant and his/her health care provider should be conducted until the problem is resolved. When the problem is resolved, the RAE should be entered into IDEAS and filed in the participant's study file.

The specifications for completing each question are listed below:

Administrative Section:

Participant ID Label: Place the PID label in the designated space. DO NOT write the participant ID in this space.

Date of Associated Screening Exam: Record the date the RAE was completed. Enter the date in MM/DD/YYYY format. This should be the date that the participant received the screening examination that is considered the cause of the event. Month and day should be zero filled, and the last two digits of the year should be recorded (e.g., 02/07/2002).

Date of Adverse Event: Record the date the adverse event occurred. Enter the date in MM/DD/YYYY format. Month and day should be zero filled, and the last two digits of the year should be recorded (e.g., 02/07/2002)

Screening Center ID: Enter the two-digit SC ID number.

Screening Center Staff ID: Enter the four-digit SC staff ID number of the person completing the form.

Study Year: Record the study year the participant was in when the screening exam causing the adverse event was performed.

Visit Number: Record the visit number of the screening exam for which the form is being completed.

Event Description Section:

1. **Category of event:** Mark all categories that describe the event.

   - Death: This category should be used if the participant died.

   - Life threatening event: This category should be used if the participant experiences events such as cardiac/respiratory arrest, cardiac arrhythmia, significant blood loss, etc.

   - In-patient hospitalization: This category should be used if the event required the participant to be hospitalized. This would include visits to the emergency room during which the participant was admitted to the hospital.

   - Persistent or significant disability/incapacity: This category includes events that caused the participant a significant reduction in daily functioning and activities. This would include any paralysis or loss of organ function.

   - Medical or surgical intervention to prevent one of the above outcomes: This category should be used if the participant required a major medical or surgical intervention as a result of the event. This would include surgery performed or medication given to repair internal injury or organ damage.

   - Other, Specify: This category should be used if the participant did not experience a catastrophic or life threatening event, an event which required in-patient hospitalization, an event that caused the participant significant disability or incapacity, or an event which required major medical or surgical intervention as described in the above categories. Specify the type of event in the space provided. This category should be used if the participant required no or minimal medical intervention. Further details can be outlined in the sections "Description of the event" and "Outcome of the event."

2. **Description of participant who experienced the adverse event:** Include items such as gender, age, and race. It is also important to note any other characteristics of the participant that may have played a role in the event, such as comorbidities or medications. Note: please be sure that this description does not contain any participant identifiers such as name and address.

3. **Brief description of the event**: This item should give a description of the participant's experiences that may have led to the adverse event. Report symptoms, the timing of the onset of these symptoms, and the manner in which the SC became aware of the event.

4. **Description of the outcome of the event**: This should be a description of any medical interventions that the participant received and their outcome. Any persistent or significant disability/incapacity (as described above) should be described here as well.

5. **Using your best judgment, do you believe that the adverse event was study related?** The PI should decide whether or not the event reported by the participant was related to their involvement in the NLST/LSS. The four responses are:

    - Yes, study related: This should be used if the PI feels certain that the event occurred as a result of the participant's screening exam.

    - Possibly study related: This should be used if the PI is not certain that the event occurred as a result of the participant's involvement but it is likely.

    - Not study related: This should be used if the PI feels certain that the event did not occur as a result of the participant's screening exam.

    - Unknown: If the PI is unsure if the event was related to the screening examination, this response should be used.

6. **Do you feel revision to the consent form is necessary?** The PI should indicate whether s/he believes that the event warrants revision of the consent form to mention it as a possible danger. The four responses are:

    - Yes, revision of the consent form is necessary: This should be used if the PI feels certain that all participants should be made aware of the potential danger.

    - Revision of the consent form may be necessary: This means that the PI is not certain that all participants should be made aware of the potential danger but it may be necessary.

    - No revision of the consent form is necessary: This should be used if the PI feels certain that the event does not warrant announcement in the consent form.

    - Unknown: If the PI is unsure whether the event warrants announcement in the consent form.

After these questions are completed, the PI is required to sign and date the form as well as print his/her last name and first initial below the signature. The SC may attach any relevant examination forms or other documentation regarding the event. If any other documentation is attached, the SC should be sure that no personal identifying information is present.

After completing the form:

- The form should be checked to make sure it is accurate, legible, and complete.

- The SC staff member who completed the form should write his/her initials in the space labeled "Initials Complete" in the box at the top right corner of the first page.

- The SC staff member who checked the form for completion should write his/her initials in the space labeled "Initials QC" in the box at the top right corner of the first page. This should not be the same SC staff member who completed the form.

- Enter the form into IDEAS.

- Copy the form
- Send the original form to the CC.
- File a copy of the form in the participant's study file.

Appendix 11-13 Sample Call Record

National Lung Screening Trial / Lung Screening Study (NLST/LSS)

Participant Name: _____

Address: _____

_____

PID

Telephone Number: (H) |__|__|__|-|__|__|__|-|__|__|__|__|

(W) |__|__|__|-|__|__|__|-|__|__|__|__|

(Other) |__|__|__|-|__|__|__|-|__|__|__|__|

Date of First Mailing: |___|___|-|___|___|-|___|___|

Date of Last Contact: |___|___|-|___|___|-|___|___|

Gender: (M/F) |___|

Day:_____ Date: |__|__|-|__|__|-|__|__|__|__| Time of Call: ____:____ am ____:____ pm Initials: |___|___|___|	Outcome of Call: ☐ No Answer ☐ Busy ☐ Call Back ☐ Left Message ☐ Form Complete ☐ Refusal	Reason for Refusal: ☐ Too Busy ☐ Not Interested ☐ Other (Specify): _____ _____ _____ _____	Level of Refusal: ☐ Mild ☐ Firm ☐ Hostile	Comments: _____ _____ _____ _____ _____ _____ _____
Day:_____ Date: |__|__|-|__|__|-|__|__|__|__| Time of Call: ____:____ am ____:____ pm Initials: |___|___|___|	Outcome of Call: ☐ No Answer ☐ Busy ☐ Call Back ☐ Left Message ☐ Form Complete ☐ Refusal	Reason for Refusal: ☐ Too Busy ☐ Not Interested ☐ Other (Specify): _____ _____ _____ _____	Level of Refusal: ☐ Mild ☐ Firm ☐ Hostile	Comments: _____ _____ _____ _____ _____ _____ _____

Appendix 11-13 Sample Call Record

<table>
<tr><td>Day:____________________
Date: |__|__|-|__|__|-|__|__|__|__|
Time of Call: ____:____ am
____:____ pm
Initials: |___|___|___|</td><td>Outcome of Call:
☐ No Answer
☐ Busy
☐ Call Back
☐ Left Message
☐ Form Complete
☐ Refusal</td><td>Reason for Refusal:
☐ Too Busy
☐ Not Interested
☐ Other (Specify):
____
____
____
______________</td><td>Level of Refusal:
☐ Mild
☐ Firm
☐ Hostile</td><td>Comments:
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______________________________</td></tr>
<tr><td>Day:____________________
Date: |__|__|-|__|__|-|__|__|__|__|
Time of Call: ____:____ am
____:____ pm
Initials: |___|___|___|</td><td>Outcome of Call:
☐ No Answer
☐ Busy
☐ Call Back
☐ Left Message
☐ Form Complete
☐ Refusal</td><td>Reason for Refusal:
☐ Too Busy
☐ Not Interested
☐ Other (Specify):
____
____
____
______________</td><td>Level of Refusal:
☐ Mild
☐ Firm
☐ Hostile</td><td>Comments:
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______________________________</td></tr>
<tr><td>Day:____________________
Date: |__|__|-|__|__|-|__|__|__|__|
Time of Call: ____:____ am
____:____ pm
Initials: |___|___|___|</td><td>Outcome of Call:
☐ No Answer
☐ Busy
☐ Call Back
☐ Left Message
☐ Form Complete
☐ Refusal</td><td>Reason for Refusal:
☐ Too Busy
☐ Not Interested
☐ Other (Specify):
____
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____
______________</td><td>Level of Refusal:
☐ Mild
☐ Firm
☐ Hostile</td><td>Comments:
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______________________________</td></tr>
<tr><td>Day:____________________
Date: |__|__|-|__|__|-|__|__|__|__|
Time of Call: ____:____ am
____:____ pm
Initials: |___|___|___|</td><td>Outcome of Call:
☐ No Answer
☐ Busy
☐ Call Back
☐ Left Message
☐ Form Complete
☐ Refusal</td><td>Reason for Refusal:
☐ Too Busy
☐ Not Interested
☐ Other (Specify):
____
____
____
______________</td><td>Level of Refusal:
☐ Mild
☐ Firm
☐ Hostile</td><td>Comments:
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______________________________</td></tr>
</table>

National Lung Screening Trial / Lung Screening Study (NLST/LSS)

Transmittal Log

Study:	
Center ID:	
Shipment Date:	
Total No. of Forms:	
Form:	
Sr No.	PID Selected

NLST/LSS Guidelines for SC Data Security

- Do not store files directly on the IDEAS workstation's hard drive. Instead, the IDEAS server should be used for storing and retrieving all electronic files. The IDEAS server provides a more secure environment for electronic files and scheduled daily back-ups provide additional protection against data loss. The Coordinating Center (CC) System Administrator will perform initial workstation audits and will move files from the workstations to the server as needed. The CC System Administrator will continue to perform random workstation audits to ensure proper storage of electronic files.
- Store IDEAS backup tapes in a secure location. At least one copy is to be maintained in an off-site location for added protection against data loss due to unforeseen circumstances such as fire or water damage.
- Store all images in a secure location. For electronic images, the file storage system must be protected from outside access (e.g. password control or locked system).
- Participant level NLST data containing personal identifiers should not be stored on a laptop that leaves the SC offices.
- Any NLST data that have been stored on non-NLST workstations to facilitate SC operations should be removed or encrypted on an ongoing basis.
- All study materials containing personal identifiers such as name, address, or Social Security number should be kept in a secure area and shredded when no longer needed.
- Avoid copying NLST data to any removable media (CDs, floppy disks, USB flash drives, etc). If there is a legitimate need to store NLST data on removable media, the data must be encrypted using a zip utility.
- Do not connect any unauthorized devices to the NLST network, including laptops. There should be no need to attempt to attach to the NLST network in this manner.
- Do not leave workstations unattended while logged in to IDEAS. The CC will provide additional security by installing a "time-out" feature to all workstations. Once installed, the workstation will "lock" after ten minutes of inactivity and can only be "unlocked" by entering a valid username and password. It is also recommended that workstations be shut down at the end of each work day.
- Do not leave computers unattended while logged in to the NLST EVICT or Data QA system Web sites.
- Strive to keep the NLST SC study area secure and free from unauthorized personnel. Access to NLST information systems including the IDEAS workstations, EVICT, and Data QA systems should be limited to necessary NLST SC staff. The SC should immediately notify the CC Coordinator of any staffing change so user accounts can be deactivated as needed.
- Use a zip utility to encrypt and password protect all NLST data that are sent via e-mail. The CC System Administrator will also zip data files sent via e-mail and will transmit NLST data to SCs by uploading to NLST servers rather than by e-mail.

July 7, 2008

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Appendix 11-16 CC Edit Form

National Lung Screening Trial / Lung Screening Study (NLST/LSS)

CC EDIT FORM

THE SC WILL RECEIVE THIS FORM WITH SHADED ITEMS FILLED IN BY THE CC. THE SC MUST FILL IN THE RESOLUTION COLUMN AND THE DATE. RETURN THE ORIGINAL TO CC AND KEEP A COPY FOR SC FILES.

Initials Complete: _____

Initials QC:

Report Date: |___|___|/|___|___|/|_2_|_0_|___|___| Page _____ of _____ To: Screening Center ID: |___|___|

Participant ID	Form	Item No.	Description of Error	RESOLUTION

Date returned to CC: |___|___|-|___|___|-|_2_|_0_|___|___|
MO DAY YEAR

Questions? Please contact _____at _____

National Lung Screening Trial / Lung Screening Study (NLST/LSS)

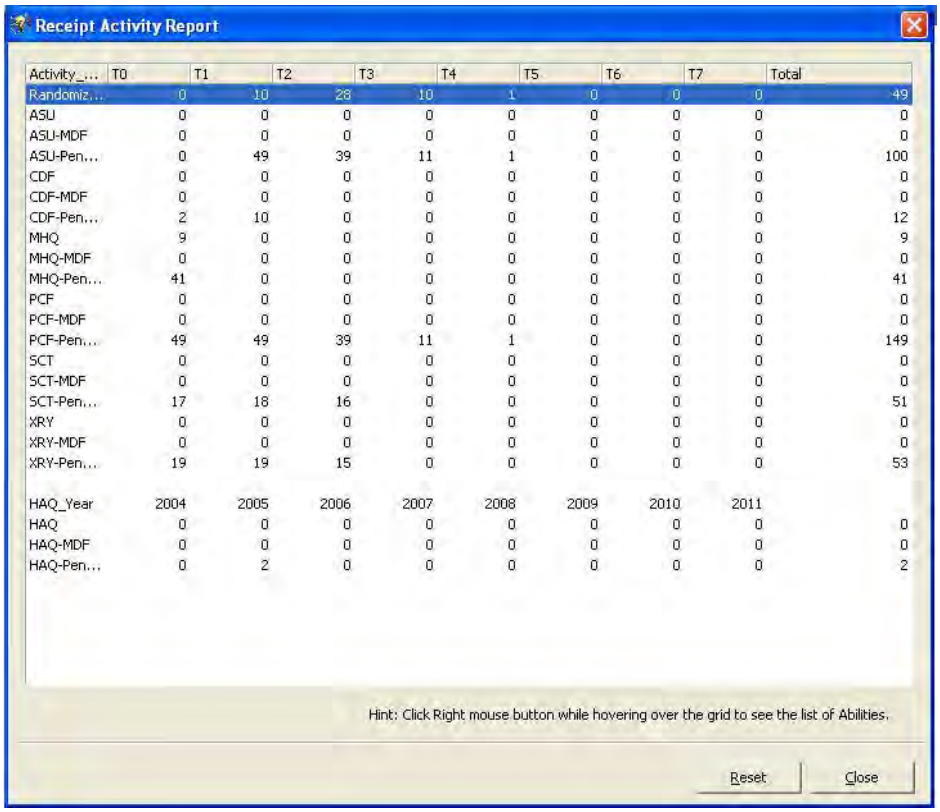
SC Cumulative Recruitment Summary Report

Recruitment Activity	SC										TOTAL
	01	02	03	04	05	06	08	09	10	11	
Recruitment packets mailed											
Eligible participants pending randomization											
Ineligible participants											
Number randomized											
Spiral CT											
Chest x-ray											
Screening exams scheduled, but not yet complete											
Spiral CT											
Chest x-ray											
Number screened*											
Spiral CT											
Chest x-ray											
Percent screened**											
Spiral CT											
Chest x-ray											
Screened+Scheduled											
Percent Screened+Scheduled											
Week ending											

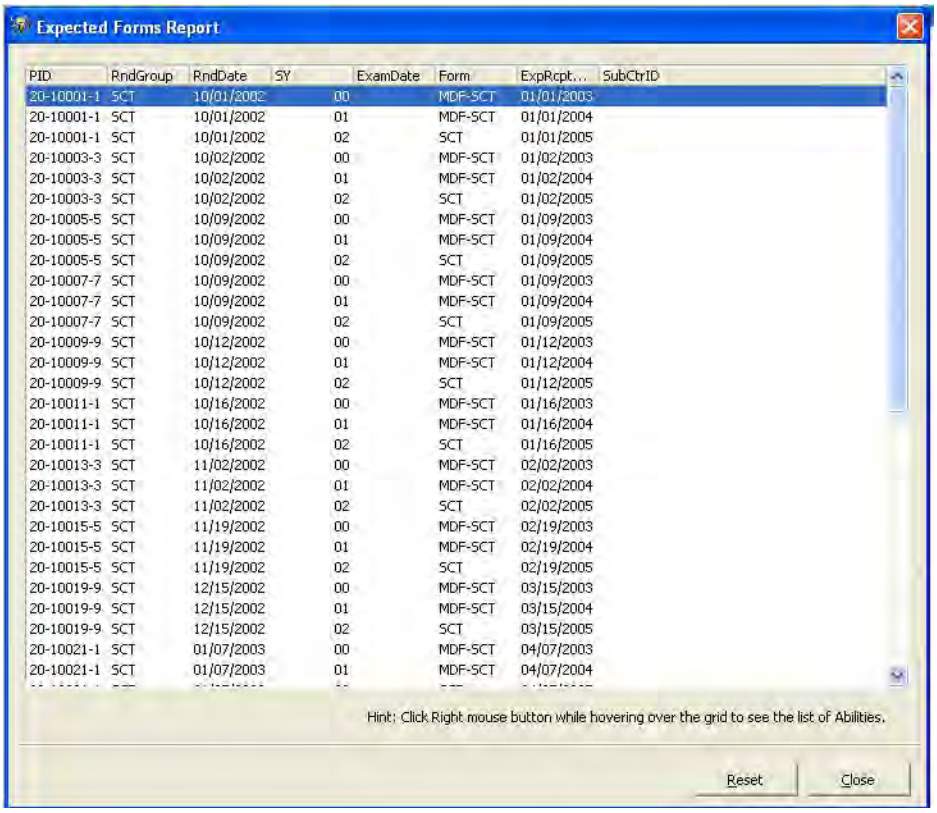
* Number screened = Number of screening exams completed regardless of whether or not radiologist has read

** Percent screened = Number screened/number randomized

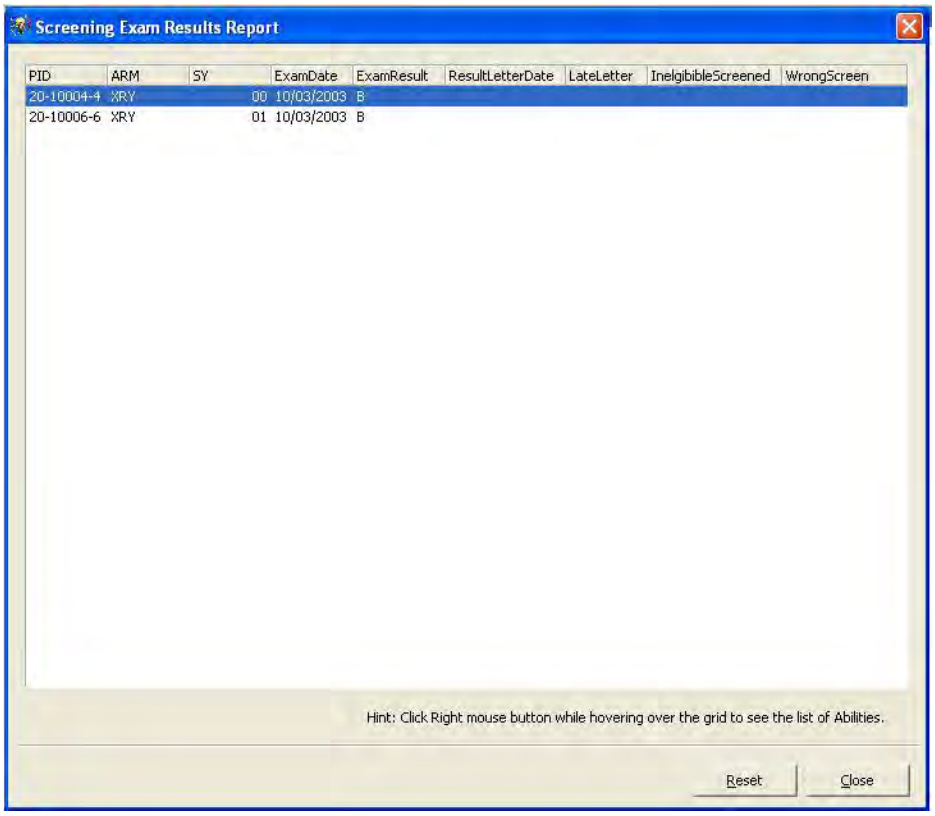
Appendix 11-18 SC Receipt Activity Report



Appendix 11-19 Expected Forms Report



Appendix 11-20 Screening Exam Results Report



Appendix 11-21 Participant Overview Report (POR)

NLST/LSS Participant Overview Report

Participant Information

Participant Name:

PID: 20-10001-1 *Status:* Active

Study Year: 03 *Insurance:*

Randomization Date: 10/01/2002 *Date of Birth:* 11/01/1933

Group: SCT *Date of Death:*

Gender: M

Current Home Address:

H Phone:

W Phone:

Vacation Home/Other Residence:

H Phone:

Scheduling Notes

3/8/2006 10:30:28 AM PID: 20-10001-1 Page 1 of 2

Physician and Hospital Information

Physicians

DR FRANK D GEISER
6666 RESEARCH BLVD SUITE # 2222
ROCKVILLE, MD 20850

Study Form Activity

Study Year	Form	MDF Form(s)	Visit	Receipt Date	Exam Result	Exam Date
00	DE		1	10/14/2005		
00	RAE		1	08/31/2004		
00	SCT		1	04/12/2005	A	02/12/2003
01	ASU			07/28/2005		
01	CDF			09/12/2005		
01	CNF			10/06/2005		
01	DE		1	04/21/2004		

Expected Forms Information

Study Year	Study Form	Expected Receipt Date
00	MDF-MHQ	01/01/2003
00	TI	01/01/2003
01	MDF-CDF - ASU(A)	01/21/2006
01	MDF-CDF - CNF(A)	08/05/2005
02	DE	
02	MDF-ASU	01/01/2005
03	ASU	01/01/2006
03	PCF	01/01/2006

Cancer Information

Study Year	Source	Cancer Description	Status	Status Date
00	SCT	Primary Lung	Confirmed	05/05/2005

Appendix 11-22 Study Progression Report (SPR)

NLST/LSS

Study Progression Report

Study Year		T0	T1	T2	T3	T4	T5	T6	T7	Overall
Randomized Participants	In Window	0	10	28	10	1	0	0	0	49
	Randomized Eligible	0	8	26	10	1	0	0	0	45
	Randomized Ineligible	0	2	2	0	0	0	0	0	4

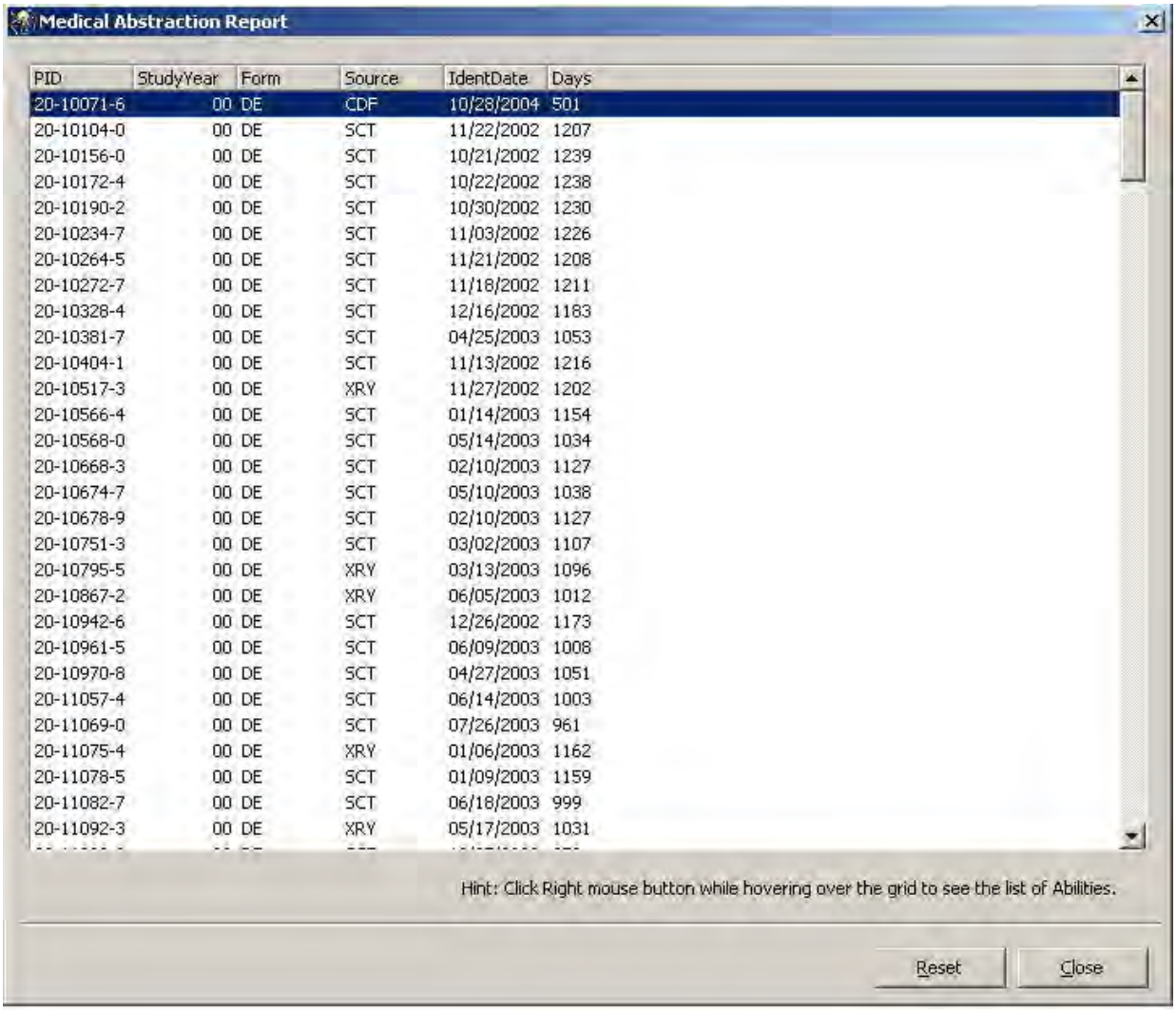
Study Year		T0	T1	T2	T3	T4	T5	T6	T7	Overall
SCT Screens	Screens Eligible	22	22	19	6	0	0	0	0	69
	Screens Completed	0	0	0	0	0	0	0	0	0
	% Screens Completed	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
	Screening MDF	0	0	0	0	0	0	0	0	0
XRY Screens	Screens Eligible	23	23	18	5	1	0	0	0	70
	Screens Completed	0	0	0	0	0	0	0	0	0
	% Screens Completed	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
	Screening MDF	0	0	0	0	0	0	0	0	0

3/9/2005 12:12:26 PM

Page 1 of 1

National Lung Screening Trial / Lung Screening Study (NLST/LSS)

Medical Abstraction Report



Appendix 11-23 Medical Abstraction Report

12. PATHOLOGY TISSUE COLLECTION

12.1 Overview

The CC and SCs will implement the collection of pathology tissue from NLST/LSS participants with resected lung cancer. The period of performance will be twelve months, beginning September 30, 2008.

Pathology tissue from lung cancer patients provides increasing opportunities for the study of biological questions relevant to tumor etiology. The pathological material obtained from this study is expected to have a special role in elucidating the contribution of genetic and proteomic factors that initiate and sustain lung cancer. The pathology specimens for this effort are formalin-fixed, paraffin-embedded (FFPE) tumor tissue blocks.

12.1.1 Study Objectives

The main objective of the Pathology Tissue Collection effort is to answer crucial questions about lung cancer etiology. This collection will be a valuable resource because the tissue will be obtained from a sample of participants who have been well characterized with regard to exposure. In addition, the prospective nature of the trial will allow the study of questionnaire exposure data free of bias from the presence of disease.

Specific objectives are:

- To collect pathology tissue to provide opportunities for research relating risk factors to histological and molecular-pathologic sub-types of lung cancer;
- To study tissue related to epidemiological observations, and
- To study the influence of environmental exposures, hereditary factors, and other types of exposures on molecular lesions.

These goals will be achieved through the collaboration of the NCI, the ten SCs, the CC, the University of Colorado Pathology Department (Colorado), and the UCLA Tissue Array Core Facility (UCLA).

12.1.2 Scientific Background

Pathology tissue specimens previously obtained from NLST/LSS participants will be collected from pathology labs and used to generate tissue microarrays (TMAs). TMAs are produced by removing minute cores from conventional histologic paraffin blocks and placing the cores into an array on a recipient paraffin block. Multiple blocks from various individuals, which may include tumors of varying grades or stages, will be located on the same array.

Histologic slides provide an invaluable way to do evaluations of the significance of potential cancer-associated genes as diagnostic markers or as therapeutic targets for specific cancers. TMA tissue is amenable to analysis by various techniques such as histochemical stains, immunologic stains with either chromogenic or fluorescent visualization, in situ hybridization (mRNA ISH and FISH), and tissue micro-dissection. Compared with conventional paraffin-embedded material, TMAs allow these same types of analyses to be conducted, but on a high-throughput scale without exhausting limited tissue resources. TMAs are created using small cores, sized 0.6 mm in diameter, taken from the original tissue blocks.

Once the original tissue blocks are cored, they can be returned to the pathology lab and any remaining material may be used for conventional histologic sectioning. As a result, generation of TMAs amplifies the limited tissue resource of the tumor tissue. Another benefit of TMAs is that they allow each sample placed in the same array to be treated in an identical way, thereby eliminating slide-to-slide variability often seen with analysis of conventional histologic sections. In addition, TMA analyses require only very small volumes of reagent to analyze an entire cohort.

12.1.3 Tissue Types

The following tissue types will be collected during the Pathology Tissue Collection effort:

- Primary lung cancer – Primary tumors will be collected if the tumor size is 5 mm or greater. All histologic types will be collected.
- Adjacent normal lung tissue – Tissue blocks containing adjacent normal lung tissue will be collected; however, additional benign histologies may be sampled, if available, for the creation of TMAs.

- Resected regional malignant lymph nodes – It is estimated that up to 25% of all lung cancer cases undergoing resection may have involved intrathoracic lymph nodes resected as well. The molecular signatures of regional nodes may differ from that of the primary tumors and the collection of these specimens could yield important information about the spread of lung cancer. Every effort should be made to collect these resected, involved lymph nodes for the creation of TMAs.
- Resected sites of metastatic disease – Resected sites of metastatic disease will be available in an extremely small percentage of lung cancer cases; however, any metastatic lesions in which there has been tissue resected should be obtained for TMA creation.

Each of the tissue types obtained will be processed as specified in Section 12.6.6.

12.1.4 Pathology Tissue Collection Activities

The collection of pathology tissue includes the activities briefly listed below. These activities are described in more detail in subsequent sections of the MOOP, Chapter 12.

- The CC and NCI will develop sample selection criteria.
- The CC will apply the sample selection criteria to all NLST/LSS participants in IDEAS and will notify the SCs of the participant identification numbers (PIDs) of eligible participants.
- The CC will develop procedures and materials for SC use, will create and maintain systems for tracking authorization and requisition activities, and will supply other materials and services as needed. These will include modifications to the existing NLST/LSS data entry system, IDEAS, and the Biological and Environmental Sample Tracking (BEST) software system, the specimen tracking system used at UCLA for PLCO pathology tissue collection.
- The SC will locate pathology reports for each eligible participant to verify cancer information and obtain pathology lab contact information for specimen requests.
- The SC will verify participant consent for pathology tissue collection and, if necessary, the SC will send a Pathology Authorization Form (PAF) to participants for a signature. The SC will follow up with participants to receive outstanding PAFs, and will document the receipt of returned PAFs in IDEAS.
- The SC will abstract information from the pathology report for each participant for whom adequate authorization has been obtained and enter the information into IDEAS.
- The SC will use IDEAS to assemble a requisition packet for each participant for whom blocks will be requested and will submit a requisition packet to the appropriate pathology lab.

- The pathology lab will either ship the requested specimen to the SC, or return the requisition form indicating the reason for no shipment. Non-response by a pathology lab will be followed up with a standard procedure.
- The SC will document receipt of each specimen as well as all correspondence with the pathology lab. The SC will relabel specimens with a sample ID label and IDEAS will retain the link between the originating pathology lab and the specimen. The SC will then ship all specimens on an established schedule to UCLA.
- UCLA will document receipt and quality of each specimen, and will prepare an H & E slide of each tissue block for review by a pathologist at the University of Colorado. The pathologist will annotate regions of interest (ROIs) from which cores should be sampled.
- UCLA will construct TMAs based upon the pathologist's mapping and will retain blocks for permanent storage or, if required by the originating pathology lab, ship to the SC for return.
- SCs will return tissue blocks to the originating pathology lab using support from IDEAS.

12.1.5 Timeline for the Pathology Tissue Collection Effort

Figure 12-1 shows the timeline of activities for the Pathology Tissue Collection effort.

Figure 12-1

Task	10/08	11/08	12/08	1/09	2/09	3/09	4/09	5/09	6/09	7/09	8/09	9/09
SC Coordinator Training Conference Call (overview, authorization, pathology lab information)	X											
CC provides PID lists, template authorization materials, and pathology lab information to SCs	X											
CC provides IDEAS support for authorization and pathology lab information	X											
SCs request IRB approval if necessary	X	X	X									
SCs generate SC-specific materials and receive NCI approval	X	X	X									
SCs contact pathology labs and enter information into IDEAS	X	X	X									
SCs mail Pathology Authorization Forms (PAFs) to participants or next of kin as required, and follow up for authorization		X	X	X								
SCs send de-identified copies of pathology reports to CC		X	X	X								
SC Pathology Lead Training (central and teleconference sessions for overview, block selection, systems support)		X	X									
CC provides systems support for specimen requests, shipping, and tracking		X	X	X	X	X						
SCs abstract pathology reports and request specimens from pathology labs			X	X	X	X						
SCs ship specimens to UCLA			X	X	X	X	X	X	X	X		
UCLA returns specimens to SCs							X	X	X	X	X	X
SCs return specimens to pathology labs							X	X	X	X	X	X
CC performs data cleanup and delivery												X

12.2 Sample Selection

The CC will work with NCI to develop sample selection criteria and will select the potential participants for this effort. The CC will provide each SC with a list of selected participants. The list will be accessible in IDEAS and will include the PID, randomization date, study year of cancer diagnosis, diagnosis date, procedure date, tumor site, tumor size, and ICD-O-3 code. Upon receiving the list, and prior to sending a request for pathology tissue, SC staff will verify the identifying information for each participant by comparing the given information against the participant's pathology report that confirms the cancer diagnosis.

The SC will create a Pathology Tissue Collection (PTC) folder in the participant's study file for each participant selected for the effort. Any documentation related to the effort should be filed in the PTC folder.

12.2.1 Selection Criteria

The selection criteria will include all NLST/LSS participants, in both the spiral CT and chest x-ray arms, with a histologically confirmed diagnosis of lung cancer and the potential for available tumor tissue, as determined by the presence of specific diagnostic procedures on the Diagnostic Evaluation (DE) Form. The procedures of interest include:

- 03 "Biopsy – Lymph node, other (Specify)"
- 04 "Biopsy – Lymph node, scalene (supraclavicular) nodes"
- 09 "Biopsy – Open surgical"
- 29 "Lymphadenectomy/lymph node sampling"
- 30 "Mediastinoscopy/Mediastinotomy"
- 43 "Resection"
- 46 "Thoracotomy"
- 49 "Thoracoscopy"
- 50 "Biopsy – Thoracoscopic"

12.2.2 Confidentiality

The confidentiality of the identity of participants will be maintained. All collected information will be protected in accordance with federal regulatory guidelines. Access to study data will be limited to staff working on the study. All computer data will be maintained in a manner consistent with the Title 21 Code of Federal Regulations (CFR) Part 11. In addition, access to the data management system will be limited to designated staff through the use of a confidential log-in ID and password.

The data from the Pathology Tissue Collection effort will be maintained until the completion of the trial or until it is no longer required for research. Data will be destroyed as required by federal regulatory guidelines.

Human research subjects are protected in accordance with Title 45 CFR Part 46 and Title 21 CFR Part 50. Each SC must obtain approval from its Institutional Review Board (IRB) for the Pathology Tissue Collection effort.

12.2.3 Informed Consent

Human research subjects are protected by informed consent procedures in accordance with Title 45 CFR Part 46 and Title 21 CFR Part 50. The signing of an informed consent form was a criterion for eligibility to participate in NLST. Each SC obtained signed consent from eligible participants before enrolling participants in NLST.

In most cases, the original NLST/LSS study consent form grants permission for study investigators to request and obtain surgical material, such as pathologic tissue, and to use those samples for research involving molecular studies on the development of lung cancer and/or other diseases. If an SC-specific informed consent form does not include permission for the collection of pathology tissue specimens, the SC must administer the Pathology Authorization Form (PAF) to all participants selected for the Pathology Tissue Collection effort. See Section 12.2.5 for more information about administering the PAF.

12.2.4 Contacting Pathology Laboratories

Since a pathology lab may have special loan policy requirements such as requiring use of a proprietary authorization form, a data use agreement, or other special arrangements, the pathology lab should be contacted prior to requesting participant authorization for specimen collection.

The original pathology report from participants with the diagnosis of primary lung cancer will identify the source pathology lab. The SC should contact the pathology lab to establish a relationship and to procure contact information. The SC may find it helpful to identify all selected specimens for the

pathology lab prior to contacting the lab. This information will be helpful for discussions about work load, cost, and scheduling. Initial information to be obtained from the pathology lab includes the following:

- Pathology lab institution name
- Shipping address
- Pathology lab general phone
- Name and position of pathology lab contact person
- Direct phone and fax numbers for pathology lab contact person
- Authorization policy
- Cost per patient or per block
- Cost comments (checks payable to, sent with requests or separately, etc.)
- General loan period
- Pathology lab ID (nickname created by SC)

The SC will determine, record on the Pathology Lab Information Form (PLIF, Appendix 12-1), and enter into IDEAS, the pathology lab contact information, authorization policies, and costs for specimen loans. The SC will determine whether the lab is willing to grant permanent retention of specimens or, if not, what maximum loan period is permitted. A loan period of six months should be requested, but a minimum loan period of three months is required to ensure adequate time for shipping and processing. Payment for requests, if required by the pathology lab, will be managed by the SC in agreement with the pathology lab.

12.2.5 Participant Authorization

Each SC will review the original NLST/LSS study consent form for the selected participants to determine whether consent for pathology tissue collection was provided. The CC also recommends that SCs contact pathology labs to determine whether a copy of the participant's consent form will be accepted as authorization. The SC will send an authorization packet to each participant for whom it is required. The authorization packet will include two copies of the Pathology Authorization Form (PAF, Appendix 12-2), a personalized PAF cover letter generated using the template provided as Appendix 12-3, and a self-addressed stamped envelope. The participant will be asked to sign the PAF and return one copy to the SC in the envelope provided.

If the participant is deceased or unable to provide written authorization due to illness or other reason, the participant's proxy will be asked to give authorization. A template PAF cover letter for next of kin is provided as Appendix 12-4.

The SC will review each completed PAF, store it in the PTC folder of the participant's study file, and document that the authorization was received in IDEAS.

12.2.5.1 Non-Response Follow-Up for Authorization

SCs will need to track the mailing of PAFs to participants for whom it is required. If the SC does not receive a signed PAF from the participant or proxy within two weeks of the initial mailing, the SC Coordinator will initiate non-response follow-up efforts. Each follow-up effort will consist of at least five telephone call attempts to make contact with the participant or proxy, and re-mailing of materials if needed. If a signed PAF is not received within two weeks of the initial follow-up effort, a second follow-up effort is completed. If a signed PAF is not received within three weeks of completing the second follow-up effort, the SC will conclude the effort and document the participant response in IDEAS. The results of non-response follow-up efforts should be documented on a Call Record (Appendix 11-13) to be filed in the PTC folder of the participant's study file.

12.3 Requesting Specimens from Pathology Labs

The SC will review the pathology report for each selected participant and determine the specimens to be requested. Information will be recorded on the Pathology Report Abstraction Form (PRAF) and entered into IDEAS. The SC will then use IDEAS to generate a Pathology Request Form (PRF) and assemble a request packet for each participant for whom specimens will be requested. Additional details regarding these procedures are described in the following sections.

12.3.1 Pathology Report Abstraction

The SC will use IDEAS to generate a Pathology Report Abstraction Form (PRAF, Appendix 12-5) for each participant selected for Pathology Tissue Collection. The PRAF will include pre-filled information from the Diagnostic Evaluation (DE) Form, the Participant Contact Form (PCF), and the Pathology Lab Information Form (PLIF). The SC will review this information as well as the participant's pathology report(s) to identify specific blocks to be requested. The SC will abstract the following information onto the PRAF:

- Participant name (if not pre-filled by IDEAS from the PCF)
- Pathology report date
- Medical record number
- Accession number
- Neoadjuvant therapy
- Related procedure date and code
- Block ID
- Block section

The most representative blocks of lung tumor tissue and adjacent normal tissue should be requested. All histologic types of lung tumors will be requested; however, primary tumors less than 5 mm will not be requested. If available, resected lymph node tissue and/or tissue from a resected metastatic site should also be requested. In most cases, the number of blocks requested will be three: two primary lung and one adjacent normal tissue. If tissue from a lymph node and/or metastatic site is available, the number of blocks requested would be four: two primary lung, one adjacent normal tissue, one lymph node or one metastatic site. In extremely rare circumstances, the SC may request lymph node tissue and tissue from a metastatic site, bringing the total requested blocks to five, although it is possible that one primary lung specimen would be sufficient. Lymph node tissue, if available, should be requested even if primary lung tumor tissue is not available. The exact distribution of tissue type specimen blocks will be decided on a case by case basis. SCs should contact the CC MRA for assistance identifying tissue blocks if needed.

The SC must review the pathology report and abstract information onto the PRAF for each tissue type (primary lung, normal, lymph node, or metastatic). If one or more of the tissue types will not be requested, the SC must indicate the reason on the PRAF. For some participants, it may be determined

that no specimens will be requested. The most common reason for not requesting specimens will be a primary lung tumor that is less than 5 mm. In this situation, the SC will complete the PRAF indicating the reason why no specimens are being requested. Refer to Appendix 12-6, Specifications for Completion of the PRAF, for more information.

A copy of the pathology report for each participant selected for Pathology Tissue Collection should be de-identified and each page labeled with a PID label. Data elements to be de-identified include: personal identifiers (e.g. name, address, date of birth, Social Security number), medical record numbers, and accession numbers. De-identified, PID labeled copies of pathology reports will be shipped to:

Adam DeBaugh
Westat – TB 349
1500 Research Boulevard
Rockville, Maryland 20850

The CC will review the pathology reports to ensure proper de-identification and will scan the reports into digital files for future use at the discretion of NCI.

12.3.2 Pathology Lab Request Packets

After obtaining authorization and loan policy information from the pathology labs, obtaining participant authorization as needed, and selecting blocks to be requested, the SC will assemble a request packet for each pathology lab. Each request may include specimens from multiple participants. Each request packet will include the following items:

- Pathology Request Form (PRF) cover letter, signed by the SC Principal Investigator;
- PRF for each participant for whom specimens are being requested;
- A copy of the original NLST/LSS study consent form, PAF, or pathology lab proprietary authorization form, if required by the lab, for each participant for whom specimens are being requested;
- A copy of the pathology report for each participant for whom specimens are being requested;
- Pre-addressed, postage-paid bubble wrap lined mailer, and shipping materials for pathology lab to send specimens; and
- Payment for requested tissue specimens, if required.

12.3.2.1 PRF Request Cover Letter

The PRF cover letter was designed to simplify the request process and to facilitate rapid retrieval of specimens. The PRF cover letter explains the purpose of the request, describes how loaned specimens will be processed and returned to the originating pathology lab, and requests that specimens be shipped to the SC in the enclosed pre-addressed, postage-paid shipping containers. The PRF cover letter should be signed by the SC Principal Investigator. A template PRF cover letter is provided in Appendix 12-7.

12.3.2.2 Pathology Request Form

The SC will use IDEAS to generate a Pathology Request Form (PRF, Appendix 12-8) for each participant for whom specimens are being requested. The PRF is used by the SCs to request specimens and by the pathology labs to indicate the release of specimens or to document any problems fulfilling the request. The PRF will be returned to the SC from the pathology labs along with the requested specimens or will be returned alone to indicate barriers or reasons for refusal to provide tissues. The PRF is also used by the SC to document the outcome of each requested specimen.

Note that multiple PRFs may be included in a request packet if specimens from multiple participants are being requested at one time. Also, a pathology lab may receive additional request packets as the SC continues to work through the participant selection list, obtains participant authorizations, and abstracts information from pathology reports onto PRAFs.

12.3.2.3 Participant Authorization for Pathology Labs

A copy of the original signed NLST/LSS study consent form for each participant for whom specimens are being requested will be included in the request packet, unless specifically not required by a pathology lab. If required by the pathology lab, a signed copy of the PAF or pathology lab proprietary authorization will be included in the packet in addition to or in place of the original study consent form.

If the participant is deceased, the pathology lab may require documentation of the participant's death in addition to or in place of the study consent form. A copy of the death certificate should be used for this purpose, unless privacy regulations in the state issuing the death certificate prohibit it. If prohibited, the SC will need to ask the state for special permission or document the death for the pathology lab in another manner.

12.3.2.4 Pathology Reports

For each participant, a copy of the pathology report that confirms and describes the primary cancer of interest from which specimen samples will be collected will be included in the pathology lab request packet.

12.3.2.5 Shipping Materials

SCs should obtain and include the appropriate shipping materials in the pathology lab request packet to facilitate shipment of specimens from pathology laboratories. The shipping materials to be included in the pathology lab request packet are:

- One pre-addressed, postage-paid bubble-wrap lined mailer per request (Associated Bag Company part no. 534-2-106, dimensions 6" x 10" or equivalent);
- Zipper Bags for storing and shipping tissue blocks (Associated Bag Company part no. 270-13H, dimensions 3" x 4" or equivalent);
- Zipper Bags for storing and shipping tissue blocks (Associated Bag Company part no. 270-39, dimensions 12" x 12" or equivalent), and
- Shipping address labels.

12.3.3 Non-Response Follow-Up for Specimen Request

In the event that the requested specimens are not received at the SC within three weeks of sending the request packet, the SC Coordinator will contact the pathology lab to confirm that the request packet was received and to determine if further assistance is required. If, after two follow-up attempts,

there is still no response or if the pathology lab refuses to release or loan the requested materials, the SC Principal Investigator or designee will pursue negotiations with the pathology lab staff to gain access to the materials. The result of each follow-up effort will be documented on a hard copy Call Record (Appendix 11-13) and filed in the PTC folder of the participant's study file. SCs can monitor the return of the PRF using the Expected Forms Report in IDEAS.

12.4 Collecting Specimens at the SC

The pathology lab will receive the request packet and review the cover letter and accompanying PRF and materials. If the pathology lab is willing to release the requested specimens, the lab staff will return the PRF and specimens to the SC in the SC-provided pre-addressed, postage paid, bubble wrap-lined mailer. If the pathology lab is not willing to release the specimens, the lab staff will indicate the reason for refusal on the PRF and fax or mail it to the SC.

12.4.1 Receipting Specimens from Pathology Labs

Receipting specimen materials at the SC involves review of both the completed PRF and the specimens. The SC will implement the following procedures for receipting specimens:

1. Check to see that a completed PRF was returned. If the PRF is missing or incomplete, contact the pathology lab to obtain a completed form.
2. Verify that each specimen corresponds to tissue requested, or has been documented on the PRF by the pathology lab. If there are any undocumented discrepancies, contact the pathology lab and complete a Discrepancy Notification Form (Appendix 12-9).
3. Check each specimen for damage. If a block is damaged, contact the pathology lab to report the damage and to request a replacement block if needed and available. Damaged blocks should be returned to the originating pathology lab. If the SC is uncertain as to the viability of a block, the specimen should be shipped to UCLA to determine if the block can be processed.
4. For each specimen requested on the PRF, and for any additional specimens received and documented on the PRF by the pathology lab, enter the information from the PRF into IDEAS, including whether the specimen was received, the date received, and the status code. If no specimens were received, enter the appropriate PRF status code into IDEAS. If one block was received for multiple tissue types requested, one tissue type must be receipted into IDEAS and the remaining tissue type(s) marked as not received, using the appropriate PRF status code.

5. Label each specimen to be shipped to UCLA with a sample ID label and attach identical labels to the participant's pathology report (see Section 12.4.2). The SC may also attach identical labels to the PRAF or PRF for documentation and streamlined entry into IDEAS. The SC should ensure that any protected health information is de-identified prior to sending the specimens to UCLA.
6. Enter the sample ID label number for each specimen into IDEAS via barcode scanning as the specimen is receipted.
7. If a received specimen will not be forwarded to UCLA because it was not requested and is not needed, is an unknown specimen, or is unusable for any reason, the specimen should be receipted into IDEAS with the appropriate status code and and should not be labeled with a sample ID label. The SC must contact the originating pathology lab for problem resolution and for return and refund arrangements, as needed.

12.4.2 Labeling and Storing Specimens from Pathology Labs

For tracking purposes, the CC developed a specimen labeling scheme using Biospecimen Inventory system ID labels (BSI ID) labels. This is the labeling system used by the NCI biospecimen repository. The CC will supply each SC with pre-printed, bar-coded labels for labeling specimens and forms. As requested specimen blocks are received from pathology labs, the SC will label each specimen to be sent to UCLA with a BSI sample ID label, attach duplicate labels to a copy of the participant's pathology report, and receipt blocks into IDEAS. The SC may also attach duplicate labels to the PRAF or PRF for documentation purposes and/or to facilitate entry into IDEAS. Sample ID labels are printed in a bar-coded and eye-readable format and will be used in sequential order as specimens are received from pathology labs.

If a pathology lab applied identifier is visible on a block after application of the sample ID label, supplied blank labels should be used as needed to mask the identifier. SC sample ID labels have a removable adhesive, and they will be removed prior to eventual return to the originating pathology labs.

The BSI ID number printed on each sample ID label will identify each tissue block belonging to a participant. The sample ID numbers have a BSI format, AA NNNNN NNNN:

- AA: two letter alpha prefix
- NNNNN: zero padded 5-digit "root" number
- NNNN: 4-digit "sequence" number

If multiple blocks are obtained for a single participant, each will have the same "root" number and an incremental "sequence" number. If a single participant has multiple primary lung cancer diagnoses, each lung cancer diagnosis will have a separate "root" number. Follow the procedures given below to label the tissue blocks:

1. Peel and attach the sample ID label on the side-edge of the paraffin block cassette.
2. Attach the duplicate label on the corresponding pathology report.
3. Use blank labels to cover identifiers elsewhere on the cassette.
4. Place the cassette in a small (2" x 3") Zipper Bag.
5. Place each bag in a 5½" x 5½" x 2" (or 3") storage box.
6. Store in a cool place until the next scheduled shipping date to UCLA.

12.5 Shipping Specimens to UCLA

The pathology specimens collected for this effort are formalin-fixed and preserved in paraffin blocks by the pathology labs. Prior to shipment, the specimens should be stored in a cool, dark container and be protected from excessive light and temperature to prevent deterioration of the wax and embedded tissue.

Weather problems, holiday schedules, and end-of-week shipping may cause specimen shipment delays, which the SC should work to avoid. Shipping methods should take seasonal temperatures into account, and include use of extra insulated packaging, overnight delivery, and a cooling agent, as needed. The standard shipping package for a specimen will include a zipper bag inside a storage box inside a foam-insulated shipping box known as a bioshipper.

All non-problematic specimens obtained from pathology labs will be shipped to UCLA every two weeks by overnight courier. Specimens will be shipped with a paper copy of the IDEAS-generated UCLA Pathology Transmittal Form (Appendix 12-10) and appropriate pathology reports. A data file including data from the PRAF will also be created by IDEAS for transferring to UCLA. Information related to the specimen shipment will be automatically stored in IDEAS.

SCs will ship specimens to UCLA according to the shipping scheduled provided by the CC. On the day of shipment, the SC Coordinator will notify UCLA by e-mail of the upcoming shipment with

estimated date of arrival. Upon receipt of the specimens, UCLA will reconcile the materials and identify any missing or damaged specimens. UCLA will contact the SC to resolve any problems.

12.5.1 Shipping Materials

The appropriate shipping materials for shipping tissue specimens to UCLA are:

1. Storage boxes for blocks (Bell Metal Specialty, dimensions 5" x 5" x 2").
2. Multi-purpose insulated bio-shippers (Polyfoam Packers part 325UPS, internal dimensions 11-5/8" x 9-7/8" x 7").

12.5.2 Shipping Task Checklist

The SC should complete the following tasks on the day of a scheduled shipment to UCLA:

1. Select the specimens to be shipped and prepare a shipping transmittal in IDEAS. The SC staff member preparing the transmittal must verify the loan period for each block prior to generating the transmittal. This information is critical to UCLA for prioritizing specimen processing. In addition, special circumstances pertaining to a shipment, such as the inclusion of multiple tissue types on one block, should be handwritten on the transmittal form.
2. Mask corresponding pathology reports for personal identifiers, including PID. Do not mask the sample ID labels.
3. Prepare and send a notification e-mail (stze@mednet.ucla.edu) or fax (310-267-2940) to UCLA listing the specimens being shipped, including the number of storage boxes, courier tracking number, and the expected date of arrival.
4. Place the transmittal form, a floppy disk or CD with the data file generated by IDEAS after the transmittal, and pathology reports inside a Zipper Bag and place the bag inside the bottom of the corrugated fiberboard shipping container box (8" x 8" x 4¼").
5. Pack the storage boxes containing specimens in the shipping container.
6. Place packing materials such as paper towels or crumpled newspaper around and between the storage boxes to prevent them from shifting during transit.
7. Seal the shipping container with strong tape.
8. Label each shipping container with an express courier label and address labels.

9. Send the package using an overnight traceable courier service such as FedEx to:

   Attention: Sheila Tze
   UCLA Tissue Array Core Facility
   650 Charles E. Young Drive South
   Reed Building, Room 3243
   Los Angeles, CA 90095

10. File a copy of the transmittal form in the PTC folder of the participant's study file.
11. Upload the IDEAS-generated shipment data file into BEST.

12.5.3 Shipping Schedules

Specimens will be shipped to UCLA according to a shipping schedule developed by the CC and UCLA. Shipments to UCLA are scheduled for every two weeks for each SC and are limited to Monday, Tuesday, and Wednesday in order to minimize the chance of an over-weekend delivery delay. If no specimens are to be shipped on a scheduled day because there are no specimens to send, the SC should notify UCLA. If no specimens are to be shipped on a scheduled day for any other reason, such as holiday or office closure, the SC should contact UCLA to discuss the possibility of a make-up shipping day. If an SC would like to ship on a date other than an assigned shipping date, approval from UCLA must be obtained in advance. Such requests should only be made if necessary (e.g. to expedite a specimen with a short loan period). The CC will monitor the number of specimens shipped to UCLA so as not to exceed the maximum number of specimens that can be processed each month.

12.6 Specimen Processing at UCLA

The following sections provide an overview of the procedures used by UCLA, including specimen receipt, preparing new sections, shipping representative slides of paraffin blocks to the Colorado for standardized pathology review, pathology review at Colorado, slide receipt from Colorado, and array construction.

12.6.1 Specimen Receipt

Specimens are unpacked and inspected for shipping damage and for completeness according to the transmittal and the SC is notified of any problems. UCLA assigns a lab-specific ID to each block,

and enters this along with the BSI ID, other specimen information, and receipt and problem information. Pathology reports are assigned specimen-matching IDs and filed in ID order in a notebook for future reference if needed.

UCLA creates a "patient" in the database based on random code. This corresponds one-to-one to each participant included in a specimen shipment. A case code is assigned, corresponding one-to-one with each specimen or BSI ID root number. Blocks are entered with the BSI ID as inventory in the database. Blocks from each shipment are stored by the date the shipment was received, grouped by SC and BSI ID order in dedicated block histology boxes, marked with NLST/LSS and date of receipt. Marker cards will be used to group the blocks for each case, or specimen.

UCLA will periodically upload information that updates the status of the specimens to BEST. The SC will be able to log in to BEST to track the status of all specimens shipped to UCLA.

12.6.2 Preparing Sections

UCLA lab protocol will be followed for preparing new sections. This includes pre-labeling of slides, cutting pre-cooled blocks in 4 μm sections down to a full-face section, floating, and mounting sections on slides. Once a full-face is obtained, UCLA will cut one 4 μm slide per block for H&E staining to determine core location(s) and for nucleic acid studies. Lab protocol will be followed for H&E staining.

12.6.3 Shipping Slides to Colorado for Standardized Pathology Review

UCLA will securely package slides in a slide box within a padded, corrugated box for shipment to the University of Colorado reviewing pathologist. This shipment will include the slides to review, a copy of the corresponding pathology reports, and the NLST Colorado Unique Primary Tumor (CO) Form and the NLST Colorado Target Annotation (TA) Form (Appendix 12-11) to denote which specific blocks contain the annotated histologies. UCLA will update the database inventory to reflect the new location of the slides on the day of shipment to Colorado. Slides will be shipped to:

Department of Pathology
UCDHSC at Fitzsimons
Bldg RC-1, South Tower
Rm. L18-5104
12801 East 17th Ave.
Aurora, CO 80045-0508

12.6.4 Standardized Pathology Review

The histological description of the tissue section will be compared with that of the histology laboratory and will become the baseline diagnosis. UCLA will confirm that donor block is of good quality with adequate tissue. The reviewing pathologist at Colorado will receive an H&E slide and a copy of the corresponding pathology report for each block. The pathologist will note his/her histological diagnosis and circle representative areas for each of the following tissue types:

- Tumor: Primary invasive histology; secondary invasive histology, and carcinoma in situ
- Benign/normal: Adjacent normal lung tissue, benign lymph node tissue, proximal bronchus and distal bronchiole
- Metastatic: Involved lymph nodes (local) and distant metastases

Colorado will prepare a printed color transparency of the digitally annotated slides (one enlarged size and one actual size on the same transparency) and ship them to UCLA with the completed NLST CO and TA Forms, pathology reports, and unmarked slides with Colorado barcode labels. The review process of the slides will be given a two week turn around time.

12.6.5 Slide Receipt from Colorado

UCLA will update the database inventory to reflect the new location of the slides on the day of receipt of shipment from Colorado. A quality control check of the annotated areas matched with the corresponding blocks will be done to make sure that the area annotated on the slide has enough tissue area and depth on the block loaned from the originating pathology lab.

12.6.6 Array Construction and DNA Isolation

UCLA will perform the following for each of the four tissue types listed in section 12.1.3. The sample and coordinate information for each core taken will be recorded in the UCLA database.

Primary Tumor

- Take two (2) cores of 0.6 mm from up to three (3) sites of the primary cancer, main histology, (six total cores) for duplicate sets of TMAs. The cores should be widely sampled regionally within the main tumor regions of interest (ROI) (e.g., AdenoCa, grade 3). Cores should focus on areas matching highest case grade where available.
- Take two (2) cores of 0.6 mm from up to three (3) sites of the primary cancer of secondary invasive histology (six total cores), if available, for duplicate sets of TMAs. The cores should be widely sampled regionally within the tumor of secondary invasive histology ROI(s) (e.g BAC component, from mixed invasive AdenoCA and BAC).
- Take two (2) cores of 0.6 mm from up to three (3) sites of carcinoma in situ, (six total cores), if available, for duplicate sets of TMAs.
- Take one (1) core of 0.6 mm from up to three (3) sites of the primary cancer of main histology to place in Eppendorf tubes for DNA isolation.
- Take one (1) core of 0.6 mm from up to three (3) sites of the primary cancer of secondary invasive histology, if available, to place in Eppendorf tubes for DNA isolation.
- Take one (1) core of 0.6 mm from up to three (3) sites of carcinoma in situ, if available, to place in Eppendorf tubes for DNA isolation.

Normal Lung Tissue

- Take two (2) cores of 0.6 mm from three (3) sites of adjacent normal lung tissue (six cores total) for duplicate sets of TMAs.
- Take two (2) cores of 0.6 mm from one (1) site of normal proximal bronchus (two cores total) and one (1) site of normal distal bronchiole (two cores total), if available, for duplicate sets of TMAs.
- Take one (1) core of 0.6 mm from up to three (3) sites of adjacent normal lung tissue to place in Eppendorf tubes for DNA isolation.

Involved Lymph Nodes/Metastatic Lesions

- Take two (2) cores of 0.6 mm from up to three (3) sites of local (involved lymph node) or distant metastatic lesion (six total cores), if available, for duplicate sets of TMAs.
- Take one (1) core of 0.6 mm from up to three (3) sites of local (involved lymph node) or distant metastatic lesion, if available, to place in Eppendorf tubes for DNA isolation.

Benign Lymph Nodes

- Take two (2) cores of 0.6 mm from up to three (3) sites of benign lymph node tissue (six total cores), if available, for duplicate sets of TMAs.
- Take one (1) core of 0.6 mm from up to three (3) sites of benign lymph node tissue, if available, to place in Eppendorf tubes for DNA isolation.

If multiple blocks are obtained for a single tissue, cores may be distributed from among the blocks for improved capture of heterogeneity, selection of tumor and uninvolved tissue, and block preservation. After coring, UCLA will fill voided areas in the block with additional paraffin. The CC will work with UCLA to link CC and UCLA systems for receipt, shipment, and tracking support. TMAs are stored in lidded containers such as Petri dishes with Parafilm covers to prevent cores from sticking to the container. Room temperature allows for indefinite storage.

If the originating pathology lab limits the number of 0.6 mm core samples that can be obtained on a given block, priority will be given to the primary TMA, then to DNA cores, then to the duplicate TMA. For all cases, the maximum number of core samples to be taken should be 18 per block and 39 per case. If additional cores are to be sampled for a given block or case due to the presence of numerous tissue types, UCLA will contact the SC to obtain approval from the originating pathology lab. If additional cores cannot be taken, the priority of punches should be as follows: primary tumor histology, secondary invasive tumor histology, carcinoma in situ, adjacent normal lung tissue, metastatic lesion, benign lymph node, proximal bronchus, and distal bronchiole.

12.7 Returning Loaned Specimens

A specimen obtained for permanent retention will be stored at UCLA after processing. A loaned specimen will be returned by the SC to the originating pathology lab within the loan period. Prior to return to the SC, a processed specimen will be repaired by filling punched holes with molten paraffin. The specimen will then be "checked out" of the UCLA database inventory, packed in original packaging and shipped to the SC with advance notification, including courier tracking number. UCLA will regularly upload status information to BEST for access by the SCs.

The SC receipts each returned specimen and, if needed, contacts UCLA to resolve any discrepancy or problem with the shipment. The SC batches and ships specimens to originating pathology

labs as needed to meet loan period deadlines. A Pathology Lab Transmittal Form for returning specimens to originating pathology labs is generated in IDEAS (Appendix 12-12). Materials are packaged as described for specimen shipments to UCLA. BSI sample ID labels and any blank masking labels are removed prior to packaging for return. The SC is responsible for returning the block within the timeframe required by the pathology lab.

12.8 Coordination Activities

The CC will coordinate all activities related to the Pathology Tissue Collection effort and will serve as liaison for the SCs, NCI, and UCLA. Coordination efforts will include: development of the protocol documentation, forms, and template materials; supplying SCs with sample ID labels; and providing computerized systems support (IDEAS and BEST). Additional coordination efforts include training SC staff, maintaining regular communication with the SCs and UCLA, and reporting progress to NCI.

12.8.1 Training SC Staff

The CC will conduct a one-day central training session to prepare SC staff to successfully perform tasks in a consistent and standardized fashion. Compliance in execution of the protocols by the SCs will be critical to ensuring that the Pathology Tissue Collection effort conforms to all procedural and regulatory requirements in a standardized manner. The central training session will provide an opportunity for introduction to and discussion of procedures, timelines, data collection instruments, specimen collection materials, and systems support for the Pathology Tissue Collection effort. One staff member from each SC will attend the training to ensure that all SCs hear the same instructions and that study procedures are carried out in a standardized manner.

The SC Coordinator is responsible for identifying the appropriate staff member to attend the central training session. The SC Coordinator, or representative, will be responsible for training other SC staff members as necessary. SC staff working on the Pathology Tissue Collection effort should refer to this chapter, as well as CC-provided training materials and IDEAS documentation to ensure standardized training.

12.8.2 Communication

The CC will arrange conference calls at least monthly to address any questions or concerns about Pathology Tissue Collection and to discuss progress of the effort. Conference calls will include representatives from the SCs, NCI, and UCLA.

12.8.3 Systems Support

The CC-provided IDEAS will be used to support the Pathology Tissue Collection effort and will have the following features:

- Storage and update of sample selection information.
- Templates for generating authorization and request forms and letters. Template documents for cover letters and the PAF can be stored in IDEAS for easy access.
- Functions for storing participant and pathology lab information. IDEAS will store pathology lab and specimen data as well as dates for mailing, shipping, and receipt.
- Templates for generating transmittal forms for shipment from the SC to UCLA and for shipments from the SCs to the originating pathology labs.
- Functions for monitoring activity using the Expected Forms Report in IDEAS and the BEST system. Detailed status reports will be generated by the CC and provided to the SCs at least monthly or more often as requested. Sample status reports are included as Appendix 12-13.

SC staff should refer to the *NLST/LSS Pathology Tissue Collection IDEAS Instructions* for additional information regarding the use of IDEAS to support Pathology Tissue Collection activities.

The CC-provided BEST system will provide support for tracking specimens shipped to UCLA. Together, IDEAS and BEST will provide the SCs with the functions for shipping specimens to UCLA, and for tracking data associated with the shipment for reconciliation purposes. The SCs will utilize IDEAS to generate a data file of specimens to be shipped to UCLA and will then access BEST to upload the data file for receipt by UCLA.

Specimen tracking activities at UCLA will also be supported by BEST, which will provide UCLA with the ability to view specimens shipped from the SCs, and receipt and track the specimens. BEST supports an interface with the pathology tissue inventory system at UCLA. Additionally, the CC will use BEST to monitor and support the Pathology Tissue Collection effort. Refer to the *NLST/LSS Pathology Tissue Collection BEST Instructions* for additional information regarding the BEST system.

Appendices for Chapter 12

Pathology Lab Information Form

Lab ID* _____

Lab Institution Name* _____

Street Address 1* _____

Street Address 2 _____

City* _____

State* _____ **Zip Code** _____

Lab Phone **(_____)** _____ - _____

Contact Name _____

Contact Position _____

Contact Phone **(_____)** _____ - _____

Contact Fax **(_____)** _____ - _____

Authorization Policy* ____ **Not required (Consent form adequate)**

____ **PAF**

____ **Proprietary**

____ **No Loan Policy**

Cost _____

Cost Comments _____

Loan period* _____

Loan Period Comments _____

**denotes fields required by IDEAS*

Appendix 12-2: Participant Authorization Form (PAF)

Letterhead of Screening Center

PID Barcode
PID

National Lung Screening Trial (NLST)

Authorization to Release Surgical Material and Related Health Information
that Identifies You for Research

Your signature below gives permission to staff at <<PathLabName>> to release surgical material (also known as pathology specimen) and related health information obtained during your diagnosis or treatment of lung cancer or related condition. The surgical material will be used for research in lung cancer detection, prevention, and treatment by the ongoing National Lung Screening Trial (NLST), in which you are a participant.

The health information to be released for this research includes the surgical material and any identifying information attached to the material such as a specimen ID, medical record number, or your name. Additionally, a copy of the pathology department report on the surgical material may be released if your local NLST screening center does not already have a copy.

The materials listed above may be released to and used by your local NLST screening center, identified at the top of this form, and to the NLST central laboratory: University of California at Los Angeles Tissue Array Core Facility. Only the screening center and central laboratory staff involved with NLST research will have access to your materials listed above.

<<PathLabName>> is required by law to protect your health information. By signing this document, you authorize them to release your health information for this research. Your local NLST screening center and the NLST central laboratory have agreed to hold your health information in confidence, to use it only for study purposes, and not to release it to anyone other than the study team unless required by law.

Your medical treatment will not be affected in any way based on your decision to sign or not sign this Authorization.

You may change your mind and revoke, or take back, this Authorization at any time, except to the extent that actions have already been taken based on this Authorization. To revoke this Authorization, contact your local NLST screening center. This Authorization does not have an expiration date.

Signature of participant *or* participant's personal representative	Date signed
Printed name of participant *or* participant's personal representative	If applicable, description of personal representative's authority to sign for participant

Appendix 12-3: Cover Letter for Participant Authorization Form

Letterhead of Screening Center

National Lung Screening Trial (NLST)

<<DateAuthToPpt>>

<<ParticipantName>>
<<ParticipantAddress>>

Dear <<ParticipantTitle>> <<ParticipantName>>:

Thank you for your continuing participation in the National Lung Screening Trial.

Our records show that, since the time you started with the NLST, you have had a lung related medical procedure. We would like to obtain a small amount of the surgical material (also known as pathology specimen) that was removed and preserved after your procedure. This will help future cancer research.

To allow us to obtain the material from the pathology lab, please sign the Authorization Form included with this letter. We have enclosed two copies of the form. Please read, sign, and return one copy to us in the enclosed postage-paid envelope. The other copy is for your records.

As you know, you have already given us consent for your involvement in the NLST, but now because of the important new HIPAA laws that are designed to protect the privacy of your medical information, we are asking for this additional "authorization" to obtain a pathology specimen from the pathology lab.

If you have any questions about this request or the NLST, please call me or your NLST study coordinator, <<SCCoordinator>>, at <<SCPhone>>. Thank you very much for your help with our continuing research.

Sincerely,

SC PI
SC PI Title
SC Name
SC Address

Enclosures: Authorization Form (two copies), return envelope

Appendix 12-4: Next of Kin Cover Letter for Participant Authorization Form

Letterhead of Screening Center

National Lung Screening Trial (NLST)

<<DateAuthToNextofKin>>

<<Nextof KinName>>
<<NextofKinAddress>>

Dear <<NextofKinTitle>> <<NextofKinName>>:

We very much appreciate <<ParticipantName>>'s participation in the National Lung Screening Trial.

Our records show that, after enrolling in NLST, <<ParticipantName>> had a lung related medical procedure. We would like to obtain a small amount of the surgical material (also known as pathology specimen) that was removed and preserved after the procedure. This will help future cancer research.

To allow us to obtain the material from the pathology lab, please sign the Authorization Form included with this letter on behalf of <<ParticipantName>>. We have enclosed two copies of the form. Please read, sign, and return one copy to us in the enclosed postage-paid envelope. The other copy is for your records.

<<ParticipantName>> has already given us consent for involvement in the NLST, but now because of the important new HIPAA laws that are designed to protect the privacy of medical information, we are asking for this additional "authorization" to obtain a pathology specimen from the pathology lab.

If you have any questions about this request or the NLST, please call me or the NLST study coordinator, <<SCCoordinator>>, at <<SCPhone>>. Thank you very much for your help with this continuing research.

Sincerely,

SC PI
SC PI Title
SC Name
SC Address

Enclosures: Authorization Form (two copies), return envelope

PATHOLOGY REPORT ABSTRACTION FORM (PRAF)

ADMINISTRATIVE SECTION

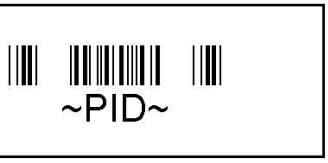
Date Abstracted: |___|___| / |___|___| / |___|___|___|___|

Staff ID: |___|___|___|___|

Screening Center ID: _____

Study Year: _____

Multiple DE#: _____



PART A: Lung Cancer Diagnosis Information

This section will be pre-filled by IDEAS

1. Date of Pathologic Confirmation: _____
2. ICD-O-3 Code: _____
3. Pathologic Type: _____
4. Grade of Primary Invasive Lung Cancer: _____
5. Pathology Lesion Size (mm): _____
6. Targeted DE Procedures:

Procedure Date	Procedure Code	Procedure Description
_____	_____	_____
_____	_____	_____
_____	_____	_____
_____	_____	_____
_____	_____	_____
_____	_____	_____
_____	_____	_____
_____	_____	_____

Appendix 12-5: Pathology Report Abstraction Form (PRAF)

~PID~

PART B: Pathology Tissue Block Information

Questions 7–9 and 13 will be pre-filled by IDEAS. Questions 10-12 and 14 are to be completed by SC Staff.

7. Participant Name: _____
8. Pathology Lab ID: _____
9. Loan Period: _____
10. Pathology Report Date: |___|___| / |___|___| / |___|___|___|___|
11. Medical Record Number: _____
12. Accession Number: _____
13. Neoadjuvant therapy? _____
14. Record block information for two blocks of primary lung tissue and one block each of normal lung tissue, lymph node tissue, and metastatic tissue. If requesting a block, record the tissue type, procedure date, procedure code, block ID, and block section, then record 02 in Status Code. If not requesting a block, record the tissue type, then skip to the Status Code field and enter the code that reflects the reason the block is not being requested. Additional blocks requested and replacement blocks from the lab are also to be recorded here.

Tissue Type	Procedure Date	Proc Code	Block ID	Block Section	Status Code	Date Received	BSI ID

Tissue Type
T – Primary lung
L – Normal lung
N – Lymph nodes
M – Metastatic site

Status Codes
00 – Not obtained
01 – Obtained, but tissue size <5 mm
02 – Requesting block
03 – Obtained, but not malignant (N or M)

Specifications for Completion of the Pathology Report Abstraction Form (PRAF)

The purpose of the Pathology Report Abstraction Form (PRAF) is to document appropriate pathology specimens from the pathology report for request from pathology labs. This form is to be completed for all participants selected for Pathology Tissue Collection that have appropriate authorization for specimen collection.

Specifications for completing each item of the form are as follows:

Administrative Section:

Participant ID Label: The PID will be pre-filled by IDEAS.

Date Abstracted: Record the date the pathology report was abstracted. This is the date the form was completed. Zero fill month and day, if necessary, and record the last two digits of the year (e.g., 12/02/2008).

Abstractor ID: Record the four-digit staff ID number assigned to the individual who is abstracting the pathology report and completing the PRAF.

Screening Center ID: The two-digit SC ID number will be pre-filled by IDEAS.

Study Year: The study year in which the participant was diagnosed with lung cancer will be pre-filled by IDEAS.

Multiple DE: The multiple Diagnostic Evaluation (DE) item will be pre-filled by IDEAS and indicates additional primary invasive lung cancers diagnosed simultaneously with or subsequent to the first primary invasive lung cancer within the same study year. Synchronous primary invasive lung cancers (diagnosed simultaneously) may be different histologies or be located in different parts of the lung and each should have been recorded on a separate DE Form.

Part A: Lung Cancer Diagnosis Information:

This section will be pre-filled by IDEAS and includes the following information as recorded on the DE Form completed for this primary invasive lung cancer diagnosis:

1. **Date of Pathologic Confirmation:** This item corresponds to the DE response in Item C.14b and represents the date that the procedure was performed that collected the most tissue and confirmed the primary invasive lung cancer diagnosis.

2. **ICD-O-3 Code:** This item corresponds to the DE response in Item C.11a and represents the classification of the primary invasive lung cancer according to ICD-O-3 and should be based on histology, if available.

3. **Pathologic Type:** This item corresponds to the DE response in Item C.14a and represents the ICD-O-3 morphology code and behavior for the type of cell composing the tumor, usually determined by the pathologist from a tissue specimen.

4. **Grade of Primary Invasive Lung Cancer:** This item corresponds to the DE response in Item C.15 and documents the histopathologic grade of the primary invasive lung cancer.

5. **Pathology Lesion Size (mm):** This item corresponds to the DE response in Item C.13 and documents the size of the tumor (lesion) at its maximum dimensions in millimeters. This information may have been determined from the pathology report, operative report, or radiology report.

6. **Targeted DE Procedures:** These items correspond to the DE responses in Item A.3 and documents diagnostic or staging procedures that may have procured tumor material or indicated a surgical approach.

Part B: Pathology Tissue Block Information:

7. **Participant Name:** The participant name will be pre-filled with the PCF data if available. The name can be modified or added as needed.

8. **Pathology Lab ID:** The pathology lab ID linked to this participant during the authorization process will be pre-filled by IDEAS.

9. **Loan Period:** The loan period that corresponds to the Pathology Lab ID from the Pathology Lab Information Form will be pre-filled by IDEAS.

10. **Pathology Report Date**: Record the month, day, and year of the pathology report. The pathology report date may be different than the date of the diagnostic or surgical procedure that procured the specimen.

11. **Medical Record Number:** Record the medical record number as it appears on the pathology report. The medical record number is used to identify an individual and his/her medical record information. The number may be either numeric or a combination of alpha and numeric characters.

12. **Accession Number:** Record the laboratory accession number as it appears on the pathology report. This is the number assigned to the sample when it arrives at the laboratory and may be either numeric or a combination of alpha and numeric characters.

13. **Neoadjuvant Therapy?:** Record whether or not the participant received neoadjuvant therapy. Neoadjuvant therapy is treatment given before the primary treatment. Examples of neoadjuvant therapy include chemotherapy, radiation therapy, and hormone therapy.

14-17. **Tissue Blocks:** Complete each of the lines in Items 14 through 17 regardless of whether any blocks of a particular tissue type will be requested. Each possible block request must be accounted for in IDEAS.

- **Procedure Date:** Record the month, day, and year of the procedure that procured the specimen. This date may be different than the pathology report date. If no blocks are requested, leave this item blank.

- **Proc Code:** Record the procedure code associated with the specimen. If no blocks are requested, leave this item blank.

- **Block ID:** Record the block ID that identifies the specimen. The block ID is the basic identifier appearing on a pathology specimen block and is usually denoted by an alpha character. If no blocks are requested, leave this item blank.

- **Block Section:** Record the block section number of the most representative section of specimen. If no blocks are requested, leave this item blank.

- **Status Code:** Record the appropriate status code for each block requested. If no blocks of a particular tissue type are being requested, record the status code that describes the reason why.

    - 00 – Not Obtained
    - 01 – Not Requesting – Tissue size < 5 mm
    - 02 – Requesting Block
    - 03 – Obtained, not malignant (N or M)

After Completing the Form

- The form should be checked to make sure it is accurate, legible, and complete.

- Enter the form into IDEAS.

- File the form in the PTC folder of the participant's study file.

Appendix 12-7: Cover Letter for Pathology Request Form

Letterhead of Screening Center

National Lung Screening Trial (NLST)

Date

Director, Pathology Department
Pathology Lab Name
Pathology Lab Street Address
Pathology Lab City, State Zip Code

Dear Director of Pathology Department,

We are writing to request your participation in a pathology tissue collection effort for the National Lung Screening Trial (NLST). *SC Name* is one of ten screening centers in the United States collaborating with the National Cancer Institute (NCI) on this study. The purpose of the NLST is to determine whether imaging-based screening reduces lung cancer-specific deaths. Pathology specimens offer great potential for increasing our understanding of lung cancer and its genetic and environmental causes as well as for improving lung cancer prevention and treatment efforts.

The formalin-fixed, paraffin-embedded tissue blocks (FFPE) collected will be used to construct tissue microarrays (TMAs). From each block, one 4μm slide will be cut for H & E staining. Based upon this slide, up to twelve 0.6 mm cores of the tumor and six 0.6 mm cores of adjacent normal tissue will be removed for TMA construction. If multiple blocks are obtained for a single tissue, cores may be distributed from among the blocks for improved capture of heterogeneity, selection of tumor and normal tissue, and core preservation. If lymph node tissue is obtained, up to nine 0.6 mm cores will be removed and, if tissue from a metastatic site is available, a minimum of four and up to twelve 0.6 mm cores will be removed. The voided areas in each FFPE block will be repaired with molten paraffin prior to their return.

The NLST participant(s) listed on the attached Pathology Request Form(s) have given signed consent and/or authorization to collect pathology material from cancer-related procedures during this trial. For each participant, a copy of the consent and/or authorization is attached along with a copy of the pathology report pertinent to this pathology material.

The Pathology Request Form specifies the material we are requesting. For tumors, we are requesting the most representative specimen(s) of primary tumor with tumor-free margin. If available, we are also requesting lymph node and/or metastatic tissue specimens. Please indicate on the Pathology Request Form your response to each request, including any problems in fulfilling our request. Please also indicate your preferred loan period for the material. We are requesting a six-month loan period; however, a minimum loan period of three-months will be required to process the specimen block(s).

Please ship the specimen(s) and a copy of the Pathology Request Form using the enclosed self-addressed, postage paid shipping materials. Please advise us of any additional costs associated with this request for preserved tissue. If you are unable to ship the requested specimen(s), please fax the Pathology Request Form to *SC Coordinator* at *SC Fax*.

Thank you for your assistance with this research. If you have any questions, please call me or our NLST study coordinator, *SC Coordinator* at *SC Phone*.

Sincerely,
SC PI
SC PI Title
SC Name
SC Address

Enclosures: Pathology Request Form, Authorization Form(s), return envelope

Appendix 12-8: Pathology Request Form (PRF)

National Lung Screening Trial (NLST)
Pathology Request Form

Path Lab Name:
Participant Name:
Date of Birth:
Medical Record Number:
Accession Number:

~PID~

The NLST participant listed above reported diagnostic procedures at your institution. Please send the paraffin blocks requested below. If there is a more representative block of primary lung tumor tissue, please send it in place of the requested primary lung tumor block, noting the relevant information in a blank grid row. Please complete the Pathology Lab columns to indicate the status of each requested specimen and **ship this form** and the requested specimens using the enclosed pre-paid packaging. If no specimens will be shipped, please indicate the reason below and **fax this form** to <<SCFax>>. Thank you for your assistance.

☐ No specimens shipped Reason ____________________

SC Status Code

Tissue Type	Procedure Date	Block ID	Block Section	Path Lab Use Only Shipping status	Path Lab Use Only Reason not shipped	SC Use Only Specimen receipt	SC Use Only Status Code	SC Status Codes	
				☐ Specimen shipped ☐ Specimen not shipped	☐ Not most representative ☐ Specimen not available ☐ Other:______	☐ Specimen received ☐ Date ______ ☐ Specimen not received	______	10 Specimen adequate 11 Specimen not available 12 Not most representative 13 Unwanted specimen 14 Too small/multiple fragments 15 Biopsy only 16 Not formalin fixed 17 Specimen damaged; not usable 18 Path lab will only release slides 19 Path lab will only release cores 20 Path lab policy changed to no loan 21 Path lab no response 99 Other (specify) ______	
				☐ Specimen shipped ☐ Specimen not shipped	☐ Not most representative ☐ Specimen not available ☐ Other:______	☐ Specimen received ☐ Date ______ ☐ Specimen not received	______		
				☐ Specimen shipped ☐ Specimen not shipped	☐ Not most representative ☐ Specimen not available ☐ Other:______	☐ Specimen received ☐ Date ______ ☐ Specimen not received	______		
				☐ Specimen shipped ☐ Specimen not shipped	☐ Not most representative ☐ Specimen not available ☐ Other:______	☐ Specimen received ☐ Date ______ ☐ Specimen not received	______		
				☐ Specimen shipped ☐ Specimen not shipped	☐ Not most representative ☐ Specimen not available ☐ Other:______	☐ Specimen received ☐ Date ______ ☐ Specimen not received	______		
				☐ Specimen shipped ☐ Specimen not shipped	☐ Not most representative ☐ Specimen not available ☐ Other:______	☐ Specimen received ☐ Date ______ ☐ Specimen not received	______		

How soon does material need to be returned to your facility? (*check one box*) ☐ Permanent retention is fine. ☐ Return in ____ months (prefer a minimum of 6 months).

SC Name
SC Address 1
SC Address 2
SC City State Zip

Appendix 12-9: Discrepancy Notification Form

NLST/LSS Pathology Tissue Collection
DISCREPANCY NOTIFICATION FORM

Date: _____

To: _____

From: _____

Subject: Problem with your shipment dated: _____

Identification of problem item (specimen ID, etc.): _____

Problem description:

_____

_____

_____

Problem resolution:

_____

_____

_____

Resolution date: _____

National Lung Screening Trial (NLST)
LSS Pathology Tissue Transmittal Form - UCLA

Screening Center: University of Maryland

Shipment Date: 01/05/2009

Shipment ID: U20001

Total # of Blocks: 4

Receipt Confirmation	Neoadjuvant Therapy	Tissue Type	BSI ID	Block ID	Block Section	Loan Policy	Comments
☐	Y	T	KC12345-0701	10	G	3	
☐	N	L	KC12345-0702	10	H	3	
☐	N	N	KC12345-0703	10	J	3	
☐	N	N	KC12346-0701	10	J	3	

Appendix 12-11: NLST Colorado Unique Primary Tumor (CO) Form and NLST Colorado Target Annotation (TA) Form

CO NLST 6654 / LSS - Colorado Unique Primary Tumor Form

Case#/ PID#: _____

Instructions: Complete this form once for each unique primary tumor (i.e. lung cancer). All slides associated with the same unique primary tumor should be listed and summarized on this form.

1. Was at least one slide associated with this tumor annotated? [1] ☐No ☐Yes

1a. If no, indicate the primary reason below: [2]

- ☐220= Insufficient target tissue: Volume
- ☐221= Insufficient target tissue: Histologic type
- ☐222= Insufficient target tissue: Histologic grade
- ☐223= Poor fixation seen histologically
- ☐224= Autolysis seen histologically
- ☐225= Extra tissue not needed for arrays
- ☐227= Slide broken
- ☐228= Slide stain poor
- ☐229= Slide not labeled
- ☐230= Slide other, specify, _____ [3]

2. Most representative topography of tumor, as per original path report? [4]

- ☐01= C34.0, Main Bronchus | Malignant neoplasm of bronchus and lung
- ☐02= C34.1, Upper Lobe | Malignant neoplasm of bronchus and lung
- ☐03= C34.2, Middle Lobe | Malignant neoplasm of bronchus and lung
- ☐04= C34.3, Lower Lobe | Malignant neoplasm of bronchus and lung
- ☐05= C34.8, Overlapping lesion of bronchus and lung | Malignant neoplasm
- ☐06= C34.9, Not otherwise specified
- ☐07= C33, Malignant Neoplasm of Trachea
- ☐88= Other, specify reason: _____ [5]

3. Which side of body was tumor located, as per original path report? [6] ☐ Right ☐ Left ☐ Not Specified

4. Longest Diameter of tumor, as per original path report: |__|__|__|. |__| [7] mm

5. List the Block IDs of all of the annotated slides associated with this tumor:

Block ID			
i. [8]	iii. [10]	v. [12]	vii. [14]
ii. [9]	iv. [11]	vi. [13]	viii. [15]

Summarize the tumor and non-tumor histology present on the slide(s) below:

6.WHO Classification [16]

|__|__|__|__|__| / |__|

7.Longest Diameter of Invasive Component [17]

|__|__|__|. |__| mm

8. Highest Grade (Select only one) [18]

- ☐1= Well differentiated
- ☐2= Moderately
- ☐3= Poorly
- ☐4= Undifferentiated
- ☐88 = Other, specify: _____ [19]

9. Likely metastases? (Select only one) [20]

- ☐1= None
- ☐2= Unlikely
- ☐3= Probable
- ☐4= Can't Determine

10. NON-Tumor: Histology (check all that apply)

- ☐01= Normal lung [21]
- ☐02= Granuloma [22]
- ☐03= Hemorrhage [23]
- ☐04= Pneumonia [24]
- ☐05= Necrosis [25]
- ☐06= Infarction [26]
- ☐07= Emphysema [27]
- ☐08= Fibrosis [28]
- ☐09= Pre-neoplastic tissue [29]
- ☐10= Chronic bronchitis [30]
- ☐88= Other, Specify: [31] _____ [32]
- ☐99= N/A [33]

11. NON-Tumor: Pre-malignant (check all that apply)

- ☐01= Squamous carcinoma *in situ* (8070/2) [34]
- ☐02= Squamous dysplasia, MILD [35]
- ☐03= Squamous dysplasia, MODERATE [36]
- ☐04= Squamous dysplasia, SEVERE [37]
- ☐05= Atypical adenomatous hyperplasia (AAH) [38]
- ☐06=Diffuse idiopathic neuroendocrine cell hyperplasia(DIPNECH) [39]
- ☐07= Reserve Cell Hyperplasia (RCH) [40]
- ☐08= Carcinoid tumorlet [41]
- ☐88= Other, Specify: _____ [42]
- ☐99= N/A [43]

_____ [44] Interpreting Pathologist's initials

_____ [45] Initials of person completing the form

____/____/_____ [46] Date Form Completed **(mm/dd/yyyy)**

CO Form, v4.4 May 15, 2009 Page 1 of 1

Appendix 12-11: NLST Colorado Unique Primary Tumor (CO) Form and NLST Colorado Target Annotation (TA) Form

TA **NLST 6654 / LSS**
Colorado Target (Region of Interest)
Annotation

Affix Barcode Slide Label Here

Case #/ PID#: ____________

Block ID: ____________________ [1]

Slide Label: S___ [2]

Complete the following questions, in columns. **Date of Slide Annotation:** ___/___/______ [3] (mm/dd/yyyy)

<table>
<tr><td>4</td><td>ROI #1</td><td>ROI #2</td><td>ROI #3</td><td>ROI #4</td></tr>
<tr><td>5</td><td>Label Color
☐ Purple = Normal Lung
☐ Yellow = Proximal Bronchus
☐ Green = Distal Bronchial
☐ Black = Invasive Carcinoma
☐ Blue = Carcinoma In Situ
☐ Red = Invasive Type II
☐ Aqua = Metastasis
☐ Orange = Normal LN
☐ Brown = Pre-Malignant
☐ Other: ____________ [6]</td><td>Label Color
☐ Purple = Normal Lung
☐ Yellow = Proximal Bronchus
☐ Green = Distal Bronchial
☐ Black = Invasive Carcinoma
☐ Blue = Carcinoma In Situ
☐ Red = Invasive Type II
☐ Aqua = Metastasis
☐ Orange = Normal LN
☐ Brown = Pre-Malignant
☐ Other: ____________ [6]</td><td>Label Color
☐ Purple = Normal Lung
☐ Yellow = Proximal Bronchus
☐ Green = Distal Bronchial
☐ Black = Invasive Carcinoma
☐ Blue = Carcinoma In Situ
☐ Red = Invasive Type II
☐ Aqua = Metastasis
☐ Orange = Normal LN
☐ Brown = Pre-Malignant
☐ Other: ____________ [6]</td><td>Label Color
☐ Purple = Normal Lung
☐ Yellow = Proximal Bronchus
☐ Green = Distal Bronchial
☐ Black = Invasive Carcinoma
☐ Blue = Carcinoma In Situ
☐ Red = Invasive Type II
☐ Aqua = Metastaasis
☐ Orange = Normal LN
☐ Brown = Pre-Malignant
☐ Other: ____________ [6]</td></tr>
<tr><td>7</td><td>Representative Histology
☐ 1 = Tumor
☐ 2 = Non-tumor (see Q17&20)</td><td>Representative Histology
☐ 1 = Tumor
☐ 2 = Non-tumor (see Q17&20)</td><td>Representative Histology
☐ 1 = Tumor
☐ 2 = Non-tumor (see Q17&20)</td><td>Representative Histology
☐ 1 = Tumor
☐ 2 = Non-tumor (see Q17&20)</td></tr>
<tr><td>8</td><td>WHO Classification
|__|__|__|__| / |__|</td><td>WHO Classification
|__|__|__|__| / |__|</td><td>WHO Classification
|__|__|__|__| / |__|</td><td>WHO Classification
|__|__|__|__| / |__|</td></tr>
<tr><td>9</td><td>Highest Grade
☐ 1= Well differentiated
☐ 2= Moderately
☐ 3= Poorly
☐ 4= Undifferentiated
☐ 88 = Other, specify:
________________ [10]</td><td>Highest Grade
☐ 1= Well differentiated
☐ 2= Moderately
☐ 3= Poorly
☐ 4= Undifferentiated
☐ 88 = Other, specify:
________________ [10]</td><td>Highest Grade
☐ 1= Well differentiated
☐ 2= Moderately
☐ 3= Poorly
☐ 4= Undifferentiated
☐ 88 = Other, specify:
________________ [10]</td><td>Highest Grade
☐ 1= Well differentiated
☐ 2= Moderately
☐ 3= Poorly
☐ 4= Undifferentiated
☐ 88 = Other, specify:
________________ [10]</td></tr>
<tr><td>11</td><td>Cellular %
|__|__|__| % (001-100)</td><td>Cellular %
|__|__|__| % (001-100)</td><td>Cellular %
|__|__|__| % (001-100)</td><td>Cellular %
|__|__|__| % (001-100)</td></tr>
<tr><td>12</td><td>Invasion Component (mm)
|__|__| . |__|</td><td>Invasion Component (mm)
|__|__| . |__|</td><td>Invasion Component (mm)
|__|__| . |__|</td><td>Invasion Component (mm)
|__|__| . |__|</td></tr>
<tr><td>13</td><td>Lymphatic invasion?
☐ NO ☐ YES</td><td>Lymphatic invasion?
☐ NO ☐ YES</td><td>Lymphatic invasion?
☐ NO ☐ YES</td><td>Lymphatic invasion?
☐ NO ☐ YES</td></tr>
<tr><td>14</td><td>Blood vessel invasion?
☐ NO ☐ YES</td><td>Blood vessel invasion?
☐ NO ☐ YES</td><td>Blood vessel invasion?
☐ NO ☐ YES</td><td>Blood vessel invasion?
☐ NO ☐ YES</td></tr>
<tr><td>15</td><td>% inflammatory cells?
|__|__|__| % (001-100)</td><td>% inflammatory cells?
|__|__|__| % (001-100)</td><td>% inflammatory cells?
|__|__|__| % (001-100)</td><td>% inflammatory cells?
|__|__|__| % (001-100)</td></tr>
<tr><td>16</td><td>Likely metastases?
☐ 1= None
☐ 2= Unlikely
☐ 3= Probable
☐ 4= Can't Determine</td><td>Likely metastases?
☐ 1= None
☐ 2= Unlikely
☐ 3= Probable
☐ 4= Can't Determine</td><td>Likely metastases?
☐ 1= None
☐ 2= Unlikely
☐ 3= Probable
☐ 4= Can't Determine</td><td>Likely metastases?
☐ 1= None
☐ 2= Unlikely
☐ 3= Probable
☐ 4= Can't Determine</td></tr>
<tr><td>17</td><td>NON-Tumor: histology
|__|__| [17] (Table 3) ☐ N/A [18]</td><td>NON-Tumor: histology
|__|__| [17] (Table 3) ☐ N/A [18]</td><td>NON-Tumor: histology
|__|__| [17] (Table 3) ☐ N/A [18]</td><td>NON-Tumor: histology
|__|__| [17] (Table 3) ☐ N/A [18]</td></tr>
<tr><td></td><td>If other specify: __________
________________ [19]</td><td>If other specify: __________
________________ [19]</td><td>If other specify: __________
________________ [19]</td><td>If other specify: __________
________________ [19]</td></tr>
<tr><td>20</td><td>NON-Tumor: pre-malignant
|__|__| [20] (Table 4) ☐ N/A [21]</td><td>NON-Tumor: pre-malignant
|__|__| [20] (Table 4) ☐ N/A [21]</td><td>NON-Tumor: pre-malignant
|__|__| [20] (Table 4) ☐ N/A [21]</td><td>NON-Tumor: pre-malignant
|__|__| [20] (Table 4) ☐ N/A [21]</td></tr>
<tr><td></td><td>If other specify: __________
________________ [22]</td><td>If other specify: __________
________________ [22]</td><td>If other specify: __________
________________ [22]</td><td>If other specify: __________
________________ [22]</td></tr>
</table>

________________________ [23]
Interpreting Pathologist's initials

________________________ [24]
Initials of person completing the form

____/____/________ [25]
Date Form Completed **(mm/dd/yyyy)**

TA Form, v3.9 May 14, 2009 Page 1 of 1

National Lung Screening Trial (NLST)
LSS Pathology Tissue Transmittal Form – Return to Pathology Lab

Screening Center: University of Maryland
Pathology Lab: Allegheny General Hospital
Shipment Date: 04/10/09
Shipment ID: S20001
Total # of Blocks: 4

Receipt Confirmation	Tissue Type	Block ID	Block Section	Accession Number	Procedure Date	Comments
☐	Tumor	10	G	27789014	2/15/05	
☐	Lung	10	H	27789014	2/15/05	
☐	Nodes	10	J	27789014	2/15/05	
☐	Tumor	10	J	41368932	11/16/04	

NLST/LSS – Pathology Status Report Summary
Site 20

	Participant Authorization Status					
Site ID	Not Required	Pending	Obtained	MDF_Refused	MDF- No Response	MDF-No Loan
20	11	0	3	1	0	1

	Case Status				
Site ID	Selected	Authorized	Request Pending	Request Complete	Shipped
20	17	15	5	10	6

Appendix 12-13: NLST/LSS SC Pathology Status Reports

NLST/LSS - Pathology Block Status Report
Site 20

PID	SY	Visit	Date Requested	Requested	Pending	Received Adequate	Received Inadequate	Date Received	Shipped	Date Shipped
20-10001-1	01	1	01/14/2009	2	0	2	0	02/06/2009	2	02/11/2009
20-10012-5	05	1	04/08/2009	3	0	3	0	04/01/2009	0	.
20-10048-1	00	1	01/14/2009	0	0	0	0	.	0	.
20-10167-7	00	1	01/06/2009	3	3	0	0	.	0	.
20-10239-4	04	1	01/06/2009	3	3	0	0	.	0	.
20-10254-1	02	1	01/06/2009	3	0	1	2	02/23/2009	1	03/11/2009
20-10345-6	01	1	01/06/2009	3	0	1	2	02/23/2009	1	03/11/2009
20-10362-3	02	1	01/06/2009	3	0	3	0	02/05/2009	3	02/11/2009
20-10401-0	05	1	04/08/2009	1	1	0	0	.	0	.
20-10483-0	02	1	.	0	0	0	0	.	0	.
20-10498-8	01	1	01/06/2009	3	3	0	0	.	0	.
20-10552-1	01	1	01/06/2009	3	0	2	1	02/05/2009	2	02/11/2009
20-10560-3	00	1	01/06/2009	3	0	3	0	02/05/2009	3	02/11/2009
20-10881-9	02	1	.	0	0	0	0	.	0	.
20-11099-4	01	1	01/14/2009	3	3	0	0	.	0	.
Totals				33	13	15	5		12	
N = 15										

Note: Received Inadequate includes blocks requested but not most representative or not adequate.

Report Date: April 14, 2009