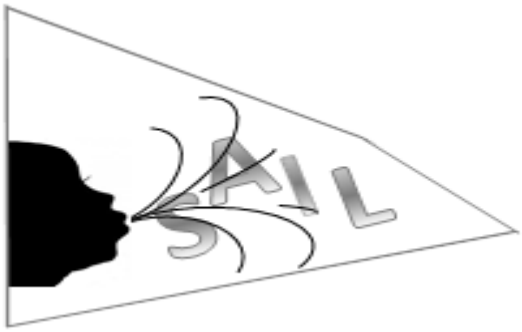

The Sustained Aeration of Infant Lungs (SAIL) Study

Manual of Procedures

Version 3.0– March 20, 2017

Prepared by the University of Pennsylvania Perelman School of Medicine, Clinical Research Computing Unit, SAIL Trial Data Coordinating Center

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1. Introduction

The SAIL Study is a prospective randomized controlled unblinded trial in preterm infants to determine which of two strategies at birth are best to optimally aerate the lung. Specifically, the trial will determine which of two lung opening strategies is superior – the current accepted Newborn Resuscitation Program (NRP) Guidelines using a standard PEEP/CPAP of 5-7 cm H2O in the Delivery Room (DR), as compared to early lung recruitment using Sustained Inflation (SI) in the Delivery Room. The primary outcome is a lower rate of the combined endpoint of death or BPD (using a standardized oxygen reduction test) at 36 weeks PMA. The study population is 600 infants of 23-26 weeks GA requiring respiratory support at birth. The study will also compare which has the lower rate of other important secondary outcomes including rates of neurodevelopmental impairment at 18 - 24 months of corrected age in survivors.

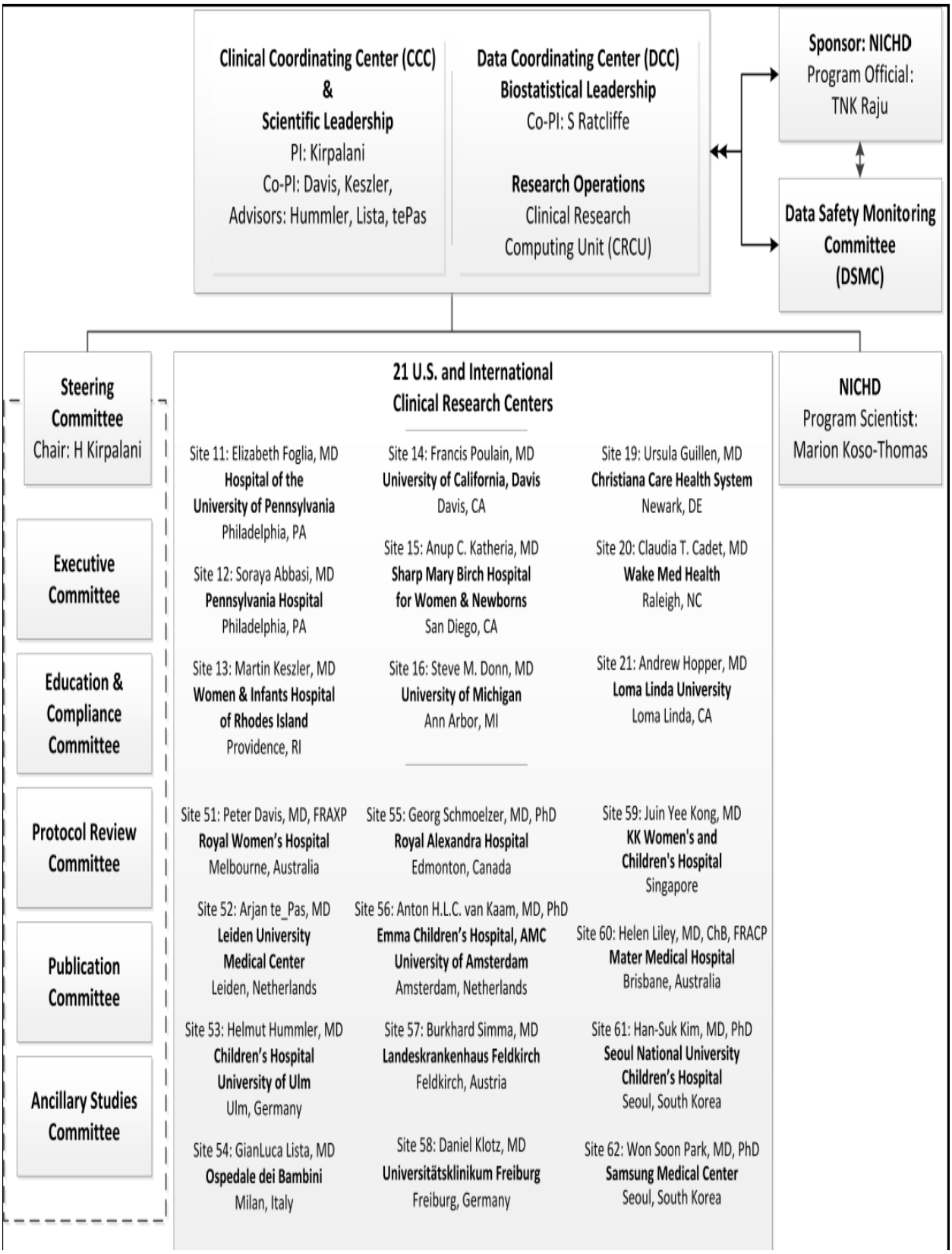
The trial is being conducted at 13 sites in the United States, Canada, Germany, Italy, the Netherlands, and Australia. The University of Pennsylvania, Perelman School of Medicine serves as the Data Coordinating Center (DCC). Funding for the study is provided by that Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD).

The SAIL Study is registered on Clinical Trials.gov - Registration number: NCT02139800
http://www.ClinicalTrials.gov

2. Study Organization

The study is sponsored by the National Institute of Child Health and Human Development (NICHD). The NICHD Program officials will provide overall scientific and administrative oversight. The scientific leadership group for the study is comprised of seven Principal Investigators. This group will also form the study Executive Committee. The trial is managed collaboratively by the Clinical Coordinating Center (CCC) and the Data Coordinating Center (DCC). The CCC is responsible for clinical leadership and the DCC is responsible for research operations. The DCC will serve as the liaison between the clinical sites, the scientific leadership and the DSMC. The diagram below depicts the research network.

2.1. SAIL STUDY RESEARCH NETWORK



2.2. Participating Clinical Sites

Each clinical site that is screening and enrolling infants must be identified. It will be assigned a 2-digit number. All data and reports will be associated with the site ID number.

Investigator	Clinical Center	Location
Elizabeth Foglia, MD, MSE.	Hospital of the University of Pennsylvania	Philadelphia, PA
Soraya Abbasi, MD	Pennsylvania Hospital	Philadelphia, PA
Martin Keszler, MD	Women & Infants Hospital of Rhode Island	Providence, RI
Francis Poulain, MD	University of California, Davis	Davis, CA
Anup C. Katheria, MD	Sharp Mary Birch Hospital for Women & Newborns	San Diego, CA
Steve M. Donn, MD	University of Michigan	Ann Arbor, MI
Ursula Guillen, MD, MSE.	Christiana Care Health System	Newark, DE
Claudia T. Cadet, MD	WakeMed Health	Raleigh, NC
Andrew Hopper, MD	Loma Linda University	Loma Linda, CA
Peter Davis, MD, FRAXP	Royal Women's Hospital	Melbourne, Australia
Arjan te_Pas, MD	Leiden University Medical Center	Leiden, Netherlands
Helmut Hummler, MD	Children's Hospital, University of Ulm	Ulm, Germany
GianLuca Lista, MD	Ospedale dei Bambini	Milan, Italy
Georg Schmoelzer, MD, PhD	Royal Alexandra Hospital	Edmonton, Canada
Anton H.L.C. van Kaam, MD, PhD	Emma Children's Hospital, AMC University of Amsterdam	Amsterdam, Netherlands
Burkhard Simma, MD	Landeskrankenhaus, Feldkirch, Austria	Feldkirch, Austria
Daniel Klotz, MD	Universitätsklinikum Freiburg	Freiburg, Germany
Juin Yee Kong, MD	KK Women's and Children's Hospital	Singapore
Helen Liley, MB, ChB, FRACP	Mater Mother's Hospital	Brisbane, Australia
Han-Suk Kim, MD. PhD	Seoul National University Children's Hospital	Seoul, South Korea
Won Soon Park,MD, PhD	Samsung Medical Center	Seoul, South Korea

2.3. Clinical Site Team

Each clinical site Principal Investigator (PI) is responsible for the oversight of the research study locally, ensuring that IRB protocol approval is obtained prior to study initiation, and that the trial is conducted according to the protocol. The PI will identify a SAIL Study team composed of

a core group (neonatologists, nurse practitioners, nurses, respiratory therapists, research coordinators) who will be responsible for adhering to the study protocol and manual of procedures.

A Neonatologist will lead the clinical team which should include clinicians trained in how to perform the delivery room (DR) intervention, clinical staff assisting in the delivery room procedures and research team members who will collect study data, communicate with the DR and NICU staff, and document trial events. The composition of the team may vary among sites.

The Research Coordinator (RC) will be responsible for the coordination of study activities at the clinical site to ensure implementation of study procedures and data quality standards. The Research Coordinator will work closely with the Project Manager of the Data Coordinating Center to facilitate study communications and information exchange.

2.4. Clinical Coordinating Center (CCC) – University of Pennsylvania

The CCC is directed by Haresh Kirpalani, BM, MSc, working with Liz Foglia, and Aasma Chaudhury and functions to:

- Provide leadership in directing the clinical aspects of protocol development and study implementation
- Develop training materials and instructions for specialized clinical procedures
- Oversee study governance
- Provide clinical site staff with training in study procedures, study implementation

The CCC works closely with the DCC.

2.5. Data Coordinating Center (DCC) - University of Pennsylvania

Under the direction of Sarah J. Ratcliffe, PhD, the DCC functions in support of the research network to assure collaboration across sites, along with standardization and uniformity of procedures, to yield high-quality data. Specific responsibilities include:

- Provide statistical leadership and oversight of study implementation; data management and information technology support for the conduct of the trial.
- Development and implementation of the data management system ; development of study randomization system; establish data collection and data entry procedures; develop and maintain study website
- Coordinate the development and distribution of study protocol, and all modifications to the study protocol; developing study forms and manual of procedures
- Conduct a review of clinical site informed consent/patient information documents prior to site IRB submission; track site IRB approvals, regulatory documentation, and providing other regulatory support as necessary

- Provide clinical site staff with training in data collection procedures and use of the data management system
- Monitor clinical site performance for protocol adherence and data integrity; continuous monitoring of data entry and data quality activities
- Participate in all study meetings; coordinate conference call meetings and provide logistical support for in-person meetings; prepare and distribute meeting materials, summaries, and follow-up on action items
- Collaborate with Principal Investigators and study leadership in the preparation of publications and presentations.

2.6. Executive Committee

The Executive Committee is the main leadership committee of the trial and is responsible for all scientific, administrative, and fiscal decisions on behalf of the trial. Membership of the Executive Committee includes the Scientific and Biostatistical Leadership investigators.

Specific responsibilities of the Executive Committee include:

- Development and implementation of trial policies and procedures
- Approval for concurrent enrollment with other trials
- Monitor the publishing of results and approve manuscripts for publication; settle issues regarding authorship
- Dispute resolution

2.7. Steering Committee

The Steering Committee is the secondary leadership committee of the trial and is responsible for its overall direction. Membership of the Steering Committee includes the Steering Committee Chair, the NICHD Program Officials, the Clinical Site PIs.

Specific responsibilities of the Steering Committee include:

- Approve study protocol and address protocol implementation issues
- Approve protocol amendments
- Review and act upon recommendations of the Data Safety Monitoring Committee
- Establish subcommittees and taskforces, as needed

2.8. Data and Safety Monitoring Committee (DSMC)

The members of the DSMC are appointed by the NICHD. The DSMC acts to independently monitor and assess study safety and efficacy. Specific responsibilities of the DSMC include:

- Conducting in-depth reviews of the progress of the study at established intervals which includes evaluating participant accrual and follow-up, data quality and monitoring, and adverse events

- Make recommendations regarding continuation, modification, or early termination of the study should it become necessary to protect the safety and welfare of the participants

3. Information Distribution

The DCC will use a variety of tools to provide research team members with information about the trial.

3.1. SAIL Trial Website

A web page will provide all SAIL Trial members with one interface from which to access training videos, study news, calendar, documents, case report forms, the data management system and tools for entering study data and all other relevant study information. This private section of the website will require a username and password. All study team members should have a website username and password. (A *different* username and password is needed for the limited group who will enter data into the REDCap system.)

3.2. Gaining Access to the SAIL Trial Website

The SAIL Trial home page is located at www.sailtrial.org. This page has a brief summary of the trial and a link to the study listing on clinicaltrials.gov.

The SAIL Trial website will be used as the gateway to all of the study documents, case report forms, newsletters, training materials, tools and reports. In order to gain access to the private section of the website, each user must complete a brief application. The DCC project manager will provide this form to you. After completing it, return it to the DCC project managers at sail-pjm@lists.upenn.edu

You will then be issued a username and password (via email) to the protected sections of the website where documents are stored. In order to log into this section, follow the steps below.

1. Navigate to the SAIL Trial website at www.sailtrial.org
2. Click on the tab at the top left of the screen labeled 'SAIL Portal' and login with your username and password.

3.3. Distribution Lists

The following distribution lists will be used to communicate with groups and clinical sites and to distribute study information. The DCC will manage list membership. The clinical site staff should inform the DCC about research team member additions or departures to ensure that all team members receive study information.

LIST NAME	MEMBERS
Sail-pi@lists.upenn.edu	Clinical site principal investigators
Sail-rc@lists.upenn.edu	Clinical site research team members (nurses, respiratory therapists, coordinators, etc.)
Sail-steering@lists.upenn.edu	All Steering committee members (all site investigators)
Sail-pjm@lists.upenn.edu	DCC project and data managers

3.4. Email

DCC personnel will also use email to send documents and current information to SAIL Trial members. DCC staff members are easily accessible by email and will reply to questions and requests for information as soon as possible.

3.5. Contact List

A contact list will be developed and revised regularly to provide clinical site staff members with current email and phone contact information for the DCC team and the CCC team .

3.6. DCC Project Managers

The DCC project managers will provide assistance to research team members in gaining access to study tools, implementing the trial, collecting data, using the data management system, responding to data queries, etc. Use this email address→ sail-pjm@lists.upenn.edu to reach the DCC team of project and data managers.

3.7. REDCap Helpdesk

The SAIL DCC will operate a helpdesk to assist users in accessing the web-based REDCap data management system (DMS). Assistance from the DCC helpdesk is focused on access to tools and technology. If you need assistance with your username and password, or if the system is not accessible to you, contact the REDCap helpdesk. The DCC will be available to respond to helpdesk questions Monday through Friday from 9 AM to 5 PM (Eastern). The following is the helpdesk contact information :

Phone: (215) 573-4623
Fax: (215) 573-6262
Email: crcuhelp@mail.med.upenn.edu

3.8. Clinical Questions and Concerns

Urgent clinical questions and concerns, and questions about eligibility should be directed to the following Clinical Coordinating Center (CCC) team members:

Haresh Kirpalani, BM, MSc	KIRPALANIH@email.chop.edu	
Liz Foglia, MD	foglia@email.chop.edu	267-441-7144
Aasma Chaudhary, BS, RRT	Aasma.Chaudhary@uphs.upenn.edu	215-917-2322

4. Training and Documentation

4.1. Training on Sustained Inflation (SI) Maneuver

At each site, the Site PI or his/her delegate will be responsible for local training. Specific training will be required for all clinicians who will be performing the Sustained Inflation (SI) maneuver during resuscitation. Training activities include the following:

- review of the SAIL protocol or the protocol slides;
- reviewing SAIL manual of procedures sections on enrollment, delivery room procedures, and the study interventions [**see MOP *Sections 6, 7,and 8***]
- watching the training videos [**see below Section 4.2]**
- practicing the SI maneuver method with the resuscitation team;
- attending local inservice session on infant resuscitation.

Upon completion of the training activities, the clinician will complete a Training Attestation Checklist *[see Appendix 1]* to document their training. **The Training Attestation form is completed only by the clinicians who will be performing the Sustained Inflation maneuver**.

4.2. Accessing the SAIL Trial Training Videos

To facilitate training, the Penn CCC team has developed 4 brief videos for use in training the delivery room team about the SAIL Study Sustained Inflation (SI) procedure. The videos show the SI procedure and highlight the timing and coordination of events in implementing the SI.

Aside from training the delivery room team during the trial planning and preparation stages, the videos can be viewed by any DR team before a SAIL eligible baby is born to reinforce the procedure and timing. The videos show the team huddle, the SI maneuver and 2 alternate scenarios and are not intended to show all possible scenarios. To view the SAIL trial videos

1. Navigate to the SAIL Trial website at www.sailtrial.org
2. Click on the tab at the top left of the screen labeled 'Training Videos.'

3. When prompted for a username and password, enter '**sailvideo**' in both fields. [See below.]
4. Click on each video to view it.
5. Users who access the training videos from this entry are not able to see any of the protected content on the SAIL Trial website.

4.3. Training on Protocol and Data Management Procedures

The DCC will hold a training webinar with site research team members, befor trial start-up at the site. This webinar will review key elements of the protocol, manual of procedures (MOP) and data collection methods. Specific data management system training will be required for users of the REDCap remote data capture web-based system.

4.4. Research Training in Human Subjects Protection

Training in Human Subjects Protection is a National Institutes of Health (NIH) educational requirement of principal investigators, sub- or co-investigators, study coordinators, and all "key research personnel" involved in the design or conduct of NIH-funded human subjects research. This requirement applies to all NIH studies conducted both nationally and internationally. Training in Human Subjects Protection should be received before research involving human subjects is begun at the clinical site. A current certificate issued from a training program provided at the clinical site institution or a certificate issued from completion of the

NIH on-line "Protecting Human Research Participants" training course will fulfill this requirement. The NIH training course takes approximately one to two hours to complete, and is available at: http://phrp.nihtraining.com/users/login.php

4.5. Summary of Training Requirements

Though the composition of the delivery room clinical team and research team varies at each site, some members of the delivery room clinical team may also be members of the site research team. The following table is a summary of study training required for clinical and research team members.

Role	Performs Resuscitation Sustained Inflation Maneuver?	Receives Training in Sustained Inflation Maneuver and Completes Attestation	Is a Member of the Research Team?	Receives Training in Human Subjects Protection
Neonatologist in charge of Delivery Room Team (team leader)	YES	YES	YES	YES
			NO	NO
Principal Investigator and/or Co-Investigators in charge of Research Team	YES	YES	YES	YES
Neonatal Attending Physician; Neonatal Fellow	YES	YES	YES	YES
			NO	NO
Other Delivery Room Clinicians such as: Respiratory Therapist; Nurse Practitioner; Nurse; Pediatric Resident; Physician Assistant	YES	YES	YES	YES
	NO	NO	NO	NO
Neonatal Nurse assisting with delivery room care/or recording resuscitation information	NO	NO	NO	NO
Research Coordinator	NO	NO	YES	YES
	YES	YES		

4.6. Approvals and Documents

Prior to the SAIL Study initiation at each individual clinical site, the following documents must be submitted to the DCC:

- Each clinical site must have IRB/Ethics Committee review of the study protocol and receive approval to conduct the study. A copy of the IRB/Ethics Committee approval letter and and a copy of the approved informed consent/patient information document(s) must be on file with the DCC before a site can begin study start.

- A copy of the Investigators delegation of responsibilities log, identifying the roles and responsibilities of key research personnel involved in conducting the study.

- A copy of the Investigator Agreement page (located in forward section of protocol) signed by the Principal Investigator
- A copy of current certificate of training in Human Subjects Protection for all site research personnel involved in the design or conduct of the study.

5. Participant Enrollment Process

Participant enrollment process refers to the tasks that each site undertakes to initiate participant accrual, beginning with identifying potential participants, screening and consenting, and randomizing.

5.1. Identifying Potential Participants

The clinical research coordinator or team member will evaluate maternal admissions to the Labor and Delivery Unit at the clinical site to preliminarily assess eligibility based on estimated gestational age and maternal labor status. Mothers may also be identified at a prenatal visit if it is deemed there is a potential risk for their baby to be born prematurely. Depending upon the clinical site's consent approach, these women may be asked to consent for the trial at the prenatal visit.

5.2. Screening

All admissions for threatened premature delivery will be screened on a daily basis to ensure that eligible patients can be enrolled. The research coordinator or trained staff member or appropriately trained clinical team member will explain the study after determining if the mother is eligible. The initial step after screening is to obtain informed consent The research coordinator at each site will maintain a screening log of all screened mothers-infants indicating who is eligible and who is not, and of eligible mothers who have consented to the study and who has refused study participation. (See Section 10.1 for Instructions on completing Screening Log).

5.3. Informed Consent for Enrollment in the Study

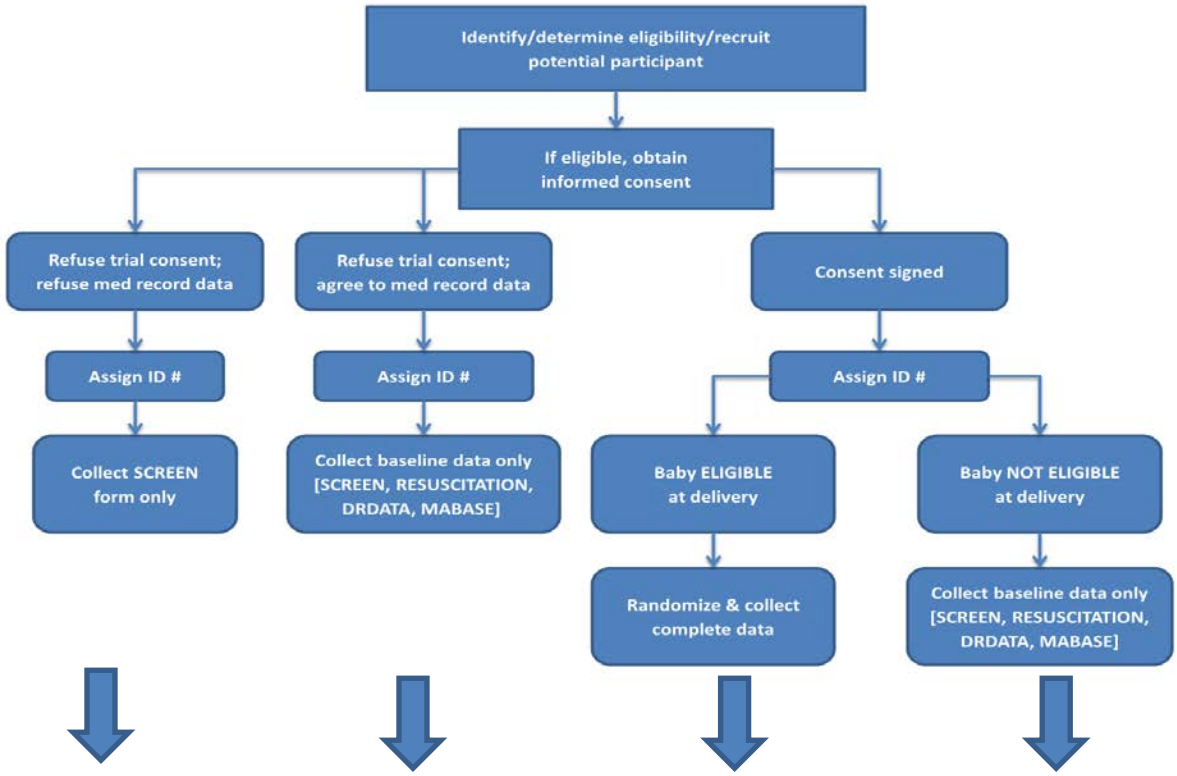
Each clinical site is responsible for ensuring that informed consent is obtained from each participant according to the guidelines of its local IRB/Ethics Board. The approach used for obtaining informed consent (antenatal or deferred conent) for the SAIL Trial, as well as the informed consent/patient information document used by the clinical site, must be approved by the local IRB/Ethics Board before the start of the study.

5.4. Antenatal Consent Approach

Based on IRB determination, a full antenatal consent procedure has been adopted for this study. Parents will be approached for informed consent to enroll their infant into the study

prior to the infant's delivery**. The Infant(s) whose parents refuse to sign informed consent <u>will not be randomized into the study</u>.** If consent for study participation/infant resuscitation is not given, the mother may be asked to give her written consent to allow her medical record (MR) data and the infant's data to be collected. The consent for medical record data will be restricted to <u>only</u> the specific medical record data collected for the SAIL study. The request for consent to collect only MR data can be made after delivery. The request for consent to collect only MR data is not to be confused with the Deferred Consent approach (see **5.5**).

Flow Diagram of Antenatal Consent Approach



Mothers who are screened and refuse consent for trial participation and refuse data collection	Mothers who are screened and refuse trial participation but give consent for data collection from medical records. Baby is NOT randomized into the trial.	Mothers who consent and whose baby is <u>eligible and randomized</u> in the trial	Mothers who consent and whose baby is **<u>NOT</u>** <u>eligible</u> [HR > 100 and vigorous] and is NOT randomized into the trial
<u>Data Collected</u>: Screening Only [1 form questions 1-5] If IRB approval given, collect minimal data set	<u>Baseline Data Collected:</u> Screening; Resuscitation; Delivery Room; Maternal Baseline [4 forms]	<u>All Data Collected:</u> Throughout course of hospitalization and follow-up period at 2 years [All data forms]	<u>Baseline Data Collected:</u> Screening; Resuscitation; Delivery Room; Maternal Baseline

IMPORTANT NOTE:

In the case where a mother has provided antenatal consent for study participation but the infant is subsequently **born beyond the eligible gestational age (≥27 weeks), the infant is no longer eligible and not included in the cohort of the study**. Therefore, only the Screening Form data [questions 1-5] will be collected.

A minimal set of data will be collected on all mothers and infants screened for the SAIL study, including those subjects who refuse consent for study participation. As specified in the SAIL Protocol Section 4.5.3 – Data Collection for Non-eligible Infants: "*To complete the patient flow description, this protocol addresses infants in the inclusion GA who are not eligible to be randomized. By definition this includes infants whose parent has refused to consent. We seek approval to capture limited data for this group of infants. There are two reasons for collecting this valuable information:*

- *The dearth of information about DR practices in this birth weight range of infants*
- *The known high potential for selection bias following the use of antenatal consent procedures.*[17, 18]

Data Collection for these infants will not include any HIPPA protected privileged information. We will be collecting the following information from parents who refused consent":

Data Collection Topic	*Specific Data Elements*
Delivery Room Data	*Month/year of birth; time of cord clamping (recorded as mm:ss after birth); birth weight; Apgar score at 1 and 5 min; gender; NRP guidelines used in the resuscitation of the infant such as respiratory status; procedures if any (intubation, chest compression, administration of epinephrine; surfactant delivery; UAC/UVC placement; chest tube placement; final respiratory status before leaving DR; and outcome of resuscitation.*
Maternal Data Form	*gravid para status, exposure to antenatal steroids and type; maternal ethnicity/race; antenatal corticosteroids (if yes, number of courses); any medications given to prolong pregnancy including tocolytics; diagnosis of diabetes during pregnancy (insulin dependent); placental abruption; chorioamnionitis; membranes rupture ≥ 24 hours before delivery; mode of delivery*

This minimal data is collected on the following case report forms: 1) screening for consent and enrollment form; 2) resuscitation data flow sheet; 3) delivery room data form; 4) maternal baseline form.

The following table outlines data collection in relation to consent status and infant eligibility:

Antenatal Consent Discussion	Gave consent for study participation	Gave Consent for Data Collection ONLY	Infant gestational age at delivery	Infant eligible?	Data Collected
Yes	Yes	N/A	23-26 $^{6/7}$ weeks	Yes	All case report forms
Yes	Yes	N/A	23-26 $^{6/7}$ weeks	No	Minimal data forms
Yes	Yes	N/A	≥ 27 weeks	No	Screening form only
Yes	No	Yes	23-26 $^{6/7}$ weeks	N/A	Minimal data forms
Yes	No	No	Any time	N/A	Screening form only
No	N/A	N/A	23-26 $^{6/7}$ weeks	N/A	Minimal data forms

ADDITIONAL NOTE: Sites should obtain written IRB approval for permission to collect minimal data set on participants who refuse to give consent regardless of consent approach used. (Please also refer to Section 12.1. Screening form and Section 12.2. Screening for Consent and Enrollment Data Instructions for details on completing the Screen form).

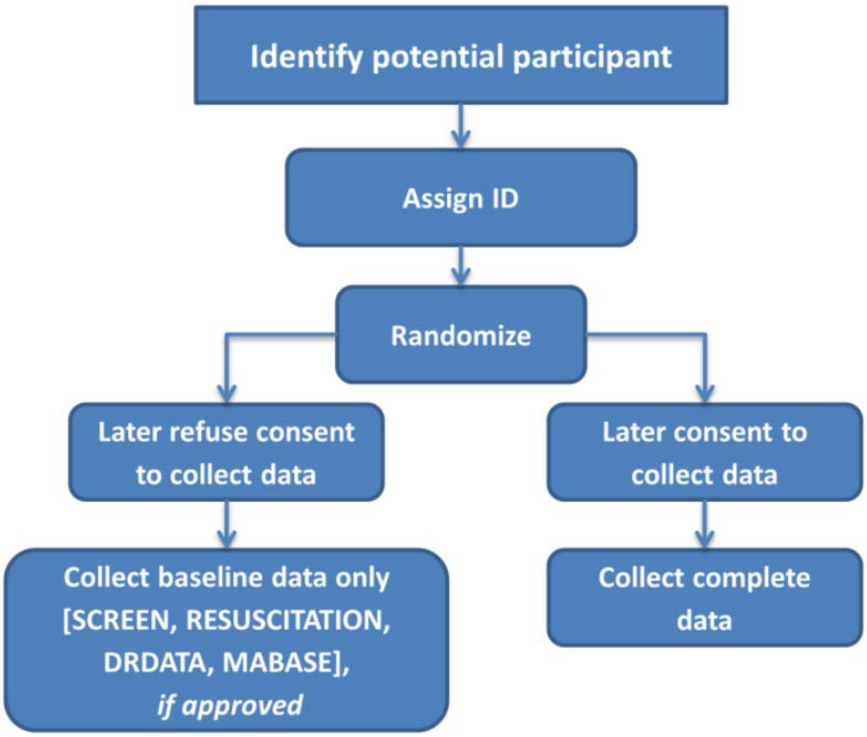
5.5. Deferred Consent Approach

If a deferred consent approach is approved at a clinical site, then all eligible infants can be randomized into the study. We define a deferred consent approach as a consent that is obtained after delivery, randomization, and resuscitation of the infant has occurred. In the SAIL trial, the deferred consent approach can only be used if this approach has been approved in advance by the local IRB/Ethics Board and indicated as such in the IRB/Ethics approval letter. If a deferred consent is obtained after resuscitation is completed in the DR, it is recommended that the parents are approached for consent to continue to collect study data as soon as possible and within 48 hours after delivery, depending on the mother's health status.

If a *deferred consent* approach is being employed and mother has refused to consent for data collection, the site may be able to collect minimal data set only [SCREEN, RESUSCITATION, DRDATA, MABASE], provided the IRB has approved this data collection.

If the IRB does not approve collection of minimal data set, the site will not collect *any* data [beyond the SCREEN Form questions 1-5], if a mother refuses to participate in the trial when approached after delivery.

Flow Diagram – DEFERRED CONSENT APPROACH



5.6. Administering the Antenatal Consent

The Research Coordinator (RC) or designated research staff member will provide the potential participant with a copy of the Informed Consent/Patient Information Form so that she can read and consider participation in the SAIL Trial. The informed consent form should be reviewed in a setting where the participant is able to make a free choice without undue influence.

Allow ample time for a participant to read and process the information. Because the consenting process for this study may occur in a limited time period, it is important that the research staff be particularly mindful of time influence during the administration of the informed consent and not allow time limits to unduly effect how they administer the informed consent or convey study information.

The Research Coordinator will discuss the purpose of the study, the study procedures, the risks and benefits, and the duration of the study. The potential subject must be told that she is not obligated to participate, that there will be no penalty for declining to participate, and that treatment will not be compromised for her or her infant, if she refuses to participate in the study. The RC should review the consent with the potential participant and answer any questions. If the potential participant expresses uncertainty about participation or indicates a need to delay in making a decision, the RC should suspend the consent process and return at a

scheduled time or ask the participant to contact the clinical site staff if she would like to resume the process. If the potential participant has difficulty reading or cannot read for any reason, the staff may read the consent form aloud to her. It is also permissible for participants to have a friend/relative assist them in reading or discussing the consent form.

The Informed Consent Form must be signed and personally dated by the participating mother and father (depending on approach) and the person obtaining consent. A participant should not be asked to sign the consent statement if she has doubts about participating or if the staff believes she does not understand what participation involves.

The Coordinator will maintain the original signed consent document in each participant's confidential research study file and provide a copy of the signed and dated informed consent to the participant. It is recommended that a second copy of all informed consent(s) should be made as a back-up and stored together in the study-confidential file. In addition, a signed/dated note should be written in each participant's research file documenting that the informed consent was obtained. To ensure confidentiality, the Coordinator will not send copies of the informed consent form(s) signed by the participant to the DCC or keep any copies of the informed consent form with the case report forms (CRFs).

5.7. HIPAA

For the USA clinical sites, participants are required to sign a Health Insurance Portability and Accountability Act (HIPAA) Authorization in addition to the Informed Consent Form. (The non-US sites have a parallel arrangement.) The HIPAA Authorization may or may not be incorporated into the text of the Informed Consent document, depending on the policy of the clinical site. If the HIPAA language is incorporated into the Informed Consent document, the regulation mandates that it be submitted to the IRB for prior approval. This form describes both the kinds of health information collected in this study and also all of the disclosures of health information that will be made. The form must also list parties to whom disclosures of personal health information will be made.

6. Enrollment

Any mother/parents who consents to the trial is considered enrolled in the study. If at the time of birth, the infant is not eligible for the study because he/she is breathing well on CPAP and does not need resuscitation or for some other reason, this baby will not be randomized. However, this child is considered enrolled and should be followed for the duration of the time hospitalized. This information will be recorded on the Screening and Enrollment [SCREEN] form and the full set of data will be collected on this baby according to the SAIL trial schedule.

6.1. Participant Eligibility

Only infants who are born in participating NICUs (which do not use prophylactic surfactant) and who are deemed at birth to be eligible will be randomized into the study ***(please also refer to MOP Section 7.7 Assessing Eligibility and Defining Respiratory Effort)***

6.2. Inclusion Criteria

In order to qualify for participation in the study, the infant must meet the following inclusion criteria at birth:

a. Gestational age (GA) at least 23 weeks but less than 27 completed weeks by best obstetrical estimate

b. Requiring resuscitation/respiratory intervention at birth – "apneic, labored breathing, gasping"

6.3. Exclusion Criteria

Infants who have any of the following at birth will be excluded:

a. Considered non-viable by the attending neonatologist

b. Known major anomalies, pumonary hypoplasia

c. Refusal of antenatal informed consent

d. Mothers who are unable to consent for their medical care and who do not have a surrogate guardian will not be approached for consent.

It is anticipated that there will be a small number of infants who, because of acute clinical deterioration are treated according to the preference of their medical team rather than as assigned by randomization in study protocol. In this case, record this information on the Screening and Enrollment form [SCREEN]

6.4. Trial Withdrawals

Parents are free to withdraw from the trial at any time. Withdrawal of consent could be made after signing consent and before the birth of the infant, or at anytime after the birth of the infant. It is important to note that parents' withdrawal from the trial does not indicate refusal

to data collection unless the parents specifically inform the research team that they withdraw consent for the collection of their child's medical data. When the research staff becomes aware of a study withdrawal, the RC should complete a STUDY STATUS form and enter it in the REDCap data management system. [See Study Status Data Instructions –Section 16.1].

6.5. Concurrent Research Enrollment

The SAIL Study has been cleared for concurrent enrollment with the NICHD Neonatal Research Network (NRN) trials with the exception of the *Inositol to Reduce Retinopathy of Prematurity (INS 3)* trial. This approval will enhance recruitment efforts at those SAIL clinical sites that are part of the NICHD Neonatal Research Network (NRN).

The policy on Concurrent Research is as follows:

i. All randomized trials that likely involve patients who are also eligible for the SAIL trial, must be discussed with the SAIL executive committee, and the protocols shared.

ii. All such studies may or may not be compatible with the SAIL trial, and full discussion will be undertaken to resolve potential for co-enrollment.

iii. Enrollment of SAIL participants in concurrent studies that involve consent for the child and family should be documented on the SAIL Screening For Consent and Enrollment [SCREEN] case report form.

7. Delivery Room Procedures

Upon the birth of the infant in the delivery room, determination of the infant's eligibility for the trial will be made. If deemed eligible, the infant will be randomly assigned to receive either resuscitation based on NRP Guidelines, or Sustained Inflation (SI) intervention followed by standard of care.

7.1. Delivery Room Resuscitation Team

A Neonatologist or designee will lead the resuscitation team, which is comprised of the clinical providers who will perform the delivery room (DR) intervention and all delivery room procedures. Some members of the clinical team may also be members of the research team. It is the members of the SAIL research team who will collect study data, communicate with the DR and NICU staff, and document trial events. The exact composition of the delivery room team may vary among sites.

In the following table, the composition and role designation for members of the team at U Penn are described. This might serve as a potential model especially for US and Canadian sites, but the SAIL team recognizes that each site may have differing solutions. However, while team composition is likely to vary considerably across sites, the site PI in general and the team leader at an individual resuscitation should consider which members of the available clinical team are responsible for performing these duties.

7.2. Table showing Team Composition used at U Penn

Role	***Performed by***	***Responsibilities***
Team Leader	Neonatal Attending or Fellow	• Leads pre-resuscitation huddle • Makes final determination of study eligibility and directs RT to open the randomization envelope • Ultimately responsible for ensuring adherence to study algorithm • Generally not involved with hands-on care
SAIL Study Coach	Neonatal nurse practitioner, fellow, or nurse	• Assists leader in ensuring adherence to intervention algorithm for infants assigned to SI arm. • Uses stopwatch to ensure appropriate time intervals are used, counts down these intervals aloud for the team. • Anticipates and announces next step of algorithm in advance.
Airway provider	Neonatal fellow or nurse practitioner	• Clears airway and manages the facemask • Assesses for visible spontaneous breathing pattern
Additional medical provider	Pediatric resident or neonatal nurse practitioner	• Stimulates infant and wraps in plastic • Performs clinical HR assessment and assessment of breathing pattern • Occludes Neopuff to deliver the SIs, so that airway provider can use 2 handed hold on mask
Respiratory therapist	Respiratory therapist	• Opens randomization envelope and announces allocation • Sets and adjusts appropriate settings on the Neopuff, titrates FiO2

Role	***Performed by***	***Responsibilities***
Bedside nurse	Neonatal nurse	• Stimulates infant, wraps in plastic • Applies pulse oximeter probe • Assists with clinical assessment of HR, breathing pattern
Recorder	Neonatal nurse	• Not involved in hands-on care • Real time recording of HR, respiratory effort every 30 seconds for the first 2 minutes: may need to prompt team for these assessments • Records all study interventions and infant's response to interventions • Thereafter records resuscitation per unit protocol

7.3. The Team Huddle

If time allows, it is suggested that the team leader should lead a brief huddle of the team prior to the delivery of the infant ('Just-in-time training). This should review the tasks and assignments of each participating team member involved in the delivery room and study procedures.

1. Ensure all required roles (see table above) are taken by a specific individual
2. Review initial steps and timing for assessment, determination of eligibility, process for randomization.
3. Ensure randomization envelope for correct gestational age stratum is available.
4. Perform checklist to ensure all equipment is present and functional
5. Review resuscitation algorithms for the control arm and sustained inflation arm
6. If time permits, briefly review SI intervention training video**
7. Address all questions and concerns

A SAIL training video demonstrating the team huddle, the sustained inflation (SI) maneuver, and the SI algorithm following alternate clinical scenarios is available at: http://www.sailtrial.org

Click on the tab at the top left of the screen labeled 'Training Videos.' The User Name and Password are the same: Log in: User Name: **sailvideo** Password: **sailvideo**

7.4. Steps in Determining Eligibility and Resuscitation

7.5. Time Zero

After birth and cord clamping as per each unit's normal practice, potentially eligible infants ($23^{0/7}$ -$26^{6/7}$weeks GA) will be taken to a resuscitation trolley, placed in a plastic wrap, stimulated, and have a pulse oximeter probe placed on the right hand. The time the infant is received by the resuscitation team is when the SAIL resuscitation time clock starts and is taken to be time 'zero.'

After ensuring airway patency, the infant will be placed on facemask, nasopharyngeal tube, or nasal prong CPAP at 5-7 cm H2O and FiO2 0.30, via a T-piece resuscitator.

7.6. Cord Clamping

This trial does not specify the duration of cord clamping, recognizing that this remains an area of controversy and uncertain uptake into clinical practice for this group of infants. But the time of cord clamping will be recorded.

7.7. Assessing Eligibility and Defining Respiratory Effort

Within 30 seconds of receiving the infant upon the resuscitation trolley (SAIL Time Zero), the resuscitation team will assess respiratory effort and heart rate. Throughout the resuscitation, inadequate respiratory effort is defined as apnea or gasping respirations, and bradycardia is defined as heart rate (HR) <100 beats per minute (bpm).

Infants with adequate respiratory effort and HR>100 bpm will not meet inclusion criteria and will not be enrolled in the trial. Those infants subsequently will be treated according to local resuscitation protocols. Infants with inadequate respiratory effort (defined as apnea or gasping respirations) or HR <100 bpm will be eligible for trial enrollment. At the moment an infant is deemed eligible for enrollment, the resuscitation team leader should instruct the responsible member of the resuscitation team to randomize the infant (See below). **In the case of multiple births, each infant will be assessed for study eligibility individually.** The same treatment allocation will be used for all eligible infants within the set of multiples.

In most cases, the process of determining trial eligibility should occur within 30 seconds of receiving the infant on the resuscitation table, and this process should always be complete within 60 seconds of receiving the infant. If the infant is deemed eligible before 30 seconds have elapsed, the team should randomize the infant immediately at that point (i.e., the team need not wait 30 seconds to make this assessment).

There are situations in which judging "adequacy" of respiratory effort is difficult due to the inherent subjectivity of this assessment. In general, infants who are deemed ineligible for trial enrollment should have unequivocal and sustained strong respiratory effort. **If providers are in doubt regarding the adequacy of respiratory effort because the assessment is not unequivocal as described, the infant should be randomized.**

7.8. Randomization Process

An infant is randomized into the SAIL Trial when he/she has been assessed as eligible regarding respiratory effort and heart rate to either the Control Arm (NRP-PPV) or the Intervention Arm (Sustained Inflation). The resuscitation team leader/neonatologist should instruct the RT/ responsible member of the resuscitation team to open the randomization envelope. The team member should loudly and clearly announce the randomization arm.

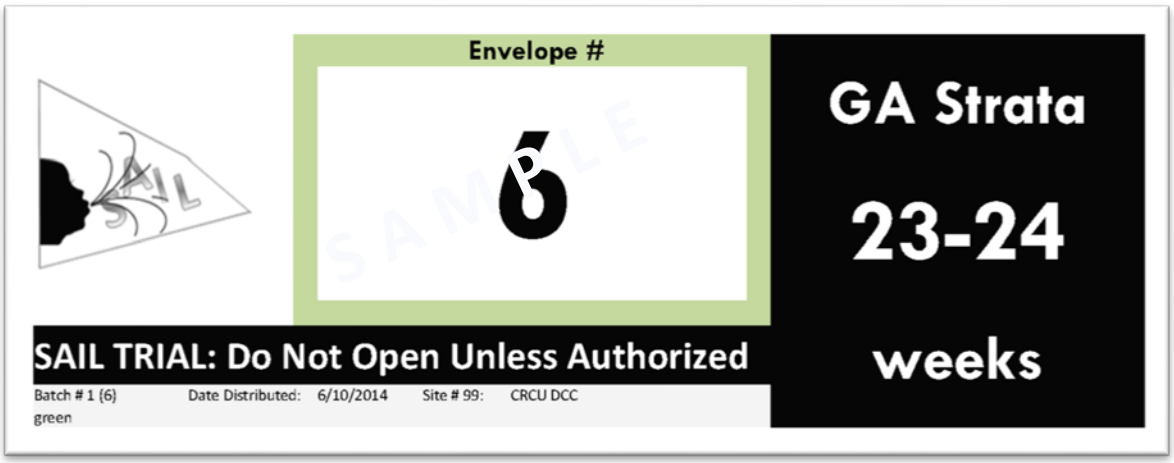
7.9. Randomization Envelopes

Randomization envelopes are color-coded to reflect the different stratification scheme based on the 2 GA groups: 1) 23 & 24 weeks (Green) and 2) 25 & 26 weeks (Orange).

The DCC will send to each clinical site a total of 24 envelopes which will be delivered in batches of 12 envelopes for each strata. The envelopes in each strata will be sequentially assigned to infants in that strata.

Envelope is Color Coded by Age Group*

GREEN – is for Infants born at 23 & 24 weeks



ORANGE – is for Infants born at 25 & 26 weeks

Envelopes should be stored in a secure but accessible location in the delivery room (DR).

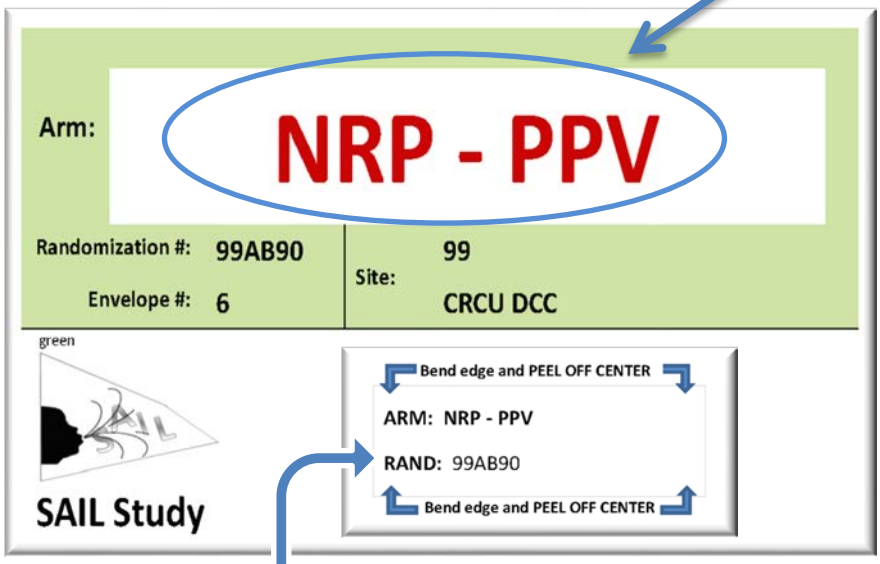
Before the infant's imminent delivery in the DR/resuscitation unit, the person responsible for opening the randomization envelope should select the next envelope in the sequence based on the infant's estimated GA. The envelope should be nearby and ready to open for allocation once the lead clinician has verified eligibility.

Inside the Envelope is the Randomization Card

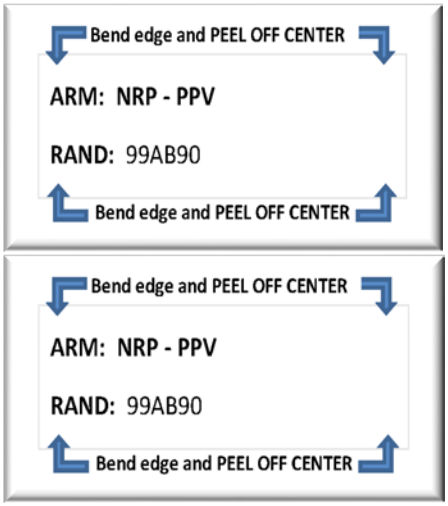
This Card tells you the treatment arm assignment the infant is to receive

The treatment arm assignment is either NRP-PPV or SI Intervention

Here is where you find the treatment arm assignment…



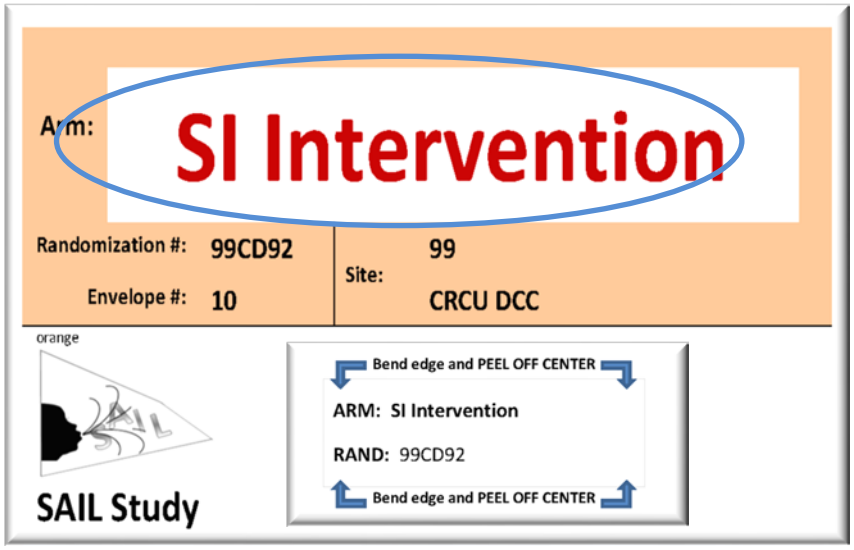
LABELS ON CARD BACK



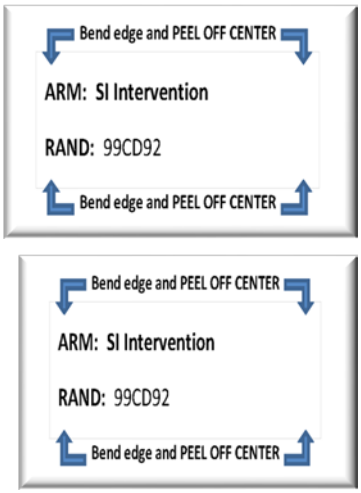
Peel off the SMALLER LABEL and stick it on the bottom of the resuscitation form

Additional labels are on back of card.

- **Use these labels if twins or triplets are born**
  - **Each infant is assigned to the same**



LABELS ON CARD BACK



As indicated above, a card containing 3 labels is *inside* of the randomization envelope. Remove the label from the front of the card and place it in the space indicated at the bottom of the RESUSCITATION form. This label has the following information: Arm assignment (*NRP-PPV* **OR** *SI Intervention* AND Randomization Number

For quality assurance, it is important that the torn opened envelope is saved and returned to the DCC. A scan or copy of the opened randomization envelope will be sent to the DCC project manager via e-mail (sail-pjm@lists.upenn.edu or fax: 215-573-6262) in a timely manner, after the infant leaves the delivery room. Once all envelopes for both strata have been used at your site, please mail the used envelops to the DCC using the UPS return label provided with the batch. It is important to note that after six randomizations have occurred in each strata, you must send an e-mail notification to the DCC project manager so that the next batch of randomization envelopes can be mailed to your site.

7.10. Important Randomization Guidelines

1. The envelope with the lowest available sequential number for a given stratum should be used.

2. The randomization envelope should not be opened in advance in anticipation of the baby's birth.

3. If a randomization envelope is opened that is not used, that randomization label should not be used for another qualified infant, and it should be reported to the DCC as soon as possible as this will alter the randomization scheme. Such envelopes should also be saved and returned to the DCC.

4. In the event that twin or additional infants are born, they will all be given the same randomization number and treatment arm assignment as the first born infant. Two additional labels are on the back of the enclosed card.

5. If a randomization envelope is opened in error, the protocol violation form should be completed and sent to the DCC project manager to explain the situation.

7.11. When is the Randomization Envelope Not Opened?

The randomization envelope is not opened when:

- It is determined at birth that baby is not eligible for the trial
- Parents refuse to gives consent or give consent to only allow collection of data

8. The Study Interventions

8.1. NRP -PPV

Infants randomized to this arm will be treated with intermittent positive pressure ventilation (IPPV) with PEEP via T-piece resuscitator and either facemask, nasopharyngeal tube (NPT) or nasal prongs, following NRP compliant practice.

Peak pressures will be set initially at 20 cm H_2O. Ongoing assessment of adequacy of IPPV will be made using heart rate and respiratory effort. Ventilation corrective steps are applied as needed (See MR SOPA below) as recommended by NRP guidelines, including increasing peak pressure to 25 H_2O cm, or as local clinical practices allow.

8.2. Sustained Inflation (SI)

Infants randomized to this arm should receive respiratory support via the T-piece resuscitator and either facemask, nasopharyngeal tube (NPT) or nasal prongs – according to local preference. A summary timeline of interventions for the SI group is given below.

Infants will be given the first SI for 15 seconds using pressure of 20 cm H_2O. An assessment for respiratory effort and heart rate will be made. Infants with adequate respiratory effort and heart rate above 100 bpm after the first SI will continue on CPAP, as study intervention has ended for these infants and they revert to standard NRP procedures.

After the first SI, if the infant has persistent inadequate respiratory effort (apnea or gasping) or bradycardia (HR<100 bpm), a second SI using a pressure of 25 cm H_2O for 15 seconds will be given. Between the first SI and the second SI, the team will follow standard NRP procedures as described in the next paragraph (MR SOPA). Decisions about need for a second SI will be based on repeat assessment of HR and respiratory effort.

During this period between SIs, as per NRP recommendations, ventilation corrective steps can be made to ensure no residual lack of seal or obstruction is impeding the infant using the MR SOPA mneumonic as described in the U.S. NRP manual:

M: Mask adjustment

R: Reposition

S: Suction Airway

O: Open Mouth

P: Pressure

A: Airway

If the infant is eligible for a second SI due to inadequate respiratory effort (apnea or gasping) or HR<100, the clinician will ensure airway patency and deliver the second SI with a pressure 5 cm higher than the initial pressure. This step is in accordance with the P (Pressure) step of MR. SOPA.

The final 'A' in MR. SOPA stands for Airway. There will be rare situations where the clinician must respond with intubation immediately – such infants will be also randomized into an SI or standard arm. While these infants data will be pooled, it will also be treated separately in a sub-group analysis.

At any point in the algorithm, if the HR is < 60 and not increasing, PPV may be given with rate in accordance with NRP and peak inspiratory pressure equal to the SI that would otherwise be performed. Observation after a 15 second period will assess whether there is an improving heart rate. If the heart rate improves to >60, the algorithm will be resumed from the point of departure.

Throughout the entire period, cardiac compressions will start if HR remains < 60 despite effective respiratory support for > 30 seconds.

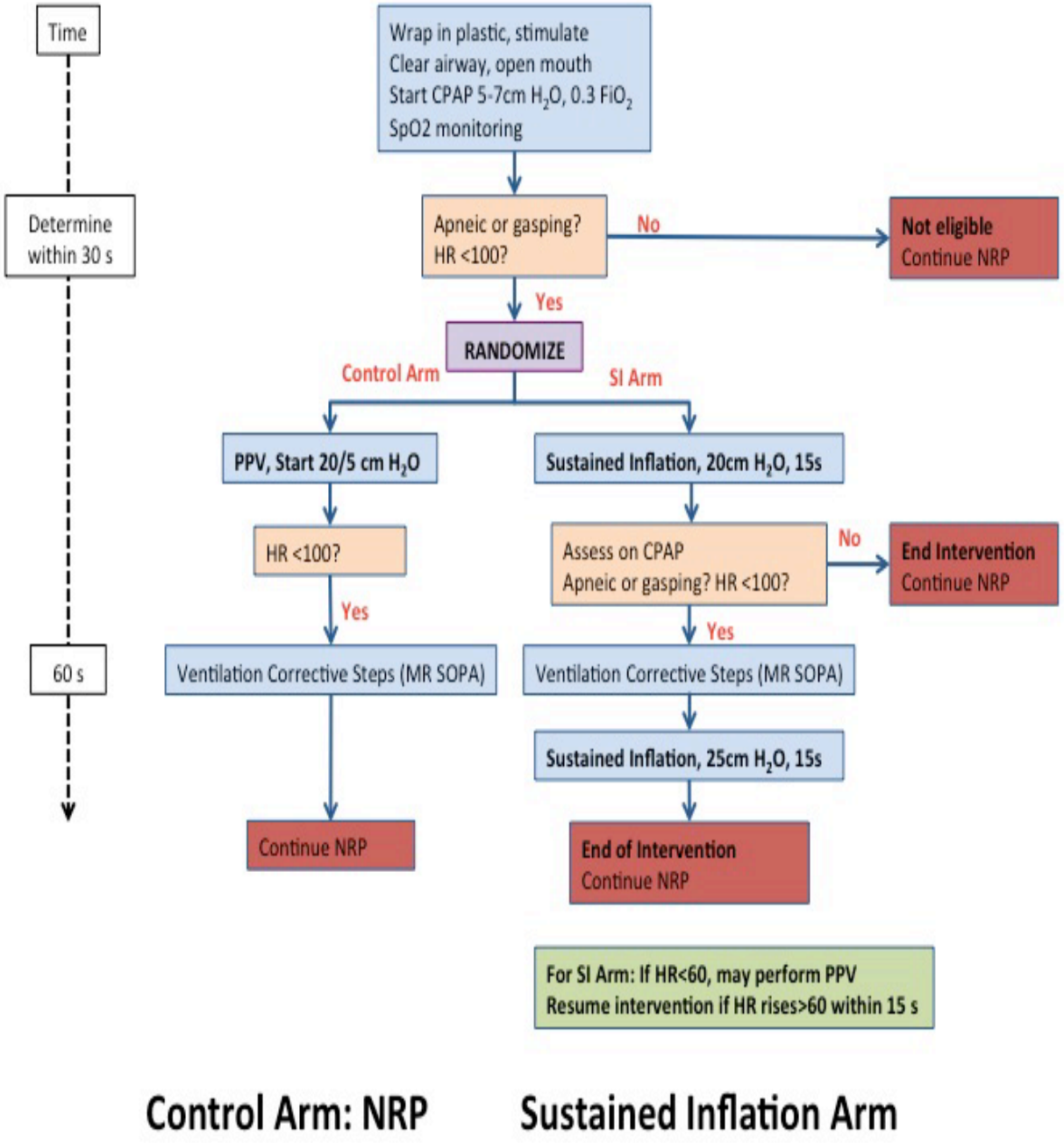


Figure: Algorithm depicting flow of assessments and interventions for infants in both arms of the trial.

8.3. Sustained Inflation Intervention - Resuscitation Timeline

The following describes the timing and flow of assessment and intervention steps for infants assigned to the Sustained Inflation (SI) Intervention arm. ***The time intervals listed are relative to Time Zero, the time the infant is placed on the resuscitation trolley.*** In the case that clinical assessments and interventions result in deviations from performing interventions within the intervals described, teams should still conform to the proscribed duration of time required for key interventions (i.e., a SI should still last 15 seconds, even if it starts at 40 seconds into the resuscitation, rather than at 30 seconds).

Time of birth: Time of birth (defined as when the body is delivered) should be recorded, but this is **not** considered time 0 for the resuscitation.

Time zero: Time zero for the resuscitation is defined as the moment the infant is placed on the resuscitation trolley.

Time 0-30 seconds: Start resuscitation and determine eligibility for trial

1. Baby is received on resuscitation trolley by resuscitation team
2. Placed immediately under radiant warmer on gel mattress, wet towels removed, placed in plastic covering (neowrap or plastic bag), hat placed on head, stimulated by team (bedside nurse, medical provider, airway provider, RT).
3. Airway cleared and mask CPAP initiated via T piece with initial settings of 5-7cm H_2O, 0.3 FiO_2, breathing pattern assessed and announced by airway provider.
4. Pulse oximeter placed on right hand by bedside nurse.
5. Clinical assessment of HR determined and announced by medical provider
6. HR, respiratory effort, intervention, and determination of eligibility recorded at 30 seconds by recording nurse
7. *<u>Before or at 30 seconds: Determine eligibility for SAIL study</u>. If infant has inadequate respiration effort (defined as apnea or gasping) <u>OR</u> has HR<100, s/he is eligible for the SAIL trial. Team leader will announce eligibility and instruct the provider responsible for randomization to open stratified randomization envelope and announce the treatment allocation.*

Time 30-45 seconds: Perform first SI, if so randomized

1. Airway provider holds mask in place with 2-handed technique
2. Assisting medical provider occludes T-piece
3. SI delivered with PIP 20cm H_2O for 15 seconds
4. Coach monitors stopwatch, counts down final 5 seconds to team

Time 45-60 seconds: Evaluate response to first SI

1. Infant maintained on CPAP, response to first SI (HR and breathing pattern) assessed, announced, and recorded.
2. *If infant has inadequate respiratory effort (apnea or gasping) <u>OR</u> has HR<100, s/he is eligible for a **second SI**. It is expected that most infants will require a second SI.*

a. Infants who have a strong respiratory effort AND HR>100 after the first SI will be maintained on CPAP, with further resuscitative efforts dictated by local protocols. The intervention is complete for this subset of infants.
    3. Corrective ventilation steps performed if necessary: airway cleared, mouth opened, and mask repositioned.
    4. It is expected that most infants who require a second SI will need corrective ventilation steps performed, to ensure airway patency and a good mask seal prior to performing the second SI.
    5. The process of determining response to the first SI and performing corrective steps should take no more than 15 seconds

Time 60-75 seconds: Perform second SI

1. Airway provider holds mask in place with 2-handed technique
2. Assisting medical provider occludes T-piece
3. Respiratory therapist increases PIP on T-piece to 25cm H_2O
4. SI delivered with PIP 25cm H_2O for 15 seconds
5. Coach monitors stopwatch, counts down final 5 seconds to team

Time 75-90 seconds: Evaluate response to second SI

1. Infant maintained on CPAP, response to second SI assessed, announced, and recorded (HR and breathing pattern)
2. Intervention is complete at this point
3. Further resuscitative efforts to be determined by local protocols

8.4. Additional Clinical Guidelines

The SAIL Study CCC team has developed the clinical guidelines below for incorporation into the clinical research site practice, as applicable.

8.5. Intubation and Extubation

Guidelines for **Intubation** include meeting any of the following criteria:

1. FiO2 ≥0.5 to maintain SpO2 ≥88%
2. pH ≤7.22 or PCO2 ≥70 mm Hg
3. >1 apneic event requiring IPPV within 6 hours
4. ≥6 apneic events requiring stimulation within 6 hours
5. Hemodynamic instability
6. Need for surgery

Extubation should be attempted within 24 hours after meeting all following criteria:

1. PCO2 ≤ 55 mm Hg
2. pH ≥7.25
3. FiO2 of ≤ 0.4 with an SpO2 of ≥ 88%
4. Mean airway pressure of ≤ 8 cm of water
5. Hemodynamic stability

8.6. Caffeine Use

The use of caffeine and the timing of caffeine administration will vary among the clinical site delivery room standard practices. The SAIL Study CCC advocates that if at the end of the resuscitation maneuver, the baby is NOT intubated and the intention is to leave the Delivery Room on CPAP, then a loading dose of caffeine should be administered within the first 4 hours of life. This information is recorded on the Growth and Medication Assessment [GMA] case report form. Document the time of the initial caffeine load the first time caffeine is given after birth. Future caffeine bolus doses given once a baby is on maintenance caffeine therapy do not need to be documented.

9. Data Management

9.1. Centralized Data Management System (DMS)

The Data Coordinating Center (DCC) provides a REDCap (Research Data Capture) data management system (DMS) for the secure entry and storage of SAIL Trial data. REDCap is a secure, web-based application for building and managing online surveys and databases. The DCC will use a REDCap installation to create a practice or development environment and an identical " live" or production environment. This system access will be granted to individual clinical site users by the DCC project or data manager.

9.2. DMS Training and Certification

All research staff responsible for data collection and data entry should be identified on the site delegation of responsibilities log. Staff members delegated to this role are required to attend a training session and participate in a certification exercise that involves entry of practice data, before being given access to the REDCap Remote Data Capture System (production DMS) for the SAIL Study. The staff member will attend a data entry webinar which will present principles of data integrity, data entry and an overview of the SAIL REDCap system.

The DCC will provide a unique username and password to each user which permits access to the SAIL *training* data management system (DMS). A mock data packet will be sent via email to enable data entry practice using the training data management system.

Upon completion of the mock data, the staff member will notify the DCC data manager who will score the data. If the error rate is less than the established threshold, the staff member will be certified to enter data into the SAIL Trial production DMS. (If the error rate is too high the user will be provided a list of corrections to make in the database.)

9.3. Acquiring a Data Management System (DMS) Username and Password

A unique REDCap DMS username and password is required for *each* person who is responsible for entering data into the electronic DMS. Each designated staff member must complete and submit a REDCap DMS access account application before a DMS username and password can be issued.

- Complete the account application in the link below and click SUBMIT.
- REDCap account request link - https://redcap.med.upenn.edu/surveys/?s=YbCvd4

You will be notified by the Data Coordinating Center when your account has been created. Please note the following:

1. A username and password will first be issued for access to the ***training DMS*.**

2. After the training and mock data entry exercise has been successfully completed, the staff member will be notified of username and password permission granting him/her access to enter data into the ***live (production) DMS***.

3. To ensure data security and confidentiality, it is of utmost importance that your individual DMS user name and password **not be shared** among site staff members.

Data integrity and use of the data management system will be tracked through the log feature in the electronic data capture system. When changes are made to the data within the system it will be tracked via each individual's username.

10. Participant Identification (PID) Number

10.1. Screening Log and Assignment of Participant Identification (PID) Number

A Screening and Enrollment Log (Screening Log) containing a list of the Participant Identification (PID) numbers assigned for the particular clinical site will be distributed to the lead Research Coordinator(RC) at the clinical site. The lead RC who will be responsible to ensure that each person who is screened and/or enrolled is assigned a unique PID number. The Screening Log provides documentation of all potential study participants who are reviewed for study eligibility. The screening log contains an identification number and mother's initials, and screening date. Since the potential study participant is screened prior to the birth of the infant, the screening log will include the following information obtained at the antenatal visit.

- Gestational age of fetus at antenatal visit (weeks and days)
- Date fetus will reach 27 weeks
- Date consent obtained for study participation and infant resuscitation
- If consent for study participation/infant resuscitation is not given, mother will be asked to give consent to allow her medical record (MR) data and the infant's data to be collected. The date that consent was received will be recorded on the log.

Every mother screened in this study will have a unique five digit study participant identification number (PID). The first two digits will be the site identification number. The next three digits will be a sequential order of participation. Example: 12035 = Mother's PID

This same unique five digit number (PID) will be assigned to the infant once the infant is born and screened for eligibility, except the digit of one (1) will be added to the identification number to indicate a single infant. Thus every infant screened at birth will have a six digit PID number. (Mothers PID + 1)

Example: 120351 = Infant's PID

In the case of *multiple births*, the Mother's PID will remain the same for all siblings, and the last digit of the PID number for each infant will reflect the sequential birth order of the siblings.

Example: 120352 = infant #2 PID number (Mothers PID + 2); and 120353 = infant #3 PID number (Mothers PID +3).

Once the infant is born, the remainder of the log will be completed to include the following information:

- Infant date of birth
- Gestational age at birth (recorded in weeks and days)
- Number of multiple births (00 = no multiple births)
- Indicate whether infant was randomized at birth (yes or no)

In addition to completing the PID assignment Screening Log, the RC will keep a separate Patient Screening Log (paper or electronic document) that will be used to link the assigned PID of the mother and baby (or babies) to their personal identifying contact information. This information linking the mother's name to the PID number must be maintained in a locked office secure file or in a password protected electronic file.

All communication and correspondene with the DCC regarding participant eligibility status or participant data should be documented by using the complete PID number only. Do not send participant names or other identifying information to the DCC. If copies of participant imaging reports or other clinical reports or medical documentation is sent to the DCC, please obscure all participant identifiers from the document, and only include the PID number on the document.

11. Collecting Participant Data

The study data are obtained by documenting specific aspects of the infant's health status over the course of his/her hospitalization on study case report forms (CRFs). Participant data for this study will be collected in the following broad groups: Infant screening and enrollment data; Infant delivery room, resuscitation and respiratory support data; Maternal demographic, antenatal, and delivery data; Detailed evaluation of infant's course in hospital; Follow-up evaluation.

11.1. Acquiring Case Report Forms

Case Report Forms (CRFs) are located on the website: http://www.sailtrial.org in the Study Documents/Case Report Form (CRF) section. CRFs are available as Adobe Portable Document Files (pdf) in visit packets or as single forms.

It is not recommended to print complete CRF visit packets for each infant at the time of enrollment (e.g. full set of CRFs through Discharge) because forms may change over the course of the study. Instead, print only a few CRFs in advance. This will ensure that all CRFs printed represent the current version of the approved CRFs.

The DCC will notify the clinical centers of CRF revisions which include changes to old CRFs and the introduction of new CRFs and flag the forms on the website. The DCC will instruct the staff about how to incorporate CRF changes into the study and how updates will impact the REDCap System.

There are 2 types of case report forms – data CRFs and administrative CRFs.

1. Data CRFs contain participant data and are entered in the database.
2. Administrative CRFs are used for study organization and are not entered in the database.

11.2. Paper Case Report Forms

The following are guidelines used when collecting data on paper CRFs :

- Print legibly and clearly on all study documents. Use a ballpoint pen with black or blue ink. Do not use pencil, erasers or correction fluid.
- Complete the study information at the top right corner of each CRF. Double check the ID # and date as that is often the source of data mistakes. Dates must match the source documentation. The approved format for collecting dates is Month/Day/Year.
- Time is documented in the 24-hour clock format.
- Provide signature and date as required on forms.

- If an error is made, draw a single straight line through the incorrect entry and enter the correct data above it. All such changes must be clearly initialed and dated. The correct response may be circled for clarification, if necessary.
- Site staff should review all CRFs for inconsistencies and missing information before entering data into the DMS and should attempt to collect missing data.
- The CRF FORM CODE is located in a box in the bottom right corner of the CRF pages; this is an abbreviation of the form name and is used in structuring the form layout in the REDCap database.
- Each CRF is dated and identified with a version number, located in the bottom left corner. This number is important should a CRF become revised at a later date. Note the version number and date of each form; should it change for any reason you will be notified.
- Keep in mind, that all information must be entered into the database to be considered study data.

IMPORTANT NOTE: There is only one form for which it is required that data be collected on the paper case report form prior to data entry in the DMS, namely the **RESUSCITATION** form. This form should be stored as source documents and may be queried for data quality inspection.

11.3. Paperless Data Collection

In most situations and provided that it is a permitted practice at your institution, data can be collected and recorded directly from the institution's Electronic Health Record (EHR) into the electronic REDCap system, using the electronic CRFs as a guide to data entry. Data may also be collected on paper CRFs for subsequent data entry, or some combination of the 2 methods may be used.

Each data collection method has different risks and benefits. Entering data into the SAIL REDCap database directly from viewing the EHR without using paper CRFs may be faster than writing on CRFs but it can result in errors that are difficult to resolve when correcting and validating data. However, transmission errors can also result when writing data on CRFs, particularly on dates and ID numbers.

Collecting daily and weekly data can result in transposition errors, often in date fields, which can cause erroneous calculations and reports. To ensure accuracy while collecting data it is helpful to have a schedule for collecting and entering data, ideally limited to 2 designated staff members. The process for correcting data that generate discrepancies or resolving queries generated by the DCC will be a topic of instruction provided on study RC webinars.

11.4. Data Collection Schedule

The data collection schedule is referred to as Visit Schedule, and identifies the standardized data collection forms and the designated time points at which the data for each form is collected on infants.

The following table outlines the schedule by study visit time points and data case report forms collected at each time point. Rows represent the data forms, while columns represent each visit time point that data collection occurs.

Data Collection Schedule/Visit Schedule in Table Format

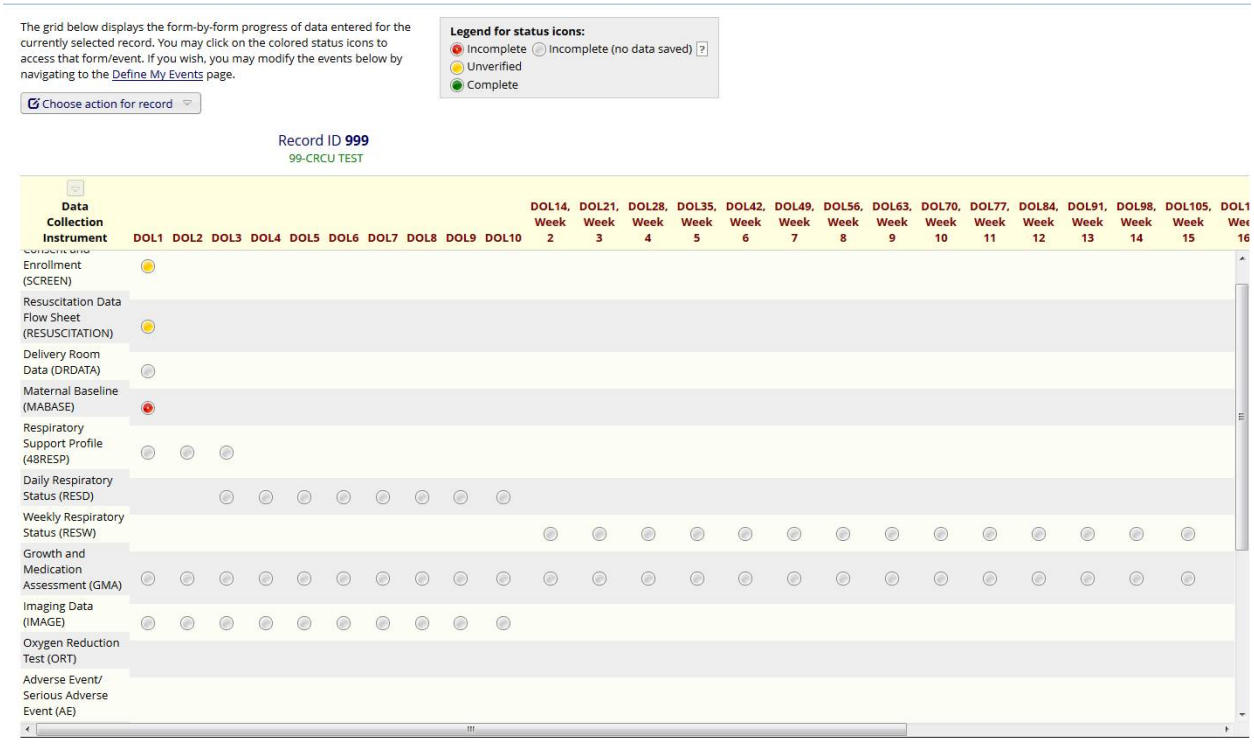
Sustained Aeration of Infant Lungs Study (SAIL)

Visit Schedule

Form Name	Form Code	Baseline					W44 PMA, Discharge, Withdrawal, Transfer or Death	Follow Up
		DOL1	DOL2	DOL3	Daily DOL3-DOL10	Weekly DOL14-Week36		22-26 Months Corrected Age
Data Collection Instruments								
Screening and Enrollment Data	SCREEN	X						
Resuscitation Data Flow Sheet	RESUSCITATION	X						
Delivery Room Data Form	DRDATA	X						
Respiratory Support Profile	48RESP	X	X	X				
Maternal Baseline	MABASE	X						
Growth and Medication Assessment	GMA	X	X	X	X	X (Weekly)		
Respiratory Status_Daily	RESD				X			
Respiratory Status_Weekly	RESW					X (Weekly)		
Imaging Data	IMAGE	X	X	X	X			
Neonatal Outcome Data	OUTCOME						X	
Study Status	SSTATUS						X	
Neurodevelopmental Data	NEURO							X
22-26 Month Follow Up	FUP							X
Readmission	READMIT						X	
Tests								
Oxygen Reduction Test	ORT					W36		
PRN Visit								
Adverse Event/ Serious AE Form	AE	PRN	PRN	PRN	PRN	PRN	PRN	PRN

Data Collection /Visit Schedule Displayed in REDCap Database

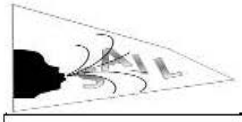
The REDCap database also displays the data collection schedule per each PID in the tab labeled Event Grid (see image of schedule shown below). The Event Grid serves as a guideline to monitor data entry for each patient. For example, Day of Life (DOL 1) column lists the data collection forms to be entered at that scheduled time point, and highlights the status of data entered on each form by indicating if the form is complete, incomplete, or unverified.



12. Completing the Data Case Report Forms

The accuracy and integrity of the SAIL Study data are of highest importance, and are considered essential to the research goals of the SAIL Study. To ensure site data quality management practices, each site Research Coordinator should maintain a consistent schedule for the timely entry of study data into the DMS, as it is collected. Typically, data should be entered into the DMS within 24 hours of its collection. The following pages provide instructions for completing the data case report forms.

12.1. Screening for Consent and Enrollment [SCREEN] Form:



SUSTAINED AERATION OF INFANT LUNGS STUDY
SCREENING FOR CONSENT AND ENROLLMENT

PID __ __ __ __ __ __ __
DATE __ __/__ __/__ __ __ __

Note: Complete this form for all screened babies regardless of consent status. Record above date as the screening date or baby's DOB. If multiple birth, complete 1 form for *each* baby.

1. What type of consent is in use for trial participation? ☐1 Antenatal ☐2 Deferred
2. Was consent obtained for resuscitation procedures? ☐1 Yes ☐0 No
3. If consent was not obtained for resuscitation procedures, was consent obtained to collect medical record data? ☐1 Yes ☐0 No

If No is checked for Questions #2 or #3, select all reasons consent was not obtained. (Check all that apply)

- ☐1 Mother is unable to consent for her medical care and does not have a surrogate guardian
- ☐2 Parents refused
- ☐3 Parents were not available
- ☐4 Baby was enrolled in another research study
- ☐5 Screening oversight
- ☐6 On request of responsible physician
- ☐7 Language Barrier
- ☐8 Imminent delivery
- ☐98 Other, Specify _____

4. Baby met eligibility criteria regardless of consent? ☐1 Yes ☐0 No
   a. If No, select all exclusion criteria (Check all that apply.)
      - ☐1 Adequate respiratory effort and HR>100 (if known), PPV not indicated
      - ☐2 Considered non-viable by either the attending neonatologist, obstetrician or both
      - ☐3 Major anomaly(ies)
      - ☐4 Stillborn
      - ☐5 Baby was born outside of Eligibility window
      - ☐98 Other, specify _____
5. Randomization envelope opened? ☐1 Yes ☐0 No
   (If yes, complete Resuscitation form and questions below.)
   a. Enter Randomization Number: __ __ __ __ __ __
   b. If envelope was opened in error, explain: _____

---

6. Baby's date of birth __ __/__ __/__ __ __ __ (Month/Day/Year)
7. Gender ☐1 Male ☐2 Female
8. Was this a multiple birth? ☐1 Yes ☐0 No
   a. Indicate the baby's birth order __ Number of __ Number
9. Gestational age __ __ Weeks __ __ Days
10. Birth weight __ __ __ __ grams
11. Apgar score __ __ 1 min. __ __ 5 min.
12. Is the baby enrolled in any other randomized trial? ☐1 Yes ☐2 No ☐88 Unknown
    a. If Yes, enter name of other clinical trial _____
    b. If Yes, enter name of other clinical trial _____

V6.0.20150105 PAGE 1 OF 1 SCREEN

12.2. Screening for Consent and Enrollment Data Instructions

Data on the SCREEN form should be completed for all infants of mothers who have been screened for the study (regardless of consent status). Completing the SCREEN form is considered mandatory and a paper case report form must exist for the data collected on this form. Please Note: In those instances when a baby is born outside of the eligibility window, or when mother refuses to consent for study participation or data collection, complete ONLY questions 1-5 of the SCREEN form. If multiple births occur, complete 1 form for *each* baby. Include the birth order even if one of the babies is stillborn. For instance: If twins were born and baby 1 of 2 was randomized and baby 2 of 2 was stillborn and thus ineligible , complete 1 form for each baby. Check "Stillborn" on second screen form for baby 2 under Question 4.

In the Header of the form record the PID and date. The date can be either the mother's screening date or infant's date of birth.

Q.1: Indicate the type of consent obtained. (Check either antenatal or deferred).If antenatal consent is used, please respond to Q.2 and Q.3. If deferred consent is used, skip to Q.3.

Q.2: Indicate if consent was obtained for resuscitation procedures (Check either Yes or No).

Q.3: If consent for resuscitation procedures was not obtained, indicate if consent was obtained for medical record data collection. (Check either Yes or No).
If response to above Q. 2 OR Q.3 is No, select all reasons why consent was not obtained.

Q.4: Indicate whether baby met all eligibility criteria regardless of consent. (Check Yes or No).

Q.4a: If the baby did not meet eligibility criteria, indicate all exclusion criteria that apply.

Q.5: Indicate (Yes or No) if randomization envelope was opened.

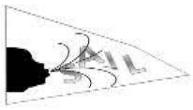
Q.5a: If infant was randomized into the study, enter the 6 digit randomization number. (Number is obtained when envelope is opened at resuscitation) NOTE: **Multiple births** will be randomized as a unit so only one envelope is opened and the same randomization number is applied to all of the infants.

Q.5b: If a **randomization envelope** is opened in error, briefly explain. Complete **protocol violation** form (see Appendix 2) and submit it to the DCC within 2 days, along with the opened envelope and the randomization slip that was enclosed.

Questions 6 thru 11: Complete all requested birth-related data. Accuracy of these data are essential to generating ongoing reports about the SAIL infants and are used in many places to indicate data collection points during and after hospitalization.

Q.12: Indicate whether infant is enrolled in any other randomized trial. If the infant is enrolled in another randomized trial, provide the name of the study or studies.

12.3. Resuscitation Data Flow Sheet [RESUSCITATION] Form



SUSTAINED AERATION OF INFANT LUNGS (SAIL) STUDY

RESUSCITATION DATA FLOW SHEET

PID: _ _ _ _ _ _ Mother's Initials _ _ _ _ _ _

DATE: _ _ / _ _ / _ _ _ _ Recorder's Initials _ _ _ _ _ _

TIME: _ _ : _ _ : _ _

Record baby's date and time placed on resuscitation trolley above.

		INTERVENTION			Post Intervention Status
Time Note: Mandatory- Record time at *start* of resp. action.	**Time Zero** Baby on resuscitation trolley	**Period 1 – Mandatory Immediate up to 30 sec**	**Period 2 - Mandatory Post 1st Action**	**Period 3** Was period 3 assessment performed? ☐ Yes ☐ No	**Period 4** Was period 4 assessment performed? ☐ Yes ☐ No
		Assessment on CPAP _ _ _ cmH2O	Assessment	Assessment	Assessment
Record Elapsed Time →	0 0	_ _ _ sec	_ _ : _ _ min:sec	_ _ : _ _ min:sec	_ _ : _ _ min:sec
	Heart rate	☐ < 60 ☐ 60-100 ☐ >100	☐ < 60 ☐ 60-100 ☐ >100	☐ < 60 ☐ 60-100 ☐ >100	☐ < 60 ☐ 60-100 ☐ >100
	Respiratory Effort	☐ None ☐ Inadequate (Gasping/apnea) ☐ Adequate	☐ None ☐ Inadequate (Gasping/apnea) ☐ Adequate	☐ None ☐ Inadequate (Gasping/apnea) ☐ Adequate	☐ None ☐ Inadequate (Gasping/apnea) ☐ Adequate
Respiratory Mode Data fields are mandatory.	Randomized ☐ **SI** ☐ **NRP** ☐ **NA, Baby not Randomized**	Actions	Actions	Actions	Actions
	MR SOPA		☐ Yes ☐ No	☐ Yes ☐ No	☐ Yes ☐ No
	CPAP		☐ CPAP _ _ cmH_2O	☐ CPAP _ _ cmH_2O	☐ CPAP _ _ cmH_2O
	SI	☐ SI @ 20 cmH_2O x 15 sec	☐ SI @ 25 cmH_2O x 15 sec		
	PPV	☐ PIP/PEEP x f _ _ _/_ _ _ x _ _ _	☐ PIP/PEEP x f _ _ _/_ _ _ x _ _ _	☐ PIP/PEEP x f _ _ _/_ _ _ x _ _ _	☐ PIP/PEEP x f _ _ _/_ _ _ x _ _ _
	FiO_2	_ _ _ %	_ _ _ %	_ _ _ %	_ _ _ %
	Interface	☐ Mask ☐ Mononasal ☐ ETT	☐ Mask ☐ Mononasal ☐ ETT	☐ Mask ☐ Mononasal ☐ ETT	☐ Mask ☐ Mononasal ☐ ETT
	Intubation?	☐ Yes ☐ No	☐ Yes ☐ No	☐ Yes ☐ No	☐ Yes ☐ No
	Compressions?	☐ Yes ☐ No	☐ Yes ☐ No	☐ Yes ☐ No	☐ Yes ☐ No
SpO2 (if available)		_ _ _ _ %	_ _ _ _ %	_ _ _ _ %	_ _ _ _ %
Additional information					
Affix randomization slip here. →		*Sample:* SAIL Trial Site #11 Envelope #4 of 5	Randomization #113001 **Arm – Intervention Sustained Inflation (SI)**		

V4.0.20150112 **RESUSCITATION**

Important Note: If your clinical site has integrated the SAIL RESUSCITATION form into an existing delivery room clinical form, the Research Coordinator must transcribe the data from the integrated clinical form onto the RESUSCITATION paper CRF. If using an integrated clinical form, ensure that all data elements contained in the RESUSCITATION CRF have been accurately represented in the integrated delivery room clinical form in its entirety and that the CRF content has not been altered. These forms will be subject to periodic audit by the Coordinating Center throughout the course of the study.

12.4. Resuscitation Data Flow Instructions

Data collected on this form **must be collected and recorded in real time** and a paper case report form must exist for these data. NOTE: Clinical assessment and respiratory intervention actions are outlined on the form in four (4) separate columns, representing four (4) time periods during resuscitation in which specified data elements are recorded. Complete all data elements listed in the Period 1 and Period 2 columns on this form; these are **mandatory** fields. If applicable, complete data in Period 3 and Period 4 columns as indicated on the form. (This form is completed on all eligible infants who are randomized. This form is also completed on infants whose parents have consented to allow data collection only or if a deferred consent approach is permitted by local IRB).

a. In the right header section of the form, record the following: Infant PID number (6 digits); Date of infant birth; Time infant is placed on reuscitation trolley which is to is reported in 24 hr. clock time including seconds, if seconds is available. If seconds is not available, record the seconds as zero (example: Time: 11:15:00). Also record the mother's initials and the initials of the person recording the data on this form.

b. After the infant is placed on the resuscitation trolley, the Elapsed time is recorded using a stop watch, beginning at Time Zero (0 0)At the start of Period 1 within the first 15-30 seconds, the airway is cleared, CPAP initiated, and the infant is assessed for SAIL elegibility. Record in the section: ASSESSMENT on CPAP - the initial CPAP pressure measurement (cm H2O setting) and seconds in time when initiated; Check boxes to indicate the heart rate and respiratory effort.

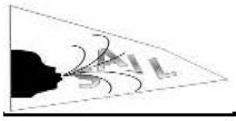
c. When the randomization envelope is opened and treatment arm announced, indicate in Check Box the randomization arm [SI or NRP] assignment and affix the randomization sticker in the space indicated at the bottom of the form. Check Box NA Baby not randomized, if the infant is not randomized into the study.

d. Period 1 - Record in the ACTIONS section the respiratory mode data indicated for either SI or PPV (if PPV mode, indicate pressure setting and duration); Indicate Fraction of Inspired Oxygen (FIO2) value: Check box of type of airway interface used; Indicate if intubation and compressions were performed (Check box Yes or No). Record Oxygen Saturation (SpO2) measurement, if available. **IMPORTANT NOTE:** In the **Additional Information section of the Resuscitation form, please record any other delivery room research required data items that may not be routinely recorded in the delivery room record**.

e. Period 2- Record Assessment data for elapsed time, heart rate and respiratory effort; Record in the ACTIONS section the respiratory mode data as indicated.

f. If Period 3 or Period 4 assessments and respiratory actions are performed (which means the first box in the column is checked □ Yes), the data fields in these periods will also become mandatory.

12.5. Delivery Room Data [DRDATA] Form- Page 1:



SUSTAINED AERATION OF INFANT LUNGS STUDY
DELIVERY ROOM DATA

PID: __ __ __ __ __ __ __
DATE: __ __ / __ __ / __ __ __ __

DELIVERY ROOM DATA LIST

Note: Record information from DR resuscitation or from the NICU within the first 2 hours of life.

1. Time of Birth — __ / __ / __ __ __ __ & __ __ : __ __ : __ __ (MM-DD-YYYY and 24 Hour Clock (HH:MM:SS))
2. Time of cord clamping — __ / __ / __ __ __ __ & __ __ : __ __ : __ __ (MM-DD-YYYY and 24 Hour Clock (HH:MM:SS))
3. Oxygen Saturation (SpO2) at specific time intervals:
   a. 3 minutes — __ __ __ %
   b. 5 minutes — __ __ __ %
   c. 10 minutes — __ __ __ %
4. Surfactant administered? ☐1 Yes ☐0 No
   a. Start Time — __ __ : __ __ (24 Hour Clock)
   b. Dose completed? ☐1 Yes ☐0 No
5. Epinephrine administered? ☐1 Yes ☐0 No
   a. Number of doses ____
6. Chest compressions? ☐1 Yes ☐0 No
7. First temperature recorded — __ __ __.__ ☐1 ○C ☐2 ○F
   a. Time of temperature recording — __ __ : __ __ (24 Hour Clock)
8. Blood Gas and Laboratory results

Time (24 Hour Clock)	__ __ : __ __ ☐99 NA
Sampling site	☐0 Cord- Umbilical Artery ☐1 Cord- Umbilical Vein ☐98 Other, specify
pH	__ __.__ __
PCO2	__ __ __.__
PO2	__ __ __.__
HCO3	__ __.__
Base excess/deficit (include +/-)	__ __.__
Hemoglobin	__ __.__
Hematocrit	__ __.__
Glucose (mg/dL)	__ __ __

9. Respiratory Settings at time of blood gas
   a. CPAP ☐1 Yes ☐0 No ☐99 NA, Umbilical Cord
   b. Non-invasive positive pressure ventilation ☐1 Yes ☐0 No ☐99 NA, Umbilical Cord
   c. Conventional Mechanical Ventilation (CMV) ☐1 Yes ☐0 No ☐99 NA, Umbilical Cord
   d. FiO2 __ __ __ % ☐99 NA, Umbilical Cord
10. Volume given? ☐1 Yes ☐0 No
    a. If yes, check all that apply
    ☐1 Normal Saline
    ☐2 Packed Red Blood Cells

V7.1.20141215 PAGE 1 OF 2 DRDATA

12.6. Delivery Room Data – Page 1 Instructions

Data on this form can be collected from the delivery room clinical records or the NICU clinical records after the infant resuscitation activity is completed.

a. All of the data fields on this form (except for Question #8 & 9) are considered **mandatory** and cannot be missing.

Q.1: Record time of birth according to 24 hour clock time including seconds. If seconds is not available, record the seconds as zero

Q. 2: Record time of cord clamping according to 24 hour clock time including seconds. If seconds is not available, record the seconds as zero.

Q.3: Record percent oxygen saturation (SpO2) for each specified time interval indicated in Q.3a-3c.

Q.4: Check box (Yes or No) to indicate if Surfactant was administered.

Q.4a: If Yes, record start time of dose administration.

Q.4b: Check box (Yes or No) to indicate if dose was completed.

Q.5: Check box (Yes or No) to indicate if Epinephrine was administered.

Q.5a: If Yes, record number of Epinephrine doses given.

Q.6: Check box (Yes or No) to indicate if chest compressions were performed.

Q.7: Record the numerical value of the first temperature obtained on the infant. Check box to indicate the temperature scale used, either Celsius or Fahrenheit.

Q.7a: Record the time the temperature was obtained.

Q.8: Complete these data elements if blood sample is drawn and data is available. Record time blood sample was drawn; check box to indicate sampling site (cord or other); record blood gas values, base excess/deficit, and other indicated laboratory values.

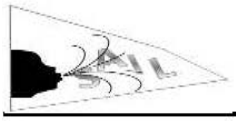
Q.9a - Q9c: Check (Yes or No or NA) to all listed items to indicate respiratory setting at the time of the blood gas draw.

Q.9d: Record percent value of Fraction of Inspired Oxygen (FiO2).

Q.10: Check box Yes or No to indicate if a volume infusion was given.

Q.10a: If Yes, indicate type of infusion given by checking boxes of all that apply.

12.7. Delivery Room Data [DRDATA] Form– Page 2



SUSTAINED AERATION OF INFANT LUNGS STUDY
DELIVERY ROOM DATA

PID: _ _ _ _ _ _ _ _
DATE: _ _ _ / _ _ _ / _ _ _ _ _ _

11. Procedures in the delivery room or in the NICU within 2 hours - Indicate if procedure was performed:

a.	UAC	☐1 Yes	☐0 No
b.	UVC	☐1 Yes	☐0 No
c.	Peripheral arterial stick	☐1 Yes	☐0 No
d.	Peripheral IV	☐1 Yes	☐0 No
e.	Paracentesis	☐1 Yes	☐0 No
f.	Thoracentesis	☐1 Yes	☐0 No
g.	Needle Thoracotomy (decompression)	☐1 Yes	☐0 No
h.	Chest tube - R	☐1 Yes	☐0 No
i.	Chest tube - L	☐1 Yes	☐0 No
j.	Intubation	☐1 Yes	☐0 No

If intubated, check most relevant indication (Select one)
☐1 Respiratory Distress
☐2 Resuscitation
☐3 Persistent Apnea after stabilization
☐4 Surfactant administration
☐98 Other, specify _____

12. Additional Medications? ☐1 Yes ☐0 No
If Yes, check all that apply

a.	Inotrope	☐1 Yes	☐0 No
b.	Bicarbonate	☐1 Yes	☐0 No
c.	Other, specify: _____	☐1 Yes	☐0 No

13. Complications in Delivery Room (DR)? ☐1 Yes ☐0 No
If Yes, check all that apply

a.	Pneumothorax	☐1 Yes	☐0 No
b.	Pulmonary Hemorrhage	☐1 Yes	☐0 No
c.	Hypotension	☐1 Yes	☐0 No
d.	Bleeding other than pulmonary hemorrhage	☐1 Yes	☐0 No
e.	Other, specify: _____	☐1 Yes	☐0 No

14. Final Disposition at end of resuscitation:
☐1 Alive
a. Time at end of resuscitation _____
24 Hour Clock
☐2 Infant Died
a. Time of death _____
24 Hour Clock

15. Were there any protocol violations? ☐1 Yes ☐0 No
a. If Yes, specify: _____

Final respiratory settings on admission to NICU
16. Select final respiratory setting
☐1 CPAP @ ___ ___ cmH2O
☐2 PPV @ ___ ___ PIP/___ ___ PEEP/ ___ ___ f
☐98 Other, specify: _____

17. Fraction of Inspired Oxygen (FiO2): _ _ _ _ %

18. Airway device (Select one): ☐1 Mask ☐2 NP tube ☐3 ETT ☐4 Prongs

19. If applicable, initials of person performing respiratory resuscitation _ _ _ _

V7.1.20141215 PAGE 2 OF 2 DRDATA

12.8. Delivery Room Data – Page 2 Instructions

Q.11a – Q.11j: Check box (Yes or No) of all listed delivery room/NICU admission procedures (*items a-j*) to indicate what procedures were performed.

If *item j* (Intubation) is checked Yes, check only one box selection to indicate most relevant reason for intubation.

Q.12: Check box (Yes or No) to indicate any additional medications administered. If Yes, indicate yes or no to all that apply (12a-c).If other medication, specify in text box.

Q.13: Check box (Yes or No) to indicate if complications occurred in the Delivery Room. If Yes, indicate yes or no for all listed complications that apply (13 a-d). If other complication, specify in text box.

Q.14: When Delivery Room resuscitation has ended, indicate the final disposition of the infant (alive or death) and write in the 24 hour clock time that the selected final disposition occurred.

Q.15: Indicate if any protocol violations occurred by checking either Yes or No. If Yes, specify violation in text box (15a).

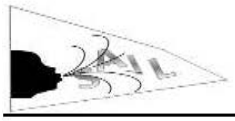
Q.16: Indicate the final respiratory settings upon admission of the infant to the NICU (select CPAP, PPV or Other). If other selected, specify in text box.

Q.17: Record percent value of Fraction of Inspired Oxygen (FiO2).

Q.18: Select and check one box to indicate airway device used
(Mask; NP Tube; ETT; Prongs).

Q.19: Indicate the initials of the clinician who performed the respiratory resuscitation in the delivery Room.

12.9. Maternal Baseline [MABASE] Form - Page 1



SUSTAINED AERATION OF INFANT LUNGS STUDY PID: _ _ _ _ _ _

MATERNAL BASELINE DATE: _ _ / _ _ / _ _ _ _

Maternal Demographic Data:

1. What is the mother's date of birth? Month _ _ / Day _ _ / Year _ _ _ _
2. Gravida _ _
3. Parity _ _
4. What is the mother's ethnicity?
   - ☐ 1 Hispanic / Latino
   - ☐ 0 Not Hispanic / Latino
5. What is the mother's race (Check all that apply)?
   - ☐ 1 North American Indian / Native Alaskan
   - ☐ 2 Asian
   - ☐ 3 Black / African American
   - ☐ 4 Native Hawaiian / Other Pacific Islander
   - ☐ 5 White / Caucasian
   - ☐ 98 Other, specify: _____
6. What is the family arrangement?
   - ☐ 1 Single parent family
   - ☐ 2 Two parent family
   - ☐ 88 Unknown
7. What is the mother's highest level of education?
   - ☐ 1 Less than 7th grade
   - ☐ 2 7th – 9th grade
   - ☐ 3 10th – 12th grade
   - ☐ 4 High school degree
   - ☐ 5 Partial college
   - ☐ 6 College degree
   - ☐ 7 Graduate degree
   - ☐ 88 Unknown
8. Maternal Occupation (at time of delivery) (Check all that apply)
   - ☐ 1 Self Employed as: _____
   - ☐ 2 Employed as: _____
   - ☐ 3 Unemployed
   - ☐ 4 Full-time Homemaker
   - ☐ 5 Student
   - ☐ 88 Unknown
   - ☐ 98 Other, specify: _____
9. Were antenatal corticosteroids given? ☐ 1 Yes ☐ 0 No
   a. If **Yes**, total number of completed courses:
      - ☐ 0 None
      - ☐ 1 One course
      - ☐ 2 Two courses
      - ☐ 3 Three courses
   b. Number of incomplete courses:
      - ☐ 0 None
      - ☐ 1 One or more courses

V2.0_20140910 PAGE 1 OF 2 MABASE

12.10. Maternal Baseline Data – Page 1 Instructions

Maternal baseline data for this CRF may be located in maternal antenatal medical records and delivery room medical records. If information needed to complete data questions on this form is not in the mother's medical record, the research coordinator should obtain the information directly from the mother. In the case of multiple births, complete one MABASE form for each baby. All of the data fields on this form are considered **mandatory** and should not be missing.

Q.1: When recording mother's date of birth, check the reported date against the reported age to verify the accuracy of the information. Record the date of birth in mm/dd/yyyy format.

Q.2: Gravida indicates the number of times the mother has been pregnant, regardless of whether these pregnancies were carried to term. The most current pregnancy is included in this count. Record the numeral in 2 digits designating the number of times the mother has been pregnant. Example: Gravida 03 = three pregnancies.

Q.3: Parity refers to the number of deliveries the mother had. (Note: A woman who has never carried a pregnancy beyond 20 weeks is nulliparous, or para 0). Record the numeral in 2 digits indicating the number of times the mother has given birth. Example: Parity 02 = two deliveries. A delivery consisting of multiples, such as twins or triplets, count as one birth for the purposes of recording parity.

Q.4: Ethnicity is self-reported and the participant should be asked about their ethnic background before checking the appropriate box.

Q.5: Race is self-reported and multiple categories may be reported by the participant when responding. If the participant is uncertain how to reply, ask them to make the best possible choice. If mother reports race & ethnicity as the same, check off the box for "Other" and specify the race that is reported by the mother regardless of whether it is the same as the ethnicity reported.

Q.6: This question refers to the family unit. Verify this information with the participant. Check *Unknown* only if you cannot verify this information.

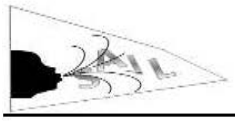
Q.7: Mothers Highest Level of Education. Verify this information with the participant before checking the appropriate box. Check box *Unknown* if you cannot verify this information.

Q.8: Maternal Occupation at time of delivery should be verified with mother. Multiple response boxes can be checked such as student and employed as ___.

Q.9: Check box Yes or No to indicate if antenatal corticosteroids were given.

Q.9a-Q.9b: If Yes, check one box for total number of completed courses. If No, check one box for number of incomplete courses.

12.11. **Maternal Baseline Data [MABASE] Form – Page 2**



SUSTAINED AERATION OF INFANT LUNGS STUDY PID: _ _ _ _ _ _

MATERNAL BASELINE DATE: _ _ / _ _ / _ _ _ _

10. Did the mother take any medications to prolong pregnancy? ☐1 Yes ☐0 No

    a. If **Yes**, check all that apply:
    - ☐1 Progesterone
    - ☐2 Cyclooxygenase inhibitors (Indocin)
    - ☐3 Oral betamemetics
    - ☐4 Calcium Channel Blockers
    - ☐5 Oxytocin receptor antagonist
    - ☐6 Magnesium Sulfate
    - ☐98 Other, specify:_____

11. Was magnesium sulfate given for any reasons other than tocolysis? ☐1 Yes ☐0 No
    a. If **Yes**, check the primary indication:
    - ☐1 Preeclampsia / eclampsia
    - ☐2 Prevention of Cerebral Palsy

12. Did the mother have diabetes during pregnancy? ☐1 Yes ☐0 No
    a. If **Yes**, did she receive insulin for her diabetes? ☐1 Yes ☐0 No

13. Were antibiotics given prior to delivery? ☐1 Yes ☐0 No

    a. If **Yes**, why were antibiotics given (check all that apply)?
    - ☐1 Chorioamnionitis
    - ☐2 Group B Streptococcus (GBS) prophylaxis
    - ☐3 Preterm labor
    - ☐98 Other, specify:_____

14. Was there placental abruption? ☐1 Yes ☐0 No

15. Did the membrane rupture ≥ 24 hours before delivery? ☐1 Yes ☐0 No
    a. If **Yes**, did the membrane rupture more than 7 days before delivery? ☐1 Yes ☐0 No ☐88 Unknown

16. Was placental pathology obtained? ☐1 Yes ☐0 No
    a. If **Yes**, was there histologic evidence of chorioamnionitis? ☐1 Yes ☐0 No

17. What was the mode of delivery?
    - ☐1 Vaginal Vertex
    - ☐2 Vaginal Breech
    - ☐3 Caesarian Section

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12.12. Maternal Baseline Data – Page 2 Instructions

Q.10: Check box (Yes or No) to indicate if mother received medications to prolong pregnancy in the antenatal period.

Q10 a: If box is checked Yes, then check boxes of all listed medications that apply.

Q.11: Check Box (Yes or No) to indicate if magnesium sulfate was given for any reason other than tocolysis (suppress premature labor).

Q11a: If box is checked Yes, then check only one box for the primary indication.

Q.12: Check Box (Yes or No) to indicate if there was maternal diabetes during pregnancy.

Q12a: If box is checked Yes, then check box (Yes or No) to indicate if mother received insulin.

Q.13: Check box (Yes or No) to indicate if mother received antibiotics prior to delivery.

Q13a: If box is checked Yes, then check boxes of all listed reasons that apply.

Q.14: Check box (Yes or No) to indicate if there was a placental abruption.

Q.15: Check box (Yes or No) to indicate if membrane rupture occurred ≥ 24 hours before delivery.

Q15a: If box is checked Yes, check box (Yes or No or Unknown) to indicate if there was a membrane rupture more than 7 days before delivery.

Q.16: Check box (Yes or No) to indicate if placental pathology was obtained.

Q16a: If box is checked Yes for placental pathology, then check box (Yes or No) to indicate if there was histologic evidence of chorioamnionitis (inflammation of the fetal membranes due to a bacterial infection).

Q.17: Check one box to indicate the mode of infant delivery.

13. Generating an Individual Patient Visit Schedule

An indiviual visit schedule can be generated for each baby once the following **key data fields** have been entered into the Screening for Consent and Enrollment (SCREEN) form in the REDCap database:

- Baby's Date of Birth (**question 6** on SCREEN form)
- Gestational age in Weeks and Days (**question 9** on SCREEN form)

The visit scheduling report will display all of the milestones and forms expected to be completed from date of birth (Day of Life 1) to Week 44 corrected age and it should be used to inform the study team of the study activites that occur on particular days and dates.

Date	Day	Gestational Age		Week	Day of Life	Data Collection/Milestone
		Weeks	Days			

Column Descriptions:

Date: Begins with the DOB and end with the date of the Week 44 milestone

Day: Begins with the DOB and list all days of the week in sequential order according to the date

Day of Life: Begins with DOB as Day of Life 1 to day of life 10, then DOL 14, 21, 28, 35, 42 etc. until Week 44

GA Weeks: Based on the data entered for Gestational Age in Weeks and mark each sequential week up to Week 44

GA Days: Based on the data entered for Gestational Age in days and mark each sequential day of the week up to Week 44. **There are 7 GA Days in one week, however, they are numbered starting with 0.** One gestational week will be marked with days 0, 1, 2, 3, 4, 5, 6.

Week: Indicates the weeks life, Week 1 begins with the DOB, DOL 1

Procedure Schedule/ Milestones:

DOL1: Baseline data (SCREEN, RESUSCITATION, DRDATA, MABASE), Respiratory Support Profile (48 RESP), Growth and Medication Data (GMA), Imaging Data (IMAGE)

DOL2: Respiratory Support Profile, Growth and Medication Data, Imaging Data (IMAGE)

DOL3: Respiratory Support Profile, Daily Respiratory Status (RESD), Growth and Medication Data, Imaging Data

*DOL 4 to 10: Collect DAILY: Daily Respiratory Status (RESD), Growth and Medication Data, Imaging Data

*DOL 14–week 36: Collect ONCE A WEEK ONLY: Weekly Respiratory Status (RESW), Growth and Medication Data

DOL28, Week 4: Indicates end of AE collection

Week 36: Weekly Respiratory Status, Growth and Medication Data, Oxygen Reduction Test (ORT)

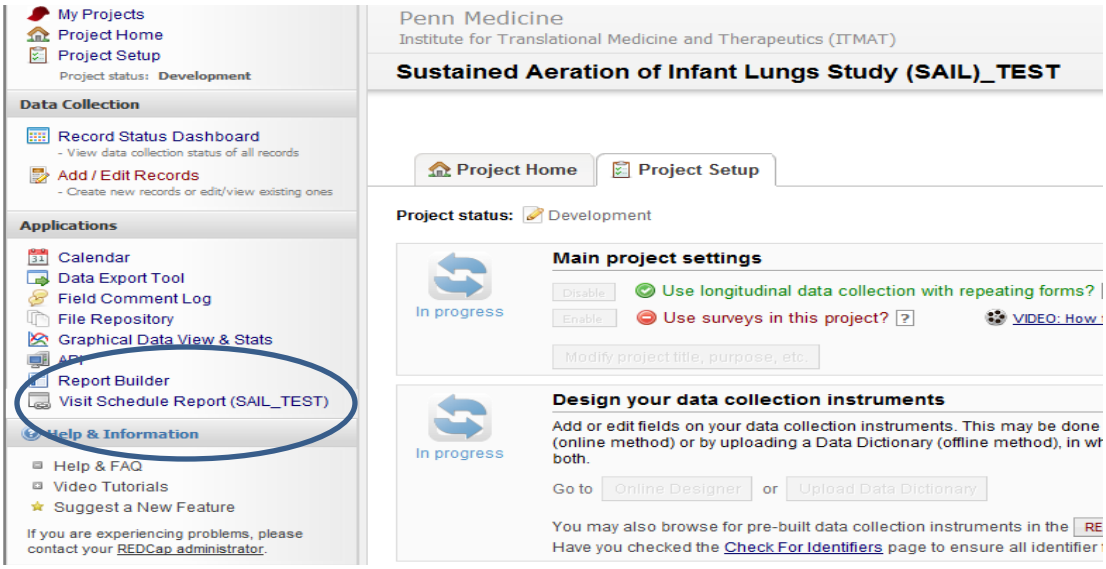
Week 37 to Week 43: Schedule and enter Study Status (SSTATUS) and Neonatal Outcome Data

Week 44: Late Outcomes if still hospitalized

13.1. Creating a New Visit Schedule Report

Data entry personnel will have access to the scheduling report in the REDCap database. It will be very helpful in organizing work flow at the site to generate a Visit Schedule for each patient enrolled in the study. Steps to run the Visit Schedule Report follow:

1) Login to REDCAP
2) Choose the SAIL TEST or SAIL LIVE study once you have access
3) In the menu options, under 'APPLICATIONS', look for the link "Visit Schedule Report" (SAIL TEST) on the left side. Clicking on the link will take the users to the report page.



4) Enter Subject No. which is the PID
5) Click Submit
6) The Scheduling Report for that PID will be displayed in your web browser.

Sustained Aeration of Infant Lungs Study - Visit Schedule Report (TEST Study)

Disconnect

Subject No. [ ]
Submit

Program finished

Key Fields for this report
PID: 110013
DOB: 2014-07-03
GA weeks: 25
GA days: 5

VISIT SCHEDULE REPORT - 110013

Date	Day	Gestational Age Postmenstrual age		Week	Day of Life	Procedure Schedule/ Milestone
		Weeks	Day			
07/03/2014	Thursday	25	5	Week 1	1	Baseline data, Respiratory Support Profile, Maternal Baseline, Growth and Medication Data
07/04/2014	Friday	25	6	Week 1	2	Respiratory Support Profile, Growth and Medication Data, Imaging Data
07/05/2014	Saturday	26	0	Week 1	3	Respiratory Support Profile, Daily Respiratory Status, Growth and Medication Data, Imaging Data
07/06/2014	Sunday	26	1	Week 1	4	Daily Respiratory Status, Growth and Medication Data, Imaging Data
07/07/2014	Monday	26	2	Week 1	5	Daily Respiratory Status, Growth and Medication Data, Imaging Data
07/08/2014	Tuesday	26	3	Week 1	6	Daily Respiratory Status, Growth and Medication Data, Imaging Data
07/09/2014	Wednesday	26	4	Week 1	7	Daily Respiratory Status, Growth and Medication Data, Imaging Data
07/10/2014	Thursday	26	5	Week 2	8	Daily Respiratory Status, Growth and Medication Data, Imaging Data
07/11/2014	Friday	26	6	Week 2	9	Daily Respiratory Status, Growth and Medication Data, Imaging Data
07/12/2014	Saturday	27	0	Week 2	10	Daily Respiratory Status, Growth and Medication Data, Imaging Data
07/16/2014	Wednesday	27	4	Week 2	14	Weekly Respiratory Status, Growth and Medication Data
07/23/2014	Wednesday	28	4	Week 3	21	Weekly Respiratory Status, Growth and Medication Data
07/30/2014	Wednesday	29	4	Week 4	28	Weekly Respiratory Status, Growth and Medication Data , AE form
08/06/2014	Wednesday	30	4	Week 5	35	Weekly Respiratory Status, Growth and Medication Data
08/13/2014	Wednesday	31	4	Week 6	42	Weekly Respiratory Status, Growth and Medication Data
08/20/2014	Wednesday	32	4	Week 7	49	Weekly Respiratory Status, Growth and Medication Data

14. Collecting Daily and Weekly Data

When documenting respiratory status over the course of the study, the date field in the header of the form and in the REDCap system should reflect the date of the clinical event (not the date on which you are collecting data).

It is possible to retrospectively collect data from the patient medical record to complete the required case report forms and enter data into the REDCap system; however, in order to stay up to date, study data should be entered into the REDCap system within 1 week of the event.

Recording Time: Recording time on the paper case report forms and in the REDCap Data Management System will be done according to the 24 hour clock. When recording the 24 hour clock time on the paper case report form, you must remember to insert the leading "0" or "00".

The following is a 24-Hour Clock Conversion Sheet to reference:

STANDARD	24-HOUR	STANDARD	24-HOUR
12 MIDNIGHT	0000	12 NOON	1200
12:01 AM	0001	12:01 PM	1201
12:15 AM	0015	12:15 PM	1215
12:30 AM	0030	12:30 PM	1230
12:45 AM	0045	12:45 PM	1245
1 AM	0100	1 PM	1300
2 AM	0200	2 PM	1400
3 AM	0300	3 PM	1500
4 AM	0400	4 PM	1600
5 AM	0500	5 PM	1700
6 AM	0600	6 PM	1800
7 AM	0700	7 PM	1900
8 AM	0800	8 PM	2000
9 AM	0900	9 PM	2100
10 AM	1000	10 PM	2200
11 AM	1100	11 PM	2300

14.1. Respiratory Support Profile [48RESP] Form

RESPIRATORY SUPPORT PROFILE

FORM IS COMPLETED FOR THE FIRST 48 HOURS OF LIFE.

PID:__ __ __ __ __ __

DATE:__ __ / __ __ / __ __ __ __

1. Collect **hourly respiratory support profile** over first 48 hours post-delivery.
   a. Count time as a 24 hour cycle from time of birth as it occurs over the first 48 hours of life.
   b. Record FiO2 (%), SpO2, Modality and ventilation settings every hour for the first three hours and then every 3 hours for the first 48 hours of life.
   c. Complete one form for each Day of Life. Note: Date of Birth= Day of Life 1, regardless of time of birth.

Time	Hour 24 Hour Clock	FiO2	SpO2	Modality Use code number	If Other, specify vent modality	MAP cmH2O	PEEP cmH2O	CPAP cmH2O	Rate	Flow Lpm	Pressure High	Pressure Low cmH2O	Tidal Volume	PIP
1	__ __:__ __													
2	__ __:__ __													
3	__ __:__ __													
4	__ __:__ __													
5	__ __:__ __													
6	__ __:__ __													
7	__ __:__ __													
8	__ __:__ __													
9	__ __:__ __													
10	__ __:__ __													

Codes to identify ventilation modality		Support Measurements
1	Conventional Mechanical Ventilation (CMV)	MAP, PEEP, Rate, Tidal Volume, PIP (Measured)
2	High Frequency Oscillation Ventilation (HFOV)	MAP
3	High Frequency Jet Ventilation (HFJV)	MAP
4	Nasal Intermittent Positive Pressure Ventilation (NIPPV)	MAP, PEEP, Rate, PIP (Set)
5	Continuous Positive Airway Pressure (CPAP)	CPAP
6	Nasal Cannula with flow rate	Flow
7	Bilevel CPAP or SiPAP	Pressure: High and Low, Rate
8	No Respiratory Support	No support measurements
98	Other, specify	

2. Was there an oxygen requirement of FiO2 ≥ 40% for 2 or more hours? ☐1 Yes ☐0 No

3. Was a chest X-ray done today? ☐1 Yes ☐0 No
   a. If yes, was a ***new*** air leak identified? ☐1 Yes ☐0 No
   b. If yes, indicate what type of air leak (Check all that apply)
      ☐1 Pneumothorax
      ☐2 Pneumomediastinum
      ☐3 PIE
      ☐98 Other, specify _____
   c. Indicate number of chest tubes in place at 1200 noon today. ___ ___

4. Was an intubation/reintubation performed on the baby today? ☐1 Yes ☐0 No
   a. If yes, indicate the reason(s) why the baby was intubated/reintubated
      ☐1 Increasing respiratory distress
      ☐2 Stridor
      ☐3 Apnea and Bradycardia
      ☐4 For diagnostic or therapeutic procedures, including surgery
      ☐5 Unplanned extubation(s), indicate the number of occurrences this day: ____
      ☐98 Other, specify: _____

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14.2. Respiratory Support Profile [48RESP] Data Instructions

The Respiratory Support Profile form is completed for the first 48 hours of life from the time of birth. This form records detailed information regarding the respiratory support provided to the infant. **One form is to be completed for each Day of Life.**

Q#1: Collect hourly respiratory support profile

IMPORTANT! FiO2 (%), SpO2, ventilation and modality settings are recorded ***every hour for the first 3 hours and then every 3 hours for the first 48 hours of life***.

Note: Date of Birth= Day of Life 1, regardless of time of birth.

EXAMPLE: Baby born at 0030 on 6/12/2014 = Day of Life 1; collect respiratory data as indicated in the table below. On 6/13/2014 = Day of Life 2; collect respiratory data at 3 hour intervals beginning at about 0130.

Hour 24 Hour Clock	(%) FiO2	SpO2	Modality Use code number	If Other, specify vent modality	MAP cmH2O	PEEP cmH2O	CPAP cmH2O	Rate	Flow LPM Lpm	Pressure High cmH2O	Pressure Low cmH2O	Tidal Volume	PIP
0030	40	91	5				5						
0130	40	90	5				7						
0230	45	89	5				7						
0530	45	88	4		4	7		10					16
0830	45	92	4		4	7		10					16
1130	45	93	4		4	5		8					16
1430	40	95	4		3	5		5					16
1730	35	92	5				5						
2030	35	93	5				4						
2330	35	92	6						1.0				

Hour: Timestamp is recorded as 24 hour clock (00:00 to 23:59)
FiO2: Record delivered oxygen setting as % value
SpO2: Record saturation data
Modality: Enter code from the Key below.

Codes to identify ventilation modality:		Record Support Measurements:
1	Conventional Mechanical Ventilation (CMV)	MAP, PEEP, Rate, Tidal Volume (Measured), PIP (Measured)
2	High Frequency Oscillation Ventilation (HFOV)	MAP
3	High Frequency Jet Ventilation (HFJV)	MAP
4	Nasal Intermittent Positive Pressure Ventilation (NIPPV)	MAP, PEEP, Rate, PIP (Set)
5	Continuous Positive Airway Pressure (CPAP)	CPAP
6	Nasal Cannula with flow rate	Flow
7	Bilevel CPAP or SiPAP	Pressure: High and Low, Rate
8	No Respiratory Support	No support measurements
98	Other, specify	

14.3. **Respiratory Support Profile [48RESP] Form *[continued]***

RESPIRATORY SUPPORT PROFILE

FORM IS COMPLETED FOR THE FIRST 48 HOURS OF LIFE.

PID:__ __ __ __ __ __

DATE:__ __ / __ __ / __ __ __ __

1. Collect **hourly respiratory support profile** over first 48 hours post-delivery.
   a. Count time as a 24 hour cycle from time of birth as it occurs over the first 48 hours of life.
   b. Record FiO2 (%), SpO2, Modality and ventilation settings every hour for the first three hours and then every 3 hours for the first 48 hours of life.
   c. Complete one form for each Day of Life. Note: Date of Birth= Day of Life 1, regardless of time of birth.

Time	Hour 24 Hour Clock	FiO2	SpO2	Modality Use code number	If Other, specify vent modality	MAP cmH2O	PEEP cmH2O	CPAP cmH2O	Rate	Flow Lpm	Pressure High	Pressure Low cmH2O	Tidal Volume	PIP
1	__ __:__ __													
2	__ __:__ __													
3	__ __:__ __													
4	__ __:__ __													
5	__ __:__ __													
6	__ __:__ __													
7	__ __:__ __													
8	__ __:__ __													
9	__ __:__ __													
10	__ __:__ __													

Codes to identify ventilation modality		Support Measurements
1	Conventional Mechanical Ventilation (CMV)	MAP, PEEP, Rate, Tidal Volume, PIP (Measured)
2	High Frequency Oscillation Ventilation (HFOV)	MAP
3	High Frequency Jet Ventilation (HFJV)	MAP
4	Nasal Intermittent Positive Pressure Ventilation (NIPPV)	MAP, PEEP, Rate, PIP (Set)
5	Continuous Positive Airway Pressure (CPAP)	CPAP
6	Nasal Cannula with flow rate	Flow
7	Bilevel CPAP or SiPAP	Pressure: High and Low, Rate
8	No Respiratory Support	No support measurements
98	Other, specify	

2. Was there an oxygen requirement of FiO2 ≥ 40% for 2 or more hours? ☐1 Yes ☐0 No

3. Was a chest X-ray done today? ☐1 Yes ☐0 No
   a. If yes, was a ***new*** air leak identified? ☐1 Yes ☐0 No
   b. If yes, indicate what type of air leak (Check all that apply)
      ☐1 Pneumothorax
      ☐2 Pneumomediastinum
      ☐3 PIE
      ☐98 Other, specify _____
   c. Indicate number of chest tubes in place at 1200 noon today. ___ ___

4. Was an intubation/reintubation performed on the baby today? ☐1 Yes ☐0 No
   a. If yes, indicate the reason(s) why the baby was intubated/reintubated
      ☐1 Increasing respiratory distress
      ☐2 Stridor
      ☐3 Apnea and Bradycardia
      ☐4 For diagnostic or therapeutic procedures, including surgery
      ☐5 Unplanned extubation(s), indicate the number of occurrences this day: ____
      ☐98 Other, specify: _____

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Once a modality is entered, provide the support measurement values in the table.

Modality	Parameters that need to be entered:
1. Conventional Mechanical Ventilation (CMV) CMV can be either volume ventilation or pressure ventilation.	• MAP in cmH2O • PEEP in cmH2O • Rate • Tidal volume (measured) This is not the set tidal volume. Record the measured volume (expiration) on the vent supported breath (not spontaneous breath) • Peak Inspiratory Pressure (PIP) –measured PIP This is not the set PIP, but measured PIP on a vent supported breath (not spontaneous breath)
2. High Frequency Oscillation Ventilation (HFOV)	• MAP in cmH2O
3. High Frequency Jet Ventilation (HFJV)	• MAP in cmH2O
4. NIPPV	• MAP in cmH2O • PEEP in cmH2O • Rate • Peak Inspiratory Pressure (PIP) – set PIP Note: This is not the measured PIP.
5. CPAP	• CPAP in cmH2O Note: SiPAP machine can be used to deliver CPAP. Must check that the setting is CPAP and not bi-phasic mode
6. NC with flow rate	• Flow rate in LPM
7. Bilevel CPAP or SiPAP (in biphasic mode)	• Peep pressure high and pressure low
8. No Respiratory Support	• No support measurements
98. Other, Specify	If another ventilation modality is used other than those listed above: • Record '98' and indicate exact vent modality used. • Record all applicable support measurements

Q.2: Check box Yes or No to indicate if there was an oxygen requirement of FiO2 $\geq$ 40% for 2 or more hours.

Q.3: Was a chest x-ray done today? Check box Yes or No

Q.3a: If Yes, check box (Yes or No) to indicate if a NEW air leak was identified on the chest x-ray done today.

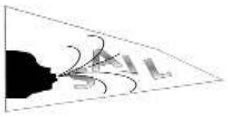
Q.3b: If Yes, indicate type(s) of air leak. If other selected, please specify.

Q.3c: Indicate the number of chest tubes in place as of 12 noon today.

Q4: Was an intubation/reintubation performed on the baby today? Check box Yes or No.

Q4a. If Yes, check off reason(s) for intubation/reintubation. If there were unplanned extubation(s), indicate the number of occurrences that day. If other is selected, please specify.

14.4. Daily Respiratory Status [RESD] Form



DAILY RESPIRATORY STATUS

COLLECTED DAILY FOR DAYS **3-10**

DAY__ __

PID:__ __ __ __ __ __

DATE:__ __ / __ __ / __ __ __ __

1. Did the baby receive any supplemental oxygen today? ☐1 Yes ☐0 No
   a. If yes, how long was the supplemental oxygen used? ☐1 12 hours or less ☐2 More than 12 hours
   b. What was the highest FiO2 delivered today? __ __ %
   c. Was the highest FiO2 setting maintained for ≥ 2 hours? ☐1 Yes ☐0 No

2. Collect **respiratory status** once **daily** for Days of Life 3 to 10

Hour	FiO2 (%)	SpO2	Modality Use code number	If Other, specify vent mode	MAP cmH2O	PEEP cmH2O	CPAP cmH2O	Rate	Flow Lpm	Pressure High cmH2O	Pressure Low cmH2O	Tidal Volume	PIP
12:00													

Codes to identify ventilation modality		Support Measurements
1	Conventional Mechanical Ventilation (CMV)	MAP, PEEP, Rate, Tidal Volume, PIP (Measured)
2	High Frequency Oscillation Ventilation (HFOV)	MAP
3	High Frequency Jet Ventilation (HFJV)	MAP
4	Nasal Intermittent Positive Pressure Ventilation (NIPPV)	MAP, PEEP, Rate, PIP (Set)
5	Continuous Positive Airway Pressure (CPAP)	CPAP
6	Nasal Cannula with flow rate	Flow
7	Bilevel CPAP or SiPAP	Pressure: High and Low, Rate
8	No Respiratory Support	No support measurements
98	Other, specify	

3. Was a chest X-ray done today? ☐1 Yes ☐0 No
   a. If yes, was a **new** air leak identified? ☐1 Yes ☐0 No
   b. If yes, indicate what type of air leak (Check all that apply)
      ☐1 Pneumothorax
      ☐2 Pneumomediastinum
      ☐3 PIE
      ☐98 Other, specify _____
   c. Indicate number of chest tubes in place at 1200 noon today. __ __

4. Was an intubation/reintubation performed on the baby today? ☐1 Yes ☐0 No
   a. If yes, indicate the reason(s) why the baby was intubated/reintubated
      ☐1 Increasing respiratory distress
      ☐2 Stridor
      ☐3 Apnea and Bradycardia
      ☐4 For diagnostic or therapeutic procedures, including surgery
      ☐5 Unplanned extubation(s), indicate the number of occurrences this day: __
      ☐6 Suspected infection
      ☐98 Other, specify: _____

V5.1_20150130 PAGE 1 OF 1 RESD

14.5. Daily Respiratory Status [RESD] Data Instructions

The RESD form is an abbreviated version of the 48RESP form. **The RESD form is completed daily starting with Day of Life 3 (DOL3) to Day of Life 10 (DOL10).** Complete a form on DOL3 even if you have completed the 48RESP form on DOL3. Collect and enter both data forms on DOL3 if applicable.

Q1: Did the baby receive any supplemental oxygen today? Check box Yes or No

Q1a: If Yes, indicate if supplemental oxygen was used less than or more than 12 hours.

Q1b: Indicate the highest FiO2 (%) delivered that day

Q1c: Was the highest FiO2 setting maintained for ≥ 2 hour? Check Yes or No

Q2: Collect respiratory status once daily for Day of Life 3 (DOL3) to Day of Life 10 (DOL10).

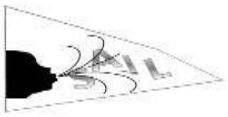
Data should be collected *at noon or as close to noon as possible*.

Hour	FiO2 (%)	SpO2	Modality Use code number	If Other, specify vent mode	MAP	PEEP	CPAP	Rate	Flow	Pressure High cmH2O	Pressure Low cmH2O	Tidal Volume	PIP
12:00													

Hour: Timestamps are recorded as 24 hour clock (12:00)
FiO2: record setting as % value
SpO2: record setting
Modality: Enter code from the Key below

Codes to identify ventilation modality		Record Support Measurements:
1	Conventional Mechanical Ventilation (CMV)	MAP, PEEP, Rate, Tidal Volume (Measured),PIP (Measured)
2	High Frequency Oscillation Ventilation (HFOV)	MAP
3	High Frequency Jet Ventilation (HFJV)	MAP
4	Nasal Intermittent Positive Pressure Ventilation (NIPPV)	MAP, PEEP, Rate, PIP (Set)
5	Continuous Positive Airway Pressure (CPAP)	CPAP
6	Nasal Cannula with flow rate	Flow
7	Bilevel CPAP or SiPAP	Pressure: High and Low
8	No Respiratory Support	No Support measurements
98	Other, specify	

14.6. Daily Respiratory Status [RESD] Form *[continued]*



DAILY RESPIRATORY STATUS

COLLECTED DAILY FOR DAYS **3-10**

DAY__ __

PID:__ __ __ __ __ __

DATE:__ __ / __ __ / __ __ __ __

1. Did the baby receive any supplemental oxygen today? ☐1 Yes ☐0 No
   a. If yes, how long was the supplemental oxygen used? ☐1 12 hours or less ☐2 More than 12 hours
   b. What was the highest FiO2 delivered today? __ __ %
   c. Was the highest FiO2 setting maintained for ≥ 2 hours? ☐1 Yes ☐0 No

2. Collect **respiratory status** once **daily** for Days of Life 3 to 10

Hour	FiO2 (%)	SpO2	Modality Use code number	If Other, specify vent mode	MAP cmH2O	PEEP cmH2O	CPAP cmH2O	Rate	Flow Lpm	Pressure High cmH2O	Pressure Low cmH2O	Tidal Volume	PIP
12:00													

Codes to identify ventilation modality		Support Measurements
1	Conventional Mechanical Ventilation (CMV)	MAP, PEEP, Rate, Tidal Volume, PIP (Measured)
2	High Frequency Oscillation Ventilation (HFOV)	MAP
3	High Frequency Jet Ventilation (HFJV)	MAP
4	Nasal Intermittent Positive Pressure Ventilation (NIPPV)	MAP, PEEP, Rate, PIP (Set)
5	Continuous Positive Airway Pressure (CPAP)	CPAP
6	Nasal Cannula with flow rate	Flow
7	Bilevel CPAP or SiPAP	Pressure: High and Low, Rate
8	No Respiratory Support	No support measurements
98	Other, specify	

3. Was a chest X-ray done today? ☐1 Yes ☐0 No
   a. If yes, was a **new** air leak identified? ☐1 Yes ☐0 No
   b. If yes, indicate what type of air leak (Check all that apply)
      ☐1 Pneumothorax
      ☐2 Pneumomediastinum
      ☐3 PIE
      ☐98 Other, specify _____
   c. Indicate number of chest tubes in place at 1200 noon today. __ __

4. Was an intubation/reintubation performed on the baby today? ☐1 Yes ☐0 No
   a. If yes, indicate the reason(s) why the baby was intubated/reintubated
      ☐1 Increasing respiratory distress
      ☐2 Stridor
      ☐3 Apnea and Bradycardia
      ☐4 For diagnostic or therapeutic procedures, including surgery
      ☐5 Unplanned extubation(s), indicate the number of occurrences this day: __
      ☐6 Suspected infection
      ☐98 Other, specify: _____

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14.7. Daily Respiratory Status [RESD] Data Instructions (cont'd)

Once a modality is entered, provide all of the support measurement values indicated in the chart.

Q3: Was a chest x-ray done today? Check box Yes or No.

Q3a: If Yes, indicate (Yes or No) if a NEW air leak is identified on the chest x-ray done today.

Q3b: If Yes, check all that apply to indicate the type of air leak. If Other is selected, please specify.

Q3c: Indicate the number of chest tubes in place at 12 noon today.

Q4: Was an intubation/reintubation performed on the baby today? Check box Yes or No

Q4a. If Yes, check the reason(s) for intubation/reintubation.

Q4a.[5] - If Unplanned extubation(s) is selected, indicate the number of occurrences that day.

14.8. Imaging Data [IMAGE] Form

IMAGING DATA

PID:__ __ __ __ __ __

DATE:__ __ / __ __ / __ __ __ __

Collect HUS and MRI for every test done during days 1-10 of life.

1. Was head imaging performed? ☐1 Yes ☐0 No

   a. What imaging technique was used?
   ☐1 Head Ultra Sound (HUS)
   ☐2 Head Magnetic Resonance Imaging (MRI)

   b. What were the results of the brain imaging, either the Worst HUS or MRI for this imaging? Check ALL that apply.
   ☐ Normal
   ☐ Subependymal hemorrhage (Grade 1 hemorrhage)
   ☐ IVH without ventricular dilation (Grade 2 hemorrhage)
   ☐ IVH distending at least one lateral ventricle (Grade 3 hemorrhage)
   ☐ Intraparenchymal echodense lesion (Grade 4 hemorrhage)
   ☐ Cystic Periventricular Leucomalacia (PVL)
   ☐ Porencephalic cyst
   ☐ Ventriculomegaly (with or without resolving IVH)
   ☐ Cortical atrophy
   ☐ Cerebellar hemorrhage
   ☐ Other, specify*: _____

   ** Do NOT report normal variants. Examples of normal variants include: Cavum septi pellucidum, connatal cysts, isolated choroid plexus cysts.*

2. Was an abdominal imaging performed? ☐1 Yes ☐0 No
   a. If Yes, what imaging technique was used?
   ☐1 Abdominal X-ray
   ☐2 Abdominal Ultrasound
   ☐3 Abdominal MRI
   ☐98 Other, specify _____

   b. Any evidence of free air or perforation on abdominal imaging? ☐1 Yes ☐0 No

V1.3_20141007 PAGE 1 OF 1 IMAGE

14.9. Imaging Data [IMAGE] Instructions

Data collected on the IMAGE form should be completed for each day of life (DOL) from DOL 1 through DOL 10. This data is collected when any of the following imaging tests are performed on the infant during days 1-10 of life:

1. Head Ultrasound (HUS)
2. Head Magnetic Resonance (MRI)
3. Abdominal X-ray, Ultrasound, or MRI

The date field in the header of this form is the day that the specific image study was performed. Record the date in the mm/dd/yyyy format.

Q.1: Choose either checkbox (Yes or No) to indicate if a head imaging test was performed.

Q1.a: If yes, indicate the type of head imaging performed: HUS or MRI

Q1.b: Indicate the results of the head imaging test. If more than one set of imaging tests were performed on that day of life, report the results of the *worst* HUS or MRI.

Results are listed by classification of hemorrhagic and/or ischemic abnormalities or other complications detected by cranial imaging. Check all results that apply. If result is not listed on the form, check Other and specify in text the reported finding.

Do not report variants that are classified as normal (see examples listed in Q1.b).

Q.2: Choose either checkbox (Yes or No) to indicate if an abdominal imaging test was performed.

Q2.a: If Yes, indicate the type of abdominal imaging performed: X-ray; Ultrasound; MRI; or Other. If Other is checked, specify in text the type of other abdominal imaging performed.

Q2.b: Choose either checkbox Yes or No to indicate if there was any evidence of free air or perforation seen on the abdominal imaging.

14.10. Growth and Medication Assessment [GMA] Form

GROWTH AND MEDICATION ASSESSMENT PID:__ __ __ __ __ __

COLLECTED DAILY FOR DAYS 1 -10, THEN WEEKLY UNTIL 36 WEEKS

DATE:__ __ / __ __ / __ __ __ __

WEEK __ __ | *DAY* __ __

Growth Data

For question 1 and 2: If more than one measurement is taken on the same day, enter the first value obtained.

1. What was the baby's body weight? __ __ __ __ gms ☐99 Not done
2. What was the baby's head circumference? __ __ . __cm ☐99 Not done

Medication Data

3. Were any of the below drugs given today? ☐1 Yes ☐0 No

If **Yes**, indicate which of the following types of drugs were given today:

a. Antibiotic	☐1 Yes	☐0 No
b. Antifungal	☐1 Yes	☐0 No
c. Surfactant	☐1 Yes	☐0 No
d. Indomethacin	☐1 Yes	☐0 No
e. Ibuprofen	☐1 Yes	☐0 No
f. Inotrope	☐1 Yes	☐0 No
g. Caffeine or other methylxanthine	☐1 Yes	☐0 No
If Caffeine, provide time of caffeine load	___ ___ : ___ ___ 24 Hr Clock	
h. Furosemide or other loop diuretic	☐1 Yes	☐0 No
i. Thiazide diuretic	☐1 Yes	☐0 No
j. Inhaled nitric oxide	☐1 Yes	☐0 No
k. Inhaled bronchodilator	☐1 Yes	☐0 No
l. Vitamin A (IM)	☐1 Yes	☐0 No
m. Erythropoietin	☐1 Yes	☐0 No
n. Red blood cell transfusion	☐1 Yes	☐0 No

V3.1.20150616 PAGE 1 OF 1 GMA

14.11. Growth and Medication Assessment [GMA] Data Instructions

Data on the GMA form is collected daily from Day of Life 1 (DOL1) to Day of life 10 (DOL10), and one form is completed for each day.

The data is then collected once every week on Day of Life 14 (DOL14), 21, 28, etc., until the baby reaches 36 Weeks PMA +/- 1 day. One form is completed for each week of data collection. **NOTE: For weekly data collection, a week is defined as 7 days plus/minus 1 day.**

Indicate the date of the assessment in the header of the form.

Growth Data

Q1: What was the baby's body weight? Record weight in grams.

a. If weight was not done, Check box Not Done.
b. If more than one measurement is taken on the same day, enter the first value obtained.

Q2: What was the baby's head circumference? Record head circumference in centimeters

a. If head circumference (HC) was not done, Check box Not Done.
b. If more than one measurement is taken on the same day, enter the first value obtained.

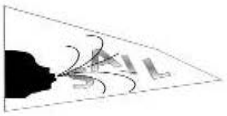
Medication Data

Q3: Were any drugs given today? Check box Yes or No.

If Yes is checked, then check the boxes (Yes or No) to indicate each type of drug given today (a-n). We are only interested in the medications listed from Q #3a – 3n. If any other meds were given, check "No" to Q. # 3.

In item g, if "Yes" is checked for caffeine, then document the time of the initial caffeine load the first time caffeine is given after birth. Once a baby is on maintenance caffeine therapy, time does not need to be documented.

14.12. Weekly Respiratory Status [RESW] Form



WEEKLY RESPIRATORY STATUS

COLLECTED WEEKLY FROM DAY 14 TO 36 WEEKS

*WEEK*__ __ | *DAY*__ __

PID:__ __ __ __ __ __

DATE:__ __ / __ __ / __ __ __ __

1. Did the baby receive any supplemental oxygen today? ☐1 Yes ☐0 No
   a. If yes, how long was the supplemental oxygen used? ☐1 12 hours or less ☐2 More than 12 hours
   b. What was the highest FiO2 delivered today? __ __ %
   c. Was the highest FiO2 setting maintained for ≥ 2 hours? ☐1 Yes ☐0 No

2. Collect **respiratory status** once **weekly** on Day 14 +/- 1 Day to Week 36 PMA.

Hour	FiO2 (%)	SpO2	Modality Use code number	If Other, specify vent mode	MAP cmH2O	PEEP cmH2O	CPAP cmH2O	Rate	Flow Lpm	Pressure High cmH2O	Pressure Low cmH2O	Tidal Volume	PIP
12:00													

Codes to identify ventilation modality		Support Measurements
1	Conventional Mechanical Ventilation (CMV)	MAP, PEEP, Rate, Tidal Volume, PIP (Measured)
2	High Frequency Oscillation Ventilation (HFOV)	MAP
3	High Frequency Jet Ventilation (HFJV)	MAP
4	Nasal Intermittent Positive Pressure Ventilation (NIPPV)	MAP, PEEP, Rate, PIP (Set)
5	Continuous Positive Airway Pressure (CPAP)	CPAP
6	Nasal Cannula with flow rate	Flow
7	Bilevel CPAP or SiPAP	Pressure: High and Low, Rate
8	No Respiratory Support	No support measurements
98	Other, specify	

3. Was a chest X-ray done this week? ☐1 Yes ☐0 No
   a. If yes, was a **new** air leak identified? ☐1 Yes ☐0 No
   b. If yes, indicate what type of air leak (Check all that apply)
      ☐1 Pneumothorax
      ☐2 Pneumomediastinum
      ☐3 PIE
      ☐98 Other, specify _____
   c. Indicate number of chest tubes in place at 1200 noon today. __ __

4. Was an intubation/reintubation performed on the baby this week? ☐1 Yes ☐0 No
   a. If yes, indicate the reason(s) why the baby was intubated/reintubated
      ☐1 Increasing respiratory distress
      ☐2 Stridor
      ☐3 Apnea and Bradycardia
      ☐4 For diagnostic or therapeutic procedures, including surgery
      ☐5 Unplanned extubation(s)
      ☐6 Suspected infection
      ☐98 Other, specify: _____

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14.13. Weekly Respiratory Status [RESW] Data Instructions

NOTE: For weekly data collection, a week is defined as 7 days plus/minus 1 day.

The Weekly Respiratory Status [RESW] form is similar to the Daily Respiratory Status [RESD] form (See Section 14.3). All data fields to complete are the same, **except for question #3 and question #4** as follows:

- **RESD form question #3**: Was a chest X-ray done **today?**
- **RESW form question #3**: Was a chest X-ray done **this week?**
  When completing question #3 on both forms, indicate a yes or no response to question #3. Complete questions #3 a-c accordingly.

- **RESD form question #4**: Was an intubation/reintubation performed on the baby **today?**
  If a Yes response is checked for question #4, indicate in #4a the reason(s) why the baby was intubated/reintubated.
  - Please note: If a response is checked for 4a[5] on the **RESD** form, you are asked to indicate the number of occurrences of unplanned extubation(s) for this day only.

- **RESW form question #4**: Was an intubation/reintubation performed on the baby **this week?**
  - Please note: If the response for 4a[5] is checked on the **RESW** form, it does not require that you record number of unplanned extubation(s).

The **RESW form is completed once every week** on Day of Life 14 (DOL 14), 21, 28, 35, etc., through the baby's hospitalization until GA 36 Weeks PMA.

Important Note: Respiratory status data collected at **day 28** of life and when the baby reaches **36 weeks PMA** are 2 significant time points in the study and it is important to enter the data at these milestones completely and promptly.

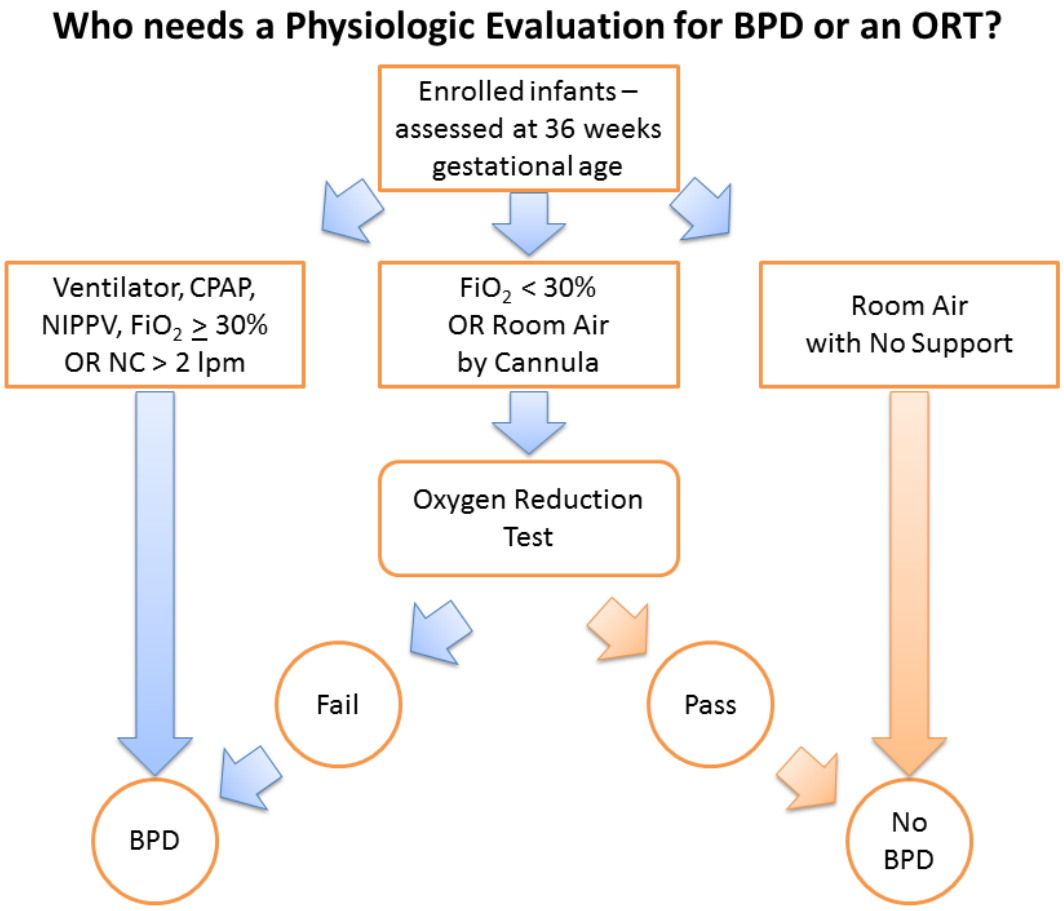
The RESW form should be completed +/- 1 day around the due date for data collection. The patient specific Visit Schedule (generated from the baby's gestational age, DOB and date) will be helpful in tracking weekly data collection.

15. Oxygen Reduction Test at Week 36

Between 36 $^{0/6}$– 36 $^{6/6}$ weeks postmenstrual age, a formal Oxygen Reduction Test (ORT) will be performed on infants receiving < 30% oxygen by low-flow. The purpose of this test is to provide an objective physiologic evaluation for BPD based on a need for supplemental oxygen.

15.1. Flow Chart of Physiologic Definition in Evaluation for BPD/ ORT

(developed by *Walsh et al.)



*Walsh, MC, Yao Q, Gettner P, Hale E, Collins M, Hensman A et al. **Impact of a physiologic definition on bronchopulmonary dysplasia rates.** *Pediatrics* 2004; 114(5): 1305-1311.

15.2. Practical Steps in Performing the ORT

1. The first step is to determine whether or not an ORT is needed. Please review the flow chart and then calculate the effective oxygen using the conversion tables provided in Section 15.7**.**
2. If the baby is in hood or isolette oxygen the oxygen concentration is measured directly by oxygen analyzer.
3. If the baby is receiving oxygen by nasal cannula or room air by nasal cannula, the delivered effective oxygen concentration will be calculated using the technique described by Benaron DA, Benitz WE. Maximizing the stability of oxygen delivered via nasal cannula. *Arch Pediatr Adolesc Med.*1994;148 :294– 300. Refer to conversion tables in Section 15.7.
4. Infants treated with pressure support (mechanical ventilation; nCPAP or NIPPV) or receiving FiO_2 > or = 30%, to keep SpO_2 > or = 90%, or NC > 2 lpm will be assigned the outcome "BPD", without further testing. **To further clarify, infants requiring nasal cannulae flow > 2lpm (regardless of the effective FiO2) will be considered in the BPD category. An ORT is not required. However, infants on nasal cannulae ≤ 2 lpm, should have an ORT performed, depending on their effective oxygen calculation (follow step #6 below).**
5. Infants being treated in room air (no support) with an oxygen saturation > or = 90% will be assigned the outcome "no BPD" without further testing.
6. If the baby is receiving effective FiO2 < 30% (to keep SpO_2 > or = 90%), or on room air (21%) nasal cannulae and is not being ventilated, the infant must undergo the oxygen reduction test as described below:
    a. Place infant in supine position and ensure pulse oximeter is placed appropriately
    b. Allow 5 minute recovery period after placing pulse oximeter and prior to baseline data collection
    c. Feedings and medications should be given 30 minutes before the evaluation
    d. Infants on continuous feeding may continue feeds during the evaluation
    e. Bolus feedings should not be given during the evaluation

15.3. Collecting Baseline Pre-test Data

Baseline or control data is to be collected in the infant's current oxygen as follows:

1. 15 minutes prior to the physiologic evaluation (ORT), a pre-test assessing saturation, apnea and bradycardia at 5 minute intervals must be done to determine the infant's stability for the reduction phase of the test and documented on the ORT CRF.
2. Assess for the following during the baseline/pre-test as well as the reduction phase;
    a. Saturations < 90% lasting for > 5 minutes.
    b. FiO2 increased > 5%

c. Need for initiation of a ventilator
d. Apnea lasting > 20 seconds
e. Bradycardia with heart rate < 80 for > 10 second
f. Severe bradycardia with heart rate < 70 for > 20 seconds

If any of the above events or symptoms is observed, **do not** continue with the ORT.

15.4. Oxygen Reduction Phase

1. **For infants on an oxygen hood or receiving oxygen in an isolette:** a stepwise 2% decrement (every 5 minutes) in supplemental oxygen to room air, can be undertaken, keeping the baby under continuous cardiorespiratory monitoring, including saturation monitoring.

2. **For infants receiving oxygen by nasal cannula:** wean flow initially by decrements of 0.1 lpm every 5 minutes to a flow of 0.1 lpm. If infant is successfully weaned to 0.1 lpm, continue as follows:

    1. **If using an oxygen blender to deliver flow to the nasal cannula:** wean Fi02 by 20% every 5 minutes to room air.

For example, from 0.1 lpm, wean FIO2 to:
0.08 FiO2
0.06 FiO2
0.04 FiO2
0.02 FiO2
Room air as tolerated in 5 min. intervals

    2. **If using low flow with 100% oxygen concentration:** wean flow from 0.1 lpm to 0.06 lpm x 5 minutes, then to 0.03 lpm x 5 minutes.

For both methods, turn off flow, gently remove cannula from nose (but do not remove nasal cannula completely from face).

3 For infants receiving room air by nasal cannula:

1. **If flow 0.5-2.0 lpm:** wean flow in decrements of 0.5 lpm every 5 minutes until a flow of 0.5 lpm is reached. Then turn the flow off.

2. **If flow is 0.001-0.49 lpm:** Turn off flow, gently remove cannula from nose (but do not remove nasal cannula completely from face).

IMPORTANT NOTES:

During the physiologic evaluation, all infants should CONTINUE to the next reduction step **ONLY** if saturation is > or = 90% during the 5 minute monitoring phase.

STOP the OXYGEN REDUCTION TEST if saturation is < 90% for 5 continuous minutes; or < 80% for 15 seconds with good signal fidelity. The infant should immediately be placed back in his/her baseline oxygen and will be considered to have NOT passed the challenge or "failed' the test.

15.5. Rapid Pass Criteria

The infant may qualify for a RAPID PASS if all saturations are > or = 96% in room air for 15 consecutive minutes.

15.6. Results of the ORT: Pass or Failure?

PASS: A pass in the ORT is the ability to safely maintain SpO_2 > or = 90% in room air for 30 minutes, i.e., no apnea or bradycardia.

Those who pass the oxygen reduction test will be assigned the outcome "No BPD."

FAILURE: Failure is defined as SpO_2 80-89% for 5 consecutive minutes, or < 80% for 15 seconds.

Those who fail the oxygen reduction test will be assigned the outcome "BPD."

All infants will be returned to their baseline supplemental oxygen at the completion of the test. Further modifications of oxygen therapy will be made at the discretion of the responsible clinician.

The primary physician caring for the patient will be given the results of the test.

15.7. Calculating FiO_2 from Low Flow Oxygen

This is a two-step process, using Table 1 and Table 2 below.

The below tables are based on data derived from equations (3) and (4) in the paper by Benaron and Benitz, "Maximizing the stability of Oxygen delivered via nasal cannula": Arch Pediatr Adoles Med. 1994; 148: 294-300.

Example:
What is the effective FiO_2 in a 2.0 kg infant on 100% cannula at a flow of 0.15 lpm?

ANSWER:
a. Use 2.0 kg and 0.15 lpm in Table 1 to get a factor of 8
b. In Table 2, use the factor of 8 and 100% FiO2 to yield an FiO_2 effective of 27%
c. Thus the effective FiO_2 is less than 30%; infant is eligible for physiologic evaluation

Table 1. Factor as a function of flow and weight

Flow (lpm)	Flow (lpm)	Weight (kg)								
		0.7	1.0	1.25	1.5	2	2.5	3	3.5	4
0.01		1	1	1	1	1	0	0	0	0
0.03	1/32	4	3	2	2	2	1	1	1	1
0.06	1/16	9	6	5	4	3	2	2	2	2
0.125	1/8	18	12	10	8	6	4	4	4	4
0.15		21	15	12	10	8	6	5	4	4
0.25	1/4	36	25	20	17	13	10	8	7	6
0.5	1/2	71	50	40	33	25	20	17	14	13
0.75	3/4	100	75	60	50	38	30	25	21	19
1.0	1.0	100	100	80	67	50	40	33	29	25
1.25		100	100	100	83	63	50	42	36	31
1.5		100	100	100	100	75	60	50	43	38
2.0		100	100	100	100	100	80	67	57	50
3.0		100	100	100	100	100	100	100	86	75
4.0		100	100	100	100	100	100	100	100	100
5.0		100	100	100	100	100	100	100	100	100
6.0		100	100	100	100	100	100	100	100	100

If exact values are not included in the table, round up or down to find the closest value.

Table 2. Effective Fi02 (x100) as a function of factor and concentration

Factor	Concentration (%)						
	21	22	25	30	40	50	100
0	21	21	21	21	21	21	21
1	21	21	21	21	21	21	22
2	21	21	21	21	21	22	23
3	21	21	21	21	22	22	23
4	21	21	21	21	22	22	24
5	21	21	21	21	22	22	25
6	21	21	21	22	22	23	26
7	21	21	21	22	22	23	27
8	21	21	21	22	23	23	27
9	21	21	21	22	23	24	28
10	21	21	21	22	23	24	29
11	21	21	21	22	23	24	30
12	21	21	21	22	23	24	30
13	21	21	22	22	23	25	31
14	21	21	22	22	24	25	32
15	21	21	22	22	23	25	33
17	21	21	22	23	24	26	34
18	21	21	22	23	24	26	35
19	21	21	22	23	25	27	36
20	21	21	22	23	25	27	37
21	21	21	22	23	25	27	38
22	21	21	22	23	25	27	38
23	21	21	22	23	25	28	39
25	21	21	22	23	25	28	41
27	21	21	22	23	25	29	42
28	21	21	22	24	26	29	43
29	21	21	22	24	27	29	44
30	21	21	22	24	27	30	45
31	21	21	22	24	27	31	47
33	21	21	22	24	27	31	47
36	21	21	22	24	28	31	49
38	21	21	23	24	28	32	51
40	21	21	23	25	29	33	53
42	21	21	23	25	29	33	54
43	21	21	23	25	29	33	55
44	21	21	23	25	29	34	56
50	21	21	23	25	30	35	60
55	21	22	23	26	31	37	64
57	21	22	23	26	32	38	66
60	21	22	23	26	32	38	68
63	21	22	24	27	33	39	71
67	21	22	24	27	34	40	74
71	21	22	24	27	34	42	77
75	21	22	24	28	35	43	80
80	21	22	24	28	36	44	84
83	21	22	24	28	37	45	87
86	21	22	24	29	37	46	89
100	21	22	25	30	40	50	100

15.8. Oxygen Reduction Test [ORT] Form – Page 1

PID:__ __ __ __ __ __

OXYGEN REDUCTION TEST

DATE:__ __ / __ __ / __ __ __ __

COMPLETED AT 36 0/7 TO 36 6/7 WEEKS PMA

Complete this form to document process and results of Oxygen Reduction Test.
Include Date of Assessment in date field above.

1. Was the Oxygen Reduction Test performed? ☐1 Yes ☐0 No
   a. If No, check primary reason infant missed test
      - ☐1 Weaned to Room Air (no resp support) within the window
      - ☐2 Respiratory support escalated to non-invasive or invasive ventilation
      - ☐3 Increased FiO2 whereby, the effective FiO2 no longer meets criteria for ORT
      - ☐4 Baby requires nasal cannula flow >2 LPM
      - ☐5 Baby was eligible but discharged or transferred
      - ☐6 Staff oversight/Staff or equipment not available to perform test
      - ☐98 Other, specify:_____

2. Time of Test ___ ___ ___ ___ 24 hour clock

BASELINE/ SAFETY PHASE

3. Starting FiO2 ___ ___ ___%
   If on low flow oxygen, use MOP instructions to calculate.

4. Time Period

a. Baseline/ Pretest	Low Saturation	☐1 Yes	☐0 No
	Apnea	☐1 Yes	☐0 No
	Bradycardia	☐1 Yes	☐0 No
b. Baseline + 5 minutes:	Low Saturation	☐1 Yes	☐0 No
	Apnea	☐1 Yes	☐0 No
	Bradycardia	☐1 Yes	☐0 No
c. Baseline + 10 minutes:	Low Saturation	☐1 Yes	☐0 No
	Apnea	☐1 Yes	☐0 No
	Bradycardia	☐1 Yes	☐0 No
d. Baseline + 15 minutes:	Low Saturation	☐1 Yes	☐0 No
	Apnea	☐1 Yes	☐0 No
	Bradycardia	☐1 Yes	☐0 No

5. Was the baby stable enough to proceed to the next phase? ☐1 Yes ☐0 No
   If **No**, do not continue to the Reduction Phase, Go to 'ORT Result, question #19, record 'Failure to establish Baseline Stability, and complete the rest of this form.
   If **Yes**, proceed to the Reduction Phase.

15.9. Oxygen Reduction Test [ORT] Data – Page 1 Instructions

This form should be completed by a member of the clinical respiratory care team at Week 36 gestational age. **Please provide the clinical respiratory team member performing the test with the ORT paper case report form, along with a copy of CRF instructions, as well as copy of the above ORT test instructions - MOP Section 15 (15.1 – 15.7), which includes Table 1 & Table 2 .**

The data collected on the ORT form will include cardiorespiratory assessment data, as well as results of the Oxygen Reduction Test. All data on this form will be recorded on the paper form. Once the data is completed on the paper form by the clinical respiratory team member performing the ORT, the research coordinator will enter the data into the data management system. The date field in the header of this form is the day that the respiratory assessment and ORT Test was performed. Record the date in the mm/dd/yyyy format.

Q 1: Check either box Yes or No to indicate if the ORT test was performed. (Please refer to Section 15.1 thru 15.3 above when answering this question)

Q1a: If No is checked, choose the appropriate box to indicate the primary reason the test was not administered. If No is checked, no further data will be collected on this form.

Q2: Time of test will be recorded in 24 hour clock time.

Questions 3 through 5 on this form refers to the Pre-Test Baseline Phase (please refer to above Section 15.1. thru 15.3. Including Tables 1 & 2 before completing this section). ***Completing the Pre-Test Baseline Phase is a required safety evaluation to determine if the infant is stable for the Reduction Phase of the ORT.***

Q3: Record pretest FiO2. If infant is receiving low flow oxygen, calculate FiO2 for low flow oxygen using Tables 1 & 2 (provided in above section 15.7) to calculate FiO2.

Q4: The time period is started at 15 minutes prior to the ORT.

Q4a: Baseline/Pretest data is recorded at the infant's current oxygen level. Assessment is made for low oxygen saturation, apnea and bradycardia symptoms. Check box YES or NO to indicate each assessment outcome.

Q 4b-4d:Assessment for low oxygen saturation, apnea, and bradycardia is done at 5 minute intervals during the 15 minute time period from baseline. Check box YES or NO to indicate assessment outcome at each 5 minute interval.

Q5: Check YES or NO to indicate if infant is assessed as stable. **Please refer to Section 15.3 above for details of assessment criteria.** If infant is assessed as not stable, DO NOT continue with ORT. Go to question #19 on page 3 of ORT form and record test result.

15.10. Oxygen Reduction Test [ORT] Form – Page 2

PID:__ __ __ __ __ __

OXYGEN REDUCTION TEST

DATE:__ __ / __ __ / __ __ __ __

COMPLETED AT 36 0/7 TO 36 6/7 WEEKS PMA

REDUCTION PHASE

Reduce oxygen (by 2% for hood/isolette or 20% of total for low flow nasal cannula) every 5 minutes. During the reduction phase, if baby has low saturations (80-89 for > 5min or <80 for 15 sec), or serious bradycardia, or serious apnea, then discontinue the ORT and record as 'Fail'.

☐99 NA

6.	5 Minutes	Low Saturation	☐1 Yes	☐0 No
		Apnea	☐1 Yes	☐0 No
		Bradycardia	☐1 Yes	☐0 No
7.	10 Minutes	Low Saturation	☐1 Yes	☐0 No
		Apnea	☐1 Yes	☐0 No
		Bradycardia	☐1 Yes	☐0 No
8.	15 Minutes	Low Saturation	☐1 Yes	☐0 No
		Apnea	☐1 Yes	☐0 No
		Bradycardia	☐1 Yes	☐0 No
9.	20 Minutes	Low Saturation	☐1 Yes	☐0 No
		Apnea	☐1 Yes	☐0 No
		Bradycardia	☐1 Yes	☐0 No
10.	25 Minutes	Low Saturation	☐1 Yes	☐0 No
		Apnea	☐1 Yes	☐0 No
		Bradycardia	☐1 Yes	☐0 No
11.	30 Minutes	Low Saturation	☐1 Yes	☐0 No
		Apnea	☐1 Yes	☐0 No
		Bradycardia	☐1 Yes	☐0 No
12.	Was the baby stable enough to proceed to the next phase? If No, record the ORT result as 'Fail'.		☐1 Yes	☐0 No

V2.0_20150130 PAGE 2 OF 3 ORT

15.11. Oxygen Reduction Test [ORT] Data –Page 2 Instructions

Reduction Phase:

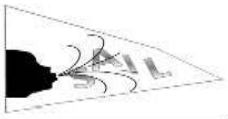
All data on this page will be recorded on the paper form. Once the data is completed on the paper form by the clinical respiratory team member performing the ORT, the research coordinator will enter the data into the data management system.

During the Reduction Phase, the oxygen is gradually reduced at 5 minute intervals over a 30 minute period of time with continuous cardiorespiratory and saturation monitoring maintained throughout each interval.

Questions 6-11: Assessment for low oxygen saturation, apnea, and bradycardia is done at 5 minute intervals during the 30 minute time period. Check box YES or NO to indicate assessment outcome at each interval.

Q 12: Check box YES or NO to indicate if infant is assessed as stable enough to proceed to the next phase of the ORT. If No, DO NOT continue with ORT. Go to Question 19 – Page 3 and record the ORT result as “Fail”.

15.12. Oxygen Reduction Test [ORT] – Page 3



OXYGEN REDUCTION TEST

COMPLETED AT 36 0/7 TO 36 6/7 WEEKS PMA

PID:__ __ __ __ __ __

DATE:__ __ / __ __ / __ __ __ __

POST -REDUCTION STABILITY PHASE

When a baby is down to room air (21% oxygen), monitor for 30 minutes. Baby must be stable (saturations >90%) for 30 minutes. Note: Rapid Pass- all saturation values ≥ 96% for 15 minutes.

13.	5 Minutes	Low Saturation	☐ 1 Yes	☐ 0 No
		Apnea	☐ 1 Yes	☐ 0 No
		Bradycardia	☐ 1 Yes	☐ 0 No
14.	10 Minutes	Low Saturation	☐ 1 Yes	☐ 0 No
		Apnea	☐ 1 Yes	☐ 0 No
		Bradycardia	☐ 1 Yes	☐ 0 No
15.	15 Minutes	Low Saturation	☐ 1 Yes	☐ 0 No
		Apnea	☐ 1 Yes	☐ 0 No
		Bradycardia	☐ 1 Yes	☐ 0 No
16.	20 Minutes	Low Saturation	☐ 1 Yes	☐ 0 No
		Apnea	☐ 1 Yes	☐ 0 No
		Bradycardia	☐ 1 Yes	☐ 0 No
17.	25 Minutes	Low Saturation	☐ 1 Yes	☐ 0 No
		Apnea	☐ 1 Yes	☐ 0 No
		Bradycardia	☐ 1 Yes	☐ 0 No
18.	30 Minutes	Low Saturation	☐ 1 Yes	☐ 0 No
		Apnea	☐ 1 Yes	☐ 0 No
		Bradycardia	☐ 1 Yes	☐ 0 No

Return to pre-test oxygen amount.

19. **Oxygen reduction test result**

☐ 1 Pass
☐ 2 Rapid Pass
☐ 3 Fail
☐ 4 Failed to establish baseline stability

a. If Fail, provide reason(s)

☐ 1 Low Saturation
☐ 1 Apnea
☐ 1 Bradycardia

20. Who performed the test?

☐ 1 RT, print name _____
☐ 2 Nurse, print name _____
☐ 3 Physician, print name _____

V2.0_20150130 PAGE 3 OF 3 ORT

15.13. Oxygen Reduction Test [ORT] Data – Page 3 Instructions

Post-Reduction Stability Phase and ORT Test Result

All data on this page will be recorded on the paper form. Once the data is completed on the paper form by the clinical respiratory team member performing the ORT, the research coordinator will enter the data into the data management system.

During the Post-Reduction Phase, the infant is monitored and assessed at room air for 30 minutes. The infant must remain stable (saturations >90%) in room air during each interval of the 30 minute assessment period in order to have a "Pass" test result.

Once the ORT is completed, the infant is returned to the pre-test oxygen amount.

Questions 13-18: Assessment for low oxygen saturation, apnea, and bradycardia is done at 5 minute intervals during the 30 minute time period. Check box YES or NO to indicate assessment outcome at each interval.

Q .19: Record the Result of the ORT. Check appropriate box to indicate result: Pass; Rapid Pass; Fail; Failed to establish stability.

Q.19a: If a "Fail" result is selected, indicate all reasons for failure that apply.

Q.20: Select title of clinical team member who performed the test, and print their name in the text line.

16. Other Outcome Data and Follow-up Assessment

Other outcome data is collected after Week 36 and include Study Status Data, Neonatal Outcome Data, and Readmission data (if SAIL participatant is readmitted to clinical center). At 22-26 months GA, data are collected on the Follow up and the Neurological forms.

16.1. Study Status [SSTATUS] Form

STUDY STATUS
AT DISCHARGE, WITHDRAWAL, TRANSFER, DEATH OR WEEK 44 PMA ASSESSMENT, WHICHEVER OCCURS FIRST

PID:__ __ __ __ __ __
DATE:__ __ / __ __ / __ __ __ __

1. What was the baby's disposition?
   - ☐ 1 Discharged Home
   - ☐ 2 Still hospitalized at 44 Weeks PMA
   - ☐ 3 Transfer to another hospital
   - ☐ 4 Baby died at study center
   - ☐ 5 Baby died post discharge
   - ☐ 6 Baby withdrawn from study
   - ☐ 98 Other, specify: _____

   a. If still hospitalized at 44 Weeks PMA, record reason for continued hospitalization
   _____
   _____
   _____

2. What was the baby's discharge date, date of death, withdrawal, transfer or date of last contact?
   __ __ / __ __ / __ __ __ __ mm/dd/yyyy

3. Was this baby enrolled in any other randomized clinical treatment trial?
   ☐ 1 Yes ☐ 0 No
   a. If Yes, provide clinical trial name(s) and infant ID number in other study. E.g. Monitor #2105
   _____
   _____
   _____
   _____

4. Was this baby enrolled in any other long term follow-up studies?
   ☐ 1 Yes ☐ 0 No
   a. If Yes, provide clinical trial name(s) and infant ID number in other study. E.g. Monitor #2105
   _____
   _____

5. Final Respiratory Status (Select one):
   - ☐ 0 No Respiratory Support
   - ☐ 1 O_2 alone
   - ☐ 2 Tracheostomy and ventilation
   - ☐ 3 CPAP
   - ☐ 4 IPPV
   - ☐ 98 Other, specify: _____

If baby died, please complete questions 6-7a.

6. What was the baby's primary cause of death?
   (Specify cause of death from the death certificate*)
   _____
   _____

   a. Was active care withdrawn? ☐ 1 Yes ☐ 0 No

7. Was an autopsy performed? ☐ 1 Yes ☐ 0 No ☐ 88 Unknown
   a. If Yes, what were the findings?
   _____
   _____
   _____
   _____
   _____

*If a death certificate is not available, please contact the primary care physician for a description of the events leading to death.

If baby withdraws early from study, please complete question 8.

8. Indicate the primary reason participation stopped
   - ☐ 1 Unable to contact parents/ caregivers
   - ☐ 2 Parents/Caregivers refuse further participation
   - ☐ 98 Other, specify: _____

V3.0_20170228 PAGE 1 OF 1 SSTATUS

16.2. Study Status [SSTATUS] Data Instructions

The Study Status form is completed when infant is discharged from the hospital; infant is withdrawn from study participation; infant is transferred to another care facility; death of infant, OR at Week 44 PMA assessment, whichever occurs first.

Q.1: Check one box to indicate the infant's disposition (discharged home, transferred to another facility, etc.)

Q.1a: If infant is still hospitalized at Week 44, write in reason for continued hospitalization.

Q.2: Indicate date (mm/dd/yyyy) of status change.

Q.3: Indicate if infant was enrolled in another randomized trial-Check Box YES or NO.

Q.3a: If YES to Q #3, provide the clinical trial name and ID number for that study.

Q.4: Indicate if infant was enrolled in any long term follow-up study/studies-Check Box YES or NO.

Q.4a: If YES to Q #4, provide the clinical trial name and ID number for that study.

Q.5: Indicate the final respiratory status of the infant – select one choice.

Q.6: Complete this question if the infant has died. Indicate the cause of death. If cause of death cannot be obtained from a death certificate, this information may also be found in the clinical chart discharge summary or physician summary note. If feasible, contact primary care physician to obtain cause of death information. If cause of death information cannot be obtained, write "unknown" in text area of form.

Q6a: Indicate if active care was withdrawn for the baby – Check Box YES or NO.

Q7: Indicate if autopsy report was obtained and if known – Check Box YES or No.

Q7a: If YES to Q #7, write a brief summary of autopsy report findings in text area of form.

Q.8: Complete this question if the infant is withdrawn early from the study (before Week 44). Check one box to indicate the primary reason for the early withdrawal. If other is selected, please specify in text line.

16.3. Neonatal Outcome [Outcome] Form - Page 1

NEONATAL OUTCOME DATA
AT DISCHARGE, WITHDRAWAL, TRANSFER, DEATH OR WEEK 44 PMA ASSESSMENT, WHICHEVER OCCURS FIRST

PID: _ _ _ _ _ _

DATE: _ _ / _ _ / _ _ _ _

Cardio-Pulmonary

1. Did the baby have any of the following types of air leaks? ☐1 Yes ☐0 No
   If **Yes**, indicate the type(s) of air leak by answering Questions 1a-1d
   a. Pneumothorax: ☐1 Yes ☐0 No
   If **Yes**, complete $1a_1$ and $1a_2$
   $1a_1$. Was a chest tube placed? ☐1 Yes ☐0 No
   $1a_2$. Has there been evidence of a bronchopleural fistula? ☐1 Yes ☐0 No
   b. Pulmonary Interstitial Emphysema (PIE): ☐1 Yes ☐0 No
   c. Pneumomediastinum: ☐1 Yes ☐0 No
   d. Pneumopericardium: ☐1 Yes ☐0 No

2. Did the baby have any pulmonary hemorrhages? ☐1 Yes ☐0 No
   If **Yes**, complete 2a and 2b
   a. Did these hemorrhages require transfusion of blood products? ☐1 Yes ☐0 No
   b. Did these hemorrhages require increased concentrations of supplemental oxygen and / or ventilator support? ☐1 Yes ☐0 No

3. Was there a diagnosis of Patent Ductus Arteriosus (PDA) requiring therapy? ☐1 Yes ☐0 No
   If **Yes**, complete 3a-3c
   a. Treated with Indomethacin? ☐1 Yes ☐0 No
   b. Treated with Ibuprofen? ☐1 Yes ☐0 No
   c. Surgical ligation performed? ☐1 Yes ☐0 No

4. Did the baby have a tracheotomy? ☐1 Yes ☐0 No
   If **Yes**, complete 4a
   a. Indicate the procedure date: _ _ / _ _ / _ _ _ _ (Month / Day / Year)

5. Were open-label systemic corticosteroids administered? ☐1 Yes ☐0 No ☐9 Enrolled in Hydrocortisone Study

   If **Yes or Enrolled in Hydrocortisone study**, complete 5a-5d
   a. Select corticosteroid therapy ☐1 Hydrocortisone ☐2 Dexamethasone ☐3 Both
   b. Indicate number of courses _ _
   c. Start date of the first course? _ _ / _ _ / _ _ _ _ (Month / Day / Year)
   d. Start date of the last course? _ _ / _ _ / _ _ _ _ (Month / Day / Year)

6. Were inhaled corticosteroids administered? ☐1 Yes ☐0 No

16.4. Neonatal Outcome [OUTCOME] Data - Page 1 Instructions

The Neonatal Outcome form is completed at the Week 44 PMA Assessment visit or when during the course of their participation in the study the infant is discharged from the hospital; infant is withdrawn from study participation; infant is transferred to another care facility; death of infant.

Q.1: Check Box YES or NO to indicate if infant had any of the air leak types from those listed in 1a thru 1d. If YES is answered to Q.1, indicate by checking box YES or NO for each type of air leak listed. (Q1a – 1d).

Q.2: Check Box YES or NO to indicate if infant had any pulmonary hemorrhages. If YES is answered to Q.2, complete questions 2a and 2b.

Q.2a: Indicate if hemorrhages required a transfusion of blood product (Yes or No).

Q.2b: Indicate if hemorrhages required increased concentration of oxygen supplement or ventilation support (Yes or No).

Q.3: Check Box YES or NO to indicate if infant was diagnosed with Patent Ductus Areteriosis (PDA) that required treatment. If YES is answered to Q.3, indicate treatment received (check box YES or No for questions 3a-3c).

Q.4: Check Box YES or No to indicate if infant received a tracheotomy. If YES is answered, answer Q.4a and indicate the date the tracheotomy procedure.

Q.5: Check Box YES or NO to indicate if infant received any open-label systemic corticosteroids. If the baby was enrolled in the Hydrocortisone study, please check the new option “Enrolled in Hydrocortisone Study”. If infant received any open-label systemic corticosteroids or if the baby was enrolled in the Hydrocortisone study, proceed to complete Q#5a – 5d. If enrolled in the Hydrocortisone study, please complete the form assuming the infant is randomized to the active arm even though you may not know if baby was given active drug or not

Q.5a: Select type of corticosteroid therapy given.

Q.5b: Indicate number of therapy courses received.

Q.5c: Record start date of first therapy course.

Q.5d: Record start date of last therapy course.

Q.6: Check Box Yes or NO to indicate if infant received any inhaled corticosteroids.

16.5. Neonatal Outcome [Outcome] Form - Page 2

NEONATAL OUTCOME DATA
AT DISCHARGE, WITHDRAWAL, TRANSFER, DEATH OR WEEK 44 PMA ASSESSMENT, WHICHEVER OCCURS FIRST

PID: _ _ _ _ _ _ _

DATE: _ _ / _ _ / _ _ _ _

Infection

7. Did the baby have one or more episodes of the following types of infection? ☐1 Yes ☐0 No
   If **Yes**, complete 7a-7d
   a. Blood culture-proven sepsis: ☐1 Yes ☐0 No
      If **Yes**, check all that apply
      - ☐ Coagulase-negative staphylococci
      - ☐ Other gram positive (+) bacteria
      - ☐ Gram negative (-) bacteria
      - ☐ Fungal
      - ☐ Viral

   b. CSF culture-proven meningitis? ☐1 Yes ☐0 No
      If **Yes**, check all that apply
      - ☐ Coagulase-negative staphylococci
      - ☐ Other gram positive (+) bacteria
      - ☐ Gram negative (-) bacteria
      - ☐ Fungal
      - ☐ Viral

   c. Presumed, but not culture-proven meningitis? ☐1 Yes ☐0 No
   d. Pneumonia? ☐1 Yes ☐0 No
      If **Yes**, confirmed by (check all that apply)
      - ☐ Chest X-ray
      - ☐ ETT aspirate growth
      - ☐ Peripheral blood culture positive
      - ☐ Persistent colonization and isolation

Gastro Intestinal

8. Did the baby have any confirmed Necrotizing Enterocolitis (NEC)? ☐1 Yes ☐0 No
9. Any bowel perforations associated with NEC? ☐1 Yes ☐0 No
10. Any surgical treatment for NEC or bowel perforations associated with NEC? ☐1 Yes ☐0 No
    a. If **Yes**, check all that apply
    - ☐ Peritoneal drain
    - ☐ Laparotomy
    - ☐ Bowel resection

11. Did the baby have any isolated bowel perforations not considered to be associated with NEC? ☐1 Yes ☐0 No

12. Any surgical treatment for any isolated bowel perforations not considered to be associated with NEC? ☐1 Yes ☐0 No
    a. If **Yes**, check all that apply
    - ☐ Peritoneal drain
    - ☐ Laparotomy
    - ☐ Bowel resection

V6.0_20150616 PAGE 2 OF 3 OUTCOME

16.6. Neonatal Outcome [OUTCOME] Data - Page 2 Instructions

The data questions on page two of this form include infection outcomes (Q 7), and gastrointestinal outcomes (Q8-12).

Q.7: Indicate YES or NO if infant had one or more episodes of the types of infections listed in 7a thru 7d. If YES is answered, complete Q7a-d. Indicate by check box YES or NO for presence of each listed infection and check specific answers related to each infection listed.

Q.7a: If response is YES for blood culture proven sepsis, check all infection types that apply.

Q.7b: If response is YES for CFS culture proven meningitis, check all infection types that apply.

Q.7c: Check Box YES or NO if it is presumed and not culture-proven meningitis.

Q.7d: If response is YES for pneumonia, check all tests that were performed to confirm diagnosis.

Q.8: Check Box YES or NO to indicate whether infant had confirmed Necrotizing Enterocolitis (NEC).

Q.9: Check Box YES or NO to indicate whether infant had any bowel perforations associated with NEC.

Q.10: Check Box YES or NO to indicate whether infant received any surgical treatment for NEC or bowel perforations associated with NEC.

Q.10a: If response to Q.10 is YES, check box or boxes to indicate all surgical treatments that apply.

Q.11: Check YES or NO to indicate if infant had any isolated bowel perforations NOT associated with NEC.

Q.12: Check YES or NO to indicate if there was any surgical treatment for isolated bowel perforations NOT associated with NEC.

Q.12a: If response to Q.12 is YES, check box or boxes to indicate all surgical treatments that apply.

16.7. Neonatal Outcome [OUTCOME] Form – Page 3

NEONATAL OUTCOME DATA
AT DISCHARGE, WITHDRAWAL, TRANSFER, DEATH OR WEEK 44 PMA ASSESSMENT, WHICHEVER OCCURS FIRST

PID: __ __ __ __ __ __

DATE: __ __ / __ __ / __ __ __ __

Ophthalmologic

13. Were any Retinopathy of Prematurity (ROP) examinations performed prior to discharge from the SAIL study center? ☐1 Yes ☐0 No

14. Was this baby diagnosed with ROP? ☐1 Yes ☐0 No
If Yes, complete 14a-14e

a. What was the worst stage ever reported in any zone?
__ Left Eye (1-5)
__ Right Eye (1-5)

b. Did the baby undergo laser or cryo-surgery?
Left Eye: ☐1 Yes ☐0 No
Right Eye: ☐1 Yes ☐0 No

c. Did the baby undergo Bevacizumab (Avastin) treatment?
Left Eye: ☐1 Yes ☐0 No
Right Eye: ☐1 Yes ☐0 No

d. Did the baby undergo Ranibizumab (Lucentis) treatment?
Left Eye: ☐1 Yes ☐0 No
Right Eye: ☐1 Yes ☐0 No

e. Did the baby undergo vitrectomy?
Left Eye: ☐1 Yes ☐0 No
Right Eye: ☐1 Yes ☐0 No

Neurologic

15. Did the baby receive a ventricular shunt? ☐1 Yes ☐0 No

a. If **Yes**, provide the date of first shunt placement: __ __ / __ __ / __ __ __ __
Month Day Year

16. What imaging technique was used to report the WORST head imaging results during the NICU admission?
☐1 Head Ultra Sound (HUS)
☐2 Head Magnetic Resonance Imaging (MRI)

a. Date of worst HUS or MRI? ____ / ____ / ____ __ __
Month Day Year

b. What were the results of this brain imaging? Check ALL that apply.
☐ Normal
☐ Subependymal hemorrhage (Grade 1 hemorrhage)
☐ IVH without ventricular dilation (Grade 2 hemorrhage)
☐ IVH distending at least one lateral ventricle (Grade 3 hemorrhage)
☐ Intraparenchymal echodense lesion (Grade 4 hemorrhage)
☐ Cystic Periventricular Leucomalacia (PVL)
☐ Porencephalic cyst
☐ Ventriculomegaly (with or without resolving IVH)
☐ Cortical atrophy
☐ Cerebellar hemorrhage
☐ Other, specify*: _____

** Do NOT report normal variants. Examples of normal variants include: Cavum septi pellucidum, connatal cysts, isolated choroid plexus cysts.*

16.8. Neonatal Outcome [OUTCOME] Data - Page 3 Instructions

Data questions on page 3 include Ophthalmologic (Q13-14) and Neurologic Outcomes Q15-16).

Q.13: Check Box Yes or No to indicate if any retinopathy of prematurity (ROP) examinations were performed prior to discharge form the study clinical center.

Q.14: Check Box Yes or No to indicate if the infant was diagnosed with ROP. If YES is checked, complete questions 14a – 14 e.

Q.14 a: Indicate for left and right eye the worst reported ROP stage (1-5) in any zone.

Q.14b: Indicate if infant underwent laser or cryo-surgery. Check Yes or No for left and right eye.

Q.14c: Indicate if infant underwent Avastin treatment. Check Yes or No for left and right eye.

Q.14d: Indicate if infant underwent Lucentis treatment. Check Yes or No for left and right eye.

Q.14e: Indicate if infant underwent vitrectomy. Check Yes or No for left and right eye.

Q.15: Check Box YES or NO to indicate whether infant received a ventricular shunt.

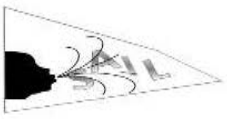
Q.15a: If response is Yes, provide date of first shunt placement.

Q.16: Indicate the imaging technique used to report the WORST head imaging results during NICU admission. Check box for either head ultra sound (HUS) or Head Magnetic Resonance Imaging (MRI).

Q.16a: Provide date of worst HUS or MRI.

Q.16b: Indicate the results of the head imaging. Check the box of all that apply in the list provided. If the box for Other is checked, please specify the results in the text line provided. Do not include any report of normal variants in the text line.

16.9. READMISSION [READMIT] Form



READMISSION PID:__ __ __ __ __ __

COMPLETE FORM FOR READMISSIONS BETWEEN 36 WEEKS AND 44 WEEKS PMA DATE:__ __ / __ __ / __ __ __ __

1. Date of readmission _____ mm/dd/yyyy

2. Primary reason for readmission _____

3. Respiratory support during readmission
   - ☐ 0 No Respiratory Support
   - ☐ 1 O_2 alone
   - ☐ 2 Tracheostomy and ventilation
   - ☐ 3 CPAP
   - ☐ 4 IPPV
   - ☐ 98 Other, specify: _____

Please note: For all readmissions up to and including 44 weeks 6/7 days PMA, update the Neonatal Outcome (OUTCOME) form and complete an additional Study Status (SSTATUS) form in the PRN visit upon discharge, withdrawal, transfer or death.

V1.0_20150108 PAGE 1 OF 1 READMIT

16.10. READMISSION [READMIT] Form - Instructions

This form is completed between 36-44$^{6/7}$ weeks PMA whenever an infant who was previously discharged or transferred, is readmitted to the SAIL clinical center facility for further treatment.

Q.1 Indicate the date of the readmission to the clinical center facility.

Q.2 Indicate the reason for readmission – provide a brief text of reason.

Q.3 Check Box to indicate the type of respiratory support that the infant was receiving at the time of readmission.

Note: When the infant is readmitted, update the Neonatal Outcome (OUTCOME) form and complete additional Study Status (SSTATUS) form in the PRN visit upon discharge, withdrawal, transfer or death.

16.11. 22-26 Month Follow Up [FUP] Form – Page 1

22-26 MONTH FOLLOW UP

PID:__ __ __ __ __ __ __

DATE:__ __ / __ __ / __ __ __ __

Patient Status

1. Was a Follow Up visit conducted? ☐1 Yes ☐0 No
   If Yes, answer questions 1a-1b. If No, skip to 1c

   a. Date of contact __ __ / __ __ / __ __ __ __ (mm/ dd/ yyyy)
   b. Indicate how follow up was conducted
      ☐1 Child lives at home, interview by phone
      ☐2 Child lives at home, follow up performed during outpatient visit
      ☐3 Child readmitted to hospital
      ☐4 Child has never been discharged from hospital
   c. If no, indicate primary reason follow up was not conducted:
      ☐1 Unable to contact
      ☐2 Refused interview
      ☐3 Child died (Please complete the SSTATUS form Q1-7a in the PRN visit)
      ☐88 Other, specify: _____
      _____
      _____

Medical History

2. Has the child been diagnosed or readmitted to the hospital for any of the following medical issues? Check all that apply
   ☐1 Respiratory Infection
   ☐2 Asthma
   ☐3 Failure to thrive
   ☐4 Short gut syndrome
   ☐5 Seizures/Seizure Disorder
   ☐6 Shunt complication
   ☐7 Meningitis with or without shunt
   ☐8 Microcephaly
   ☐9 Head Injury
   ☐10 Vocal Cord Paralysis
   ☐88 Other medical admissions or other serious injuries, specify: _____
   _____
   _____
   ☐99 None of the above

3. Have any of the following medications been prescribed for at least 2 months since first discharge home?

a.	Inhaled Corticosteroids	☐1 Yes	☐0 No
b.	Systemic Corticosteroids	☐1 Yes	☐0 No
c.	Bronchodilators	☐1 Yes	☐0 No
d.	Anticonvulsants	☐1 Yes	☐0 No
e.	Diuretics	☐1 Yes	☐0 No

V1.1_20160119 PAGE 1 OF 2 FUP

16.12. 22-26 Month Follow Up [FUP] Form – Page 1 Instructions

The Follow Up form is to be completed at 22-26 months corrected age and entered in the 2 YR CA visit in the database. The header date indicates the date of form entry. All dates are in MM-DD-YYYY format.

Q.1: Check Box YES or NO to indicate whether a Follow Up visit was conducted. If Yes is checked, complete questions 1a-1b. If No is checked, skip to 1c.

Q.1a: Enter Date of contact

Q.1b: Check box to indicate how follow up was conducted. Please note that if the child is unwell, the interview or visit should be rescheduled.

Q.1c: If the follow up visit was not conducted, check box to indicate primary reason why it was not completed. Select only one option.

- If the child died, complete the SSTATUS form
- If the box for 'Other' is checked, please specify the reason

Q.2: Record all medical issues applicable to the child. Check the box of all that apply in the list provided. If the box for 'Other' is checked, please specify any other medical admissions or other serious injuries. If the box for "None of the above" is checked, no other medical issues should be selected.

Q.3: Check Box YES or NO to indicate whether any of the medications (questions 3a-3e) listed were prescribed for at least 2 months. This question is intended to capture continuous semi-chronic dosing over a two month period any time after discharge.

Q.3a: Check Box YES or NO to indicate whether Inhaled Corticosteroids were prescribed

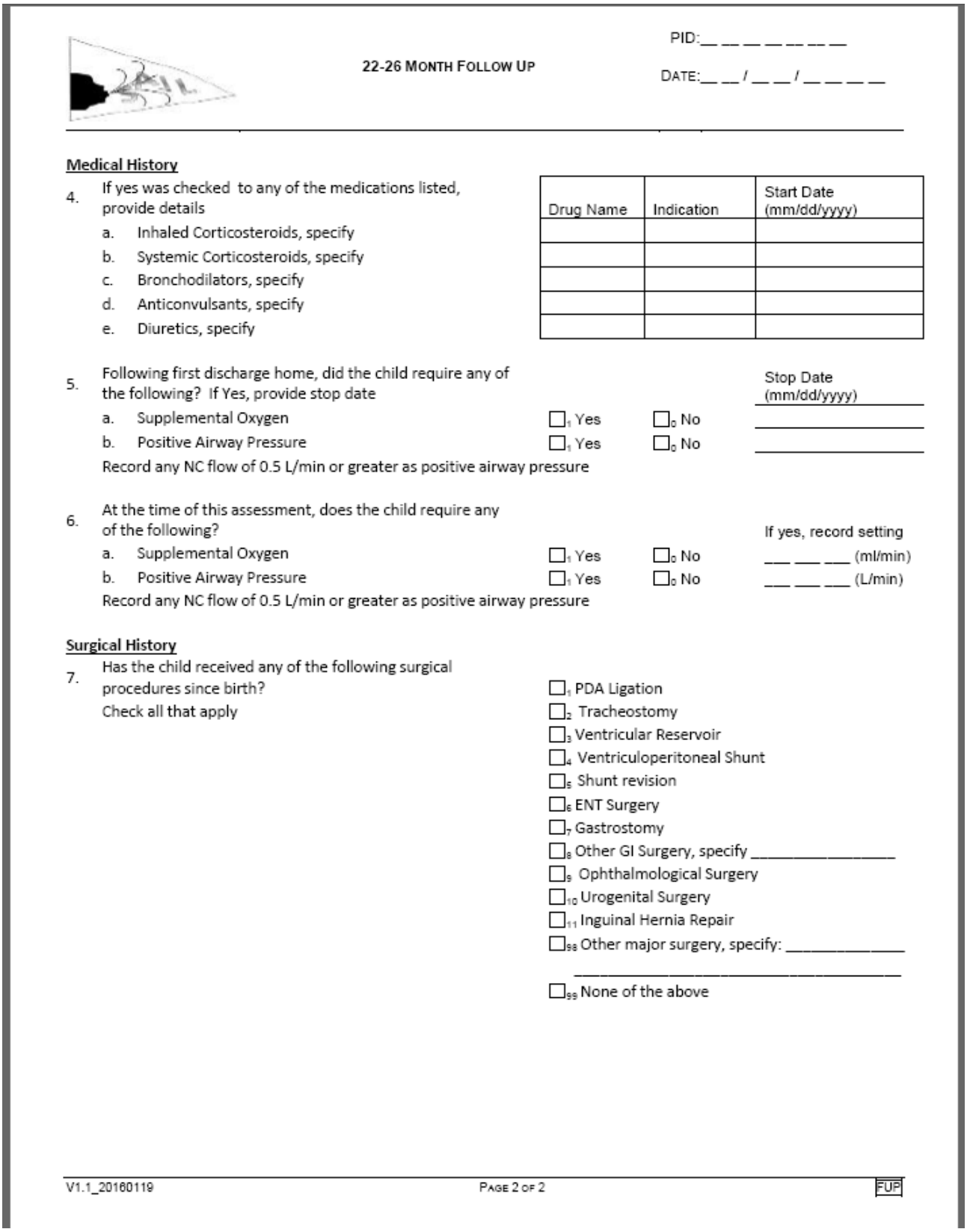
Q.3b: Check Box YES or NO to indicate whether Systemic Corticosteroids were prescribed

Q.3c: Check Box YES or NO to indicate whether Bronchodilators were prescribed

Q.3d: Check Box YES or NO to indicate whether Anticonvulsants were prescribed

Q.3e: Check Box YES or NO to indicate whether Diuretics were prescribed

16.13. 22-26 Month Follow Up [FUP] Form – Page 2



22-26 MONTH FOLLOW UP

PID:__ __ __ __ __ __ __

DATE:__ __ / __ __ / __ __ __ __

Medical History

4. If yes was checked to any of the medications listed, provide details

	Drug Name	Indication	Start Date (mm/dd/yyyy)
a. Inhaled Corticosteroids, specify			
b. Systemic Corticosteroids, specify			
c. Bronchodilators, specify			
d. Anticonvulsants, specify			
e. Diuretics, specify			

5. Following first discharge home, did the child require any of the following? If Yes, provide stop date

			Stop Date (mm/dd/yyyy)
a. Supplemental Oxygen	☐1 Yes	☐0 No	_____
b. Positive Airway Pressure	☐1 Yes	☐0 No	_____

Record any NC flow of 0.5 L/min or greater as positive airway pressure

6. At the time of this assessment, does the child require any of the following?

			If yes, record setting
a. Supplemental Oxygen	☐1 Yes	☐0 No	___ ___ ___ (ml/min)
b. Positive Airway Pressure	☐1 Yes	☐0 No	___ ___ ___ (L/min)

Record any NC flow of 0.5 L/min or greater as positive airway pressure

Surgical History

7. Has the child received any of the following surgical procedures since birth?
Check all that apply

- ☐1 PDA Ligation
- ☐2 Tracheostomy
- ☐3 Ventricular Reservoir
- ☐4 Ventriculoperitoneal Shunt
- ☐5 Shunt revision
- ☐6 ENT Surgery
- ☐7 Gastrostomy
- ☐8 Other GI Surgery, specify _____
- ☐9 Ophthalmological Surgery
- ☐10 Urogenital Surgery
- ☐11 Inguinal Hernia Repair
- ☐88 Other major surgery, specify: _____
  _____
- ☐99 None of the above

V1.1_20160119 PAGE 2 OF 2 FUP

16.14. 22-26 Month Follow Up [FUP] Form – Page2 Instructions

Q.4: If any of the above medications were checked Yes, specify details of the medication history

Q.4a: If Inhaled Corticosteroids were prescribed, specify Drug name, Indication and Start date

Q.4b: If Systemic Corticosteroids were prescribed, specify Drug name, Indication and Start date

Q.4c: If Bronchodilators were prescribed, specify Drug name, Indication and Start date

Q.4d: If Anticonvulsants were prescribed, specify Drug name, Indication and Start date

Q.4e: If Diuretics were prescribed, specify Drug name, Indication and Start date

Q.5: Indicate if the child required respiratory support following first discharge home.

Q.5a: If Supplemental Oxygen was required, record Stop Date

Q.5b: If Positive Airway Pressure was required, record Stop Date
-Record any NC flow of 0.5 L/min or greater as positive airway pressure

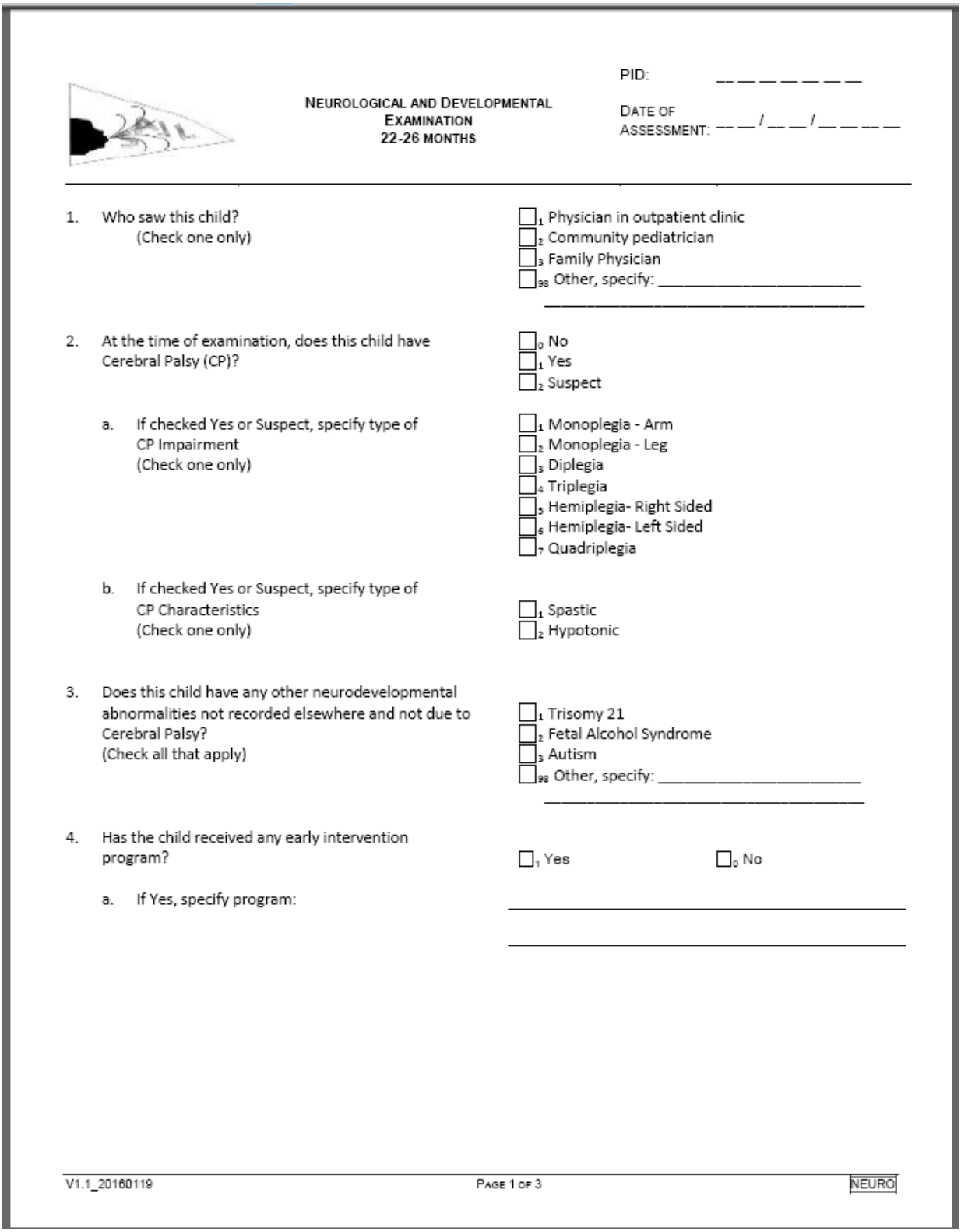
Q.6: Indicate if the child currently requires respiratory support at time of assessment

Q.6a: If Supplemental Oxygen is required, indicate Yes and record setting

Q.6b: If Positive Airway Pressure is required, indicate Yes and record setting
-Record any NC flow of 0.5 L/min or greater as positive airway pressure

Q.7: Record all surgical procedures the child received since birth. Check the box of all that apply in the list provided. If the box for 'Other, GI Surgery' or 'Other major surgery' is checked, please specify what the procedure was. If the box for "None of the above" is checked, no other surgical procedures should be selected.

16.15. Neurological and Developmental Examination 22-26 Months [NEURO] Form – Page 1



NEUROLOGICAL AND DEVELOPMENTAL EXAMINATION
22-26 MONTHS

PID: _ _ _ _ _ _ _ _

DATE OF ASSESSMENT: _ _ / _ _ / _ _ _ _

1. Who saw this child? (Check one only)
   - ☐ 1 Physician in outpatient clinic
   - ☐ 2 Community pediatrician
   - ☐ 3 Family Physician
   - ☐ 98 Other, specify: _____

2. At the time of examination, does this child have Cerebral Palsy (CP)?
   - ☐ 0 No
   - ☐ 1 Yes
   - ☐ 2 Suspect

   a. If checked Yes or Suspect, specify type of CP Impairment (Check one only)
   - ☐ 1 Monoplegia - Arm
   - ☐ 2 Monoplegia - Leg
   - ☐ 3 Diplegia
   - ☐ 4 Triplegia
   - ☐ 5 Hemiplegia- Right Sided
   - ☐ 6 Hemiplegia- Left Sided
   - ☐ 7 Quadriplegia

   b. If checked Yes or Suspect, specify type of CP Characteristics (Check one only)
   - ☐ 1 Spastic
   - ☐ 2 Hypotonic

3. Does this child have any other neurodevelopmental abnormalities not recorded elsewhere and not due to Cerebral Palsy? (Check all that apply)
   - ☐ 1 Trisomy 21
   - ☐ 2 Fetal Alcohol Syndrome
   - ☐ 3 Autism
   - ☐ 98 Other, specify: _____

4. Has the child received any early intervention program?
   - ☐ 1 Yes ☐ 0 No

   a. If Yes, specify program: _____

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16.16. Neurological and Developmental Examination 22-26 Months [NEURO] Form – Page 1 Instructions

The NEURO form is to be completed at 22-26 months corrected age (CA) and entered in the 2 YR CA visit in the database. The header date indicates the date of form entry. All dates are in MM-DD-YYYY format.

Q.1: Indicate who saw this child and performed the NEURO exam. Select best option. If the box for 'Other' is checked, please specify

Q.2: Indicate if the child has Cerebral Palsy (CP) at the time of the examination based on the examiner's clinical judgement. If 'Yes' or 'Suspect' is checked, answer questions 2a and 2b.

Q.2a: Check box to specify type of CP impairment. Select only one option

Q.2b: Check box to specify CP characteristics. Select only one option

Q.3: Indicate if the child has any other neurodevelopmental abnormalities not recorded anywhere else and not due to Cerebral Palsy. Check the box of all that apply in the list provided. If the box for 'Other' is checked, please specify

Q.4: Check Box YES or NO to indicate if the child received any early intervention program

Q.4a: If Yes is checked, specify the program

16.17. Neurological and Developmental Examination 22-26 Months [NEURO] Form – Page 2

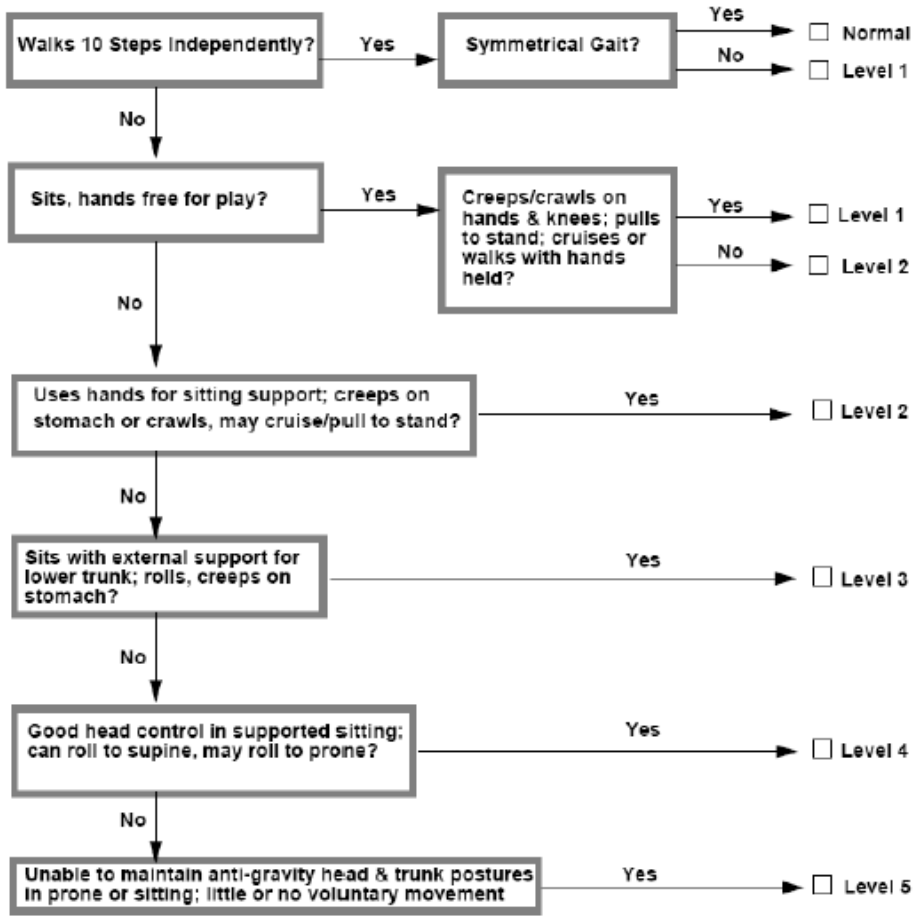
NEUROLOGICAL AND DEVELOPMENTAL EXAMINATION
22-26 MONTHS

PID: _ _ _ _ _ _ _ _

DATE OF ASSESSMENT: _ _ _ _ / _ _ _ _ / _ _ _ _ _ _

Gross Motor Function Score (GMFCS)

5. Follow the algorithm below to determine the LEVEL that most closely describes the child's current GROSS MOTOR FUNCTION (see Manual for detailed explanation of Levels)



V1.1_20160119 PAGE 2 OF 3 NEURO

16.18. Neurological and Developmental Examination 22-26 Months [NEURO] Form – Page 2 Instructions

We recommend using the Gross Motor Function Classification System - Expanded & Revised (GMFCS - E&R). It is available in 22 languages using the following link:

Reference Link: https://canchild.ca/en/resources/42-gross-motor-function-classification-system-expanded-revised-gmfcs-e-r

Listed below is the 5 level classification system that differentiates children with cerebral palsy based on the child's current gross motor abilities, limitations in gross motor function, and need for assistive technology and wheeled mobility

GMFCS Level I

- Can walk indoors and outdoors and climb stairs without using hands for support
- Can perform usual activities such as running and jumping
- Has decreased speed, balance and coordination.

GMFCS Level II

- Has the ability to walk indoors and outdoors, and climb stairs with a railing
- Has difficulty with uneven surfaces, inclines or in crowds
- Has only minimal ability to run or jump.

GMFCS Level III

- Walks with assistive mobility devices indoors and outdoors on level surfaces
- May be able to climb stairs using a railing
- May propel a manual wheelchair (may require assistance for long distances or uneven surfaces).

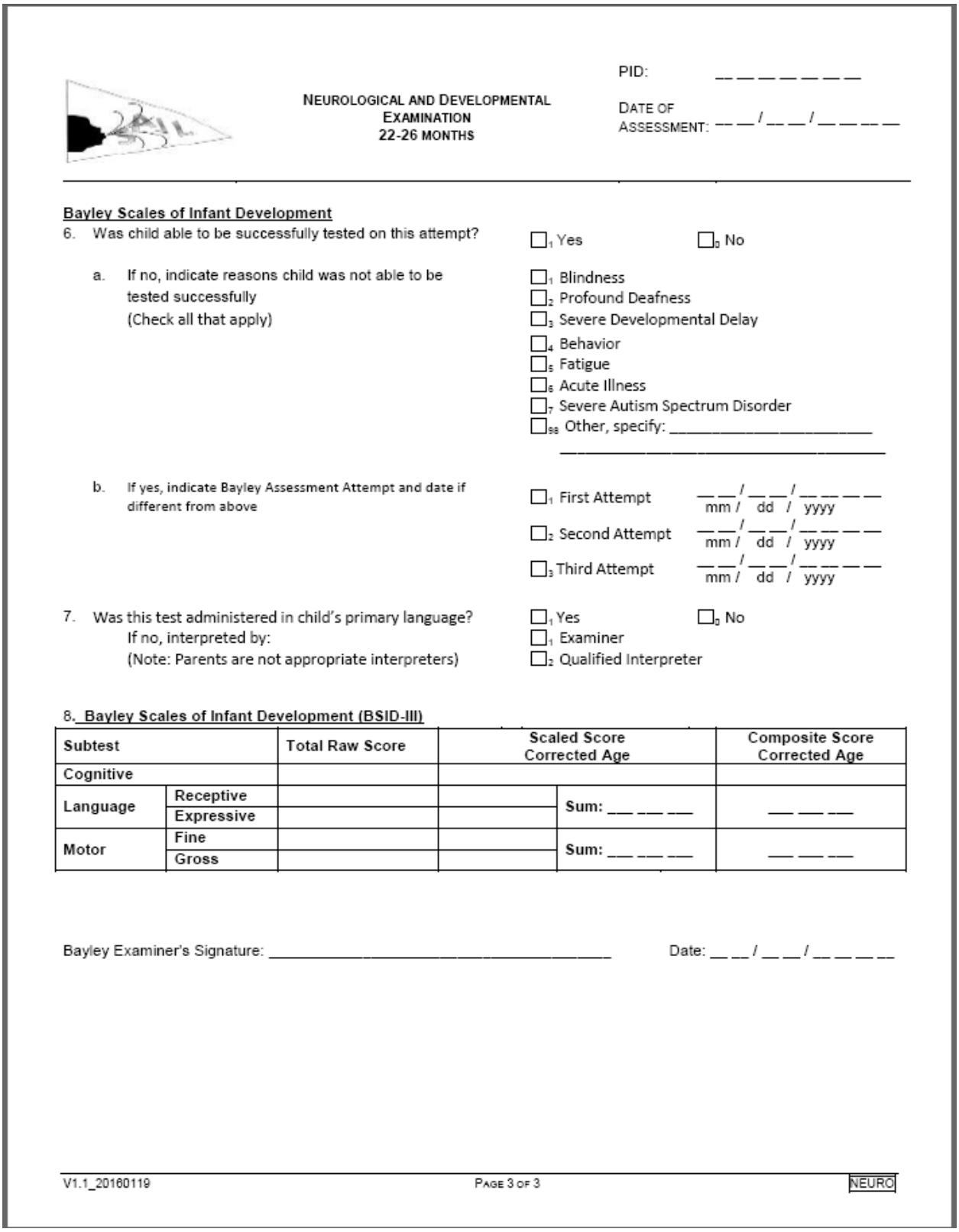
GMFCS Level IV

- Walking ability is severely limited even with assistive devices
- Uses wheelchairs most of the time and may propel their own power wheelchair
- May participate in standing transfers.

GMFCS Level V

- Has physical impairments that restrict voluntary control of movement and the ability to maintain head and neck position against gravity
- Is impaired in all areas of motor function
- Cannot sit or stand independently, even with adaptive equipment
- Cannot independently walk, though may be able to use powered mobility.

16.19. Neurological and Developmental Examination 22-26 Months [NEURO] Form – Page 3



NEUROLOGICAL AND DEVELOPMENTAL EXAMINATION
22-26 MONTHS

PID: __ __ __ __ __ __ __

DATE OF ASSESSMENT: __ __ / __ __ / __ __ __ __

Bayley Scales of Infant Development

6. Was child able to be successfully tested on this attempt? ☐1 Yes ☐0 No

   a. If no, indicate reasons child was not able to be tested successfully (Check all that apply)
   - ☐1 Blindness
   - ☐2 Profound Deafness
   - ☐3 Severe Developmental Delay
   - ☐4 Behavior
   - ☐5 Fatigue
   - ☐6 Acute Illness
   - ☐7 Severe Autism Spectrum Disorder
   - ☐88 Other, specify: _____

   b. If yes, indicate Bayley Assessment Attempt and date if different from above
   - ☐1 First Attempt __ __ / __ __ / __ __ __ __ (mm / dd / yyyy)
   - ☐2 Second Attempt __ __ / __ __ / __ __ __ __ (mm / dd / yyyy)
   - ☐3 Third Attempt __ __ / __ __ / __ __ __ __ (mm / dd / yyyy)

7. Was this test administered in child's primary language? ☐1 Yes ☐0 No
   If no, interpreted by:
   - ☐1 Examiner
   - ☐2 Qualified Interpreter

   (Note: Parents are not appropriate interpreters)

8. **Bayley Scales of Infant Development (BSID-III)**

Subtest		Total Raw Score	Scaled Score Corrected Age		Composite Score Corrected Age
Cognitive					
Language	Receptive			Sum: ___ ___ ___	___ ___ ___
	Expressive				
Motor	Fine			Sum: ___ ___ ___	___ ___ ___
	Gross				

Bayley Examiner's Signature: _____ Date: __ __ / __ __ / __ __ __ __

V1.1_20160119 PAGE 3 OF 3 NEURO

16.20. Neurological and Developmental Examination 22-26 Months [NEURO] Form – Page 3 Instructions

Reference: Bayley N. Bayley Scales of Infant and Toddler Development. 3rd ed. San Antonio, TX: Harcourt Assessment Inc; 2006

Q.6: Check Box YES or NO to indicate if the child was able to be successfully tested. If No is checked, answer question 6a. If Yes is checked, answer questions 6b.

Q.6a: If No is checked, select all reasons child was not tested successfully. Select all that apply. See guidelines below:

a. Blindness: Review notes from the child's previous Retinopathy of Prematurity (ROP) exam, if it was done. Diagnosis will be made after reviewing all ophalmology notes in the medical chart after the last known ROP exam. Previously diagnosed and stable visual problems do not reqire a new exam if they are well documented in previous ophthalmologic reports. Children without any functional vision are to be categorized as not successfully tested.
b. Deafness: Medical chart records indicating profound deafness as defined by sensorineural hearing loss. In addition, any hearing impairment requiring amplification or hearing impaired despite amplification constitutes deafness. If the child has profound hearing loss that cannot be corrected with a hearing aid, the child should be categorized as not successfully tested.
c. Behavior: Behavior should be determined on the physician's assessment of the child on the day of the interview. If the child has a diagnosis of Attention Deficit Hyperactivitiy disorder (ADHD), the child should be categorized as not succesfully tested.
d. Fatigue: Fatigue should be determined based on the physician's assessment of the child on the day of the interview. If the box for 'Other' is checked, please specify reason

Q.6b: If Yes is checked, record which attempt was successful and date if different from form entry date. If the first attempt is unsuccessful, we advise sites to reschedule the interview. The number of possible attempts will vary according to your institution's practices. Please be sure to schedule the interview within the 22-26 month follow up window.

Q.7: Check Box YES or NO to indicate if the test was administered in the child's primary language. If No is checked, record who interpreted the test. Parents, relatives or friends of the child's family are not appropriate interpreters.
-Select option for either Examiner or Qualified Interpreter.If an interpreter is needed, inform the interpreter to translate instructions as closesly as possible, and not to repeat instructions unless permitted by the examiner. If the family refuses an interviewer, the test should not be conducted.

Q.8: Enter all scores obtained for the BSID-III:
-Cognitive: Total Raw Score, Scaled Score and Composite Score
- Language: Total Raw Score, Scaled Score, Sum of Receptive and Expressive Language Score and Composite Score
-Motor: Total Raw Score, Scaled Score, Sum of Fine and Gross Motor Score and Composite Score

17. Adverse Event Reporting and Recording

Adverse events will be monitored during the study to ensure timely detection of events that may affect safety or continued participation. Protocol defined adverse events, as well as any unanticipated adverse events deemed possibly or probably related to study procedure, that occur within the first 28 days of life must be reported and entered in the data management system.

17.1. Protocol Adverse Event Definitions

The SAIL study population (critically ill preterm infants) has a high risk of adverse events (AEs) and serious adverse events (SAEs). The protocol has designated study specific AEs and SAEs that are to be reported within certain defined time frames.

The following table illustrates the specific AEs defined in the SAIL protocol and the time frame in which they are to be observed for reporting:

Adverse Event definitions:	Time Frame of Occurrence
Oxygen requirement of Fi02 ≥ 40% for 2 hours or more	Within the **first 48 hours** post delivery
Grade 1 or 2 IVH	Head ultrasound findings within the **first 10 days of life** (report based only)
Infant requiring > 30% Oxygen or mechanical support	**Respiratory support assessment only at day of life 28**

The above protocol defined AEs occurring in the specified time frame are reported by recording the event on the Adverse Event case report form AND entering the event in the data management system (DMS).

17.2. AE Reporting Examples

AE Example A: If a baby has a Grade 1 IVH on **day 3** of life:

1. Complete the AE case report form and enter event in the DMS.
2. Complete the IMAGING form to document the HUS/MRI findings.

AE Example B: If a baby has a Grade 1 IVH on **day 30** of life:

1. This event falls **outside of the protocol defined time frame** and after day 10 of life and **does not need to be reported or entered** in the DMS

AE Example C: For a baby requiring >30% Oxygen:

1. Report this protocol defined event **ONLY at Day 28 of life**.
2. Complete the AE case report form and enter event in the DMS.

17.3. Protocol Serious Adverse Event Definitions

The following table illustrates specific SAEs defined in the SAIL protocol and and the time frame in which they are to be observed for reporting.

Serious Adverse Event definitions:	Time Frame of Occurrence
Death	Within the **first 48 hours** post delivery
Administration of epinephrine or use of chest compressions	Within the **first 48 hours** post delivery
Pneumothorax, pulmonary interstitial emphysema (PIE) and pneumopericardium. These will be supplemented by data on: a) any chest tube in-situ post DR b) need for new chest tube after arrival in NICU	Radiographic evidence within the **first 10 days of life**
Grade 3 or 4 IVH	Head ultrasound findings within the **first 10 days of life** (report based only)

Reporting any of the above protocol defined SAEs involves the following steps:

1. Complete the AE form and enter event in the data management system (DMS)
2. Complete the Investigator SAE Report form (which includes additional clinical information) and submit it to the DCC.

Any of the above **protocol defined SAEs that occur outside of the specified time frame or any additional event deemed serious by the Principal Investigator** are documented on the AE case report form and entered in the DMS. No written Investigator SAE Report is required.

17.4. SAE Reporting Examples

SAE Example A: If a baby dies at **30 hours** of life:

1. Complete the AE form, indicate the event is serious, and enter it in the DMS. Send a brief alert e-mail or phone message to the DCC indicating that an SAE occurred and information will follow. Alert message should be sent within 24 hours of first knowledge of the event.
2. Within 3 days of the alert message, send an initial Investigator SAE report form to the DCC which includes a written narrative signed by the investigator.
3. Complete the STUDY STATUS form to indicate that the baby has died.
4. Submit a final Investigator SAE Report form to the DCC within one week of the event.

SAE Example B: If a baby dies on **day 30** of life:

1. Complete the AE form, indicate the event is serious, and enter it in the DMS.
2. Complete the STUDY STATUS form to indicate that the baby has died.

SAE Example C: If a baby has a pneumothorax on **day 3** of life:

1. Complete the AE form, indicate the event is serious, and enter it in the DMS. Send a brief alert e-mail or phone message to the DCC indicating that an SAE occurred and information will follow. Alert message should be sent within 24 hours of first knowledge of the event.
2. Submit an initial Investigator SAE Report form with narrative signed by the Investigator to the DCC within 3 days of the alert message.
3. Submit a final SAE Report form to the DCC within one week of the event.

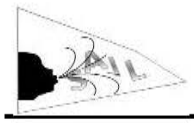
SAE Example D: If a baby has a Grade 4 IVH on **day 15** of life:

1. Complete the AE form, indicate that the event is serious, and enter it in the DMS.

17.5. Summary of Time Frame For Protocol Defined AE/SAE s

Time Frame of Occurrence	Events by Type
Within the first 48 hours post delivery	a. Oxygen requirement of Fi02 ≥ 40% for 2 hours or more [AE] b. Death [SAE] c. Administration of epinephrine or use of chest compressions [SAE]
Within the first 10 days of life	a. Grade 1 or 2 IVH [AE] b. Grade 3 or 4 IVH [SAE] c. Pneumothorax, pulmonary interstitial emphysema (PIE), pneumopericardium [SAE]
Day of life 28 assessment	a. Infant requiring > 30% Oxygen or mechanical support [AE]

17.6. Adverse Event Form – Page 1



SUSTAINED AERATION OF INFANT LUNGS (SAIL) STUDY

Adverse Event Form

PID: _ _ _ _ _ _

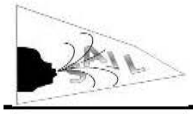
Event #	AE Code	AE description	Severity/ Grade	Serious Event?	AE Expected?	Attribution	Start Date *mm/dd/yyyy*	Stop Date *mm/dd/yyyy*	Outcome
1									
2									
3									
4									
5									
6									
7									
8									
9									
10									

AE Key				
Severity/ Grade	Serious event?	AE Expected?	Attribution to Rescusitation	Outcome
1 = Mild 2 = Moderate 3 = Severe 4 = Life Threatening/disabling 5 = Death	1 = Yes 0 = No	1 = Yes 0 = No	1 = Definitely 2 = Probably 3 = Possibly 4 = Unlikely 5 = Unrelated	1 = Recovered/resolved with no Sequelae 2 = Recovering/resolving 3 = Not recovered/not resolved 4 = Recovered/resolved with Sequelae 5 = Fatal

Signature of Investigator: _____

V2.1.20150130 Page 1 **AE**

17.7. Adverse Event Form – Page 2



SUSTAINED AERATION OF INFANT LUNGS (SAIL) STUDY

Adverse Event Form

PID: _ _ _ _ _ _

	Adverse Event Code Table and definitions:	Time Frame
1	Oxygen requirement of Fi02 ≥ 40% for 2 hours or more	Within the **first 48 hours** of life
2	Infant requiring > 30% Oxygen **or** NC > 2 LPM	**ONLY** at **Day 28 of life**
3	Infant on mechanical support (includes CPAP, NIPPV, invasive ventilation via ETT)	**ONLY** at **Day 28 of life**
4	Grade 1 IVH	Head imaging findings in the **first 10 days of life** (report based only)
5	Grade 2 IVH	Head imaging findings in the **first 10 days of life** (report based only)
6	Any additional event possibly or probably related to study procedure	Up to 28 Days of Life

	Serious Adverse Event Code Table and definitions:		Time Frame
7	Death		Within the **first 48 hours**
8.	Administration of Epinephrine		In the first 48 hours of life
9.	Use of Chest Compressions		In the first 48 hours of life
10	Grade 3 IVH		Head imaging findings in the **first 10 days of life** (report based only)
11	Grade 4 IVH		Head imaging findings in the **first 10 days of life** (report based only)
12	Pneumothorax- supplemented by data on:		Radiographic evidence within the **first 10 days of life**
	a) any chest tube in-situ		
	b) need for new chest tube		
13	Pulmonary interstitial emphysema (PIE)- supplemented by data on:		Radiographic evidence within the **first 10 days of life**
	a) any chest tube in-situ		
	b) need for new chest tube		
14	Pneumopericardium- supplemented by data on:		Radiographic evidence within the **first 10 days of life**
	a) any chest tube in-situ		
	b) need for new chest tube		
15	Any additional event deemed to be serious by the site Principal Investigator		Duration of study

V2.1.20150130 Page 2 **AE**

17.8. Adverse Event [AE] Form – Pages 1 & 2 Instructions

The Adverse Event paper case report form (pages 1 & 2) is featured above. Protocol defined adverse events and their severity, expectedness, attribution to resuscitation, outcome and start/stop dates are recorded on the AE form. Adverse events are recorded in an on-going log format for each individual patient. The codes for each protocol specific adverse and serious adverse event is listed on page 2 of the Adverse Event Form. The Adverse Event information can be recorded on the paper case report form and then entered into the data management system (DMS), or entered directly into the DMS. The AE form is located in the PRN visit tab in the DMS. Protocol defined AEs and any additional AEs deemed possibly or probably related to study procedure that occur within the **first 28 days of life** are recorded on this same AE form (AE log) which is then updated in the DMS with each new event. AE data should be entered into the data management system within 1 week of the occurrence.

1. Did an Adverse Event or Serious Adverse Event occur within the first 28 Days of Life?
    - Check Yes or No.

2. If Yes, enter AE code and provide a description of the event.

3. Using the AE Key table at the bottom of the page, indicate the severity/grade of the event, if the event was serious, expected, and if it was attributable to resuscitation.

4. Indicate the start date, which is the date the adverse event occurred.

5. For the stop date, enter the date the baby recovered from the event or the date the event was resolved**.**

6. Indicate the Outcome using the AE Key table. Data entry of the AE would be made when the event occurs, but date of AE resolution will not be entered until final resolution of the event. Note: Some adverse events may not have an outcome or stop date recorded. In this case, if the baby did not recover or the event was not resolved by Day 28, reassess the event at 36 weeks, discharge or transfer, whichever occurs first and enter this date as the stop date.

Example: An O_2 requirement of FIO2 >40% for more than 2 hours occurs at day one of life. The event is recorded on the AE form along with the start date and entered in the DMS. At 48 hours of life the oxygen requirement of FIO2>40% continues, thus a stop date for the event is not entered in the DMS. If at day 28 of life, should the Oxygen need for FIO2 >40% continue, the date of resolution would be left blank on the AE form and in the DMS. Should the AE be resolved or remain unresolved by the time the infant is discharged or at week 36 (whichever occurs first), record that date as resolution date and enter it in the DMS.

17.9. Serious Adverse Event Report Form - Page 1

Principal Investigator Serious Adverse Event (SAE) Report

When to Use This Form: Complete this form and submit it with related attachments for the study specific Serious Adverse Events described below that occurred within the specified time frame. If reporting more than one event, complete an additional SAE Report Form.

SAE DEFINITIONS

Serious Adverse Event	Time Frame
• Death	Within the **first 48 hours** post delivery
• Administration of epinephrine or use of chest compressions	Within the **first 48 hours** post delivery
• Pneumothorax, pulmonary interstitial emphysema (PIE) and pneumopericardium. These will be supplemented by data on: a) any chest tube in-situ post DR b) need for new chest tube after arrival in NICU	Radiographic evidence within the **first 10 days of life**
• Grade 3 or 4 IVH	Head ultrasound findings with the **first 10 days of life** (report based only)

REPORT TYPE: ☐ **Initial Report** ☐ **Follow-up Report** ***Date of Report:*** _____

Clinical Site: _____ ***Date of Serious Adverse Event:*** _____

PID # : _____ **Date of Birth:** _____

Gestational Age: _____ **weeks** _____ **days** **Birth Weight:** _____

Specify Serious Adverse Event:

Was this an Unexpected Adverse Event? ☐ Yes ☐ No

Relatedness [Check only one}

- ☐ Unrelated
- ☐ Unlikely
- ☐ Possibly
- ☐ Probably
- ☐ Definitely

Category of Seriousness (Check all that apply):

- ☐ Life-threatening
- ☐ Hospitalization/Prolongation of hospitalization
- ☐ Persistent or significant disability/incapacity
- ☐ Important medical event
- ☐ Death

If Death Occurred : Date of Death: _____

Cause of Death: _____

Autopsy Performed: ☐ Yes ☐ No

17.10. Serious Adverse Event Form – Page 2

If there is a reasonable possibility that the event is related to a Concomitant Drug(s), specify:	*If infant is also enrolled in concurrent research and there is a reasonable possibility that the event is related to that study(s), specify study(s):*

SERIOUS ADVERSE EVENT NARRATIVE

(Provide description of the event).

What was subject's participation level after the event?	☐ Parents withdrew infant from further participation ☐ Investigator withdrew infant from further participation ☐ Infant continues in study participation
What steps do you plan to take as a result of the adverse event reported above?	☐ no action required ☐ amend consent document ☐ amend protocol ☐ inform current subjects ☐ terminate or suspend protocol ☐ other, describe:

Signature of Person Completing this Form	***DATE***
SIGNATURE OF PRINCIPAL INVESTIGATOR	***DATE***

17.11. Serious Adverse Event Report Form – Pages 1 & 2 Instructions

The Serious Adverse Event Report Form-Principal Investigator SAE Report (shown above) is a two page administrative report form. This form is not entered in the data base. It **is only completed for protocol defined SAEs** that occur within the designated time frame as outlined on Page 1 of the form.

A written narrative of the protocol defined SAE will be completed on the Serious Adverse Event Report Form and signed by the Investigator and sent to the DCC project manager. The report should contain a thorough description of the SAE and sufficient clinical information should be provided. All protocol specified SAEs will be independently adjudicated in this study. Supporting clinical documentation should be provided with the SAE written narrative report, such as clinical reports on medical imaging (e.g. ultrasounds, MRIs, chest x-rays), or any additional clinical information from the subjects record that is relevant to the event (e.g. progress reports, discharge summary, hospital death summary). All supporting clinical documentation will be de-identified and redacted of any patient identifying information before being sent to the DCC.

When to complete this form: This form is completed each time that a protocol defined SAE occurs on an infant within the specified time frame.

A written SAE narrative is NOT required for any protocol defined SAE that occurs outside the specified time frame**. Any other SAE (not protocol defined) that occurs during the study and is deemed serious by the Principal Investigator should be recorded on the AE form and entered in the DMS, however.**

NOTE: In this study, any congenital anomaly/birth defect is not considered to be a reportable SAE. In addition, any intervention (drug or surgical) needed to prevent permanent impairment or damage to the infant is not considered a reportable SAE.

17.12. Timeline for Reporting Serious Adverse Events

A preliminary SAE alert message is sent to the DCC within 24 hours of first knowledge of the event. This alert message may be sent via e-mail or phone to the DCC project manager. An initial Investigator SAE report should be sent within 3 days of the alert message which includes a written narrative signed by the investigator. A final SAE report is submitted by the site to the DCC within one week. This report will be submitted to the DSMC Chair for independent adjudication of relatedness to the intervention.

The Program Scientist at NICHD and/or the DCC will determine whether expedited DSMC reviews are necessary. The DSMC can recommend further action and the DCC will be responsible for notification to the local site team and NICHD.

17.13. Reporting Unanticipated Problems

The Serious Adverse Event form is also used to report any **unanticipated problem** that may occur. To determine whether an adverse event is an unanticipated problem, the following questions should be asked:

1) Is the adverse event unexpected?
2) Is the adverse event related or possibly related to participation in the research?
3) Does the adverse event suggest that the research places subjects or others at a greater risk of harm than was previously known or recognized?

If the answer to **all three questions** is Y*es,* then the adverse event is an unanticipated problem and must be reported on the SAE Report Form as such and submitted to the DCC.

18. Appendix 1: Sustained Inflation Training Attestation

SAIL TRIAL TRAINING

Attestation - Sustained Inflation Maneuver

Name: _____

Initials: _____

Clinical Site: _____

I attest that I have completed the following training activities required of all clinicians who perform the Sustained Inflation (SI) maneuver during resuscitation in the SAIL Trial.

TRAINING ACTIVITES CHECKLIST		Date completed
1	Read SAIL Trial protocol or viewed the protocol slides.	
2	Watched the SAIL training Video.	
3	Practiced the SI method with the resuscitation team.	
4	Read SAIL Trial MOP.	
5	Attended local in-service on infant resuscitation.	

Attester's Signature: _____

Date Signed: _____

Instructions:

1. **This form should be completed by each clinician member of the resuscitation team who will perform the Sustained Inflation maneuver.**
2. Send this completed form to the DCC project managers at: sail-pjm@lists.upenn.edu
3. Keep a copy of this form on file in your study training records.

19. Appendix 2: Reporting a SAIL Protocol Violation

Any failure to follow a major component of the protocol will result in a protocol violation. Examples of a protocol violation include:

- Failure to obtain informed consent from the parent(s) prior to enrollment of infant.
- Failure to follow randomized treatment arm assignment in delivery room resuscitation of enrolled infant.
- Opening of randomization envelope prior to the birth of the infant; opening more than one randomization envelope for an enrolled infant.
- Enrollment and randomization of an infant who is ineligible for the study.
- Failure to follow the approved study protocol that affects participant safety or data integrity
- Failure to report serious adverse event to sponsor/DCC.
- Continuing research activities after IRB approval has expired.

Guidelines for Reporting Protocol Violation

1. Complete SAIL protocol violation report form, indicating date of occurrence of violation, participant identification number, clinical site number. Provide a written description of the violation and any actions taken.
2. Report violation internally as per site IRB/Ethics Board requirements.
3. Submit written report to the DCC Project Manager via e-mail or fax.

19.1. Protocol Violation Form

SAIL PROTOCOL VIOLATION REPORT			
Site #	Participant ID #	Date Violation Occurred:	Submitted by :
Protocol Violation: Provide a description of the event.			
Action Taken: Identify corrective actions taken and parties notified (if applicable).			
Additional Information:			

Signature of person completing form

Date Reported

Submit completed report to the DCC Project Manager.

20. Appendix 3: Study Policies

20.1. Co-Enrollment / Concurrent Research

In order to have the best chance of success in both this trial and others, we have adopted a policy on Concurrent Research as follows;

i) All randomized trials that likely involve patients who are also eligible for the SAIL trial, must be discussed with the SAIL executive committee, and the protocols shared.
ii) All such studies may or may not be compatible with the SAIL trial, and full discussion will be undertaken ito resolve potential for co-enrollment
iii) In the CRFs we request that all studies that involved consent for the child-family, should be documented somewhere.

Ultimately, SAIL sites wishing to co-enroll infants into another study must have the co-enrollment study approved by the SAIL executive committee. Generally, in order to be considered for co-enrollment, studies will need to show:

1) Potential to dilute main effects of SAIL study no more than standard clinical practice; particularly important if co-enrollment is high (approx. >50%) as sample size for SAIL may need to be adjusted.
2) Outcome is not a competing risk with BPD.
3) Co-enrollment study is not operating under an IND (investigational new drug).
4) The intervention arms for the co-enrollment study are unrelated to the SAIL arms.
5) Will not create known serious adverse event risks beyond those already expected in the SAIL population.
6) Balanced randomization within SAIL arms, or the ability to work with the SAIL statistician to create a 2xN factorial randomization for both studies combined.
7) If the co-enrollment study is blinded and the SAIL executive committee determines the co-enrollment intervention could affect the primary SAIL analysis, then intervention assignment unblinding must be possible before the final analyses for SAIL are completed (expected unblinding needed by 1/2018).

20.2. Data Access Policy

Access to SAIL data requires an association with the study, and agreement to abide by study policies and procedures. Non-participating site investigators may request ancillary analyses, but in any such case SAIL investigators must be directly involved as co-investigators.

Note that all relevant data for all studies conducted under the auspices of SAIL, will contain no personal identifiers; i.e. are de-identified, unless otherwise noted.

Each recruiting site will have access to the complete data from their site after the completion of the SAIL study (i.e. after primary analyses have been completed). This data may be used for

investigation purpose but may not be used for publication without prior approval of the steering committee of the trial. No secondary paper can be submitted for publication until the primary results are accepted.

In order to maximize the benefits of participating in the study, to maximize scientific benefit from the study, and to acknowledge the generosity of parents in enabling their child to participate in the study, we encourage sites to consider meaningful secondary or ancillary studies. These must follow the following guidelines.

Data access is provided to Investigators, Collaborators or Ancillary Study Investigators for scientific research upon completion of the following procedures.

1. Secondary (ancillary) Paper proposal

A paper proposal must be submitted for each paper, prior to request for data. This need not be lengthy, but at minimum 2 pages that describes the research question, main goals, and initial analytical approach. We encourage multi-site collaboration for these secondary studies. The proposal is reviewed by the Steering Committee for consistency with the goals of the SAIL study, lack of overlap with other work, and scientific integrity. All persons who will have access to study data need to be named on the proposal. If there is a change of analyst (someone new who will access the data), the name of the new analyst needs to be communicated to the Steering Committee coordinator for study records.

Upon review of the proposal, the Steering Committee will either vote for either (i) approval of proposal; (ii) resubmission based on questions / concerns raised, or (iii) rejection of the proposal. Note that approval of the proposal does not guarantee receipt of the requested data. Both a data use agreement (step 2) and costs associated with data extraction (step 3) need to be completed/covered before the data will be released to the investigator.

2. Data Use Agreement (DUA)

Following the scientific approval of the study, a Data Use Agreement must be completed to obtain study data. This requires IRB review from the recipient investigator's institution. Investigators outside the University of Pennsylvania who are located at a SAIL site need to confirm with their own institution that their IRB approval for study activities includes receiving and analyzing data from all study sites.

3. Data Request

Data may be obtained from the Coordinating Center by submitting a Data Request Form to the Project Manager. Costs associated with extraction of the requested data must be covered by the requestor prior to the data being pulled. These costs will depend upon the complexity of the data being requested. An estimate of these costs will be provided upon request.

4. Publication

No ancillary study can be published until the primary paper(s) are published.

20.3. Publication Policy

All SAIL manuscripts and abstracts ("publications") must, before submission, be reviewed by the Steering Committee. The Steering Committee will form the writing committee of the main primary paper. The author line must conclude with "and the SAIL Study investigators," and NICHD funding must be acknowledged, specifying the grant number if applicable.

Note: "publications" include abstracts and posters for presentation at national and international meetings.

Manuscripts are assigned a primary reviewer(s) from the Steering Committee who is responsible for final approval. The manuscript is returned to the lead author with major comments (required changes) and minor comments (recommended changes). If there are required changes, the manuscript must be revised and resubmitted for further review. This process is repeated until no required changes remain. In case of persistent disagreement between authors and reviewers, final judgment rests with the Steering Committee chair. Abstracts undergo a similar but abbreviated review.

Additionally, if the analysis is done at the local site: the lead author is required to submit the analytical plan and computer code used to produce the results in the publication from the original dataset. If results cannot be reproduced, the publication will not be approved for submission.

20.4. Authorship

SAIL supports and subscribes to the policies of the International Committee of Medical Journal Editors' Uniform Requirements for Manuscripts Submitted to Biomedical Journals (http://www.icmje.org/). These Requirements state:

> *"Authorship credit should be based on 1) substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; 2) drafting the article or revising it critically for important intellectual content; and 3) final approval of the version to be published. Authors should meet conditions 1, 2, and 3."*

For the purposes of reporting results, SAIL will consider substantial contributions to patient accrual as meeting criterion 1), as accrual is critical for the "acquisition of data".

In general, authors will be named as individuals with as many authors included **as permitted by the intended journal**. Situations may exist where it is more appropriate to have authors named under an umbrella term. In these situations, a Writing Committee will be named and will include members of the SAIL Study investigators. If permitted, authorship will start with the members of the steering committee and then work through collaborating center PIs in order of number of enrolled and randomized infants. Additional authorship positions will be determined by SAIL site accrual. When a site has contributed a a large percentage of accrual, additional authors from that center may be selected (e.g. 2 authors from the site if >15% of total accrual, 3 for >25%, etc). The additional authors will be determined by the site PI.

When appropriate for unusual contribution, SAIL staff will be considered for inclusion as other contributing authors. Examples include the DCC Project Manager and, for papers with detailed statistical analysis, the staff statistician. The life span of SAIL may mean that sustained involvement by a single Project Manager is not possible. In these circumstances, all staff with direct project-specific responsibilities will be included in the Acknowledgements.

Where journal policies permit, all investigators who played a contributing role in the study, including to its accrual, will be included in an Acknowledgement section. DCC and site staff with direct project-specific responsibilities will also be acknowledged.