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INFORMATION AND CONSENT FORM FOR PATIENTS WITH COPD (including Sputum assessment)

STUDY TITLE: Observational study in healthy subjects and patients with COPD to assess the relationship between clinical, imaging and biomarker measurements, and progression of emphysema over three years.

PROTOCOL No.: 352.2069 FOOTPRINTS™

SUBJECT No.: _____

EudraCT No.: NA

SPONSOR: Boehringer Ingelheim Pharma GmbH & Co. KG
Birkendorfer Straße 65, 88397 Biberach an der Riss, Germany

STUDY DOCTOR: Name, address, telephone number

Dear Study Participant,

You are being asked to participate in this observational study because:

- You are a 40 to 70 year old ex-smoker, having quit smoking more than 9 months and you have been diagnosed with Chronic Obstructive Pulmonary Disease (COPD)

  Or

- You are a 30 to 70 year old ex-smoker, having quit smoking more than 9 months you have an alpha 1-antitrypsin (A1AT) deficiency phenotype zz and you have been diagnosed with COPD.

This is a 3 year observational study to investigate if there are biomarkers, specific for chronic obstructive pulmonary disease (COPD) and especially emphysema. COPD is a common cause of lung problems and is most often due to smoking. At first, COPD may cause no symptoms or only mild symptoms. As the disease gets worse, symptoms usually become more severe. People with COPD often have symptoms such as cough, abnormal sputum production and shortness of breath, due to narrowing and blockage of the breathing tubes through which air flows in and out of the lungs. Apart from smoking cessation, there is no treatment that can prevent the progression of the disease. Destruction of lung tissue (called emphysema) is a characteristic of COPD involving damage to the air sacs (alveoli) in the lungs which are needed for gas exchange. As a result, the body does not get the oxygen it needs. Many patients with COPD, but not all, develop emphysema at some point. Biomarkers are medical signs, which can be measured, such as blood tests, imaging

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and lung tests. Biomarkers identified in this study could contribute to discovery of new drugs for treatment of COPD and associated lung tissue destruction.

Please read the following information carefully. It contains important information to help you decide whether to participate in this research study. The study staff will have a detailed discussion with you to inform you about the study and the possible benefits and risks of your participation. Ask questions about anything that is not clear at any time. You may take home an unsigned copy of this information to think about and discuss with your family, friends or family doctor before you make your decision to participate or not.

After reading and discussing the information you should know:

- Why this research study is being done;
- What will happen during the study;
- Any possible benefits to you;
- The possible risks to you;
- Other options you could choose instead of being in this study;
- How your personal information / health information will be treated during the study and after the study is over, and which data privacy rights you have;
- Whether being in this study could involve any cost to you; and
- What to do if you have problems or questions about this study.

Participation in this study is voluntary (your choice). If you join this study, you can still stop at any time. You have the right not to sign this consent form. If you do not sign, you cannot take part in this research study. If you decide to participate, you will be asked to sign and date at the end of this form.

PURPOSE OF THE STUDY

The purpose of this study is to evaluate biomarkers correlating to the development and progression of the COPD disease, in particular the emphysema. This study is an observational study. The study does not include administration of any investigational medicinal product and you are allowed to continue and change your standard medication during the study.

COPD is a common disease of lower airways, which significantly affects the quality of life. The disease progresses over time and eventually results in complete disability. Despite major advances in COPD treatment, none of existing drugs can stop the progression of the disease, nor lung tissue destruction (called emphysema), which occurs in every 5th patient with COPD. Also, there are no reliable biological markers (biomarkers) of the disease in sputum and blood, which would allow for earlier recognition of COPD, its progression and response to treatment other than lung function tests. Such biomarkers would also contribute to faster discovery of new drugs for COPD. This study is undertaken to collect data on various biomarkers in induced sputum and blood as well as markers derived from imaging techniques (like chest CT or MRI) in patients with different degrees of COPD and of healthy subjects, who serve as control group. It will also be checked if any of these markers reflect COPD severity or presence or progression of emphysema. This research can lead to the discovery of new diagnostics and medicines and improve the treatment of COPD including associated emphysema in the future.

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We estimate that approximately <enter number of participants assigned to your OPU> people will participate in this study in <insert country of OPU> and approximately 455 participants worldwide.

This study has been approved by <insert applicable local authorities, if required, otherwise this statement can be deleted>.

DESCRIPTION OF THE STUDY

The study is multi-national and involves approximately 12 participating countries. It consists of 2 consecutive periods, a screening and an observational period. The screening period lasts up to 28 days. The observational period lasts 3 years and includes 6 clinic visits and 7 additional phone contacts.

FLOW CHART OF THE STUDY

Study Periods	**Screening Period**	**Observational Period**												
Visit	**1**	**2**	**3**	**4**	☎	**5**	☎	☎	☎	**6**	☎	☎	☎	**7**
Weeks			**12**	**26**	**39**	**52**	**65**	**78**	**91**	**104**	**117**	**130**	**143**	**156**
Interview MESI Check	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Physical examination & Vital Signs	X					X				X				X
Blood collection for safety and biomarkers	X	X	X	X		X				X				X
Urine collection (smoking status)	X	X	X	X		X				X				X
Questionnaires	X	X				X				X				X
Pulse oximetry	X	X		X		X				X				X
Lung function testing	X	X	X	X		X				X				X
Review of the diary		X	X	X	X	X	X	X	X	X	X	X	X	X
Chest CT		X				X				X				X
MRI (optional)		X		X		X				X				X
Induced sputum		X	X	X		X				X				X
Exercise testing (6 MWT)	X	X								X				X

STUDY PROCEDURES

Pre-study procedures

Before any study-related procedures are performed, you will be asked to read and sign this consent form to confirm that you wish to participate. The study will be explained to you. You can ask questions and if you agree to take part in the study, you need to sign the consent form.
By signing the Informed Consent you confirm your participation in this study.

Please note, that you are also asked to agree to collection of unspecified blood and sputum samples for biobanking. A biobank is a place where samples are long term stored until they are needed for

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further research. This is part of this study. Please read the respective descriptive sections in this document.

Study procedures taking place at each visit

At each clinic visit or scheduled phone visit

- You will be asked about your overall health and changes in medication.
- Please use your reminder diary and note your respiratory symptoms, hospitalization or doctor's visits and all medication you are taking.

Study procedures at the screening visit (Visit 1)

- The study will be introduced to you.
- You will be asked for your demographics, such as sex, race, year of birth.
- Your medical and smoking history will be reviewed.
- You will have a complete physical examination, which will include measurements of blood pressure, pulse rate, temperature, weight, and height.
- An electrocardiography (ECG) will be performed. The ECG is a painless test which measures the electrical activity of the heart.
- Blood (approximately 15 ml or 3 teaspoons) will be drawn from a vein in your arm for different laboratory tests, including a genetic test to look whether you have a genetic variation called alpha 1-antitrypsin deficiency (A1ATD). A1ATD is a genetic disorder that causes defective production of alpha 1-antitrypsin (A1AT). There are several forms and degrees of the deficiency. The most common abnormal genes are the S and Z alleles. In this study only patients with the zz-gene mutation can participate. Severe A1ATD can lead to liver disease and emphysema.
- A urine sample will be taken for nicotine testing.
- For all women of child bearing potential a urine pregnancy test will be done.
- You will complete the mMRC (Modified Medical Research Council) questionnaire.
- You will have a lung function test before and after taking salbutamol/albuterol [OPU to adapt locally]. You will be asked to blow hard into the mouthpiece of the measuring device. The test determines how well your lungs work. The procedure will be explained in detail before the test.
- You will have a lung diffusion test called D_{LCO} after taking salbutamol/albuterol [OPU to adapt locally]: this lung diffusion test measures how well the lungs exchange gases. This is an important part of lung function testing, because the major function of the lungs is to allow oxygen to "diffuse" or pass into the blood from the lungs, and to allow carbon dioxide to "diffuse" from the blood into the lungs. You breathe in (inhale) air containing a very small amount of carbon monoxide, a gas existing in the atmosphere but given to you in a higher concentration. You hold your breath for 10 seconds, and then rapidly blow it out (exhale). The exhaled gas is tested to determine how much of the carbon monoxide gas was absorbed during the breath. The remaining gas will easily be eliminated from your body by normal breathing.
- A 6-minutes walking exercise test will be done. You will be asked to walk as far as possible for 6 minutes and the distance will be measured. You will get sufficient time to recover from the walking test.
- Pulse oximetry: this test measures how much oxygen your blood is carrying. By using a small device put on your forefinger your blood oxygen level can be checked.

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- You get a reminder diary to write down if your health conditions have gotten worse, if you experienced symptoms and all medication that you are taking.

The results of the tests and/or questions at the screening visit will help the study team to decide whether you can continue in this study. If these tests show that you are eligible to participate, you will be able to continue the study. If you do not meet the eligibility criteria, you will not be able to continue.

Even if you are eligible for the study, your participation cannot be guaranteed. At the moment when the maximum number of subjects who can be included is reached, you will not be able to enter the observational phase of the study.

Visit 1 will last approximately 3 - 4 hours.

You will be scheduled to return for Visit 2 within the next 28 days.

Study procedures in the observational period (Visits 2 to 7)

You will be scheduled to return to the clinic for 6 observational period visits. All visits during the observational period will be scheduled to begin between 06:00 and 09:00 in the mornings. Please come fasted to the visits. Please do not have anything to eat or drink, except water, for 6 hours before the visit. This is very important to get good laboratory measurements.

- First at each visit you will be asked about your medication intake, your diet and life style and your smoking status.
- You will have a complete physical examination, which will include measurements of blood pressure, pulse rate, temperature, weight, and respiratory rate at visits 5, 6 and 7.
- For all women of child bearing potential a urine pregnancy test will be performed at visits 2, 4, 5, 6 and 7.
- You will complete at visits 2, 5, 6 and 7 three questionnaires prior to pulmonary function testing. The questionnaires contain questions about your health, the breathing and COPD status:
  All questionnaires together will take approximately 60 minutes to complete.
- Lung function testing (each performed twice), D_{LCO} and pulse oximetry will be performed at each clinic visit, except at visit 3.
- Body plethysmography will be performed at each clinic visit, except at visit 3. You sit in a small, airtight room known as a body box. You breathe against a mouthpiece. Clips are put on your nose to shut off your nostrils. As your chest moves while you breathe, it changes the pressure and amount of air in the room and against the mouthpiece. From these changes an accurate measure of the amount of air in your lungs can be determined.
- Between lung function tests salbutamol/albuterol [OPU to adapt locally] will be administered.
- Induced sputum will be collected at each clinic visit. Sputum induction is a procedure to help you cough up secretions from your lungs more easily. The principle is to create extra moisture in the airways of the lungs by inhaling a saline enriched aerosol, which will help loosen the sputum deep in your lungs. The sputum sample will be examined further. In case you are not able to produce an acceptable sputum sample at Visit 2 and at the Visit 2 retest you will continue in the study, but no more sputum induction will be performed in the study.

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- Blood samples for safety laboratory testing, and biomarker assessments will be drawn at each clinic visit (about 90 ml or 9 tablespoons).
- A urine sample for nicotine testing will be taken at each clinic visit.
- Your reminder diary will be reviewed at each visit.
- An ECG will be performed at visits 5, 6 and 7.
- A chest computer tomography (CT), a radiologic imaging method, enabling a detailed look into your body, will be performed at visits 2, 5, 6 and 7 between 1h and 4h after salbutamol/albuterol [OPU to adapt locally] administration for the lung function testing.
- The 6-minute walk test will be performed at visits 2, 6 and 7 after the lung function testing.

Visits 2 – 7 will last approximately 4 – 7 hours. Some visit procedures like induced sputum and/or chest CT can be rescheduled to another day (within 14 days of the original visit), e.g. if you have time constraints. In this case you will be administered with salbutamol/albuterol [OPU to adapt locally] prior to the assessment(s).

Telephone contacts

Additionally, you will have 7 telephone contacts between clinic visits 4, 5, 6 and 7 to follow up and collect information by telephone interviews. Your reminder diary helps you to remember your respiratory symptoms, any COPD exacerbations (COPD flare up with symptoms worsened suddenly), hospitalization or health care visits, and all medication you were taking.
Please remember to inform your study team prior to scheduled telephone interviews in case you have been hospitalized. Telephone calls might take about 30 minutes.

Study completion

Visit 7 or the discontinuation visit, in case you terminate the study early, will mark the end of the study and you have completed the study.

Early discontinuation

If you terminate the study during the observational period for any reason, you will be asked to come to the clinic for a discontinuation visit at the time of your next scheduled visit. You will undergo the procedures of this particular visit as outlined in the flowchart. If you do not agree to undergo all procedures of the next scheduled visit, you are asked to do at least the safety assessments.

Women who become pregnant will be discontinued from further study participation and will undergo the procedures for safety assessments like for example blood collection and physical examination.

Phone calls after early discontinuation

After you have discontinued the study early, the study team will contact you for further follow up, if you agree. You will be asked if you have experienced COPD exacerbations. If your discontinuation takes place between:

Discontinuation date between Visit 2 and 5, three telephone calls:

1. First call: 52 weeks after your Visit 2
2. Second call: 104 weeks after your Visit 2

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3. Third call: 156 weeks after Visit 2

Discontinuation date between Visit 5 and 6, two telephone calls:
1. First call: 104 weeks after your Visit 2
2. Second call: 156 weeks after your Visit 2

Discontinuation date between Visit 6 and 7, one telephone call:
1. Call: 156 weeks after Visit 2

YOUR RESPONSIBILITIES

- While participating in this study, you should not take part in another medication research study. You must tell your study doctor if you have been in another research study in the past 6 weeks or are currently in another research study.
- You must follow the study instructions provided by the study staff, come to all scheduled study visits and be reasonably available for the scheduled telephone visits.
- Prior to and during the lung function assessments you have to stay in in the building where the measurements are performed.
- You must tell the study doctor about all prescription and non-prescription drugs, herbal preparations and food supplements that you are taking or planning to take.
- Please refrain from strenuous activity for at least 12 hours prior to lung function testing, also avoid cold temperatures, environmental smoke, dust or areas with strong odors (e.g. perfumes).
- Please do not donate blood during the observational period of the study.
- You must fast, not have anything to eat or drink, except water, for 6 hours before all study visits.
- You might be asked to provide an additional sputum sample prior to Visit 2 that will be used for quality assurance of sputum processing. This sputum sample will be taken as described above.

POTENTIAL BENEFITS

This study is an observational study with no change in your usual medication treatment. There will be no direct benefit for you, except for the benefit which derives from the extensive examinations and periodic monitoring of your health or disease status.

RISKS AND/OR DISCOMFORTS

Your participation in this study requires standard medical procedures which are well known to patients with respiratory diseases. The examinations include procedures like physical examination, blood sampling, ECGs, lung function testing, D_{LCO} measurements, bodyplethysmography, chest CTs and sputum induction.

Computed tomography

A CT scan will be done at four visits. This is a painless test, a type of X-ray exam, which shows detailed lung structures. You will be asked to strip to the waist and lie on the narrow table that will slide through a hole in the center of the CT scanner. You have to stay still during the procedure

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and follow the instructions when to hold your breath. The actual CT scanning takes less than 30 seconds and the entire process is usually completed within 15 minutes.
The scientific unit of measurement for radiation dose is the millisievert (mSv). Chest CT scans involve exposure to radiation equivalent to 20 chest x-rays (approximately 4 millisievert). Although the amount of radiation exposure is higher than a typical x-ray, the risk of harmful effects from a single exam is small. Persons are exposed to radiation from natural sources in the environment all the time. These natural "background" doses vary from area to area. The natural background radiation is 2.4 mSv per year. The additional risk of developing a fatal cancer from a single 4 mSv exposure in a person 50 years old is approximately 1 in 5000 or 0.02%. If it were to occur, it could take many years or decades for you to develop cancer related to this study. The latent period for cancer is estimated to be 6 to 10 years for blood borne cancers (leukemia, lymphoma) and 10 to 25 years for solid organ cancers. Please keep in mind that the risk from all sources of radiation is cumulative over a lifetime.
The chest CT is a very sensitive diagnostic method and reveals lung nodules in approximately 20% of people. The chest CT scan may detect lung abnormalities much earlier than other diagnostic methods, which may be life-saving in subjects at risk of lung cancer (e.g. smokers). Such finding causes anxiety and triggers further diagnostic work-up to confirm or reject malignancy. While an early diagnosis of lung cancer is critical for successful treatment, most lung nodules accidentally found on the chest CT scan turn out to be benign.

ECG

You may experience skin irritation from the ECG electrode pads or pain when pads are removed.

Lung function measurement (spirometry and diffusing capacity of the lungs for carbon monoxide)

Risks and discomforts associated with lung function testing may include shortness of breath, dizziness, or headache during the breathing tests. Should this occur, you may receive treatment.

6-minute walk test

The 6-minute walk test measures the distance that you can quickly walk on a flat, hard surface in a period of 6 minutes. To prevent any risk to your health you will be constantly supervised by specially trained medical personnel and your health will be monitored. The test may be stopped if you are unable to continue safely in the opinion of the supervising personnel. After the test you will have enough time to recover and to leave the office/clinic in good health.

Sputum induction

Sputum induction is a painless and safe procedure. Rarely, it may cause transient wheeze or chest tightness. Let your study doctor know immediately if you feel any of these symptoms at any time during the induction procedure. These symptoms could be quickly relieved by inhaling an appropriate drug. The procedure is performed after inhalation of salbutamol/albuterol [OPU to adapt locally] that helps open up the air passages. Side-effects of salbutamol/albuterol [OPU to adapt locally] are rare and further details can be found below.

Laboratory tests

Blood draw may cause some discomfort or mild pain, as well as redness or bruising at the site of puncture. In rare cases the puncture site can also become infected or nerves may be damaged,

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inducing long lasting abnormal sensations (paresthesia), impaired sensation of touch and persistent pain.
A total blood volume of about 500mL will be withdrawn over a period of about 3 years. Approximately 90 mL will be drawn per time point (Visit 2 – 7). The estimated blood loss will not impact your health.

Bodyplethysmography

Some people may feel uncomfortable in the small plethysmography chamber called body box. Tell the study staff if you feel uncomfortable in any way during the test and keep in mind that you can open the door from the inside at any time.

Salbutamol/Albuterol [OPU to adapt locally]

Salbutamol/Albuterol [OPU to adapt locally] is a short-acting bronchodilator used to treat narrowed airways like in asthma or COPD. It is taken by the inhaled route for direct effect on bronchial smooth muscle. In general, salbutamol/albuterol [OPU to adapt locally] is well tolerated even at large doses. In this study, salbutamol/albuterol [OPU to adapt locally] is used only at clinic visit days in combination with some diagnostic tests like PFTs, imaging assessments or induced sputum. It is not administered for the treatment of a disease.
The most common side effects are shaking of fingers, anxiety, headache, muscle cramps, dry mouth, and palpitation (awareness of heart beat). Other symptoms may include increase in heart rate, irregular heartbeat, flushing, myocardial ischemia (reduced blood supply of the heart muscle) (rare), and disturbances of sleep and behavior. Rarely occurring, but of importance, are allergic reactions like unexpected narrowing of the airways (can be life threatening in rare cases), rapid swelling of the facial skin rarely with life threatening breathing difficulties, skin hives with itching and redness, decrease in blood pressure, and collapse. High doses or prolonged use may cause hypokalemia (low levels of potassium in your blood).

ALTERNATIVES

This study is for research purposes only. Your participation is voluntary. The alternative is not to participate in the study.

Please talk to the study doctor about your options before you decide whether you will take part in this study.

NEW INFORMATION ABOUT THE STUDY

During the study, you will be notified of changes to study procedures, which may affect your health or willingness to participate. You may be asked to sign a new consent form that shows that you have been informed of changes.

INFORMATION ON BIRTH CONTROL

You cannot participate in this study if you are pregnant or plan to become pregnant due to the planned radiologic procedures. If you should nevertheless become pregnant or you think you could be pregnant during the study, it is important for you to tell the study doctor or study staff prior to each clinic visit. In case of pregnancy, you will be removed from the study procedures and you will be followed up by phone calls.

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WITHDRAWAL FROM THE STUDY PARTICIPATION

Your participation in this study is voluntary. You may choose to leave this study completely at any time. Your decision will not result in any penalty or loss of benefits to which you are otherwise entitled. Leaving the study will not affect your future medical care.
All data and samples that had already been collected up to the time of withdrawal of your consent, including data and samples gathered at any of your final assessments, will still be used to ensure the correct completion and documentation of the trial and comply with applicable law.

Your study doctor might decide to stop your study participation early without your consent when, in the study doctor's judgment, it is in your best health interest to do so or under certain circumstances listed below:

- Your inability to participate as instructed.
- Study cancellation by the sponsor or [if applicable regulatory authority/EC].
- Or for other unforeseen reasons that make it necessary to stop your participation in the study.

If you are removed from the study, the study doctor will explain to you why you were removed.

CONFIDENTIALITY / PRIVACY AND DATA SHARING

Use of your personally identifiable information

The part of your personal information that directly identifies you such as your name, address, or birth date will remain at the study site and can be accessed by the study doctor and other people at the site who are assisting with the study or your care. This information may also be checked at the study site by the

- sponsor, or the sponsor's representatives (including monitors hired by the sponsor through a service provider),
- ethics review board/committee that reviewed the ethical aspects of this study, and/or
- [Please adapt or delete if not applicable] domestic or foreign regulatory agencies such as the U.S. Food and Drug Administration (FDA) and European Medicines Agency (EMA) that approve medicines.

These persons check that the study is carried out correctly at the study site. They are bound by a duty of confidentiality.

Use of your coded data

Your personally identifiable information and health information collected for the purpose of the study as well as the samples will be labelled with a unique code number. Coded data may also include data/information such as images (e.g. CTs/MRTs). The code number will be used in place of your name and other information that directly and easily identifies you, for example, address and birth date. Only the study site will have the link between your personal information and the coded data. This link will not be provided to the sponsor; only your coded data such as medical data, biomarker data, images and all other information collected in the study will be sent to the sponsor and/or contractors of the sponsor. The sponsor and/or contractors of the sponsor will take measures to protect the confidentiality and security of your coded data and your privacy in accordance with current law.

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The sponsor and other members of the Boehringer Ingelheim Group of Companies and those working with them such as their associates, collaborators, research partners, assignees, licensees and designees, and its/their affiliated companies and agents, and other individuals and organizations, may use your coded data for the following purposes:

- Keep it electronically and analyze it to understand the study and the study results;
- Share it with domestic or foreign regulatory agencies worldwide such as the U.S. Food and Drug Administration (FDA) and European Medicines Agency (EMA), that approve medicines;
- Share it with ethics review boards/committees worldwide, or steering committee that checks whether the study was run properly.
- Analyse it to improve the quality of this study and other clinical trials

The coded data may be transferred within your country or to other countries for analysis. Where the data protection rules in other countries are not as strict as the rules in your country, the sponsor will adopt appropriate measures to provide an adequate level of protection according to EU law.

Use of anonymized data for additional research

Anonymized data refers to data from which the subject cannot be identified by the recipient of the information. Anonymizing data is one of the strongest safeguards for the protection of subjects' identity.

The sponsor may give scientists and medical researchers in other companies, research organizations, or academic institutions access to anonymized data for further research and education beyond the disease investigated in this study. This may include research looking into improving patient care or quality and efficiency in conducting clinical studies in general. Details on the anonymization and data sharing process are set forth in the Boehringer Ingelheim "Policy on Transparency and Publication of Clinical Study Data" available at: http://trials.boehringer-ingelheim.com.

Information and correction rights

You have the right to review which personal data the trial site and sponsor store about you. You can also request that incorrect personal data is corrected or that processing is restricted. You can request a copy of the contractual safeguards implementing adequate protection of personal data if your data is shared outside the EU/EEA.

In order to exercise your rights please contact the study site [if applicable: and its data protection officer (ADD EMAIL)] who will align with the sponsor. You can also ask to receive the personal information you have provided for the study in a standardized electronic format or to have them transmitted to another person of your choice. You can also contact your local data protection authority in case of questions or concerns about the handling of your personal data. In some cases, your rights can be limited under applicable laws, especially where they conflict with the conduct of the study and mandatory archiving requirements. In this case you will be informed accordingly.

If you have signed an Information and Consent Form for the optional DNA banking sample, all the information provided in this form under section "Confidentiality / Privacy and Data Sharing" your rights under data protection laws and the information on how to exercise them applies as well to the optional DNA banking consent form.

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Clinical study websites and publication

A description of this clinical study will be available on http://www.clinicaltrials.gov, as required by U.S. Law. This web site will not include information that can identify you. At most, the web site will include a summary of the results. You can search this web site at any time.

The results of the study will be published on Boehringer Ingelheim' s study web site (http://trials.boehringer-ingelheim.com) and may also appear in other clinical study/study registries in countries in which the study is conducted. The results will not include information that can identify you.

The results of the study may also be published in a professional journal or presented at scientific meetings. Your identity will not be disclosed in those presentations.

USE OF SAMPLES IN THIS STUDY

Blood and sputum will be collected for pre-specified as well as for unspecified analyses. Urine samples will also be collected. All samples collected during the study as described under the section "Study Procedures" will be coded and sent to the central laboratory (except pregnancy test). A part of the analyses will be done at the central laboratory. In addition, samples will be further distributed to Boehringer Ingelheim and contractors of Boehringer Ingelheim for analyses.

Urine samples

Urine samples will be collected from all patients for the purpose of nicotine testing and (if applicable) additionally for pregnancy testing in women. Pregnancy testing will be done at the site and the sample will be discarded right after testing. Urine samples for nicotine testing will be shipped to and analyzed by the central laboratory and neither kept nor used for any future analyses.

Pre-specified biomarker assessment

The pre-specified analyses done in blood samples comprise safety laboratory testing, testing of A1ATD and biomarker assessment. Pre-specified biomarkers will also be analysed in sputum samples. All blood and sputum samples will be collected to gain a better understanding of COPD and the influence of A1ATD. Those biomarkers include but are not limited to markers of inflammation and tissue destruction, which have been reported and/or hypothesized to be indicative of physiological and pathophysiological changes in the lungs. In addition investigations aiming at identification of new biomarkers will be done.

The DNA sample used to determine A1ATD and left over of other biomarker samples for prespecified analyses will be destroyed once this analysis has been completed.

Left over sputum samples that were not used for the pre-specified biomarker analyses will be transferred to the biobank (see section "Unspecified biomarker assessment").

Unspecified biomarker assessment (Biobanking)

Since knowledge in the biomarker field is steadily increasing, we also ask you to consent to the collection of samples for unspecified biomarker analyses. These samples including left over sputum samples described above will be stored up to 15 years after the final study report has been written to enable these additional explorative investigations

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Approximately 50 ml blood will be collected per visit during the observational period. All analyses aim at increasing our understanding of COPD and other respiratory diseases. This may help to develop new therapies for COPD in the future. Samples will be sent to Boehringer Ingelheim or a storage CRO for long term storage.

The future research on your samples will not affect your present medical care. Reports from any future research with your samples and data will not be given to you or your doctor. Summaries of the research results may be published in scientific journals, on the internet, in data repositories or presented at meetings for other researchers, so that other doctors and researchers can find out about the results. In any case, your identity will not be disclosed in any publications or presentations. Subjects who donate her/his samples to BI do not retain any property rights to the materials such as samples and their derivatives and the related data.

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COMPENSATION / COSTS

[Amend in accordance with local legal requirements or insurance.]
This study is funded by the sponsor. The sponsor has signed a contract with <insert CRO, applicable> to conduct this study. The sponsor <CRO on behalf of CRO> will pay the study doctor's and/or institution's for his/her expenses, time and effort to conduct this study. The study doctor and the institution/Hospital have no other financials ties to Boehringer Ingelheim.

There will be no additional costs to you for your participation in this study. All study procedures including lab work, tests, and doctor visits are provided to you free of charge by the sponsor, Boehringer Ingelheim, and will not be billed to you or your insurance carrier as long as you are participating in the study. You will receive <enter amount and/or a description of a payment schedule> to cover out-of-pocket expenses such as meals and parking for visits that are required as part of the study.

The sponsor will be owner of the study results. If commercial products or other valuable discoveries result from research using your samples and/or data, these products and discoveries may be owned, patented, licensed, or otherwise developed for commercial sale by sponsor, other researchers, or companies. If this should occur, you will not receive any financial benefits or compensation or other proprietary interest from any commercial products or discoveries that may result from such research.

INJURY

You will receive necessary medical treatment in the event that an injury results because of your participation in this study. Financial compensation for lost wages, disability or discomfort due to an injury is not generally available. You do not give up any legal rights by signing this form. You do not release the sponsor, institution, study doctor or their agents from any liability for negligence by signing this form.

EMERGENCY CONTACT / ETHICS CONTACT

If you have questions concerning the conduct of the study, or for any other reason you may contact Dr. _____ at _____ or the Study Coordinator _____ at _____.

In case of an emergency, please go to the nearest hospital emergency department and inform your study doctor as soon as possible.

If you have any questions about your rights as a study subject, please contact your family doctor, lawyer, or write to the committee that reviewed the ethical aspects of this study at: <insert ethics committee name and contact here>

A B CD

DECLARATION OF INFORMED CONSENT

STUDY SUBJECT No.: _____

My signature on this consent form means that:

- I understand that I am being asked to participate in a research study entitled: Observational study in healthy subjects and patients with COPD to assess the relationship between clinical, imaging and biomarker measurements, and progression of emphysema over three years.
- I have had this study explained to me by _____.
- I have read each page of this document.
- I have had all of my questions answered fully and to my satisfaction.
- I was given sufficient time to think in peace and quiet and decide whether to participate.
- I have been told that my participation is voluntary and I can withdraw at any time without giving any reasons.
- I agree to the collection, storage, processing, transfer and use of my personal data and biological samples (blood, urine and sputum) as explained in the above information.
- I agree that blood will be collected for biobanking and will be used for future unspecified analyses.
- I agree that left over of my sputum samples can be stored for future unspecified analyses.
- I agree that further, today unspecified analysis of my biological samples can be done during and after the study.
- I hereby expressly declare and agree that I transfer all rights of ownership of the collected samples and sample-related data to Boehringer Ingelheim Pharma (GmbH & Co. KG) so that the same may use them as described in this Informed Consent Form.
- I voluntarily consent to participate in this study.
- I will be given a signed copy of this consent document for my records

It is important that your personal doctor is aware that you are in a research study because you are undergoing examinations that could affect your health. With your permission, we will notify him/her that you are taking part in this study.

I consent to my personal doctor being notified that I am taking part in this study.

❑ YES, I agree. ❑ NO, I don't agree.

I agree that in case I discontinue the study early, the study team can contact me as described above, for further follow up by telephone.

❑ YES, I agree. ❑ NO, I don't agree to be contacted after early discontinuation.

A B CD

I consent that in case I die during the time of this study my study doctor is allowed to contact my family members to ask after the circumstances and that he can review my relevant medical records.

❑ YES ❑ NO

Name of Study Participant (*please print*)	**Consent Signature of Study Participant**	**Date** (dd mmm yyyy)
Name of Person Obtaining Consent (*please print*)	**Signature of Person Obtaining Consent**	**Date** (dd mmm yyyy)

STATEMENT OF INVESTIGATOR / STUDY DOCTOR:

I certify that I have explained to the above individual(s) the nature and purpose of the study and the possible benefit and risks associated with participation. I have answered any questions that have been raised and the potential study participant has received a copy of this signed consent document.

I acknowledge my responsibility for the care and well-being of the above study participant, to respect the rights and wishes of the participant, and to conduct the study according to applicable Good Clinical Practice guidelines and regulations.

Investigator Name (*please print*)	**Investigator Signature**	**Date** (dd mmm yyyy)