LOS ANGELES BIOMEDICAL RESEARCH INSTITUTE
AT HARBOR-UCLA MEDICAL CENTER

Human Subjects Research Consent Form

This form describes a research study. Please discuss the content of this form with the study doctor or a member of his study team before you agree to take part.

Subject's Name:_____ Date:_____

An Investigator Initiated, Randomized, Double Blind, Placebo Controlled, Two Period, Crossover Study to Assess the Effect of BEVESPI AEROSPHERE™ Therapy (Glycopyrrolate/Formeterol) on Exercise Tolerance and Dynamic Hyperinflation in Patients with Chronic Obstructive Pulmonary Disease

Who is conducting this study?

Drs. William Stringer, Richard Casaburi, Harry Rossiter and Janos Porszasz are researchers from the Rehabilitation Clinical Trials Center at the Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center (LA BioMed) and they are conducting this research study.

Why am I invited to take part in this research study?

We are asking you to take part in this study because you have chronic obstructive pulmonary disease (COPD, also known as emphysema or chronic bronchitis) with shortness of breath that limits your ability to exercise.

What should I know about a research study?

- Someone will explain this research study to you.
- Research studies only include people who choose to take part.
- Whether or not you take part is up to you.
- You can choose not to take part in the research study.
- You can agree to take part now and later change your mind.
- Whatever you decide will not be held against you.
- Feel free to ask all the questions you want before you decide.

Please take your time to make your decision about taking part. You may discuss your decision with your friends and family. You can also discuss it with your health care team. If you have questions, you can ask the study doctor to explain the study more.

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

Why is this study being done?

The purpose of this research study is to try to find a way to improve the breathing of COPD patients while they exercise, thereby increasing the time they are able to exercise. People who have COPD have difficulty with breathing, especially exhaling. This breathlessness will often reduce their ability to exercise and they will stop exercising early. A major component causing the breathlessness is "dynamic hyperinflation" which means that the lungs get bigger and bigger during exercise since the patient has trouble exhaling. Treatment with inhaled medications (bronchodilators) can improve breathing for COPD patients. This study will see if a twice-daily bronchodilator (Bevespi Aerosphere™) will increase the ability to exercise and reduce hyperinflation in patients with COPD.

This is a "crossover" study, which means that you will receive both the active drug (Bevespi Aerosphere™ Glycopyrrolate/Formeterol) and placebo (no active drug) during the course of the study. Also, you will be required to stop taking other long-acting bronchodilator medications throughout this study. Because you will not be taking a long-acting bronchodilator at all times during the study, it is possible that you may experience a worsening of your COPD symptoms, such as shortness of breath, coughing or wheezing. You will receive an albuterol and/or Combivent inhaler (albuterol and ipratropium), which are short-acting bronchodilator medications, that you can use if you find that your breathing becomes difficult. Also, if you currently take a long-acting bronchodilator in combination with an inhaled corticosteroid, the corticosteroid part of this medication will be given to you in a non-combination inhaler.

Are there potential conflicts of interest?

The study doctor and his staff will be reimbursed by AstraZeneca Pharmaceuticals for the work that they do as part of this study. Dr. Casaburi, a Co-investigator, has received consulting and speaking fees from Astra Zeneca in the past twelve months. Dr. Casaburi was involved in designing the study. Please feel free to ask any further questions you may have about this matter.

The person inviting you to take part in this research study may also be your treating doctor. In such cases, the doctor has an interest in both your care and promoting the successful conduct of this research. Sometimes these two interests may cause conflict. You can choose not to take part in the study and still receive treatment from your doctor. If you wish, you may also request to speak to another doctor who is not a member of the study team about your options.

How many people will take part in the study?

About 50 people will take part in this study. This research study is only being done at this one site.

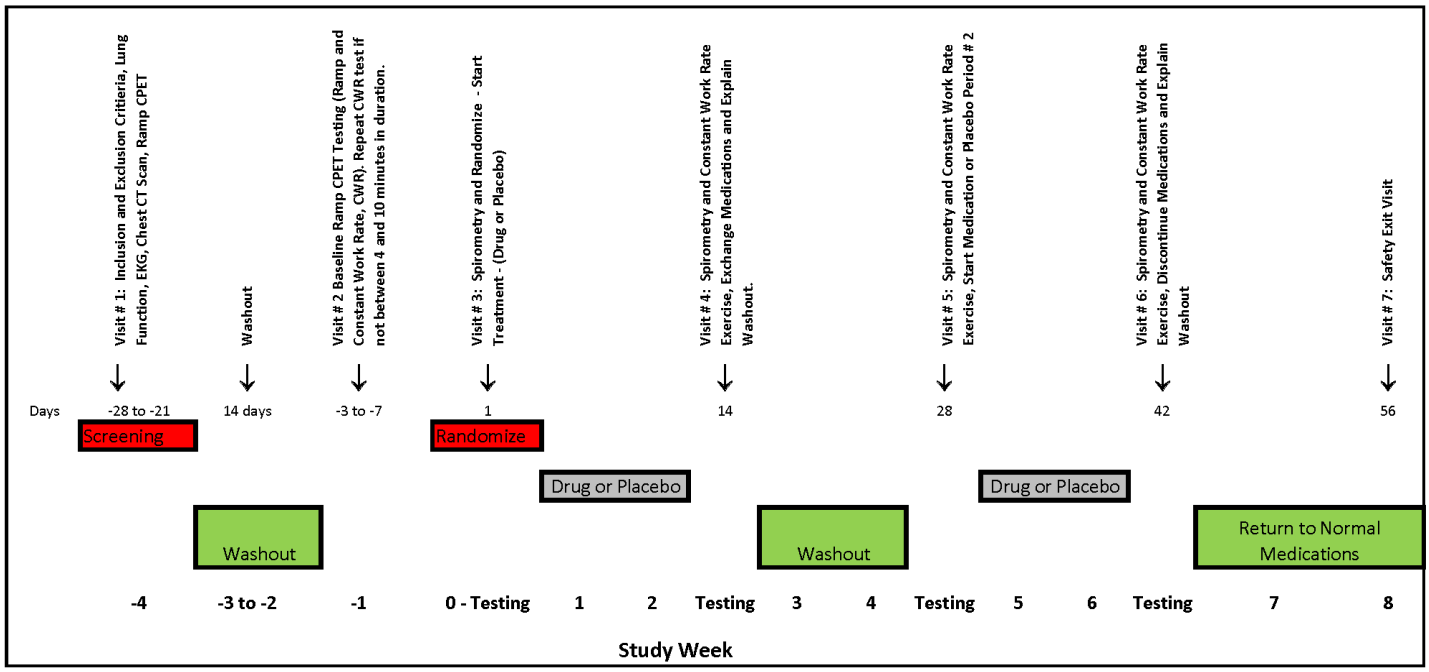
What will happen if I take part in this research study?

Over the next 12 weeks, you will visit the research center 7 times, during which we will ask you questions about your health and medical history, and perform lung function and exercise tests.

We are studying a medication (Bevespi Aerosphere™) that is inhaled twice a day. This drug consists of two different bronchodilators that are designed to help your breathing. We are going to compare it to no active medication (placebo). While you are on either Bevespi or placebo, you can always use your "rescue" inhaler (either albuterol, or albuterol and ipratropium).

There are two (2) treatment periods during this study, each lasting 2 weeks. This is a "crossover" study, which means that you receive both Bevespi Aerosphere™ and placebo during this study. Initially, we will "randomize" you to get either Bevespi Aerosphere™ first or the placebo first, after which you will "crossover", or take the one you didn't get the first time. Between the two treatment periods you will not receive either medicine. This period will last 2 weeks and is called a "Washout Period." Randomization means that you are put into a group by chance (like tossing a coin). Neither you nor the study doctors or staff will know when you are receiving Bevespi Aerosphere™ or when you are receiving placebo. Someone not involved in this study (the pharmacist) will keep record of who is receiving what during this study. However should a medical emergency occur where knowing what medication you are on is helpful for your medical care, this information could be made available to your treating doctor.

The diagram below shows the timeline of the study. In this diagram, drug A or B refers to Bevespi Aerosphere™ or placebo.



During this study you will return to see the study doctor every 2 weeks for up to 12 weeks (7 visits total). Each study visit will last between 1 and 4 hours depending on the tests and procedures that you will undergo. During Visits 2, 4, 5 and 6 you will exercise, so it is important that you eat a light meal roughly 3 hours prior to these

visits. After this meal we recommend that you do not eat again until after the testing is over. You may continue to drink water as you feel necessary throughout the day.

Occasionally it becomes necessary to repeat measurements (tests) made in the study (for example, if the measurement was not clear on the first try). In such cases, we may ask you to complete an extra visit within about 2 days after the originally scheduled visit.

Procedures and Schedule of Visits

Below you will see a description of the procedures to be performed at each visit.

Visit 1 (-4 Weeks - 4 weeks before the start of the study which is at Visit 3 or Day 0/Baseline)
This visit last about 1 hour.

- **Consent.** We will thoroughly explain the study to you and go over the information provided in this consent form. We will answer any questions you have. If you agree to take part in this study, we will ask that you sign this consent form.
- **Medical history and current medications.** We will ask you about your past and present illnesses, treatments and surgeries, your history of smoking, alcohol and drug use.
- **Physical exam.** You will have a physical examination, which will include measuring your height and weight and checking your vital signs (blood pressure and heart rate) and amount of oxygen in your blood (device is placed on the tip of one of your fingers to do this).
- **ECG.** You will have an electrocardiogram (ECG) which is a test that measures the electrical activity of your heart. For the ECG, we will place a number of adhesive patches on the skin of your chest, abdomen and sides. We will connect wires from the ECG machine to the patches.
- **Questionnaires.** You will complete two questionnaires related to how your breathing issues affect your daily life. It should take about 15-20 minutes to complete both questionnaires.
- **Urine pregnancy test.** If you are capable of becoming pregnant, you will provide a urine sample for a pregnancy test at screening. You will be asked about changes in your pregnancy status as the study progresses, and will perform another urine pregnancy test if needed.
- **6 minute walk test.** You will walk back and forth in a hallway as far as possible in 6 minutes. We will measure the distance you were able to walk in these 6 minutes.
- **Lung function (breathing) tests.** The lung function tests measure how much air is in the lungs and how well the air moves in and out of the lungs when you breathe. You will blow hard into the mouthpiece of the measuring device several times. We will explain the procedures in detail before the tests are done.
- **Chest CT.** High Resolution Chest CT Scans: At the visit, you will have three chest CT scans. Before the CT scan, we will ask you about any recent bronchodilator (opens the airways in the lungs) medication that you may have taken. For the CT scan, you will lie on a table and the table will move through the middle of an x-ray machine that looks like a large round donut. You will need to lie quietly and take a deep breath in and hold it for the scan. You will have the second scan done after another deep breath. Then, at the end of a normal breath, you will hold your breath to have the third scan. The total amount of time needed to do the 3 CT scans is about 15 minutes.
- **Rescue medication.** Because you will be required to stop taking certain breathing medications (long acting bronchodilators) used to control your COPD symptoms, you will receive an albuterol inhaler, or in some cases, a Combivent inhaler (albuterol and ipratropium). These are short-acting bronchodilator medications that you can use if you find that your breathing becomes difficult while you are taking part in this study. Also, if you currently take a combination inhaled corticosteroid plus bronchodilator, the

active corticosteroid part of this medication will be given to you in a non-combination inhaler. You will return to using your normal breathing medications 6 weeks after randomization.

First Washout Period – 2 Weeks
If the results of the above tests and procedures allow you to be in the study, and you are willing to take part, you will have to stop taking any medications (long acting bronchodilators) that are not allowed in the study, and instead you will use short acting medications (albuterol or albuterol and ipratropium) if you find that your breathing becomes difficult. Again, because you will not be taking a long-acting bronchodilator at all times during the study, it is possible that you may experience a worsening of your COPD symptoms, such as shortness of breath, coughing or wheezing.

Visit 2 (about 5-7 days before the study starts on visit #3)
This visit will last about 4 hours.

- **Review of symptoms.** We will ask you about how you have been feeling since your last visit.
- **Vital signs.** We will measure your blood pressure and heart rate.
- **Breathing (lung function) tests.** You will perform the same breathing tests. We will again explain the procedures for these tests in detail prior to them being done.
- **Exercise tests.** We will fit you for a mouthpiece and nose clip, to monitor your breathing during exercise. We will place sticky patches on your chest and attach them to an ECG machine (to monitor your heart). We also will place a device on one of your fingers to measure your blood oxygen levels and measure your blood pressure from a cuff placed on your upper arm several times during the testing and recovery. During exercise you will begin cycling against no resistance, and we will slowly increase the work (the pedaling will become more difficult) until you can no longer pedal. At the point that you can no longer continue, we will remove the cycling resistance (pedaling will become easy) and monitor your recovery. The entire exercise test will take about 20-30 minutes. You will rest for about 2 hours and then complete another exercise cycle test where you will ride the bicycle at a constant work rate (pedaling resistance doesn't change) for as long as you can. As done in the first exercise test, we will monitor your breathing, heart rate, and the amount of oxygen in your blood.

If the study doctor determines that the exercise tests need to be repeated, we will ask you to return 2 or 3 days later to repeat the tests.

Washout Period Continues - ***For the 5-7 days following Visit 2, you will use only the rescue medicines to treat your symptoms.***

First Treatment Period (Visits 3 and 4)

If the exams, tests and procedures show that you can be in the study, and you choose to take part, then you will begin the first Treatment Period of the study.

Visit 3 (Day 0/Baseline - Start of First Treatment Period)
This visit will last 2 hours since we want to have you take your first dose of study medication in the laboratory. At this visit we will "randomize" you to receive either Bevespi Aerosphere™ or placebo.

- **Review of symptoms/adverse events.** We will ask you how you have been feeling since your last visit.
- **Vital signs**. We will measure your blood pressure, heart rate, amount of oxygen in your blood and your weight.

- **Questionnaires.** You will complete the same 2 questionnaires related to how your breathing issues affect your daily life.
- **Breathing Tests –** We will check your lung function before and after the study medication.
- **Study drug.** You will begin to take (inhale) either Bevespi Aerosphere™ or placebo every day for the next 14 days (2 weeks, 2 puffs, twice a day). We will give you a supply (inhaler) of the study drug (Bevespi Aerosphere™ or placebo) to last until your next visit and you will need to bring the inhaler with you to your next study visit.

Visit 4 (Week 2 – End of First Treatment Period)
You will return to see the study doctor 2 weeks (14 days) after Visit 3. You will need to bring the study drug with you and take your last dose at this visit. This visit will last about 2 hours.

- **Vital signs**. We will measure your blood pressure, heart rate, amount of oxygen in your blood and your weight.
- **Review of symptoms/adverse events.** We will ask you how you have been feeling since your last visit.
- **Questionnaires.** You will complete the same 2 questionnaires related to how your breathing issues affect your daily life.
- **Breathing tests.** You will undergo breathing tests as before.
- **Exercise test.** You will complete a constant work rate exercise cycle test (CWR) at the same work rate as before (Visit 2) with all the same measurements being made.
- **Study drug.** You will take your last dose of the study drug (either Bevespi Aerosphere™ or placebo) at this visit in the presence of the study doctor or member of the study team.

Second Washout Period - ***For the 2 weeks following Visit 4, you will use only the rescue medicines to treat your symptoms.***

Visit 5 (Week 4 – End of Washout Period, Start of Second Treatment Period)
You will return to see the study doctor 2 weeks (14 days) after Visit 4. This visit will last about 2 hours.

- **Vital signs.** We will measure your blood pressure, heart rate, amount of oxygen in your blood and your weight.
- **Review of symptoms/adverse events**. We will ask you how you have been feeling since your last visit.
- **Questionnaires.** You will complete the same 2 questionnaires related to how your breathing issues affect your daily life.
- **Breathing tests.** You will undergo breathing tests as before.
- **Exercise test.** You will complete a constant work rate exercise cycle test (CWR) at the same work rate as before (Visits 2 and 4) with all the same measurements being made .
- **Study drug.** You will begin to take (inhale) either Bevespi Aerosphere™ or placebo every day for the next 14 days (2 weeks, 2 puffs, twice a day). You will take whichever study drug (Bevespi Aerosphere™ or placebo) you did not receive during the first treatment period. We will give you a supply (inhaler) of the study drug (Bevespi Aerosphere™ or placebo) to last until your next visit and you will need to bring it with you to your next study visit

Visit 6 (Week 6 – End of Second Treatment Period)
You will return to see the study doctor 2 weeks (14 days) after Visit 5. You will need to bring the study drug with you and take your last dose at this visit. This visit will last about 2 hours.

- **Vital signs.** We will measure your blood pressure, heart rate, amount of oxygen in your blood and your weight.
- **Review of symptoms/adverse events.** We will ask you how you have been feeling since your last visit.
- **Questionnaires.** You will complete the same 2 questionnaires related to how your breathing issues affect your daily life.
- **Breathing tests.** You will undergo breathing tests as before.
- **Exercise test.** You will complete a constant work rate exercise cycle test (CWR) at the same work rate as before (Visits 2, 4 and 5) with all the same measurements being made .
- **Study drug.** You will take your last dose of the study drug (either Bevespi Aerosphere™ or placebo) at this visit in the presence of the study doctor or member of the study team. You will return your supply of study drug at this visit.
- **Resume Medications.** You will resume (start taking again) the medicines you were taking that you had to stop taking to be in this study.

Visit 7 (Week 8 – End of Study Visit)
You will return to see the study doctor 2 weeks (14 days) after Visit 6. This is you last study visit and it should last no more than 1 hour. You will have been back on your usual medications for 2 weeks, and this is a safety visit regarding the study.

- **Vital signs.** We will measure your blood pressure, heart rate, amount of oxygen in your blood and your weight.
- **Review of symptoms/adverse events.** We will ask you how you have been feeling since your last visit.

What are my responsibilities if I take part in this research?

If you take part in this research, you are responsible for following the instructions given by the study doctor and his staff. You are also responsible for taking the study medication as instructed, for returning to the site for each study visit, and undergoing all study required testing and procedures. It is your responsibility to tell the study doctor or his staff about any injury or change in your health or medication. It is your responsibility to return for a final visit to return all study medications and complete a safety visit, even if you decide not to continue with the study. .

How long will I be in the study?

You will take part in this study for about 12 weeks (about 3 months).

Can I stop being in the study?

Yes. You can decide to stop at any time. You can withdraw your consent at any time. Please tell the study doctor if you are thinking about stopping or trying to decide to stop. S/he will tell you how to stop safely, return for a final visit, and return any unused medication.

It is important to tell the study doctor if you are thinking about stopping so any risks from the Bevespi Aerosphere™, albuterol and rescue medicines can be evaluated by your study doctor. Another reason to tell your study doctor that you are thinking about stopping is to discuss what follow-up care and testing could be most helpful for you.

The study doctor may decide that it is not safe for you to continue in the study. This may be because you have a medical condition or situation that requires immediate withdrawal from the study.

The study doctor may stop you from further participation in this study at any time without your consent if he believes it is in your best interest, if you do not follow the study rules or instructions given to you, or if the study is stopped by the sponsor.

If you stop being in the study, data that has already been collected (information collected from and about you while you are in the study) may not be removed from the study database.

What treatments and/or procedures are experimental?

We are carrying out all of the procedures and/or treatments described above for research or experimental purposes. The drugs used in this study (Bevespi Aerosphere™, albuterol, Combivent (albuterol and ipratropium), or inhaled corticosteroids) are all approved by the US Food and Drug Administration (FDA) for treating COPD.

What side effects or risks can I expect from being in the study?

You may have side effects while on the study. We will you closely while taking part in the study for any side effects. However, doctors don't know all the side effects that may happen. Side effects may be anything from mild to very serious. Your study doctor or his/her staff may give you medicines to help lessen side effects. Many side effects go away soon after you stop taking the Bevespi Aerosphere™ and rescue medicines. In rare cases, side effects can be serious, long lasting, or may never go away.

You should talk to your study doctor about any side effects that you have while taking part in the study even if you think they may not be caused by the medicines.

Washout Period Risks
Because you will not be taking a long-acting bronchodilator during two washout periods (2 weeks each, you may experience a worsening of your COPD symptoms, such as shortness of breath, coughing, wheezing, or a reduction in your exercise tolerance. You will receive short acting breathing medications, also known as rescue medicines (described above) that you can use if you find that your breathing changes or becomes difficult. There is a risk of needing to take additional medication for a COPD exacerbation (for example antibiotics or prednisone), needing to go visit a doctor, needing to go to an emergency room, or a very small risk of being hospitalized.

We will provide you with a card that describes the study you are in, and the number to contact if any of your treating doctor(s) needs more information on the study. We have also included the phone numbers of your

study coordinator. We would like you to give us a call if you notice any increase in difficulty breathing or exercising while in the washout periods. The types of symptoms to look for will also be listed on the card.

Placebo (No Treatment) Risks
When you are receiving placebo the risks are the same as those listed above for the Washout Period. It is important that you understand that there will be a period of about 2 weeks during this study when you will not be receiving any long-acting bronchodilator (Bevespi Aerosphere™). This is because you will be receiving a similar inhaler to the Bevespi Aeroshere, but it will contain placebo or inactive components. You may experience a worsening of your COPD symptoms, such as shortness of breath, coughing, wheezing, or a reduction in your exercise tolerance. You will receive rescue medicines (described above) that you can use if you find that your breathing becomes difficult. There is a risk of needing to take additional medication for a COPD exacerbation (for example antibiotics or prednisone), needing to go visit a doctor, needing to go to an emergency room, or a very small risk of being hospitalized during the placebo period.

Rescue Medications

Albuterol: You will take 4 puffs of albuterol at Visit 1 during the lung function tests. You will also be given albuterol to take home with you in case you need it during the study. Side effects caused by normally used inhaled doses of albuterol are mild and they usually disappear with continued treatment. Reported side effects include:

- Very common (greater than 10%): pharyngitis (sore throat)
- Common (3% -7%): headache, rapid heart rate, muscle and joint pain, dizziness, stuffy and runny nose, and unpleasant awareness of palpitations (strong heart beat)
- Uncommon (less than 3%): chest pain, infection, diarrhea, inflammation of the tongue, accidental injury, anxiety, shortness of breath, ear disorder, ear pain and urinary tract infection.

Combivent (albuterol and ipratropium): If you currently take a long-acting bronchodilator medicine, you must stop taking it before you can begin this study. We may give you a replacement short-acting medication (Combivent) to use during the study. This medication contains albuterol and ipratropium bromide. Side effects may include:

- Common (greater than 2%): cough, shortness of breath, headache, bronchitis, sore throat, respiratory infection
- Uncommon (less than 2%): high blood pressure, dizziness, tremor (shaking), muscle spasms or muscle pain, diarrhea, nausea, dry mouth, constipation, vomiting, weakness, flu-like illness, chest discomfort, eye pain, low blood potassium, palpitations (strong heartbeat), fast heartbeat, skin itching or rash, pain in nose or throat, wheezing

Inhaled corticosteroid: If you currently take an inhaled corticosteroid in a medicine combined with a long-acting bronchodilator, you must stop taking it before you can begin the study. We will provide you with the same active corticosteroid part of this medication in a non-combination inhaler to use during this study. Reported side effects include:

- Common (greater than 3%): upper respiratory infections, throat infection, upper respiratory inflammation, sinus infection, hoarseness, mouth or throat infection, cough, bronchitis (inflamed airways in the lungs), headache

- Uncommon (less than 3%) runny nose or post-nasal drip, nasal sinus disorders, laryngitis (hoarseness), diarrhea, viral (caused by virus) gastrointestinal infection, dyspeptic symptoms (painful digestion), gastrointestinal discomfort and pain, dry mouth, joint pain, muscle pain, muscle stiffness/tightness/rigidity, dizziness, migraines, fever, viral infections, pain, chest symptoms, viral skin infections, muscle injuries, soft tissue injuries, urinary infections

Bevespi Aerosphere Therapy™: The safety of Bevespi Aerosphere Therapy™ has been tested in controlled clinical trials (research studies).

The most common side effects (in more than 3 in 100 (3%) patients) in patients with COPD are:
- cough (4%)
- urinary tract infection

Other side effects that occurred in more than 1%, but less than 2% of patients are:
- arthralgia (joint pain)
- chest pain
- tooth abscess
- muscle spasms
- headache
- oropharyngeal (mouth/throat) pain
- vomiting
- pain in extremity (legs or arms)
- dizziness
- anxiety
- dry mouth
- fall
- influenza (flu)
- fatigue
- acute sinusitis (symptoms are pain , tenderness, swelling and pressure around eyes, cheeks, nose and forehead)
- contusion (bruise)

There are risks associated with the procedures used in this study.

Electrocardiogram (ECG): There may be some irritation when removing the sticky patches from your skin at the end of the recording.

Lung function (breathing) test: The lung function tests may make you short of breath or feel tired.

Chest CT Scan: The CT scan will expose you to radiation (x-rays). The maximum amount of radiation exposure during the chest CT scan is about 13 mSv (mSv stands for milliSievert, which is a measure of the dose of low levels of radiation.). The average amount of background doses of radiation that the general population is exposed to in the United States is 3 mSv per year. Thus, the maximum amount of radiation you will receive equals about 4.5 years of normal background radiation. The more radiation received over the course of a life,

the greater risk of having cancerous tumors or of inducing changes in genes. The changes in genes possibly could cause abnormalities or disease in your future offspring. The radiation in this study is not expected to greatly increase these risks, but the exact increase in such risks is not known.

The chest CT scan can provide important clinical information, such as the presence of lung nodules (growths or tumors), which may require additional medical testing. We will share the results of your chest CT scan with you and your primary physician.

Questionnaires: Reading and filling out questionnaires may cause some psychological discomfort or anxiety.

Exercise tests: You will perform high-intensity exercise (pedaling at times will be hard) that may lead to physical discomfort (for example, fatigue or shortness of breath). The risks associated with taking part in this testing may include muscle cramps, muscle strain and/or joint injury, light-headedness, and fatigue (feeling tired). You may feel delayed muscle soreness for 24-48 hours after the exercise testing. There is a rare chance (about 1 in 10,000) of experiencing a heart attack or irregular heartbeat.

To manage the risks, a physician will be present during your exercise test. If at any time during the test you want to stop, you can signal or tell us and we will stop the test. You will feel very tired at the end of the test, but should recover within a few minutes. We recommend that when you leave the lab that you do no strenuous exercise for the rest of the day.

For women. Women who are pregnant cannot take part in this study. If you are of childbearing potential you must confirm, to the best of your knowledge, that you are not now pregnant, and that you do not intend to become pregnant during the study. If you are of childbearing potential we will collect a urine sample from you and use it for a pregnancy test to confirm that you are not pregnant. This pregnancy test will be performed before any CAT scan (x-ray) studies. You will not be allowed to continue in the study if you are pregnant. We will ask you during the study if there is any change in your status, and administer a urine pregnancy test if there is any question.

Unknown and unforeseeable risks: In addition to the risks listed above, there may be some unknown risks related to the study procedures.

For more information about risks and side effects, ask your study doctor.

Are there benefits to taking part in the study?

You will not receive any direct benefit from being in this study. However, the information we get from this study may be useful scientifically and may, therefore, be helpful to other COPD patients in the future. On your request, we will make the results of the lung function and exercise tests as well as CT scans available to you and your primary physician.

What other choices do I have if I do not take part in this study?

This is a research study and is not a treatment for your condition. You have the choice of not taking part in this study.

Talk to your doctor about your choices before you decide if you will take part in this study.

Will my personal and medical information be kept private?

We will do our best to make sure that the personal information in your medical record is kept private. However, we cannot guarantee total privacy. We may have to give out your personal information if required by law. If information from this study is published or presented at scientific meetings, we will not use your name and other personal information.

Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- Government agencies, like the Food and Drug Administration (FDA), involved in keeping research safe for people
- The Institutional Review Board at the Los Angeles Biomedical Research Institute or its staff
- The agency providing the funding for this research (AstraZeneca Pharmaceuticals LP,).

The ways your study doctor will use your study-related health information and the people who may receive it are identified in a separate form titled "Authorization For Release of Protected Health Information (PHI)".

What are the costs of taking part in this study?

You do not have to pay for study drugs, study visits, supplemental (rescue) medications or tests that are required for this study.

We will conduct all test and procedures required for this study at no cost to you.

For your time and inconvenience related to your taking part in this study, we will compensate (pay) you a total of $1,250 if you complete this study. If you do not complete the study, for any reason, you will be paid for the study visits you do complete according to the following schedule: $300 for visit 1; $200 for visit 2; $150 for visits 3, 4, 5, 6 and 7. If you are asked to repeat a visit, you will also be paid at the same rate for the visit you repeat.

Payment received as compensation for taking part in research is considered taxable income for a research subject. If you receive more than $600 in any one calendar year, LA BioMed is required to report this information to the Internal Revenue Service (IRS). If you receive research subject payments exceeding $600 during any calendar year LA BioMed will issue you a 1099 (Miscellaneous Income) form and forward a copy to the IRS.

What happens if I am injured because I took part in this study?

It is important that you tell your study doctor, William W. Stringer, MD, if you feel that you have been injured because of taking part in this study. You can tell the doctor in person or call him at **310-222-8200.** If you cannot reach your study doctor, you may call the Harbor-UCLA Medical Center emergency department (310-222-3514).

If you are injured as a direct result of taking the drugs used in this study or as a result of a procedure that would not have been performed on you if you were not in the study, you will be provided with appropriate medical care including treatment and hospitalization if necessary. The care will not necessarily be free of charge. Financial compensation for any injury from this research is not available. The study sponsor (*AstraZeneca Pharmaceuticals LP,*) and Los Angeles Biomedical Research Institute will not pay for the normal progress of your disease, or any injury or complication due to the medical condition you already have. Financial compensation for such things as lost wages, disability or discomfort due to an injury is not available."

What are my rights if I take part in this study?

Taking part in this study is your choice. You may choose either to take part or not to take part in the study. If you decide to take part in this study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your regular benefits. Leaving the study will not affect your medical care. You can still get your medical care from Harbor-UCLA Medical Center or your primary/personal physician.

We will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

In the case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.

Who can answer my questions about the study?

If you have questions, concerns, or complaints, or think the research has hurt you talk to the research team at ***310-222-8200.***

This research has been reviewed and approved by a John F. Wolf, M.D. Human Subjects Committee. You may talk to them at (310) 222-3624 for any of the following:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You want to talk to someone besides the research team.
- You have questions about your rights as a research subject.
- You want to get information or provide input about this research.

Have you taken part in any research studies within the past three months? *Circle "Yes" or "No"*

Yes **No**

If "YES", please describe: _____

If you want more information about this study, ask your study doctor.

For the Subject

I have been given a copy of this consent form in its entirety (all pages). I have read it or it has been read to me. I understand the information and have had my questions answered. I have also been given a copy of the Human Subject's Bill of Rights. I agree to voluntarily take part in this study.

Your signature documents your permission to take part in this research.

_____ _____
Signature of subject Date

_____
Printed name of subject

_____ _____
Witness to subject's signature Date

_____ _____
Signature of person obtaining consent Date

_____
Printed name of person obtaining consent

WITNESS FOR ILLITERATE SUBJECTS: My signature below documents that the information in the consent document and any other written information was accurately explained to, and apparently understood by, the subject and that consent was freely given by the subject.

_____ _____
Signature of witness to consent process Date

For the Investigator

I certify that I am the principal investigator and am responsible for this study, for ensuring that the subject is fully informed in accordance with applicable regulations, and for advising the Human Subjects Committee of any adverse reactions that develop from the study.

Principal Investigator:_____

Date _____

Principal Investigator: William W. Stringer, MD

DO NOT SIGN THIS FORM AFTER THE EXPIRATION DATE →

Telephone Number: 310-222-8200

LABioMed
Los Angeles
Biomedical
Research Institute
at Harbor-UCLA Medical Center

HUMAN SUBJECT'S BILL OF RIGHTS

Anyone asked to take part as a subject in a medical research study or asked to agree on behalf of someone else, has the right to understand the following:

1. What the study is about and why it is being done.

2. What you will have to do if you take part in the research study and what treatments, drugs or medical devices, if any, will be used.

3. Any pain or discomfort you may expect to feel and what risks you might run, if any, from taking part in the research study.

4. What benefit to your health, if any, you might get from taking part in the research study.

5. Other non-research treatments, drugs or medical devices that may be available to treat your illness and a comparison of the risks and benefits of these other treatments with the one you are being asked to agree to receive.

6. What medical treatment, if any, will be available to you after the research study, if medical complications arise as a result of the study.

7. You will be given a chance to ask questions about the research study, until you are satisfied that you understand what is involved. You should expect your questions to be answered clearly, fully and honestly.

8. If you agree to take part in the research study, you can later change your mind at any time without being penalized. Leaving the study will not affect your usual medical care.

9. You will not be pressured, forced, misled, given wrong facts, bribed or unfairly influenced to get you to agree to take part in the experiment.

10. You will be given a copy of any consent form you sign for the research study.