

**CONSENT TO TAKE PART IN A CLINICAL RESEARCH STUDY  
AND  
AUTHORIZATION TO DISCLOSE HEALTH INFORMATION**

**Sponsor / Study Title:** Boehringer Ingelheim Pharmaceuticals, Inc., “A randomised, active-controlled, double-blind, double-dummy, parallel group design, multi-center trial to compare the efficacy and safety of 2.5 µg and 5 µg Tiotropium Inhalation Solution delivered by the Respimat® Inhaler with Tiotropium inhalation capsules 18 µg delivered by the HandiHaler®”

**Protocol Number:** 205.452

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**Subject ID Number:** \_\_\_\_\_

You are being invited to take part in a research study. This informed consent document has information to help you decide if you want to participate. Take your time, read this form carefully, and ask the study doctor or staff any questions you may have.

**INTRODUCTION**

Before you agree to take part in this research study, it is important for you to read and understand all of the information that follows. This document explains the purpose, procedures, risks, benefits, discomforts and precautions of the study. It also explains what other treatments are available if you choose not to be in the study and your right to leave the study at any time. No promises can be made as to the results of the study.

If you are not completely truthful with the study doctor about your health history, you may harm yourself by taking part in this study.

The study is being conducted for Boehringer Ingelheim Pharmaceuticals, Inc.

**BACKGROUND AND PURPOSE**

You are being asked to participate in this research study because you have Chronic Obstructive Pulmonary Disease (COPD).

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*Chesapeake IRB Approved Version 11 Oct 2010*

*Subject's Initials* \_\_\_\_\_  
*Revised 11 Oct 2010*

*BIPI Protocol # 205.452*

*BIPI Trial Main, Version 4.0, Date 04 Oct 2010*

COPD is a common cause of respiratory (lung) problems and is most often due to smoking. Persons with COPD often have symptoms such as cough, sputum and shortness of breath, due to narrowing and blockage of the breathing tubes through which air flows in and out of the lungs. Patients with COPD may experience frequent exacerbations (worsening of symptoms) which can result in the need for increased medication use and in some instances, admission to a hospital. COPD is a progressive and serious disease and may be associated with people dying earlier than would happen if they did not have COPD.

There are a number of different types of medications that can be used to treat COPD. One of these, tiotropium, is an inhaled medicine marketed under the brand name Spiriva<sup>®</sup>. It is available as tiotropium HandiHaler<sup>®</sup>. Tiotropium is a bronchodilator (sometimes called a reliever), which means it works by opening up the air passages in the lungs, making it easier to breathe in and out, and relieving breathlessness and other symptoms of COPD.

Tiotropium is widely available (in over 100 countries worldwide) as a powder inhaled using a device called the HandiHaler<sup>®</sup>. In some countries, tiotropium inhaled using a device called the Respimat<sup>®</sup> is also available. The Respimat<sup>®</sup> is a different type of inhaler to the HandiHaler<sup>®</sup>. The Respimat<sup>®</sup> delivers a slow-moving mist of medicine that is easy to inhale and travels deep into the lungs. Both types of inhalers bring a similar amount of tiotropium to the lungs. Making different types of inhalers available allows doctors to choose the best treatment option for each patient.

Both tiotropium HandiHaler<sup>®</sup> and investigational tiotropium Respimat<sup>®</sup> have been shown to improve lung function (breathing), symptoms and health-related quality of life in patients with COPD. In addition, clinical research studies have shown that long term treatment with tiotropium given by either the HandiHaler<sup>®</sup> or Respimat<sup>®</sup> reduces the number and severity of COPD exacerbations. There is some evidence that tiotropium Respimat<sup>®</sup> may do more than tiotropium HandiHaler<sup>®</sup> in reducing the number and severity of COPD exacerbations, although some trials have shown a higher number of deaths with tiotropium Respimat<sup>®</sup> (2.2% of Respimat<sup>®</sup> treated patients compared to 1.7% of patients in the other treatment group), which were mainly in patients who were known to have a heart rhythm problem. The higher numbers in the tiotropium Respimat<sup>®</sup> group have not been considered related to tiotropium. There are no long-term studies conducted comparing tiotropium in the HandiHaler<sup>®</sup> to the Respimat<sup>®</sup> device. While both devices do give similar amounts of tiotropium to the lung, a study directly comparing both devices is the best way to help see if there are real differences.

The purpose of this trial will be to:

- Directly compare the effects of the currently available tiotropium HandiHaler<sup>®</sup> and tiotropium Respimat<sup>®</sup> treatments on COPD exacerbations and safety over a period of at least two years.
- Compare the tiotropium 2.5 micrograms (mcg) via Respimat<sup>®</sup> to the tiotropium Handihaler<sup>®</sup> 18 mcg and the tiotropium 5 mcg via Respimat<sup>®</sup> on the reduction of exacerbations and side effects, particularly when combined with other medications that keep the airways open (i.e. bronchodilator medications).

Tiotropium HandiHaler<sup>®</sup> 18 mcg is available by prescription for COPD. Both doses of the tiotropium Respimat<sup>®</sup> used in this study are investigational. An investigational use, dose, or formulation is one that is not approved by the United States Food and Drug Administration (FDA).

## NUMBER OF SUBJECTS / LENGTH OF PARTICIPATION

About 16,800 subjects in approximately 50 countries worldwide will participate in this study. Your participation in this study will last approximately 2 to 3½ years. We anticipate that the study will require approximately 10 study visits (at 12-week intervals) and 8 telephone contacts over a period of approximately 2 years. Depending on the overall progress of the study, you may be asked to continue taking the study drugs (tiotropium HandiHaler® and tiotropium Respimat®) and attending study visits at 12 week intervals (with interim telephone contacts) for a longer period, possibly up to 3 ½ years in total. The total number of visits could be as many as 17 and phone calls could be as many as 14.

This is an ‘event driven’ study, which means that the study will not end until a certain number of events have occurred. The events we are counting in this study are fatal (resulting in death) adverse events. When the study begins we will not know how long it will take to see the target number of events; therefore, we cannot be sure how long the study will be in total or for each patient.

This study will use competitive enrollment. This means that when a target number of subjects has entered the Study Treatment Phase, all further enrollment will be closed. Therefore, it is possible that you could be in the screening phase, ready to enter the study treatment phase, and be taken out of the study without your consent if the target number of subjects has already entered the study treatment phase.

## PROCEDURES

The study consists of Consenting and Screening Visits to determine if you qualify; a Study Treatment Phase, an End of Study Treatment Visit and a Follow-up Period. Note, the Consenting and Screening Visits may be combined if your study doctor allows this and you are not participating in the PFT Sub-Study (described in the Optional Sub-Study section of this consent document and in a separate consent form).

### Consenting Visit

#### **Visit 0**

Before any study-related tests and procedures are performed, you will be asked to read and sign this consent document.

### Screening Visit

#### **Visit 1 (May be the same day as Visit 0 or up to 4 weeks later)**

You will have the following tests and procedures performed:

- You will be asked questions about your medical history and any medications you have taken in the past 2 months.
- You will be asked questions such as gender, race, date of birth and about your past and current smoking status.
- You will be asked how you are feeling and whether you have had a worsening of COPD symptoms.
- You will be asked to rate your breathlessness using the Modified Medical Research Council (MMRC) Dyspnea Scale.

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- Physical examination.
- Height and weight will be measured.
- Heart rate and blood pressure measurements taken.
- Urine (or blood if required) taken for a pregnancy test if you are a woman who can have a child.
- ECG (electrocardiogram) – a painless test of the electrical activity of your heart.
- Pulmonary Function Test (PFT) - A breathing test to see how well your lungs are working. If you are not participating the PFT sub-study and have a PFT on file that was performed recently, you may not need to perform this test. If the PFTs will be done, you will be asked to inhale a type of medication called a bronchodilator. You will be asked to sit straight up and take in a deep breath (as deep as possible) and blow out as forcefully, rapidly and as long as possible through a mouthpiece into a machine called a spirometer at least 3 times, but not more than 8 times, before and after you inhale the medication.
- If you qualify to take part in this study, you will have the following procedures and will be randomly assigned by chance to receive either:
  - 1) Tiotropium inhalation solution 5 mcg taken once a day (2 puffs of 2.5 mcg each) through the Respimat<sup>®</sup> + Placebo (inactive substance) inhalation capsule taken once daily through the HandiHaler<sup>®</sup>  
**Or**
  - 2) Tiotropium inhalation solution 2.5 mcg taken once a day (2 puffs of 1.25 mcg each) through the Respimat<sup>®</sup> + Placebo inhalation capsule taken once daily through the HandiHaler<sup>®</sup>  
**Or**
  - 3) Tiotropium powder – one 18 mcg capsule for inhalation taken once a day through the HandiHaler<sup>®</sup> + Placebo inhalation solution taken once daily through the Respimat<sup>®</sup>
- You will receive enough study drug for 12 weeks, and you will take the first dose in the clinic under the supervision of the study doctor or nurse. If you are not participating in the PFT Sub-Study and if you have been taking tiotropium and have already taken your daily dose before you came into the study center, you will take your first dose of study drug the next day.
- You will be asked to bring your used and unused study drugs and all packaging with you to each visit.

You will have equal chance of being assigned to any of the 3 study groups.

This is a double-blind study, which means neither you nor the study doctor will know to which of these study drug groups you are assigned. In case of an emergency, however, the study doctor can get this information.

The Respimat<sup>®</sup> and HandiHaler<sup>®</sup> inhalers look very different; therefore, the study involves a ‘double-dummy’ design to hide the identity of the study drug you are taking, in other words to keep the study blind.

This means that you will have to inhale from both the Respimat<sup>®</sup> and the HandiHaler<sup>®</sup> inhalers for the whole time you are in the study treatment phase. If you are assigned to study group 1 or 2 (see above), only the Respimat<sup>®</sup> inhaler will contain active study drug, while the HandiHaler<sup>®</sup> inhaler will contain placebo. If you are assigned to study group 3, only the HandiHaler<sup>®</sup> inhaler will contain active study drug, while the Respimat<sup>®</sup> inhaler will contain placebo.

A placebo looks like the actual study drug but does not contain active ingredients and has no direct effect on your condition. In this study, all subjects will receive an active study drug; the placebo is taken in addition.

- You will be given reminder cards to record study clinic and telephone appointments, exacerbations of COPD symptoms, any medications you may have taken and other important information. You will bring these cards with you to all your visits.
- You will receive detailed instructions and training on the use of the HandiHaler<sup>®</sup> device and the Respimat<sup>®</sup> inhaler.
- You will receive a study ID card with your name, your study doctor's name and contact information, and research study information to use in case of emergency to notify your treating physician that you are taking part in this research study.
- You will be given an appointment to return in 6 weeks for Visit 2.

### **Study Treatment Phase**

#### **Visits 2 through End of Study Treatment Visit**

You will be asked to return to the clinic approximately 6 weeks after starting study drug (Visit 2). Visit 3 will be scheduled to take place approximately 6 weeks after Visit 2. Visit 4 will be scheduled to take place approximately 12 weeks after Visit 3. All subsequent visits will be scheduled to take place approximately every 12 weeks.

During each clinic visit you will have the following procedures:

- You will be asked how you have been feeling and about any medications you have taken.
- Your reminder cards will be collected and reviewed for any missed doses of study drug, exacerbations of your COPD, hospitalizations, any medications that you have taken and all other information that is to be recorded on these cards.
- Smoking status will be reviewed.
- You will be trained on the proper inhalation technique and use of the HandiHaler<sup>®</sup> and Respimat<sup>®</sup> devices.
- Study drug will be collected at each visit and you will receive a new supply of study drug for 12 weeks (except Visit 2 when study drug will be reviewed for compliance).
- You will receive a new reminder card with an appointment to return in 12 weeks (except Visit 2 when you will be asked to return in 6 weeks for Visit 3) and the next telephone contact.

#### **Telephone Contacts**

In addition to the clinic visits, the site staff will schedule regular telephone contacts with you. The telephone contacts will take place at approximately 6 week intervals between the clinic visits (from Visit 3 onwards). During the telephone contact, the site staff will ask you about any changes in your health, if you have had any COPD exacerbations and about any medications you have taken since your last visit. Other information recorded on your reminder cards since the last clinic visit will also be collected verbally.

### **End of Study Treatment Visit**

At the end of the Study Treatment Phase, or if you stop taking the study drug before the end of the study, you will have the following procedures:

- You will be asked how you are feeling and about any medications you have taken.
- You will be asked if you had any COPD exacerbations.
- Smoking status will be reviewed.
- Pregnancy test (urine or blood) for women who can have a child.
- You will return all used and unused study drug and packaging.
- You will receive an appointment for a telephone contact in about 30 days.

### **End of Study and Follow-Up Period (Telephone Visit)**

A telephone contact will be scheduled about 30 days after the last dose of study drug. You will be asked the following:

- You will be asked how you are feeling and about any medications you have taken.
- You will be asked if you had any COPD exacerbations (information from the reminder cards will be collected verbally).
- Smoking status will be reviewed.

### **Early Withdrawal and Vital Status Follow-Up**

It is important for us to be able to collect as much information as possible on the health of all subjects who take part in the study, including those who withdraw before completing the entire study period. Previous studies suggest that if health status information is not obtained for withdrawn subjects, it may be difficult to interpret results correctly.

You are, of course, free to withdraw from the study at any time, and you do not have to give a reason. However, in the event of your withdrawal from the study, it would be very helpful if we could keep in touch with you, a member of your family, or any health care professionals involved in your treatment to find out how you are.

If you withdraw from the study, we would like to contact you, a member of your family, or health care professional by phone at regular intervals (every 12 weeks after the Follow-Up Telephone Visit). You will be asked how you are feeling and about any medications you have taken. We would like to do this up until the study is completed. For example, if you started the study in December 2010, but decide to withdraw in October 2011, we would ask you to accept phone calls approximately every 12 weeks at least until December 2012.

We will ask you to confirm, by signing this consent form, that you have given your permission for us to contact you, a family member or health care professional, as described in this section, if you withdraw from the study early.

## **OPTIONAL SUB-STUDY**

### **Pulmonary Function Tests (PFT) Sub-Study**

You will only be asked to perform one PFT during Visit 1 to ensure you qualify for the study.

However, optional additional pulmonary function tests (PFT) will be performed at selected study centers. These additional PFTs are called a “sub-study.” Your study doctor or study staff will let you know if your study center is participating in this sub-study. If your center is taking part in this sub-study, you will be asked if you would like to participate or not. Participation is optional. You do not have to participate in the PFT Sub-Study to participate in this “main” study.

If you agree to participate, you will be asked to read and sign a separate Pulmonary Function Test Sub-Study consent form. Signing this consent alone does not mean you are in the sub-study.

## **EXPECTATIONS**

If you participate in this study you will be expected to:

- Come to scheduled study visits and be reasonably available for the scheduled interim telephone calls.
- Take the study drug at approximately the same time each morning.
- Bring your supply of used and unused study drug with you to each study visit, including empty tiotropium capsules and all Respimat<sup>®</sup> and HandiHaler<sup>®</sup> devices and cartridges and packaging.
- Record your COPD exacerbation symptoms, medication you have taken and other information on your reminder cards and bring the cards with you to each clinic visit.
- Store the study drug in the original container. It should not be exposed to high heat (above 77 degrees F). Do not throw the study drug in the trash. It must be kept out of reach of children and those who are unable to read the label. Only you are allowed to take the study drug.
- Tell the study doctor or staff if you do not feel well or experience any side effects, whether or not you think they have happened as a result of taking part in this study, even if they have disappeared with or without the treatment you may have taken. Contact your study doctor immediately if there is any sudden worsening in your condition or if you notice that your COPD symptoms are getting worse.
- Tell the study doctor and staff about any prescription or over-the-counter medicines you are taking. This includes any other preparations or food supplements you are taking, such as vitamin preparations, herbal products, or similar products. If you are given a new medication by your primary care physician during the time you are in this study, please inform your study doctor at your next visit.
- If you require treatment from other doctors (for example during an emergency) you should inform the doctors about your participation in the study. A card with your name, your study doctor’s name and contact information, and research study information will be provided to you at the beginning of the study.
- Not take part in other research studies while you are in this study.
- If you become pregnant or believe that you may be pregnant while you are in this study, you must tell your study doctor right away.

## **RISKS, SIDE EFFECTS AND/OR DISCOMFORTS**

### **Tiotropium (Spiriva<sup>®</sup> – tiotropium HandiHaler<sup>®</sup> and tiotropium Respimat<sup>®</sup>)**

Tiotropium is a marketed product, licensed for use in COPD throughout the world. The most common side effect (in more than 1 in 100 patients) of tiotropium is dryness of the mouth.

Uncommonly (in less than 1% of patients) the following side effects can occur: dizziness, palpitations, fast heart rate, abnormalities of heart rhythms or heart rate (atrial fibrillation, tachycardia, supraventricular tachycardia), nosebleeds, difficulty swallowing, constipation, acid reflux, sore throat, itching, rash, hoarseness, coughing, thrush (fungal infection in the mouth), difficulty passing urine, pain on passing urine, problems swallowing, and stomatitis (inflammation or ulcers in the mouth area).

Rarely (less than 1 in 1000 patients affected) side effects include increased pressure inside the eye, glaucoma, blurred vision, swelling of the tongue or gums, laryngitis (swelling of the vocal cords which may cause you to lose your voice), insomnia, urticaria (red skin welts), sinusitis (inflammation of the sinuses), intestinal obstruction (a condition where the gut becomes blocked), angioedema (where the skin becomes very swollen and red), urinary tract infections, skin infections or skin ulcers, dry skin and hypersensitivity reactions.

Other problems that may occur, although it is not possible to decide how frequently they occur, include swelling of the joints, and dehydration.

As with other inhaled drugs, tiotropium can cause bronchospasm (a narrowing of the airways which may temporarily make your breathing worse). This may occur in less than 1% of patients.

If you are assigned to the study group getting 2.5 mcg of tiotropium Respimat<sup>®</sup>, your COPD symptoms may not be controlled as well if you were assigned to a dose that is FDA-approved or previously studied in a clinical trial.

### **Bronchodilator (medication to open your airways) taken at Visit 1only**

Subjects that do not have a recent breathing test or subjects taking part in the sub-study, are required to take a bronchodilator at Visit 1 during their breathing test. There are different medications which are used for this testing. The most common medications and their side effects are listed below. You will receive just one of these medications and will be told which one by study staff.

#### **Short acting beta agonists (like albuterol)**

The most common bronchodilator medications used during breathing tests are called short acting beta-agonists. Common side effects of medications like this are rapid heart rate (tachycardia), palpitations (irregular heart beats), tremors, nervousness, sleep disturbances, and decreased potassium levels. The most common side effects of these medications are related to the amount you take and happen more with medication provided as pills than inhaled medication. Some of the most common medications are called levalbuterol, terbutaline (Bricanyl), pirbuterol (Maxair<sup>®</sup>), metaproterenol (Alupent) and fenoterol, The most common medication is albuterol and the specific side effects for this medication are listed below.

- **Albuterol**

The most common side effects of albuterol include irregular heartbeat, rapid heart rate, tremor (involuntary shaking) or nervousness.

Other side effects reported by 3% of subjects or greater than placebo (an inactive substance) in research studies included throat irritation, upper respiratory inflammation, musculoskeletal and back pain, headache, and dizziness.

Other side effects reported by less than 3% of subjects and that have the potential to be related to albuterol include chest pain, infection, vomiting, diarrhea, inflammation of the tongue, accidental injury (nervous system), shortness of breath, ear disorder or pain, and urinary tract infection.

Side effects that have been reported outside of research studies, with frequency difficult to assess are muscle cramps, gagging, swelling of the tissues just below the skin, hoarseness, low blood pressure, difficulty sleeping, and fatigue.

Albuterol should be used with caution in patients with cardiovascular (heart and blood vessel) disorders, in patients with convulsive (seizure) disorders, overactive thyroid (hyperthyroidism), diabetes mellitus or patients with sensitivity to this type of drug. This type of drug can also lower your blood potassium but this does not usually require treatment.

### **Short-acting Anticholinergic Medications (like ipratropium, called Atrovent<sup>®</sup>)**

Short-acting anticholinergic medications can also be used during the breathing tests. The side effects of ipratropium bromide (Atrovent<sup>®</sup>), which is the most common medication, are listed below.

- **Atrovent<sup>®</sup> HFA Inhalation Aerosol**

The most common drug related side effects reported for Atrovent<sup>®</sup> HFA are dry mouth and bitter taste.

Other side effects reported in 3% or more patients are: back pain, headache, influenza like symptoms, dizziness, indigestion, nausea, bronchitis, COPD exacerbation, coughing, shortness of breath, rhinitis (nasal symptoms), sinusitis, upper respiratory tract infection and urinary tract infection.

There have also been rare reports of aggravated bronchospasm (increased tightening of the breathing tubes).

## **Combination Short-acting Anticholinergic and Beta-agonist Medications (like Combivent®)**

Medications like albuterol can be combined with medications like ipratropium in one inhaler. Combivent® is an example of a combination product and the side effects are listed below.

- **Combivent® (ipratropium and albuterol)**

The most common side effects in more than 3% of patients include: headache, pain, nausea, bronchitis, dyspnea (difficulty in breathing), coughing, respiratory disorders, upper respiratory tract infections, sore throat, and sinusitis.

Each of these bronchodilator medications also have less common risks that will be explained to you before the breathing test.

### **Allergic Reactions**

Sometimes people have allergic reactions to medications. If you have a very bad allergic reaction, you could die. Some things that happen during an allergic reaction are:

- Hives or a rash
- Having a difficult time breathing
- Wheezing when you breathe
- Sudden drop in blood pressure
- Swelling around the mouth, throat or eyes
- Fast heart rate
- Sweating

You will be monitored carefully after administration of the study drug for signs of an allergic reaction. There are trained medical personnel and emergency equipment and medicines available at the research center to treat you in the event of an allergic reaction. If you think you are having a severe allergic reaction when you are not at the clinic, call 911 and seek medical attention immediately. You should then notify the study doctor or study staff to inform them of these or any other side effects during the study.

### **Procedure Risks**

You may feel discomfort during some of the tests and some tests may also have risks, such as:

#### **ECG**

Skin irritation from the ECG electrode pads or pain when removing the pads is a possible risk.

#### **Pregnancy Test Blood Draw**

The risks of a blood draw include fainting and pain, bruising, swelling, or rarely infection where the needle is inserted. If a blood pregnancy test is required, the approximate amount of blood taken will be 2 teaspoons.

## **Pulmonary Function Tests (PFT)**

Risks and discomforts from pulmonary function testing may include shortness of breath, dizziness, or headache while doing the breathing tests. Should this occur, treatment will be given.

## **Unforeseen Risks**

Since the study drug is investigational when taken alone or in combination with other medications, there could be other risks that are not known.

## **PREGNANCY / BIRTH CONTROL**

No studies have been done on tiotropium in pregnant women or women who are nursing their infants. It is not known if tiotropium is safe for pregnant women, unborn babies and infants who are nursing. It is also not known if tiotropium has an effect on sperm or eggs.

If you are pregnant, planning to become pregnant, or are nursing an infant you will not be able to take part in this study. If you are a woman who is able to become pregnant, you must have been using a medically acceptable form of birth control, such as oral contraceptives (birth control pills), intrauterine devices (IUDs) diaphragm or subdermal implant such as Norplant® for the previous three months prior to the study and agree to continue to use a medically acceptable form of birth control for the length of the study. You must discuss with your study doctor if the method of birth control you are using is reliable and effective for you. You must have a negative pregnancy test prior to treatment and must not become pregnant while in the study. If you become pregnant during the study you must tell the study doctor or staff right away.

You should also know that medications like albuterol, Atrovent® and Combivent® may have some risks in pregnant women. The FDA has given albuterol and Combivent® what is known as a Type C pregnancy warning. This means that animal studies which have been done indicate that there have been adverse effects on the fetus (unborn baby). There are no studies that have been done in pregnant women. Atrovent® has a Type B warning, which means that in animal studies, adverse effects to the fetus have not been seen, however, there are no studies conducted in pregnant women.

## **ALTERNATIVE TREATMENT**

You do not have to be in this study to receive treatment for your COPD. Many different oral and inhaled medicines are available for the treatment of COPD. Instead of being in this research study, you may have other treatment choices or you may choose no treatment at all. Your doctor may prescribe tiotropium HandiHaler® without you being in this study. You should discuss all other treatment options with your study doctor before you decide to take part in this study. You should ask your study doctor about the benefits and risks of the other choices available to you.

## **CONFLICT OF INTEREST**

A “conflict of interest” (COI) is a circumstance in which different interests could influence a person’s decisions. For example, a conflict of interest for your study doctor may involve his/her conflict in providing care as your personal physician versus overseeing your participation in a clinical research study, or it could involve financial issues.

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Your study doctor(s) must follow federal rules and IRB requirements for identifying and managing possible conflicts of interest before he/she can be approved to conduct a research study. This is to make sure that the conduct of the study and the reporting of the study results will not be influenced by any conflicting interests.

Your study doctor is being paid by Boehringer Ingelheim Pharmaceuticals, Inc., for the work he/she does as part of this study.

## **NEW FINDINGS**

Any new important information that is discovered during the study and which may influence your willingness to continue participation in the study will be made available to you in a timely manner.

## **BENEFITS**

You may benefit as a result of your participation in this study. There is, however, no guarantee that you will benefit from your participation in this study. Results from this study may benefit others in the future.

## **COMPENSATION FOR PARTICIPATION**

For your time and inconvenience related to your participation in this study, you will be paid for the study visits you complete according to the following schedule: \$12.00 for each clinic visit (Visit 0, Visits 2-End of Treatment), \$24.00 for Visit 1 and \$12.00 for each unscheduled visit. You will also be reimbursed for travel expenses related to the study. Please inquire with your study coordinator regarding the current Federal Mileage Reimbursement Rates. Reimbursement for public transportation is also available.

If you do not complete the study, for any reason, you will be paid for each study visit you do complete according to the schedule above. This will be paid to you at each study visit.

If you have any questions regarding your compensation for participation, please contact the study doctor at the telephone number listed on page one of this consent document.

## **CONFIDENTIALITY**

Your study-related medical records will be treated as private as possible under local, state, and federal laws. Whenever possible, a code instead of your name or other identifying information will be used on study documents and specimens. Information from this study will be submitted to the sponsor. "Sponsor" includes any affiliates or parent company, persons or companies working with the sponsor to conduct the study.

The information will also be given to the U.S. Food and Drug Administration (FDA). It may be given to governmental agencies in other countries where the study drug may be considered for approval. Medical records which identify you and the consent form signed by you may be looked at and/or copied for research or regulatory purposes by:

- the sponsor;
- the FDA;
- Department of Health and Human Services (DHHS);
- Governmental agencies in other countries; and
- Chesapeake Research Review, Inc.'s Institutional Review Board (IRB, a research ethics board that oversees this study).

Study-related medical records includes all medical records the sponsor believes necessary to conduct this study including but not limited to past medical history, medical information from your primary care physician and all information collected from your participation in this research study. Your study doctor may ask you to sign a separate authorization to obtain some or all of your medical records from your doctor(s) or other healthcare professionals.

Absolute confidentiality cannot be guaranteed. If the study results are published in medical or scientific journals, you will not be identified by your name.

### **COMPENSATION FOR INJURY**

If you are injured or become ill as a direct result of a study procedure or the study drug, the study center will provide or make available reasonable and customary medical care for that injury or illness at no cost to you. The Sponsor will pay for the costs of such care that are not covered by your insurance or third party coverage (excluding governmental health insurance programs) under the following circumstances:

1. It is the opinion of the study doctor and Sponsor that the injury or illness is a result of the research;
2. For studies that provide treatment of a specific condition or disease, it is the opinion of the study doctor and the Sponsor that the injury is not related to your disease/condition or to the expected complications of the usual treatment for that disease/condition;
3. If the injury is the result of a procedure and the procedure was not one that you would have normally received as part of the treatment or management for your disease/condition;
4. You have followed all of the directions of the study doctor and the information provided on how to take the study drug;
5. You have followed medical advice regarding the injury or illness; and
6. You have notified the study doctor of the injury or illness as soon as possible.

The fact that you may receive treatment or care at no cost as just described above does not mean that the study center or the Sponsor are responsible for such injury or illness. No type of compensation, such as lost wages or payment for discomfort due to any injury suffered as a direct result of this study will be paid. You do not waive any legal rights you may have or other causes of action by signing this form.

If you are injured during this study, your study doctor may discuss with you the available medical treatment options.

*Lisa M. Wheatley, M.D.*

*Chesapeake IRB Approved Version 11 Oct 2010*

*Subject's Initials \_\_\_\_\_  
Revised 11 Oct 2010*

## **COSTS**

There will be no charge to you for your participation in this study. The study drug, study-related procedures, and study visits will be provided at no charge to you or your insurance company. If necessary, the bronchodilator medication for the PFT will be supplied by the study center.

Because this is a research study, tiotropium HandiHaler<sup>®</sup> and tiotropium Respimat<sup>®</sup> will be given to you only for the duration of this study and not after the study is over.

## **EMERGENCY CONTACT / IRB CONTACT**

During the study, if you experience any medical problems, suffer a research-related injury, or have questions, concerns or complaints about the study, please contact the study doctor at the telephone number listed on page 1 of this consent document. If you seek emergency care or hospitalization is required, alert the treating physician that you are participating in a research study being run by the study doctor listed on page 1 of this document.

If you have any questions about your rights as a research subject, or concerns or complaints regarding this research study, contact:

- By mail:  
Study Subject Adviser  
Chesapeake Research Review, Inc.  
7063 Columbia Gateway Drive, Suite 110  
Columbia, MD 21046
- or call **collect**: 410-884-2900
- or by **email**: [adviser@irbinfo.com](mailto:adviser@irbinfo.com)

Please reference the following number when contacting the Study Subject Adviser: Pro00005255.

## **VOLUNTARY PARTICIPATION / WITHDRAWAL**

Your decision to participate in this study is voluntary. You may choose to not participate or you may withdraw from the study for any reason without penalty or loss of benefits to which you are otherwise entitled and without any effect on your future medical care. If you leave the study for any reason, the study doctor may ask you to have some end-of-study tests both for your safety and for the completeness of the study.

The study doctor or the sponsor can stop your participation at any time without your consent for the following reasons:

- If it appears to be medically harmful to you;
- If you fail to follow directions for participating in the study;
- If it is discovered that you do not meet the study requirements;
- If the study is canceled; or
- For administrative reasons, including competitive enrollment - the target number of subjects has entered the treatment phase.

**PRIMARY CARE PHYSICIAN / SPECIALIST NOTIFICATION OPTION**

Please initial below whether you want us to notify your primary care physician or your specialist of you taking part in this study.

\_\_\_\_\_ Yes, I want the study doctor to inform my primary care physician/specialist of my taking part in this study.

\_\_\_\_\_ No, I do not want the study doctor to inform my primary care physician/specialist of my taking part in this study.

\_\_\_\_\_ I do not have a primary care physician/specialist.

\_\_\_\_\_ The study doctor is my primary care physician/specialist.

**CONSENT**

I have read this consent form and my questions have been answered. By signing this consent form I will not give up any of my legal rights.

I authorize the release of my medical records to representatives of the sponsor, FDA, DHHS agencies, regulatory agencies in other countries, and Chesapeake Research Review, Inc.'s Institutional Review Board.

I will be given a signed and dated copy of this consent form.

I voluntarily consent to take part in this study and I understand that I may withdraw my consent at any time.

\_\_\_\_\_  
First and Last Name of Subject  
(BLOCK letters/Print)

\_\_\_\_\_  
Signature of Subject

\_\_\_\_\_  
Date

**IMPARTIAL WITNESS STATEMENT (USE ONLY IF APPLICABLE)**

**If this consent form is read to the subject because the subject is unable to read the form, an impartial witness not affiliated with the research or study doctor must be present for the consent and sign the following statement:**

I attest that the information in this informed consent form was accurately explained to, and apparently understood by the subject. I also attest that the subject freely gave their informed consent to participate in this trial.

\_\_\_\_\_  
First and Last Name of Impartial Witness (if applicable)  
(BLOCK letters/Print)

\_\_\_\_\_  
Signature of Impartial Witness

\_\_\_\_\_  
Date

\_\_\_\_\_  
Address of Impartial Witness

**STUDY PERSONNEL STATEMENT**

The person signing this consent form has had the study fully and carefully explained and has been given an opportunity to ask any questions regarding the nature, risks and benefits of the subject's participation in this research study.

\_\_\_\_\_  
First and Last Name of Person Obtaining Consent  
(BLOCK letters/Print)

\_\_\_\_\_  
Signature of Person Obtaining Consent

\_\_\_\_\_  
Date

## AUTHORIZATION TO DISCLOSE HEALTH INFORMATION

Access to your Protected Health Information (“PHI”) will be required for the purpose of conducting this research study.

PHI is medical information that identifies you as an individual such as: name, address, social security number, and other details about you.

This will include all information that is used to determine your eligibility and collected from the procedures and tests that are carried out as a part of this study. This may include, but is not limited to, the following types of medical information:

- Your past medical history, including medical information from your other health care providers.
- Physical exam and laboratory test (urine or blood) results for pregnancy.
- Smoking history.
- Pulmonary Function Test results.
- Electrocardiogram results.
- Your response to any study treatments.
- Information related to study visits and phone calls.
- Other tests or procedures that may be performed and not listed.

With your permission the study doctor and his/her support staff will be allowed to give this information to the study sponsor’s key individuals. The “sponsor’s key individuals” include any parent or affiliate company of the sponsor and any person or company working for or with the sponsor to facilitate the study. They will have the right to see your health information and know your identity during and after the study.

In addition, your PHI may also be given to the FDA, Department of Health and Human Services, government agencies in other countries, the IRB (a research ethics board that oversees this study).

The sponsor’s key individuals agree to keep all of your information confidential, which will minimize the risk that it will be released to others without your permission. However, once your PHI has been disclosed to a third party, federal privacy laws may no longer protect it from further disclosure.

This authorization does not have an ending date and permission to access your PHI will continue until such time as it is no longer required by the sponsor.

You have the right to see and copy any of the PHI gathered about you, but not until the study is complete.

You also have the right to withdraw this permission at any time by providing a written request to the study doctor. When you withdraw your permission, no new health information that might identify you will be gathered after that date, and you will not be able to continue in the study. Information that has already been gathered may still be used by the sponsor.

By signing this authorization form, you are giving your permission to use and give out your protected health information. If you do not give your permission, you will not be able to be in this study.

You will be provided with a signed copy of this form for your files.

*Lisa M. Wheatley, M.D.*

*Chesapeake IRB Approved Version 11 Oct 2010*

*Subject’s Initials \_\_\_\_\_  
Revised 11 Oct 2010*

**AUTHORIZATION**

\_\_\_\_\_  
First and Last Name of Subject  
(BLOCK letters/Print)

\_\_\_\_\_  
Signature of Subject

\_\_\_\_\_  
Date

**IMPARTIAL WITNESS STATEMENT (USE ONLY IF APPLICABLE)**

**If this authorization form is read to the subject because the subject is unable to read the form, an impartial witness not affiliated with the research or study doctor must be present for the authorization and sign the following statement:**

I attest that the information in this authorization form was accurately explained to, and apparently understood by the subject. I also attest that the subject freely gave their authorization to participate in this trial.

\_\_\_\_\_  
First and Last Name of Impartial Witness (if applicable)  
(BLOCK letters/Print)

\_\_\_\_\_  
Signature of Impartial Witness

\_\_\_\_\_  
Date

\_\_\_\_\_  
Address of Impartial Witness

**STUDY PERSONNEL STATEMENT**

The person signing this authorization form has had the authorization fully and carefully explained and has been given an opportunity to ask any questions regarding the use and disclosure of his/her protected health information as a subject in this research study.

\_\_\_\_\_  
First and Last Name of Person Obtaining Authorization  
(BLOCK letters/Print)

\_\_\_\_\_  
Signature of Person Obtaining Authorization

\_\_\_\_\_  
Date