Penn Medicine

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COVER PAGE

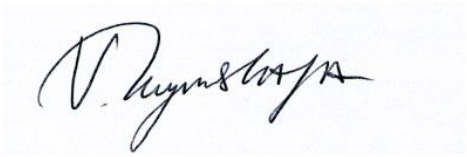
Date: 04-October-2016

TITLE: Safety of Simvastatin in LAM and TSC (SOS)

Identifiers: NCT02061397

Unique Protocol ID; The SOS Trial

Best Regards,



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UNIVERSITY OF PENNSYLVANIA
RESEARCH SUBJECT
INFORMED CONSENT AND
HIPAA AUTHORIZATION FORM

Protocol Title: The Safety of Simvastatin in Patients with Pulmonary Lymphangioleiomyomatosis and with Tuberous Sclerosis Complex (The SOS Trial)

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Why am I being asked to volunteer?

You are being invited to participate in a research study because you have either pulmonary lymphangioleiomyomatosis (LAM) or tuberous sclerosis complex (TSC) and the investigators of this study want to look at how safe it is to use a drug called simvastatin in subjects like you with LAM or TSC. Your participation is voluntary, which means you can choose whether or not you want to participate. If you choose not to participate, there will be no loss of benefits to which you are otherwise entitled. Before you can make your decision, you will need to know what the study is about, the possible risks and benefits of being in this study, and what you will have to do in this study. The research team is going to talk to you about the research study, and they will give you this consent form to read. You may also decide to discuss it with your family, friends, or family doctor. You may find some of the medical language difficult to understand. Please ask the study doctor and/or the research team about this form. If you decide to participate, you will be asked to sign this form.

What is the purpose of this research study?

The purpose of this research study is to see if simvastatin can be taken safely in patients with either LAM or TSC, who are already being treated with everolimus or sirolimus. This is the first step in looking at simvastatin as a drug that may help patients, by impacting the growth and survival of cells that make up the lung lesions that cause problems in LAM and TSC patients. The study also seeks to learn more about how simvastatin works, when given to patients being treated with everolimus or sirolimus, and to evaluate benefit or risk to patients taking this 2-drug combination.

Simvastatin is a member of a group of drugs called HMG CoA reductase inhibitors, or "statins." These drugs reduce levels of "bad" cholesterol (low-density lipoprotein, or LDL) and triglycerides in the blood, while increasing levels of "good" cholesterol (high-density lipoprotein, or HDL). Simvastatin is used by millions of people to lower the risk of stroke, heart attack, and other heart complications, in people with diabetes, coronary heart disease, or other risk factors. Simvastatin is approved by the US Food and Drug Administration (FDA) for this purpose. It is considered experimental in this study.

How long will I be in the study?

You will be one of ten evaluable patients in the study. The study involves 6 scheduled visits occurring approximately every 30 days, over a 5 month period (approximately 164 days). You will receive simvastatin as part of this study for four months. At the end of five month period, you will complete your final set of surveys and questioning. One month after completing the final study visit, you will be contacted by telephone to see how you are doing. The total number of days for this study (including all visits and telephone contacts) is approximately 164. All participants in this study will be from the University of Pennsylvania.

What am I being asked to do?

Once you have signed this consent form, study related tests/procedures will be done to ensure that you qualify for the study. If found to be eligible and you agree to participate, you will be given simvastatin at a starting dose of 20 mg, to be taken each evening by mouth. If after 2 months, you tolerate the simvastatin 20 mg dose, the dose of simvastatin will be increased to 40 mg each evening by mouth. Doses may be adjusted, as needed, should you experience side effects from simvastatin. The dose of everolimus or sirolimus that you have been taking is not expected to change, as this is a dose that you have shown to tolerate. If however, you experience side effects from the combination of drugs, the dosages may be adjusted by the study physician (investigator).

<u>Please note, you should not drink grapefruit juice or eat grapefruit or grapefruit products while taking simvastatin, because it could create an unwanted interaction with simvastatin.</u>

At screening, **Visit 1**, the following tests and evaluations will be performed (however, if done recently, some of these tests may not need to be repeated):

- Medical history review and a physical examination
- Review of the medications you are currently taking
- A urine pregnancy test, if there is a possibility you could become pregnant
- Three (3) tablespoons of blood will be drawn and the following tests will be performed on the blood:
    - **CBC:** a complete blood count provides important information about the kinds and numbers of cells in the blood
    - **Chemistry (CMP):** a blood test that looks at kidney function, liver function and electrolytes like potassium and calcium.
    - **CPK:** creatine phosphokinase (CPK) is an enzyme found mainly in the heart, brain, and skeletal muscle. This test will monitor the health status of muscle.
    - **Lipid Profile:** a panel of blood tests that serves as an initial broad screening tool for abnormalities in lipids, such as cholesterol (including LDL and HDL) and triglycerides
    - Sirolimus or everolimus test: a measurement of the amount of sirolimus or everolimus (whichever medicine you take) in your blood.
    - Any remaining blood from the sample will be stored for LAM research.
- A chest x-ray will be performed

Visit 2 will happen within 14 days of your screening visit; this will be **day 0**, since it will be the first day of treatment with simvastatin. During this visit, the following tests and evaluations will be performed:

- Review of the medications you are currently taking
- A urine pregnancy test, if there is a possibility you could become pregnant
- One (1) tablespoon of blood will be drawn as research for VEGF-D. VEGF-D is a marker frequently found in the blood of patients with LAM and/or TSC
- Spirometry testing (breathing test) performed before and after using a bronchodilator inhaler
- Completing questionnaires about your overall health, daily life and your sense of well-being (approximately 20 minutes to complete)

You will be given a 30-day supply of simvastatin 20 mg, which you will take each evening. You will also be given a calendar to write down when you took the simvastatin each day; you will be asked to bring the calendar and the pill bottle back with you, at the next scheduled study visit.

Visit 3 (day 30) will occur one month after Visit 2. During this visit, the following tests and evaluations will be performed:

- Medical history review and a physical examination
- Review of the medications you are currently taking
- Review of any side effects you may have experienced since the last visit
- A urine pregnancy test, if there is a possibility you could become pregnant
- Four (4) tablespoons of blood will be drawn and the following tests will be performed on the blood:
    - **CBC:** a complete blood count provides important information about the kinds and numbers of cells in the blood
    - **Chemistry (CMP):** a blood test that looks at kidney function, liver function and electrolytes like potassium and calcium.
    - **CPK:** creatine phosphokinase (CPK) is an enzyme found mainly in the heart, brain, and skeletal muscle. This test will monitor the health status of muscle.
    - **Lipid Profile:** a panel of blood tests that serves as an initial broad screening tool for abnormalities in lipids, such as cholesterol (including LDL and HDL) and triglycerides
    - Sirolimus or everolimus test: a measurement of the amount of sirolimus or everolimus (whichever medicine you take) in your blood.
    - VEGF-D: a marker frequently found in the blood of patients with LAM and/or TSC
    - Any remaining blood from the sample will be stored for LAM research.
- Completing questionnaires about your overall health, daily life and your sense of well-being (approximately 20 minutes to complete)

You will be given a 30-day supply of simvastatin 20 mg, which you will take each evening. You will be given a calendar to write down when you took the simvastatin each day; you will be asked to bring the calendar and the pill bottle back with you, at the next scheduled study visit.

Visit 4 (day 60) will occur one month after Visit 3. During this visit, the following tests and evaluations will be performed:

- Medical history review and a physical examination
- Review of the medications you are currently taking
- Review of any side effects you may have experienced since the last visit
- A urine pregnancy test, if there is a possibility you could become pregnant
- Four (4) tablespoons of blood will be drawn and the following tests will be performed on the blood:

- **CBC:** a complete blood count provides important information about the kinds and numbers of cells in the blood
- **Chemistry (CMP):** a blood test that looks at kidney function, liver function and electrolytes like potassium and calcium.
- **CPK:** creatine phosphokinase (CPK) is an enzyme found mainly in the heart, brain, and skeletal muscle. This test will monitor the health status of muscle.
- **Lipid Profile:** a panel of blood tests that serves as an initial broad screening tool for abnormalities in lipids, such as cholesterol (including LDL and HDL) and triglycerides
- Sirolimus or everolimus test: a measurement of the amount of sirolimus or everolimus (whichever medicine you take) in your blood.
- VEGF-D: a marker frequently found in the blood of patients with LAM and/or TSC
- Any remaining blood from the sample will be stored for LAM research.

- Spirometry testing (breathing test) performed before and after using a bronchodilator inhaler
- Completing questionnaires about your overall health, daily life and your sense of well-being (approximately 20 minutes to complete)

If you have tolerated the simvastatin 20mg dose without any problems, you will be given a 30-day supply of simvastatin **40** mg, which you will take each evening. You will be given a calendar to write down when you took the simvastatin each day; you will be asked to bring the calendar and the pill bottle back with you, at the next scheduled study visit.

Visit 5 (day 90) will occur one month after Visit 4. During this visit, the following tests and evaluations will be performed:

- Medical history review and a physical examination
- Review of the medications you are currently taking
- Review of any side effects you may have experienced since the last visit
- A urine pregnancy test, if there is a possibility you could become pregnant
- Four (4) tablespoons of blood will be drawn and the following tests will be performed on the blood:
    - **CBC:** a complete blood count provides important information about the kinds and numbers of cells in the blood
    - **Chemistry (CMP):** a blood test that looks at kidney function, liver function and electrolytes like potassium and calcium.
    - **CPK:** creatine phosphokinase (CPK) is an enzyme found mainly in the heart, brain, and skeletal muscle. This test will monitor the health status of muscle.

    - **Lipid Profile:** a panel of blood tests that serves as an initial broad screening tool for abnormalities in lipids, such as cholesterol (including LDL and HDL) and triglycerides
    - Sirolimus or everolimus test: a measurement of the amount of sirolimus or everolimus (whichever medicine you take) in your blood.
    - VEGF-D: a marker frequently found in the blood of patients with LAM and/or TSC
    - Any remaining blood from the sample will be stored for LAM research.
- Completing questionnaires about your overall health, daily life and your sense of well-being (approximately 20 minutes to complete)

If you have continued to tolerate the simvastatin 40mg dose without any problems, you will be given a 30-day supply of simvastatin 40 mg, which you will take each evening. You will be given a calendar to write down when you took the simvastatin each day; you will be asked to bring the calendar and the pill bottle back with you, at the next scheduled study visit.

Visit 6 (day 120) will occur one month after Visit 5. During this visit, the following tests and evaluations will be performed:

- Medical history review and a physical examination
- Review of the medications you are currently taking
- Review of any side effects you may have experienced since the last visit
- A urine pregnancy test, if there is a possibility you could become pregnant
- Four (4) tablespoons of blood will be drawn and the following tests will be performed on the blood:
    - **CBC:** a complete blood count provides important information about the kinds and numbers of cells in the blood
    - **Chemistry (CMP):** a blood test that looks at kidney function, liver function and electrolytes like potassium and calcium.
    - **CPK:** creatine phosphokinase (CPK) is an enzyme found mainly in the heart, brain, and skeletal muscle. This test will monitor the health status of muscle.
    - **Lipid Profile:** a panel of blood tests that serves as an initial broad screening tool for abnormalities in lipids, such as cholesterol (including LDL and HDL) and triglycerides
    - Sirolimus or everolimus test: a measurement of the amount of sirolimus or everolimus (whichever medicine you take) in your blood.
    - VEGF-D: a marker frequently found in the blood of patients with LAM and/or TSC
    - Any remaining blood from the sample will be stored for LAM research.

- Spirometry testing (breathing test) performed before and after using a bronchodilator inhaler
- Completing questionnaires about your overall health, daily life and your sense of well-being (approximately 20 minutes to complete)
- A chest x-ray will be performed

You will kindly bring the calendar and empty pill bottle back with you for this final study visit. You should bring the calendar and the pill bottle back with you at this last face-to-face visit.

A **telephone call** will occur one month (day 150) after Visit 6. During this call, the study coordinator will ask how you are doing, review any adverse events, and give you a chance to give feedback.

The chart below indicates which procedures are performed at each visit:

Visit number	1	2	3	4	5	6	7
Event	**Screen**	**Day 0**	**Day 30**	**Day 60**	**Day 90**	**Day 120**	**30 day follow-up**
Informed consent	X						
History and physical exam	X		X	X	X	X	
Chest X-ray	X					X	
Blood levels of sirolimus (target range 3-20 ng/mL) or everolimus (target range of 3-20 ng/ml)	X		X	X	X	X	
CBC, CPK, CMP, Lipid profile	X		X	X	X	X	
VEGF-D		X	X	X	X	X	
Saved serum and plasma from blood sample		X	X	X	X	X	
Urine pregnancy test	X	X	X	X	X	X	
Spirometry (breathing test)		X		X		X	
Review medications	X	X	X	X	X	X	
Review adverse events			X	X	X	X	X
Study drug (simvastatin) management		X	X	X	X	X	
Complete health questionnaires		X	X	X	X	X	

What are the possible risks or discomforts?

There may be unknown or unforeseen risks associated with study participation. There is also the possibility of previously unknown side effects occurring from simvastatin alone or from combining it with everolimus or sirolimus. It is important that you inform your study team should you experience any of these side effects, or any

other effects you think might be related to study treatment. You will be monitored for side effects and if indicated, treatment for the side effect will be offered.

Side effects of Simvastatin include:

More common

- Dizziness
- Fainting
- Fast or irregular heartbeat

Less common

- Bladder pain
- Bloody or cloudy urine
- Blurred vision
- Body aches or pain
- Chills
- Cough
- Dark-colored urine
- Difficult, burning, or painful urination
- Difficulty with breathing
- Difficulty with moving
- Dry mouth
- Ear congestion
- Fever
- Flushed, dry skin
- Frequent urge to urinate
- Fruit-like breath odor
- Headache
- Increased hunger
- Increased thirst
- Increased urination
- Joint pain
- Loss of consciousness
- Lower back or side pain

- Muscle cramps, spasms, or stiffness
- Muscular pain, tenderness, wasting, or weakness
- Nasal congestion
- Nausea
- Runny nose
- Sneezing
- Sore throat
- Stomachache
- Sweating
- Swelling
- Swollen joints
- Troubled breathing
- Unexplained weight loss
- Unusual tiredness or weakness
- Vomiting

Less common

- Acid or sour stomach
- Belching
- Burning feeling in the chest or stomach
- Dizziness or lightheadedness
- Excess air or gas in the stomach or intestines
- Feeling of constant movement of self or surroundings
- Full feeling
- Heartburn
- Lack or loss of strength
- Pain or tenderness around the eyes and cheekbones
- Passing gas
- Sensation of spinning
- Skin rash, encrusted, scaly, and oozing
- Stomach discomfort, upset, or pain
- Tenderness in the stomach area

- Trouble sleeping

Simvastatin has been extensively studied at the doses you will be taking during this study. Currently, simvastatin is not FDA approved for use in treating LAM and TSC patients. There has been a possibility of a slight risk of bleeding. If you take digoxin, there is a slight risk of raising your digoxin levels in your blood when taking simvastatin. (Digoxin is a type of medicine used to treat certain heart problems. Too much digoxin in your blood can be harmful or even toxic.)

Possible symptoms you may experience also include an upper respiratory infection, headache, abdominal pain, constipation and nausea. There is an increased risk of muscle weakness, including rhabdomyolysis (breakdown of muscle fibers into the bloodstream) with acute renal (kidney) failure. However, this has been seen in patients who have certain predisposing factors (such as advanced age of 65 years or older, are female, are taking Lomitapide for high cholesterol, have uncontrolled hypothyroidism, and have renal impairment) AND are taking a higher dose (80 mg) of simvastatin. The highest simvastatin dose used in this study is 40 mg.

If you wish to discuss the information above or any other discomforts you may experience, you may ask questions now or call the study doctor listed on the front of this form.

Side effects of everolimus or sirolimus have been previously discussed with you, when you starting one of these drugs, prior to enrolling in this study. Please talk to your doctor if you have any additional questions about side effects of everolimus or sirolimus.

Reproductive risks: The effects of simvastatin may result in serious harm to unborn children or children who are breast-feeding. This medication can cause birth defects. **Do not take simvastatin if you are pregnant. If you become pregnant during this study, stop taking simvastatin and tell your doctor right away.** Use effective birth control to avoid pregnancy while you are taking simvastatin. Simvastatin may pass into breast milk and could harm a nursing baby. Do not breast-feed while you are taking simvastatin.

It is also possible that harmful side effects that are not yet known could happen to both the mother and unborn or breast-feeding child. If you are currently pregnant, it is important that you inform the investigator, because you will not be able to participate in this study. If you are able to become pregnant, you will be given a urine pregnancy test before entering the study and at each study visit, to confirm you are not pregnant. You are required to use a medically accepted barrier method of birth control while you participate in the study. You should not become pregnant while you are taking simvastatin. If you **do** become pregnant, you must tell the investigator immediately and consult an obstetrician or maternal-fetal specialist immediately. You will be removed from the study promptly.

Risks of Chest x-rays: The radiation dose of a chest x-ray will be equivalent to the background radiation experienced by a person living in the Philadelphia area, over approximately an eight day period of time. The risk from this level of radiation exposure is too small to be measured directly and is considered to be very low, when compared with other everyday risks. The amount of radiation received in this study is unlikely to cause any side effects or problems.

Risks of Questionnaires: The risks of completing the questionnaires include fatigue; you may also feel that the questions are too personal. You may skip any questions you wish and may take as long as you need to complete the questionnaires. A staff member will be available to assist you.

Risks of Pulmonary Function Testing: The risk of performing a pulmonary function test is occasional shortness of breath or light-headedness. Occasionally after receiving the salbutamol, a temporary sensation of a racing heart, nervousness, or jitteriness may develop.

Risks of Blood Collection: Blood collection for laboratory tests involves removing blood from a vein with a needle. Risks associated with blood draws include soreness, bruising, and in rare instances, an infection at the site of the blood draw or fainting.

What if new information becomes available about the study?

During the course of this study, we may find more information that could be important to you. This includes information that, once learned, might cause you to change your mind about being in the study. We will notify you as soon as possible, if such information becomes available.

What are the possible benefits of the study?

If you agree to take part in this research study, there may not be a direct medical benefit for you. However, it is possible that your lung function may improve with the addition of simvastatin, but there is no guarantee. The information learned from this research study may benefit other patients with LAM or TSC in the future.

What other choices do I have if I do not participate?

You have the option of not participating in this research study. If you choose not to participate, you may continue to receive your usual medical care through the University of Pennsylvania.

Simvastatin is a commercially available drug. It is possible for you to receive this drug without participating in this study.

Will I be paid for being in this study?

You will receive a stipend (small payment) for your participation in this study. This stipend is intended to help offset any inconvenience associated with your participation in

this study. The stipend is $25 per completed study visit. In addition to the stipend, reimbursement for travel related to the study (such as gas, parking, hotel costs, etc.) is available for participants. This compensation will be made only after proper documentation has been provided to the study coordinator. Please speak with the study coordinator prior to study initiation for details, forms, and eligibility restrictions.

Will I have to pay for anything?

Study-related tests, study visits and the simvastatin drug will be provided free of charge. Tests that are performed only because of the study will be covered (paid for) by the study. These tests include the lipid panel, CPK measurement, VEGF-D, sirolimus or everolimus measurement and urine pregnancy test.

As a participant in this research study, you or your insurance company will have to pay for the costs of standard procedures (procedures or tests that are part of normal care for your condition) for your disease, that are also used as part of this the study. These include physician visits, hospital costs, physicians' fees for surgery, laboratory tests (blood counts, etc.), and radiologic studies (x-rays, CT Scans, etc.). Every effort will be made to establish which costs will or will not be covered by your insurance policy, prior to study enrollment and this information will be discussed with you.

There may be extra costs with this treatment. Some of the costs may not be covered by the study or your health insurance company. We encourage you to work closely with your insurance company, to find out exactly what is covered for this research study. You will also be responsible for any co-pays or deductibles required by your insurance company.

What happens if I am injured from being in the study?

We will offer you the care needed to treat injuries directly resulting from taking part in this research study. We may bill your insurance company or other third parties, if appropriate, for the costs of the care you get for the injury, but you may also be responsible for some of them.

There are no plans for the University of Pennsylvania to pay you or give you other compensation for an injury. You do not give up your legal rights by signing this form.

If you think you have been injured as a result of taking part in this research study, tell the investigator or study coordinator as soon as possible. The investigator and physician names and phone numbers are listed on the front of this consent form.

When is the Study over? Can I leave the Study before it ends?

This study is expected to end after all participants have completed all visits, and all information has been collected. This study may also be stopped at any time by your physician, the study Sponsor, or the Food and Drug Administration (FDA) without your consent because:

- The Principal Investigator feels it is necessary for your health or safety. Such an action would not require your consent, but you will be informed if such a decision is made and the reason for this decision.
- You have not followed the study instructions.
- The sponsor, the Principal Investigator, or the Food and Drug Administration (FDA) has decided to stop the study.

If you decide to participate, you are free to leave the study at anytime; your participation is voluntary. Withdrawing from the study will not interfere with your future care.

Who can see or use my information? How will my personal information be protected?

If you decide to participate in this study, the study doctor and staff will collect medical and personal information about you as part of completing the study. 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. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used. This study is being overseen by the Food and Drug Administration (FDA). The FDA may review your research records. Please refer to the information below, which explains more specifically how your personal information will be protected.

What information about me may be collected, used or shared with others?

The following personal health information will be collected and used for the purposes of this study.

- The history and diagnosis of your disease
- Specific information about the treatments you are receiving and previous treatment(s) you may have had and your response to them
- Medical data generated during this study- including physical exams, laboratory test results, radiology and pulmonary scan results and results of any other tests/procedures performed during the study
- Information on side effects you may experience, and how these were treated
- Other conditions that may affect your treatment
- Information related to study visits and other tests/procedures performed while you are participating in this study
- Date of birth
- Name
- Medical Record Number
- Telephone Number

You will be assigned a unique subject registration number upon enrollment. This number and your initials will be used to identify you throughout the course of this study, so that your identity is protected.

Electronic Medical Records and Research Results

What is an Electronic Medical Record?

An Electronic Medical Record (EMR) is an electronic version of the record of your care within a health system. An EMR is simply a computerized version of a paper medical record.

If you are receiving care or have received care within the University of Pennsylvania Health System (UPHS) (outpatient or inpatient) and are participating in a University of Pennsylvania research study, results of research-related procedures (i.e. laboratory tests, imaging studies and clinical procedures) may be placed in your existing EMR maintained by UPHS.

If you have never received care within UPHS and are participating in a University of Pennsylvania research study that uses UPHS services, an EMR will be created for you, for the purpose of maintaining any results of procedures performed as part of this research study. The creation of this EMR is required for your participation in this study. In order to create your EMR, the study team will need to obtain basic information about you that would be similar to the information you would provide the first time you visit a hospital or medical facility (i.e. your name, the name of your primary doctor, the type of insurance you have). Results of research procedures performed as part of your participation in the study (i.e. laboratory tests, imaging studies and clinical procedures) may be placed in this EMR.

Once placed in your EMR, these results are accessible to appropriate UPHS workforce members that are not part of the research team. Information within your EMR may also be shared with others who are determined by UPHS to be appropriate to have access to your EMR (e.g. health insurance company, disability provider, etc).

Will I be able to access my research records?

You have the right to see and get a copy of your medical records kept by the University of Pennsylvania. However, you will not be able to review or receive some of your records related to the study until after the entire study has been completed.

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 at any time.

Why is my information being used?

Your personal contact information is used by the research team to contact you during the study. Your information and results of tests and procedures are used to:

- do the research
- oversee the research
- to see if the research was done right
- to evaluate and manage research functions.

Who may use and share information about me?

The following individuals may use or disclose your personal health information for this research study:

- The Principal Investigator and the study team
- Authorized members of the workforce of the UPHS and the School of Medicine, and University of Pennsylvania support offices, who may need to access your information in the performance of their duties (for example: for research oversight and monitoring, to provide treatment as part of this study or as part of your routine care, to manage accounting or billing matters, etc.). This includes members of the Institutional Review Board (IRB), an Ethics Committee at the University of Pennsylvania, which is responsible for reviewing and overseeing research studies to ensure that they are safe and well managed.

Who, outside of the School of Medicine, might receive my information?

As part of the study, the Principal Investigator, the study team and others listed above, may disclose your study-related records, including the results of the research study tests and procedures, to those listed below. In all disclosures sent outside of the University of Pennsylvania Health System and School of Medicine, you will not be identified by name, social security number, address, telephone number, or any other direct personal identifier, unless disclosure of the direct identifier is required by law. In records and information sent outside of the University of Pennsylvania Health System and School of Medicine, you will be assigned a unique code number.

Individuals or organizations outside of Penn who might see your personal health information:

- The physician and laboratory staff at the University of Cincinnati, where some of the blood specimens will be analyzed.

Regulatory and safety oversight organizations who might see your personal health information:

- The Food and Drug Administration
- DHHS (Department of Health and Human Services)
- Other regulatory agencies and/or their designated representatives in the United States and other countries

Once your personal health information is disclosed to others outside of UPHS or the School of Medicine, it may no longer be covered by federal privacy protection regulations.

The Principal Investigator or study staff will inform you if there are any additions to the list above during your active participation in the trial. Any additions will be subject to University of Pennsylvania procedures, developed to protect your privacy.

How long may the School of Medicine be able to use or disclose my personal health information?

Your authorization for use of your personal health information for this specific study does not expire. If you sign this form, we will collect your health information until the end of the research study. We may collect some information from your medical records, even after you finish taking part in this study. We will keep all of the information forever, in case we need to look at it again. We will protect this information and keep it confidential.

Your information may be held in a research database. However, UPHS and the School of Medicine may not re-use or re-disclose information collected in this study for a purpose other than this study unless:

- You have given written authorization to do so
- The University of Pennsylvania's Institutional Review Board grants permission after ensuring that appropriate privacy safeguards are in place
- As permitted or required by law

The data from this study may be published or used for teaching purposes, but you will not be personally identified in any publication. Your identity will remain confidential, unless disclosure is required by law.

Can I change my mind about giving permission for use of my information?

You have the right to withdraw your permission for the use of your personal health information, but if you do so, you must stop taking part in this study. You must withdraw your permission in writing to the Principal Investigator, at the address on the first page. Even if you withdraw your permission, your personal health information that was collected before we received your written request may still be used and disclosed, as necessary for the study. If you withdraw your permission to use your personal health information, you will also be withdrawn from the research study and no new information will be collected.

What if I decide not to give permission to use and give out my health information?

Then you will not be able to participate in this research study.

Who can I call with questions, complaints or if I'm concerned about my rights as a research subject?

If you have questions, concerns or complaints regarding your participation in this research study or if you have any questions about your rights as a research participant, you should speak with the Principal Investigator listed on page one of this form. If a member of the research team cannot be reached or you want to talk to someone other than the study staff, you may contact the Office of Regulatory Affairs with any questions, concerns or complaints at the University of Pennsylvania by calling (215) 898-2614.

When you sign this form, you are agreeing to take part in this research study. This means that you have read the consent form, your questions have been answered and you have decided to volunteer. Your signature also means that you are permitting the University of Pennsylvania to use your personal health information collected about you for research purposes within our institution. You are also allowing the University of Pennsylvania to disclose that personal health information to outside organizations or people involved with the operations of this study.

A copy of this consent form will be given to you.

Please check 'yes' or 'no' if you would like to participate in the following options:

1. The study team would like to keep some of your blood and store it for future use. The precise tests to be performed are not known at this time, but the samples would only be used to help better understand LAM and/or TSC. If you agree to allow storage of your samples for future use, please indicate below. This is voluntary and may decide not to allow samples to be used for future use. This decision will in no way impact your care or your ability to participate in this clinical trial.

__ Yes, I agree to allow some of my blood to be stored for future use.

__ No, I do NOT agree to allow some of my blood to be stored for future use.

2. The study team would like your permission to continue to access and look at your medical records, after the study has ended. Your records may be reviewed for up to 2 years, in order to check, clarify and/or confirm information about your condition, treatment or any tests or procedures that have been done.

__ Yes, I agree to allow my medical records to be accessed and reviewed for up to 2 years after the study has ended.

__ No, I do NOT agree to allow my medical records to be accessed or reviewed after the study has ended.

3. The study team would like your permission to contact you after your participation in the study has ended. The team would contact you about other research studies for which you may qualify and want to participate.

__ Yes, I agree to be contacted regarding potential new studies, after this study has ended.

__ No, I do NOT agree to be contacted regarding potential new studies, after this study has ended.

Informed Consent Signature

_____	_____	
Name of Subject (Please Print)	Signature of Subject	Date
_____	_____	
Name of Person Obtaining Consent (Please Print)	Signature	Date