The Ohio State University Consent to Participate in Research

Study Title:	Nicotine Treatment for Pulmonary Sarcoidosis: A Clinical Trial Pilot Study
Principal Investigator:	Elliott Crouser MD
Sponsor:	National Heart Lung and Blood Institute

- **This is a consent form for research participation.** It contains important information about this study and what to expect if you decide to participate. Please consider the information carefully. Feel free to discuss the study with your friends and family and to ask questions before making your decision whether or not to participate.
- **Your participation is voluntary.** You may refuse to participate in this study. If you decide to take part in the 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 usual benefits. Your decision will not affect your future relationship with The Ohio State University. If you are a student or employee at Ohio State, your decision will not affect your grades or employment status.
- **You may or may not benefit as a result of participating in this study.** Also, as explained below, your participation may result in unintended or harmful effects for you that may be minor or may be serious depending on the nature of the research.
- **You will be provided with any new information that develops during the study that may affect your decision whether or not to continue to participate.** If you decide to participate, you will be asked to sign this form and will receive a copy of the form. You are being asked to consider participating in this study for the reasons explained below.
- ***Participation in a research study is not a substitute for medical care and does not provide free comprehensive doctor visits. You should maintain (or establish) a relationship with your primary care physician.***

1. Why is this study being done?

The purpose of this study is to determine if nicotine treatment is beneficial for the treatment of sarcoidosis. Sarcoidosis is a disease of unknown cause that leads to inflammation and affects your body's organs.

2. How many people will take part in this study?

The Ohio State University Wexner Medical Center and the Cleveland Clinic are participating in this study. About 25 subjects will be enrolled at each site for a total of 50 participants will be enrolled in this study. All participants will have evidence of sarcoidosis and active lung disease despite usual therapies for sarcoidosis.

Participants will be randomized, like a flip of a coin, to receive daily treatments with a skin patch containing nicotine or a patch containing no nicotine (placebo). The nicotine patch is

approved by the U.S. Food and Drug Administration (FDA), but its use in this study is considered investigational. You will continue to receive study medication for about 28 weeks.

Results of your medical testing will be collected to determine if nicotine treatment is helpful in terms of reducing signs or symptoms of the disease.

3. What will happen if I take part in this study?

If you choose to participate in this study, you will continue to receive care for your sarcoidosis from your pulmonologist. If you consent to take part in this research study, you will be asked to sign this consent form and will have the following tests and procedures. Some of the procedures may be part of your standard medical care (you will be billed for these procedures), but others are being done solely for the purpose of this research study (you will not be billed for these procedures).

There will be 5 visits to the clinic and 7 telephone calls as a part of this study.

The study staff can answer any questions you have about individual study visits or about the evaluations that will occur. The visits are outlined in the table below and then reviewed in detail.

Study Procedures	Screen	Entry	Week 1*	Week 2*	Week 6*	Week 10	Week 14*	Week 18	Week 22*	Week 26	Week 27*	Week 28*
Consent	X											
Randomize		X										
Vital Signs	X	X				X		X		X		
Urine Pregnancy Test	X	X				X		X		X		
Blood Draw		X				X				X		
Chest X-ray ***(if needed)***	X											
ECG **(Electrocardiogram)**	X									X		
CT Scan		X								X		
Pulmonary Function Test		X								X		
Adverse Events			X	X	X	X	X	X	X	X	X	X
Medication Review	X					X		X		X		
Questionnaires		X				X		X		X		

Visit weeks 1, 2, 6, 14, and 22 will be conducted by telephone. Approximately 1 month after week 28 you will also receive a phone call to see if you have had any nicotine dependency cravings.

Screening Visit:

This visit will occur at the clinic and will take about 2 hours to complete. At this visit, you will be asked to:

- Have your vital signs (blood pressure, weight, and height measured) taken;
- Have an electrocardiogram (ECG). An ECG is a non-invasive and painless procedure that uses temporary adhesive patches on your chest and limbs to measure the electrical activity of your heart;
- Have a chest x-ray if you have not had one done within the past year;
- Review your medications and medical history.

You will not be eligible to participate in this study if you have significant coronary artery disease.

Study Entry Visit

This visit will occur at the clinic and will take about 2 hours to complete. At this visit, you will be asked to:

- Have your vital signs taken;
- Have a brief physical exam by the study doctor;
- Have blood drawn. About 2 teaspoons (10mL) will be taken from a vein in your arm prior to you starting study medication. Nicotine and nicotine metabolites will be measured in the blood to determine if the rate of nicotine metabolism relates to the measured results from the CT scans and pulmonary function tests;
- Have a Pulmonary Function Test (PFT), a group of tests that measure how well the lungs take in and release air. Albuterol may be given after the spirometry, a common office test used to assess how well your lungs work by measuring how much air you inhale, how much you exhale and how quickly you exhale to dilate the breathing passages;
- Have a CT scan of your chest. This scan combines a series of X-ray views taken from many different angles and computer processing to create cross-sectional images of the bones and soft tissues inside your body;
- Complete questionnaires. Each questionnaire measures a different aspect of your quality of life, shortness of breath and level of stress.
- If you are a woman of childbearing age, you will be tested for pregnancy at no cost to you. This will require a urine sample. Pregnant women cannot participate in this study. If you become pregnant while participating in this study, you must inform the study doctor. If your urine pregnancy test is positive, blood will be drawn to perform a serum pregnancy test.

At this visit, you will be randomly divided into two groups. One group will receive a nicotine patch to use for approximately 7 months; the other group will receive placebo for nicotine patches to use for the same time period. You, the study doctor or the research staff will not know if you are receiving study drug or not.

You will be unable to tell if you have been assigned to receive nicotine or placebo patch treatments because they are designed to look the same. The treatment you are receiving will be revealed to you at the end of the study.

You should only wear one patch at a time. You may wear the patch from 16 to 24 hours. Apply one new patch at least every 24 hours on skin that is dry, clean and hairless. Remove backing from patch and immediately press onto skin. Hold for 10 seconds. Wash hands after applying or removing patch.

Keep the empty boxes and pouches and return everything at your next study visit.

Procedures and Evaluations While Receiving Study Medication

At regular time points during the study, you will be asked to have the following tests and procedures.

You will start your study medication at the minimum nicotine dose of 7mg. In seven days (week 1), we will call you to see how you are doing at this dose. If you are doing well, we will increase your dose to 14mg. We will then call you seven days later (week 2) to see how you are doing on the 14mg dose. If you are doing well, we will increase the dose to 21 mg. We will not increase any of these doses if you are feeling side effects that make you uncomfortable. We will also decrease the dose to the previous dose it you are feeling side effects that make you uncomfortable.

You will then be called at visit weeks 6, 14, 22, 27 and 28 to see if you have had any nicotine dependency cravings and to monitor for any side effects such as insomnia (unable to sleep), headaches, or feeling tired..

You will be asked to complete questionnaires week 10, week 18, and week 26, the final visit. It will take approximately 45 - 60 minutes at each visit to complete the questionnaires.

You will be asked to have blood taken from a vein in your arm. About 2 teaspoons of blood will be drawn at weeks 10 and 26.

If you are a woman of childbearing age, you will be tested for pregnancy by providing a urine sample. Pregnant women cannot participate in this study. If you become pregnant while participating in this study, you must inform the study doctor.

At week 26th of the study, you will start the “washout period.” This is the process of taking you off the nicotine patch at a slow pace. We will decrease the drug on a weekly basis. For example, if you are on the 21mg patch during the study your dose will be reduced to 14 mg for a week, then 7 mg, for a week, and then you will stop. If you are on 7 mg at the beginning of the washout period, you will just stop taking the drug.

4. How long will I be in the study?

You will be in the study for approximately 32 weeks.

We anticipate that study visits will take approximately 1-2 hours.

5. Can I stop being in the study?

You may leave the study at any time. If you decide to stop participating in the study, there will be no penalty to you, and you will not lose any benefits to which you are otherwise entitled. Your decision will not affect your future relationship or your medical care at The Ohio State University Wexner Medical Center.

If you choose to withdraw from the study please return any/all nicotine patches to the study research staff.

6. What risks, side effects or discomforts can I expect from being in the study?

Nicotine patch
Common side effects include:

- mild headache;
- burning at the site of application (redness, itching, and/or burning which subsides within 24 hours).

  To avoid skin irritation you should change the location of the patch each day. Please contact the study doctor if burning does not stop after 24 hours. You should not use any type of tobacco product while using nicotine patches.

Rare and less frequent side effects may include: change in sense of taste, increased coughing, mild dizziness or lightheadedness; drowsiness, dryness of mouth, menstrual pain, abdominal or stomach pain and/or gas, constipation, diarrhea, indigestion, mild loss of appetite and nausea or vomiting, muscle or joint pain, increased sweating, trouble sleeping or abnormal dreams, unusual irritability or nervousness. If you experience abnormal dreams or have trouble sleeping, you may take the patch off at night when you go to bed. A new patch must be used the next day, while the old one should be discarded.

Risk of nicotine dependence: The risk of developing dependence to nicotine is very low. Less than 1% of people that use nicotine to quit smoking develop dependency symptoms, such as cravings. The slower release of nicotine and gradual decrease in dose will reduce any craving for the drug. If cravings or other signs of dependency continue at the end of the washout period mentioned previously in this form, the study doctor will recommend tobacco cessation programs and will pay for medications.

There is little information known about nicotine patches being used on non-smokers and how it will affects people, or if they may be more likely to become dependent, however the nicotine patch has been used in a smaller study in patients with sarcoidosis. In this smaller study, the most common side effects found were skin irritation, headaches and changes in sleep quality however, these symptoms improved after several days of using the patch. None of these patients became addicted to the patch.

Blood draw: The risks of drawing blood include pain when the needle is inserted into the vein in the arm, bruising and rarely infection or fainting.

Spirometry: There is little risk from spirometry. Some people may have chest soreness or light-headedness from the hard blowing. The chest soreness usually goes away by itself, but can be relieved with non-prescription pain-relievers.

Albuterol: Albuterol is a medication that may be given after the spirometry to dilate the breathing passages. On rare occasions (less than 10 out of 192 people) it may cause nervousness, a rapid heartbeat or headache at the doses used in this study. If you

develop any of these problems, we will monitor you closely until the problem goes away (typically in 30 minutes). On rare occasions, albuterol may cause arrhythmias (the heart beats in an abnormal way) . This side effect is usually related to taking high doses of the medication and so are very unlikely to occur during this study.

ECG: After you have an ECG, you may have mild irritation, slight redness, and itching at the places on your skin where the recording patches are placed.

Questionnaires: You may be mentally tired or become stressed answering some of the questions.

CT Scan: If you take part in this research, you will have one or more medical imaging studies which use radiation. The tests you will have include two lung CT scans. The radiation dose from this research is about 11 millisievert. To give you an idea about how much radiation you will get, we will make a comparison with an every-day situation. Everyone receives a small amount of unavoidable radiation each year. Some of this radiation comes from space and some from naturally-occurring radioactive forms of water and minerals. This research gives your body the equivalent of about 4 extra year's worth of this natural radiation. The radiation dose we have discussed is what you will receive from this study only, and does not include any exposure you may have received or will receive from other tests.
A possible health problem seen with radiation exposure is the development of cancer later in life.

This extra cancer risk is higher at younger ages and for girls and women. The extra lifetime risk of dying of a fatal cancer due to the radiation exposure from this research may range from about one in 3,000 to about one in 1,000. At such low radiation exposures, scientists disagree about the amount of risk. These estimates are very uncertain, and there may be no extra risk at all. We can compare this possible extra cancer risk to other risks (over a lifetime) that everyone is subject to in everyday life. For example, the chances of a person dying of cancer with no extra radiation exposure are about one in 4. The chances of dying in a car crash are about one in 82, and the chances of being killed by a car while crossing the street are about one in 730.

X-Ray
A chest x-ray will be done if you have not had one in the past year. This involves a small amount of radiation. The radiation exposure from this research is about 200 microsievert. To give you an idea about how much radiation you will get, we will compare it to the amounts that people encounter in daily life. There is radiation that naturally occurs from space and from rocks in the soil. This natural radiation is greater at higher altitudes. This research gives you about the same amount of radiation as you would get from living in a high altitude city such as Denver for 12 days, or taking 4 airplane flights from New York to Los Angeles. The radiation dose we have discussed is what you will receive from this study only, and does not include any exposure you may have received or will receive from other tests.

A possible health problem seen with radiation exposure is the development of a second cancer later in life. This extra cancer risk is higher at younger ages and for girls and women. The extra lifetime risk of dying of a fatal cancer due to the radiation exposure from this research may range from about one in 200,000 to about one in 70,000. At such low radiation

exposures, scientists disagree about the amount of risk. These estimates are very uncertain, and there may be no extra risk at all.

We can compare this possible extra cancer risk to other risks (over a lifetime) that everyone is subject to in everyday life. For example, the chances of a person dying of cancer with no extra radiation exposure are about one in 4. The chances of dying in a car crash are about one in 82, and the chances of being killed by a car while crossing the street are about one in 730.

Confidentiality: Every possible effort will be made to keep personal information confidential. The researchers cannot guarantee absolute confidentiality. Personal information may be disclosed if required by law. In order to protect health information, data will be stored on a password protected network server and only authorized study personnel will have access to this confidential information. Information that would allow you to be identified such as name, medical record number, address, and phone number will be stored separately from the research test results and will be linked by a randomly generated identifier (a unique number assigned to the research participant).

Risks to Women of Childbearing Age: A urine pregnancy test will be repeated at each visit if subject is a female and of childbearing potential. If you become pregnant you will be asked to stop your study medication and you will be withdrawn from the study. If a urine pregnancy test is positive, you will have blood drawn for a serum pregnancy test.

7. What benefits can I expect from being in the study?

There may be no direct benefit for participation in this study. However, this study will benefit society as researchers learn more about the mechanisms that cause sarcoidosis and possible new treatments.

8. What other choices do I have if I do not take part in the study?

You may choose not to participate without penalty or loss of benefits to which you are otherwise entitled.

9. Will my study-related information be kept confidential?

The NIH issues Certificates of Confidentiality for all NIH-funded studies, including this study. This Certificate provides extra protection for you and your study information, documents, or samples (blood, tissue, etc.). The Certificates are issued so that we cannot be required to disclose any identifiable information collected about you as a part of this study in a lawsuit or legal proceeding. This is a layer of protection over and above the already existing protections in place for you and your information, documents, or samples.

However, these protections do not apply in some situations. For example, we may have to release your information if a law requires us to do so, if the NIH that is funding this study requests the information, or if the FDA tells us to release this information.

Please talk to your study team, or contact the Office of Responsible Research Practices at 614-688-8641, if you have questions.

Please visit the NIH website at https://humansubjects.nih.gov/coc/faqs to learn more.

Efforts will be made to keep your study-related information confidential. However, there may be circumstances where this information must be released. For example, personal information regarding your participation in this study may be disclosed if required by state law. Also, your records may be reviewed by the following groups (as applicable to the research):

- Office for Human Research Protections or other federal, state, or international regulatory agencies;
- U.S. Food and Drug Administration;
- The Ohio State University Institutional Review Board or Office of Responsible Research Practices;
- The sponsor supporting the study, their agents or study monitors; and
- Your insurance company (if charges are billed to insurance).

If a study procedure is related to your medical care (e.g., CT scan findings), your study-related information may be placed in your permanent hospital, clinic, or physician's office records. Authorized Ohio State University staff not involved in the study may be aware that you are participating in a research study and have access to your information.

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 the website at any time

If the study involves the use of your protected health information, you may also be asked to sign a separate Health Insurance Portability and Accountability Act (HIPAA) research authorization form.

10. What are the costs of taking part in this study?

Taking part in this study may lead to added cost to you or your insurance company if you need additional medical treatment other than that given as part of the study. The additional medical treatment is not covered by the study (for example, if you need to be hospitalized, then the costs related to this hospitalization will not be paid for by the study). You will need to check with your insurance providers regarding any additional costs.

11. Will I be paid for taking part in this study?

You will receive $50.00 for the completion of each of the five office visits (screening, entry, study visit weeks 10, 18, and 26). If you complete all required study visits, you will receive a total of $250.00. With appropriate documentation you may be reimbursed for travel costs (as needed) such as parking, lodging, and bus fare.

By law, payments to subjects are considered taxable income.

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

If you suffer an injury from participating in this study, you should notify the researcher or study doctor immediately, who will determine if you should obtain medical treatment at The Ohio State University Wexner Medical Center.

The cost for this treatment will be billed to you or your medical or hospital insurance. The Ohio State University has no funds set aside for the payment of health care expenses for this study.

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

If you choose to participate in the study, you may discontinue participation at any time without penalty or loss of benefits. By signing this form, you do not give up any personal legal rights you may have as a participant in this study. Follow-up is desired either in person or via records review should the intervention be halted. Subjects are encouraged to continue follow-up if withdrawn from interventions.

You will be provided with any new information that develops during the course of the research that may affect your decision whether or not to continue participation in the study.

You may refuse to participate in this study without penalty or loss of benefits to which you are otherwise entitled.

An Institutional Review Board responsible for human subject research at The Ohio State University reviewed this research project and found it to be acceptable, according to applicable state and federal regulations and University policies designed to protect the rights and welfare of participants in research.

14. Who can answer my questions about the study?

For questions, concerns, or complaints about the study you may contact Elliott Crouser, M.D. at 1-800-678-6495.

For questions about your rights as a participant in this study or to discuss other study-related concerns or complaints with someone who is not part of the research team, you may contact Ms. Sandra Meadows in the Office of Responsible Research Practices at 1-800-678-6251.

If you are injured as a result of participating in this study or for questions about a study-related injury, you may contact Elliott Crouser M.D. at 1-800-678-6495.

Signing the Consent Form

I have read (or someone has read to me) this form and I am aware that I am being asked to participate in a research study. I have had the opportunity to ask questions and have had them answered to my satisfaction. I voluntarily agree to participate in this study.

I am not giving up any legal rights by signing this form. I will be given a copy of this form.

Printed name of subject	**Signature of subject** **AM/PM** **Date and time**
Printed name of person authorized to consent for subject (when applicable)	**Signature of person authorized to consent for subject (when applicable)** **AM/PM**
Relationship to the subject	**Date and time**

Investigator/Research Staff

I have explained the research to the participant or his/her representative before requesting the signature(s) above. There are no blanks in this document. A copy of this form has been given to the participant or his/her representative.

Printed name of person obtaining consent	**Signature of person obtaining consent** **AM/PM** **Date and time**

Witness(es) - *May be left blank if not required by the IRB*

Printed name of witness	**Signature of witness** **AM/PM** **Date and time**
Printed name of witness	**Signature of witness** **AM/PM** **Date and time**