PARTICIPANT INFORMED CONSENT FORM AND AUTHORIZATION TO USE AND DISCLOSE MEDICAL INFORMATION

STUDY TITLE: Effects of rifaximin (Xifaxan®) on chronic prostatitis

PRINCIPAL INVESTIGATOR: Leonard B. Weinstock, M.D.

TELEPHONE: 314-997-0554 (weekdays)
314-388-6578 (at night or weekends)

SPONSOR: Leonard Weinstock, MD

You are being asked to participate in a medical research study. Your participation in this research study is strictly voluntary, meaning that you may or may not choose to take part. To decide whether or not you want to be part of this research, the risks and possible benefits of the study are described in this form so that you can make an informed decision. This process is known as informed consent. This consent form describes the purpose, procedures, possible benefits and risks of the study. This form also explains how your medical information will be used and who may see it. You are being asked to take part in this study because the study doctor feels that you meet the qualifications of the study. You may have a copy of this form to review at your leisure or to ask advice from others.

The study doctor or study staff will answer any questions you may have about this form or about the study. Please read this document carefully and do not hesitate to ask anything about this information. This form may contain words that you do not understand. Please ask the study doctor or study staff to explain the words or information that you do not understand. After reading the consent form, if you would like to participate, you will be asked to sign this form. You will be given a signed copy of your consent to take home and keep for your records.

WHY IS THIS STUDY BEING DONE?
You are being asked take part in this study because you have been diagnosed with chronic prostatitis (CP) by your urologist and continue to have symptoms. CP is prostate condition that can cause pain, urinary frequency and urgency when no other urological diseases are present. The symptoms of CP vary from person to person but may include discomfort, pressure, tenderness or intense pain in the bladder and surrounding pelvic area. Since no cause of CP is currently known, it has not been possible to direct treatment of this condition to a target. As a result, treatments for CP are not effective. Better understanding of CP is important because the identification of the cause of this disorder may lead to improved treatment of this condition.

This study is being done because we think an abnormality of the intestine may be responsible for CP. Specifically, we believe that small intestinal bacterial overgrowth (SIBO) may be a cause of CP. Normally, the large intestine is home to a large number of bacteria with much of the small intestine free of bacteria. In SIBO, there is growth of these friendly bacteria from the large to the small intestine. Since the small intestine has an “alarm system” to respond to bacteria, SIBO triggers the immune response of the patient (an alarm response) to generate symptoms similar to that seen in flu or a cold. Just like the aches and pains of flu, the immune response to SIBO may be detectable in the blood or urine and may cause the symptoms found in CP. We have recently shown a link between SIBO and irritable bowel syndrome (IBS), a disorder of the gastrointestinal tract that has similar symptoms and inflammatory chemical changes as in CP.

Rifaximin (Xifaxan®) is a FDA-approved antibiotic for the treatment of traveler's diarrhea. Xifaxan® has been reported to be highly effective against SIBO. Xifaxan® is not approved for the treatment of CP; therefore its use in this study is investigational.

The purpose of this study is:

1) To determine if overgrowth of bacteria in the small intestine is associated with CP
2) To determine if Rifaximin (Xifaxan®) will reduce the symptoms of CP and gastrointestinal symptoms

About 20 men ages 18 and older will take part in this study.

WHAT IS INVOLVED IN THE STUDY?

Your participation in this study will last for approximately 1 month, and will involve two clinic study visits and three telephone calls.

If you agree to participate and are eligible for the study, you will be given Rifaximin (Xifaxan®) 550 mg three times a day for 10 days

STUDY PROCEDURES

The night before you come to the clinic for the first study visit, you will be asked to:

- Eat a light dinner (a lunch sized meal with no beans)
- Not eat anything after midnight
- Not smoke cigarettes that morning

At the first visit, you will be given an informed consent document (this document) prior to any study procedures. Before signing the informed consent to participate in the study, the details and potential risks will be fully explained to you and any questions you may have will be answered. If you agree to participate in the study you will sign the document and receive a copy for your records. There are 2 clinic visits and each should take about 3 hours to complete.

Part A

<u>One Day Prior to Each Clinic Visit:</u> Participants will be asked to do the following prior to each clinic visit: 1) eat a light dinner with steamed rice as the only source of starch; 2) to refrain from eating or drinking beginning midnight the night; 3) do not have candy or gum with artificial sugars and 4) not smoke cigarettes that morning.

Clinic Visit #1:

After you have signed the informed consent document, you will have the following procedures performed to determine if you are eligible to participate in the study:

1) You will be interviewed to see if you fulfill all of the clinical criteria to be allowed into the study.

2) If you fulfill all of the criteria and do not have criteria that exclude you from participating

in the study then you will have a lactulose breath test. This test will take approximately 3 hours to complete. For this test, you will drink a liquid containing lactulose (a non-digestible sugar). If there is bacterial overgrowth in the small intestine, the lactulose will ferment, producing the gases hydrogen and methane. The breath test involves blowing into bag via a mouthpiece and then a breath sample is obtained. The breath samples will be analyzed for hydrogen and methane using a special machine. The lactulose breath test must be abnormal for you to be eligible for this research study. A tuberculosis skin test will be applied during the first clinic visit and this will need to be negative to continue with the study.

3) You will fill out questionnaires about your medical history and current symptoms. You may fill out the questionnaires during the lactulose hydrogen breath test.

4) You will be given a 10-day supply of Xifaxan which you will take at the dose of 550 mg (one pill) three times a day.

Part B

Clinic Visit 2 (Day 12-14 with Day 1 as the start of treatment)

1) You will have a second lactulose hydrogen breath test performed.
2) You will receive 2 set of questionnaires and addressed stamped envelopes to be filled out and mailed back to the clinic.

Part C

On Day 17- you will fill in the questionnaires and mail them in to the clinic.

Part D

On Day 30- you will fill in the questionnaires and mail them in to the clinic.

WHAT ARE THE POSSIBLE RISKS AND DISCOMFORTS?

While on the study, you may be at risk for certain side effects. The study doctor will review these with you and you should discuss them with your regular doctor. There also may be other side effects that we cannot predict.

Lactulose Breath Test

The lactulose mixture used in the lactulose hydrogen breath test is likely to result in some bloating and gas. In some cases, diarrhea may result for a short period of time.

Rifaximin (Xifaxan)

Side effects are possible with any drug and you might experience some side effects during this study. In previous studies and during patient care, side effects associated with the use of Rifaximin (Xifaxan) have included, but may not be limited to, abdominal pain, difficulty having bowel movement (stool), fever, flatulence (gas), headache, nausea, rectal pain, urgent need to have a bowel movement (stool), and vomiting. There is risk of developing resistance to anti-tuberculosis therapy.

Allergic Reaction
Rare or unknown side effects could occur, including life-threatening reactions. As with any drug, it is possible that you could experience an allergic reaction to the study drug or the rescue medication (if taken). Allergic reactions, such as itching, skin rash, facial swelling, an acute or sudden drop in blood pressure, may lead to shock with loss of consciousness and/or possible seizures, including the possibility of death. If an allergic reaction is severe, seek medical attention immediately.

WHAT ARE THE POSSIBLE BENEFITS OF TAKING PART IN THIS STUDY?
If you agree to take part in this study, there may or may not be direct medical benefit to you. Your participation in this study will provide information that may benefit other patients with CP in the future.

WHAT OTHER OPTIONS ARE THERE?
You do not have to participate in this study to get medical treatment for CP. Xifaxan is an antibiotic which can be prescribed by your doctor. Below are some of the drugs and other therapies outside the study that may be available to treat CP.

Current treatment of CP includes the antidepressant amitriptyline and Elmiron® (100 mg pentosan polysulfate sodium capsules), and broad spectrum absorbed antibiotics. This is not a complete list of potential therapies and medication. The effectiveness and side effects of these and other treatments may be different for different people. You may ask the investigator for more information about your condition and the possible benefits and risks of other available therapies, including no treatment at all.

WILL YOUR INFORMATION BE KEPT PRIVATE?
The study doctor and the Institutional Review Board (IRB) will keep your records for this study private as far as the law allows. We may publish the information from this study in journals or present it at meetings. If we do, we will not use your name. Confidentiality will be maintained by assigning you a code number and keeping the list linking your name with your code number separate from the research results. The research results will be kept in locked filing cabinets. Only the investigator and research assistants will have access to them.

WHAT ARE THE COSTS?
There are no costs to you for participating in this study. Neither you nor your insurance company will be billed for your taking part in this study. The study drug will be provided to you at no charge.

ARE THERE ANY PAYMENTS TO YOU FOR TAKING PART IN THE STUDY?
You will not be paid for participating in this study.

WHAT HAPPENS IF YOU GET INJURED OR NEED EMERGENCY CARE?
You are participating in this study under the supervision of Leonard B. Weinstock, M.D. All of the study procedures will be performed at the Dr. Weinstock's office. If you get hurt or sick from participating in the study, you will be offered treatment for the injury. If the injury is from the study medication or procedures performed or directed by Dr. Weinstock of his staff, we will give you the medical care you need. You will have to pay for this care.

WILL YOU RECEIVE NEW INFORMATION ABOUT THIS STUDY?
During the study, we may learn new things about the risks or benefits of being in the study. If we do, we will share this with you. You might change your mind about being in the study based on this information. If new information is provided, you may be asked to sign a new Consent Form.

UNDER WHAT CIRCUMSTANCES CAN YOUR PARTICIPATION BE TERMINATED?
If you do not follow the study doctor's instructions or if your condition gets worse, you may be removed from this study. If this happens, the study doctor will discuss other options with you.

WHAT ARE YOUR RIGHTS AS A PARTICIPANT, AND WHAT WILL HAPPEN IF YOU DECIDE NOT TO PARTICIPATE?
Your participation in this study is voluntary. Your decision whether or not to take part will not affect your current or future care at this institution. You are not waiving any legal claims or rights. If you do decide to take part in this study, you are free to change your mind and stop being in the study at any time.

ARE THERE ANY POTENTIAL CONFLICTS OF INTEREST?
This study is initiated by Drs. Weinstock and not by a drug company. Dr. Weinstock is on the Speaker Bureau of Salix Pharmaceuticals (the drug company that makes Xifaxan®).

WHOM DO YOU CALL IF YOU HAVE QUESTIONS OR PROBLEMS?
If you have any questions about this study, or if you need to report a research-related injury, you should contact Dr. Weinstock at 314-997-0554 week days or 314-388-6578 at night or weekends.
If you have questions regarding your rights as a participant in a research study, you may contact Sally P. Green, M.D., Chairman of Sterling Institutional Review Board, 6300 Powers Ferry Road, Suite 600-351, Atlanta, Georgia 30339 (mailing address) at telephone number 1-888-636-1062 (toll free).

AGREEMENT
I have read (or someone has read to me) the information provided above. I have been given a chance to ask questions. All my questions were answered. I have decided to sign this form in order to take part in this study.

Name of Participant _____

_____ _____
Signature of Participant Date

I have personally explained the research to the subject and answered all questions. I believe that he/she understands the information described in this informed consent and freely consents to participate.

Name of Investigator / Person Explaining Consent Form _____

_____ _____
Signature of Investigator/ Person Explaining Consent Form Date *(same date as above)*

Subjects initials _____

Information from Air Samples Collected as Part of This Research:

During the course of this study, you will not be given the results of research testing. This includes results of the lactulose hydrogen breath test. However, you may receive specific information about your test results and general information about what was learned from the study after the study has been completed. Please indicate below which information you would like to receive. If you change your address and/or telephone number, you should contact Dr. Weinstock or a member of the study staff at telephone number

_____.

I would like to receive specific information about my test results from this study.

Yes / No (Circle one) Initials _____

I would like to receive general information about what was learned from the study.

Yes / No (Circle one) Initials _____

CONFIDENTIALITY AND AUTHORIZATION TO COLLECT, USE AND DISCLOSE YOUR MEDICAL INFORMATION

As a part of this research, we will collect and use records that contain information or data about you and your health. These records may identify you and will be kept as confidential as possible. This is required by law.

Under the privacy laws, you have the right to decide who can use your personal health information (called PHI).

When you sign this form, you are saying that you will allow the use of your information for this study.

The Information that may be collected about you as a part of this research includes:

Name, Address, Telephone number, Birth date, Race, Sex, Social security number, Family medical history, Allergies, Medications, Information from the examinations done by the study doctor, Results of tests and procedures you have for the study, Other information from other doctor's offices, clinics, hospitals that is needed for the research

Information collected about you for the research study will be kept in a research file that is separate from your medical chart. You will not be able to see your research file until after the end of the study.

The study team will know your identity. However, they may label your records with your initials or a code assigned to you. The research staff are the only people who will have this code and it's key.

The following groups may review and use your information. They will review the study information to make sure it is correct. They will also review how the doctor(s) and study team completed the study to make sure they conducted the study correctly. These people include: The U.S. Food and Drug Administration, The Institutional Review Board, The Department of Health and Human Services, Other government agencies in other countries, other doctors and health care professionals who are involved in the study.

We need to release your information to the groups listed above. If your health information is reviewed by these people, they may need to see your entire medical record. Because of this, we cannot promise your privacy will always be protected. It is possible that your information will be shared (re-disclosed) in a way that it would no longer be protected.

Your information may also be presented at meetings or in articles written about the study (publications). You will not be identified by name in any presentation or publication that uses your research or health information.

This permission (also called an authorization) will expire on December 31, 2056. However, you may take away (withdraw) your permission for us to use your health information at any time. If you choose to take away your permission, you must write your study doctor a letter.

The study doctor's mailing address is 11525 Olde Cabin Road, St. Louis, MO 63141. The research study doctor will still be able to use the information collected about you before you withdrew your permission. Information that has already been sent to the Sponsor of the research study cannot be taken back.

If you withdraw your permission after you have entered the study, you will be discontinued from the research study.

If you do not give permission to use your health information, you cannot be in this research study. If you refuse to give permission, your medical care or your relationship with the health care providers at 11525 Olde Cabin Road, St. Louis, MO 63141 will not be affected.

_____ _____
Signature of Participant Date

_____ _____
Signature of Person Obtaining Authorization Date

EXPERIMENTAL SUBJECT'S BILL OF RIGHTS

STUDY TITLE: Effects of rifaximin (Xifaxan®) on chronic prostatitis

INVESTIGATORS: Leonard B. Weinstock, M.D.

Any person who is requested to consent to participate as a subject in a research study involving a medical experiment, or who is requested to consent on behalf of another, has the right to:

1. Be informed of the nature and purpose of the experiment.

2. Be given an explanation of the procedures to be followed in the medical experiment, and any drug or device to be used.

3. Be given a description of any attendant discomforts and risks reasonably to be expected from the experiment.

4. Be given an explanation of any benefits to the subject reasonably to be expected from the experiment, if applicable.

5. Be given a disclosure of any appropriate alternative procedures, drugs, or devices that might be advantageous to the subject, and their relative risks and benefits.

6. Be informed of the avenues of medical treatment, if any, available to the subject after the experiment if complications should arise.

7. Be given an opportunity to ask any questions concerning the experiment or other procedures involved.

8. Be instructed that consent to participate in the medical experiment may be withdrawn at any time, and the subject may discontinue participation in the medical experiment without prejudice.

9. Be given a copy of a signed and dated written consent form when one is required.

10. Be given the opportunity to decide to consent or not to consent to a medical experiment without the intervention of any element of force, fraud, deceit, duress, coercion, or undue influence on the subject's decision.

_____ _____

Signature of Subject Date

_____ _____

Signature of Person Explaining Consent Date