INFORMED CONSENT TO PARTICIPATE IN A RESEARCH STUDY

Participant

Principal Investigator  Weinstock, Leonard  MD
Last  First  Credentials

PI’s Phone Number  (314) 997-0554

Title of Project:  Effects of a Treatment Regimen Containing Rifaximin On Restless Leg Syndrome Patients With Abnormal Lactulose Breath Tests

You are invited to take part in a research study by Dr. Weinstock.

Please ask for an explanation of any words you do not understand.

You may want to talk about the study with your family or friends before you decide to be in it.

1. **Why is this study being done?**
   The purpose of this study is to determine if having too many bacteria in the small intestine is related to restless legs syndrome, and if killing some of the bacteria with the antibiotic Xifaxan will improve symptoms in people with RLS.

   Xifaxan is an antibiotic already approved by the Food and Drug Administration (FDA) for treatment of patients 12 and older with travelers’ diarrhea caused by noninvasive strains of *Escherichia coli* (e. coli). Xifaxan is experimental, not approved by the FDA, in treating patients with RLS who have an abnormal (positive) lactulose breath test.

   You can be eligible for the study if your breath test is positive. A positive recording indicates that there is bacterial overgrowth in your small intestines. This overgrowth can cause an increase level of hydrogen or methane gas in your breath. The doctors are going to measure readings of hydrogen and methane gas that is produced. If the hydrogen or methane gas value is increased by greater than 20 ppm (parts per million) from your first (baseline) value, this would be considered a positive test for bacterial overgrowth.

2. **What am I being asked to do?**
   You have been asked to participate because you have been diagnosed with RLS. Should you agree to participate and have signed this consent, you will come to the office of Specialists in Gastroenterology in Creve Coeur for up to 2 outpatient visits and 2-3 telephone contacts.

   The first visit is a screening visit. During the screening visit, medical tests will be performed. They include a complete medical history and physical, questionnaires, and a blood draw. You will be asked questions about tuberculosis (TB). If you have tested positive in the past you may not need to have a TB test, please notify the staff. Otherwise, you will need to have a TB test to make sure you do not have TB.

   You will have about two (2) tablespoons of blood drawn from your vein once at the screening visit. Blood testing for hemoglobin and iron studies will be done on the first session. If you are of child-bearing age, a urine sample will also be tested for pregnancy at visit #1.
If you meet the criteria for RLS, you will receive a lactulose breath test (LBT). The breath test takes 3 hours to complete and you will have to follow dietary instructions before each test. This appointment and the instructions will be provided to you before you set up the screening visit.

For the LBT you will drink lactulose sugar in 8 ounces of water over one or two minutes. Starting after the lactulose is taken, breath samples will be taken every 20 minutes for 3 hours. The samples will be collected by having you breathe into a small bag. The technician or coordinator will collect the bag. This will help determine if you will continue forward in the study. This procedure will be performed at the first and second visit if the first was abnormal. If the first test result is abnormal you will go ahead with the study as described below. If the test is negative, you will no longer need to complete any other testing. The study will end after the first visit for you.

If the breath test is negative you may choose to be treated with standard RLS treatment, which is based upon medical treatment and may include iron supplementation or long-term drug treatment designed for relief of the symptoms of RLS. These may include drugs that are dopamine-agonists such as ropinirole (Requip®), pramipexole (Mirapex®), or other dopamine agents. Dopamine-agonists are drugs that affect a neurotransmitter (dopamine), which is a chemical reaction in the brain.

If the breath test is positive, you will be randomized (like flipping a coin) to either the active drug or placebo (a sugar pill) for 10 days. A placebo is a substance that looks like the study drug, but does not affect you. We are using a placebo in this study so that you will not know when you are receiving the drug. This way, the results of the study will be fair. The placebo pills will look the same as the active pills.

If you are taking medication for your RLS symptoms, you may continue to take your same dose of medicine during the entire study. We ask that you not change your medication doses without notifying the research staff.

You will be contacted by phone from a coordinator from the office, which will be on day 17 and day 24 of the study to ask you questions related to your RLS symptoms. These phone calls should take about 15 minutes or less.

You may be able to continue on this drug after the trial is over – this would be arranged through a routine office visit and doctor-patient relationship with Dr. Weinstock.

**How long will I be in the study?**
You will be in the study for up to 24 days.

3. **What are the Costs?**
Doctor visits and medications are free to you and your insurance company while you are in the study. The costs of the routine blood tests and the breath tests will be charged to your insurance if it is allowed by the company. Your insurance company will be billed for some of the study procedures performed as part of this research study (laboratory work for blood samples and the breath test). It is possible that your insurance company will not pay for these expenses. You should check with your insurance company to see if they will cover these costs of your participation in a research study."

4. **What are the Risks?**
All of these risks are related to the research study. There are no procedures or tests that are being done that are standard of care for RLS.

**As related to the lactulose breath test (LBT) for research purposes:**
**Likely:** Diarrhea, abdominal discomfort, gas and bloating. These can last 1-2 hours after taking the lactulose and are more likely to occur if you have a positive breath test, which reflects bacterial overgrowth.

**As related to the research portions of the study which includes blood testing and medication:**

**Likely:**
- **Blood draw:** The blood draw may cause bleeding, bruising, or pain. Some people become dizzy or feel faint. If you have had dizziness or fainting in the past, please tell the person drawing your blood. You may lie down during the blood drawing procedure. There may also be a small chance of infection at the site of the blood draw.

**Medication:** Gas (flatulence), headache, abdominal pain, urge to have a bowel movement, nausea, vomiting, and constipation.

**Less likely:**
- **Medication:** You will only be taking this medication for 10 days and these risks are not likely to develop and should resolve once you stop taking the antibiotic:
  - abnormal blood counts including low blood counts, ear pain, motion sickness, ringing in the ears, diarrhea, dry, sore or painful throat, stool abnormality, dry lips, stomach discomfort and bloating, chest pain, fatigue and weight, pain, respiratory tract infection, sunburn, increase in aspartate aminotransferase level which is a liver test, blood in stool, blood in urine, weight decreased, anorexia, dehydration, bone pain, muscle spasms and muscle aches, neck pain, abnormal dreams, dizziness, migraines, fainting, loss of taste, trouble sleeping (insomnia), too much bile in your urine, painful urination, too much protein in your urine, urinary frequency, shortness of breath, runny nose, nasal congestion, nasal irritation and swelling, clamminess and increased sweating, swelling, rash, hives and itching, hot flashes.

Some of the questions in the questionnaires may make you uncomfortable. If this happens, please talk to the study coordinator. You may choose not to answer any question that makes you feel uncomfortable. We will contact you at the telephone number you provide to us when you begin the study.

Another potential risk of participating in this study is that confidential information about you may be accidentally disclosed. We will use our best efforts to keep the information about you secure, and we think the risk of accidental disclosure is very small. Please see the *Confidentiality* section of this consent form for more information.

Participation in this study may cause all or some of the side effects listed above which, if severe, may cause death. Your condition may not improve or may worsen while participating in this study.

You may experience all or some of the risks listed above. The PI will answer any questions you have about these risks.

### Pregnancy/Childbearing Potential

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<th>If you are a woman of childbearing potential, please read and sign below.</th>
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Some parts of this study might cause physical or mental problems in an unborn baby. If you become pregnant, taking part in this study may involve risks to your unborn baby that are unknown. You must tell the doctor immediately if there is any chance you are pregnant. You must also tell the doctor if your birth control method fails while you are on the study.

To take part in this study, you must have a pregnancy test before starting the study. You must use an acceptable medical method of birth control and must not become pregnant. Birth control pills are not acceptable. You must be willing to use a barrier method during the study.
By signing below, you agree to follow these rules.

You must tell the study doctor if you are breast-feeding.

Treatments in this study may disqualify you from other research studies.

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

Dr. Weinstock and his staff will try to reduce, control, and treat any complications from this research. If you feel you are injured because of the study, please contact the Investigator and/or the Human Studies Chairperson from Item 8.

5. **Are there Benefits to taking part in the study?**

Taking part in this study may or may not benefit you directly. It may or may not help your RLS symptoms. The study may benefit others with RLS.

6. **What other Options are there?** Taking part in this research study is voluntary. You may choose not to take part in this research study or you may withdraw your consent at any time. Your choice will not at any time affect the commitment of your health care providers to administer care. There will be no penalty or loss of benefits to which you are otherwise entitled. Other than not taking part in the research, you may be given iron supplements, or long term drug treatment for RLS symptom relief. These may include drugs that are dopamine-agonists such as ropinirole (Requip®), pramipexole (Mirapex®), or other dopamine agents.

7. **What about Confidentiality?**

Protected Health Information (PHI) is health information that identifies you. PHI is protected by federal law under HIPAA (the Health Insurance Portability and Accountability Act). To take part in this research, you must give the research team permission to use and disclose (share) your PHI for the study explained in this consent form.

In addition to health information that may be created by the study, the research team may access the following sources of your health information to conduct the study:

- Medical records
- Clinical records
- Biological specimens
- Questionnaires
- Downloaded information from actigraphy watch

**The research team will follow state and federal laws and may share your information with:**

- Government representatives, to complete federal or state responsibilities
- Hospital representatives, to complete Hospital responsibilities
- Your primary care physician if a medical condition that needs urgent attention is discovered

Once your health information is shared with someone outside of the research team, it may no longer be protected by HIPAA.

The research team will only use and share your information as talked about in this form. When possible, the research team will make sure information cannot be linked to you (de-identified). Once information is de-identified, it may be used and shared for other purposes not discussed in this consent form. If you have
questions or concerns about your privacy and the use of your PHI, please contact Paula Willis, the Privacy Officer, at 314-997-0554.

Your research record will be kept separately and will not be kept with your medical records. You will not have access to your research record.

**If you decide not to sign this form, it will not affect**
- your treatment or the care given by your health provider.
- your insurance payment or enrollment in any health plans.
- any benefits to which you are entitled.
However, it will not be possible for you to take part in the study.

**If you sign this form:**
- You authorize the use of your PHI for this research
- Your signature and this form will not expire as long as you wish to participate.
- You may later change your mind and not let the research team use or share your information (you may revoke your authorization).
  - To revoke your authorization, send a letter stating so to Specialists in Gastroenterology.

  - **If you revoke your authorization:**
    - The research team may only use and share information already collected for the study.
    - Your information may still be used and shared if necessary for safety reasons.
    - You will not be allowed to continue to participate in the study.

Please specify any contact restrictions you want to request for this study only.
(Example – no calls at home, no messages left for you, no –emails, etc.)

____________________________________________________________________________________

**Notice of Privacy Practices**
The Notice of Privacy Practices is a separate document. It describes the procedures used by Specialists In Gastroenterology to protect your information. If you have not already received the Notice of Privacy Practices, the research team will make one available to you.

I have been offered a copy of the Notice of Privacy Practices.

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8. **Who do I call if I have Questions or Problems?**
If you have any questions, concerns or complaints about the study, or feel that you are injured because of the study call Dr. Leonard Weinstock at 314-997-0554 or after hours at 314-388-6578. If you wish to talk to someone else, or have questions or concerns about your rights as a research subject, call the Chairman of the Sterling Institutional Review Board, at (888) 636-1062.
9. The Principal Investigator (PI) may withdraw you from the study without your consent if considered appropriate. For safety, it may be in your best interest to allow follow-up outside the study. The PI will share any new information that could change how you feel about continuing in the study.

10. Being in a research study does not take the place of routine physical exams or visits to your own doctor and should not be relied on to diagnose or treat medical problems.

I have read this consent form and have been given the chance to ask questions. I will also be given a signed copy of this consent form for my records. I give my permission to participate in the research described above, titled: Effects of a Treatment Regimen Containing Rifaximin on Restless Leg Syndrome Patients with Abnormal Lactulose Breath Tests

Participant’s Signature or Legally Authorized Representative  Date       Signature of person providing Informed Consent  Date

Relationship to Participant

Thank you for your important contribution to research studies that are trying to improve medical care.

Please mark all that apply. This section is optional.

[] Not Hispanic or Latino  [] Hispanic or Latino  [] Unknown

[] Asian  [] Black or African-American  [] Caucasian  [] Native American or Alaskan Native  [] Native Hawaiian or Pacific Islander  [] Other  [] Unknown

The Office of Management and Budget has declared that Hispanic/Latino is an ethnicity. National Institutes of Health, in an effort to ensure diversity in research, requests that you report your ethnicity. (http://grants.nih.gov/grants/funding/women_min/women_min.htm)