

UNIVERSITY OF MICHIGAN CONSENT TO BE PART OF A RESEARCH STUDY

INFORMATION ABOUT THIS FORM

You may be eligible to take part in a research study. This form gives you important information about the study. It describes the purpose of the study, and the risks and possible benefits of participating in the study.

Please take time to review this information carefully. After you have finished, you should talk to the researchers about the study and ask them any questions you have. You may also wish to talk to others (for example, your friends, family, or other doctors) about your participation in this study. If you decide to take part in the study, you will be asked to sign this form. *Before you sign this form, be sure you understand what the study is about, including the risks and possible benefits to you.* This study has been reviewed and has received approval from the IRB.

1. GENERAL INFORMATION ABOUT THIS STUDY AND THE RESEARCHERS

1.1 Study title: A Double-blind Placebo-controlled Cross-over Study in Fibromyalgia Subjects to Examine Effects of Pregabalin on Brain response to Mechanical Pain as assessed by Functional Magnetic Resonance Imaging, Proton Magnetic Resonance Spectroscopy, and Subjective Ratings

1.2 Company or agency sponsoring the study:

Pfizer

1.3 Names, degrees, and affiliations of the researchers conducting the study:

PI: Richard E. Harris, Ph.D., Research Assistant Professor, Department of Anesthesiology, University of Michigan

Co-I: Daniel J. Clauw, M.D., Professor, Department of Anesthesiology, University of Michigan

Co-I: Sawsun (Susie) As-Saine, M.D., Department of Obstetrics and Gynecology, University of Michigan

2. PURPOSE OF THIS STUDY

2.1 Study purpose:

The aim of the present study is to measure the effects of pregabalin, an analgesic, or pain-reducing medicine, on pain processing and on the pattern of brain activation in patients with fibromyalgia. We

will use two brain imaging methods called functional magnetic resonance imaging (fMRI) and proton magnetic resonance spectroscopy (H-MRS) to look at your brain's response to pregabalin. In addition to pregabalin capsules you will also take a placebo capsule (this capsule is a dummy capsule that contains no active medicine). You will receive both treatments during the course of the study. Pregabalin has been FDA-approved for treatment of pain nerve pain, epilepsy and fibromyalgia.

3. INFORMATION ABOUT STUDY PARTICIPANTS (SUBJECTS)

Taking part in this study is completely **voluntary**. You do not have to participate if you don't want to. You may also leave the study at any time. If you leave the study before it is finished, there will be no penalty to you, and you will not lose any benefits to which you are otherwise entitled.

3.1 Who can take part in this study?

To take part in the study, *you must*:

- 1) Meet established criteria for the diagnosis of fibromyalgia (FM) as defined by the American College of Rheumatology in 1990. These criteria are widespread pain (above and below the waist, on both sides of the body, and in the neck, back or chest) for at least 6 months and the presence of 11 of 18 tender points in specified areas.
- 2) Be between the ages of 18 and 70.
- 3) Have a negative pregnancy test at screening, if you are of child-bearing age, and must be willing to use an appropriate method of contraception during participation in this study.
- 4) Be female.
- 5) Be right-handed.
- 6) Be capable of giving written informed consent.
- 7) Have a Body Mass Index (BMI) that is compatible with MRI scanner requirements less than 36k/m².
- 8) Your fibromyalgia pain must fall within the established limits of the study.
- 9) Willing and able to comply with scheduled visits, treatment plan, laboratory tests, and other trial procedures.

You *may not* take part in the study if any of the following items apply to you:

- 1) Presence of concurrent heart, lung, kidney, neurological, gastrointestinal or liver disease or abnormal function.
- 3) Severe psychiatric illnesses (e.g., current schizophrenia, major depression with suicidal tendencies, drug or alcohol abuse within two years).
- 5) Presence of a concurrent autoimmune or inflammatory disease (e.g., rheumatoid arthritis, systemic lupus erythematosus, inflammatory bowel disease, diabetic peripheral neuropathy, post-hepatic neuralgia, etc.) that causes pain.
- 6) An abnormal laboratory (blood, urine, or ECG) value that would prevent you from participating in this study.
- 7) Patients with pending litigation or disability assessments regarding your fibromyalgia.

- 8) You have metal implants, surgical staples, pacemakers or claustrophobia or any other factor sufficiently significant that it is likely to prevent successful completion of fMRI scans.
- 9) Subjects who use a copper-containing intrauterine device (IUD) or transdermal contraceptive patches.
- 10) Previous experience with pregabalin that did not result in pain relief.
- 11) Presence of any condition possibly affecting drug absorption (e.g., gastrectomy).
- 12) A positive urine drug screen for drugs of abuse.
- 13) Treatment with an investigational drug within 30 days prior to the first dose of medication in this study.
- 14) You are pregnant or nursing.
- 15) Patients unwilling to discontinue use of prescribed opioid medications, sedatives, or tranquilizers during the course of the study.
- 16) Known allergy to pregabalin or gabapentin
- 17) Subjects with active malignancy of any type or a history of a malignancy (with the exception of subjects with malignancy surgically removed with no evidence of recurrence within 2 years enrollment and subjects with a history of treated basal cell carcinoma).
- 18) Acetaminophen taken prior to scanning on the day of the imaging visits. (Visit 3-6)
- 19) Subjects with difficulties swallowing capsules or unable to tolerate oral medication.
- 20) Subjects unwilling or unable to comply with study requirements.

3.2 How many people (subjects) are expected to take part in this study?

24 subjects are expected to be enrolled in this study at the University of Michigan.

4. INFORMATION ABOUT STUDY PARTICIPATION

4.1 What will happen to me in this study?

If you agree to participate in this study and sign this consent form, you agree to participate in all of the following activities to the best of your ability.

Screening (Visit 1; Days -14 to -1) will include the following:

- Informed consent will be obtained, including determination of your eligibility for the study.
- A medical history and brief physical exam as well as height and weight, blood pressure and pulse, an ECG (electrocardiogram) and urine and blood tests to assess your general health including urine to test for drugs of abuse.
- Calculation of your BMI (Body Mass Index) to make sure it will be safe for you to have a MRI.
- Blood, urine and ECG tests are for purposes of drug safety screening to confirm that it is safe for you to take pregabalin and to confirm your eligibility for the study (including a negative pregnancy test) as outlined in the eligibility criteria in section 3.1 above.
- A tender point exam as part of the diagnostic criteria for fibromyalgia, during which a researcher will apply pressure with his/her thumb to specific points on your body. You will tell the researcher whether the pressure results in pain or tenderness. You will rate the pain on a scale.
- Inquire about time of menstrual period (if applicable): ensure anticipated time of menstrual period does not coincide with Visits 4 and 6 (post-dose imaging).

- If you have agreed to discontinue certain medications, you will begin to gradually stop taking them now.
- Record concomitant medications.
- Instructions on the use of Life Style Guidelines and Concomitant Medications sections.

Magnet Familiarization/Randomization; (Visit 2, Day 1) will include the following:

- A Pressure Pain Tenderness procedure. You will feel a series of different pressures of 5 second duration and varying intensities to your right thumbnail. Some pressures will feel very light to you, like touch, while others will feel heavier and painful to you. You will be asked to rate the intensity of the pressure on a pain rating scale. Based on your range of tolerable pressures from this test, a second test will apply the pressures to your thumbnail randomly.
- Ask you to have a mock fMRI Scan to familiarize you to the scanner. During this time, you will receive varying pressures on your thumbnail while in the mock scanner. You will rate the discomfort of these sensations on visual scales.
- A brief series of questions and 1 questionnaire about your pain sensitivity.
- Paper diaries to record your pain daily and be shown how to use them.
- Collection of information about medications you are currently taking.
- Completion of a randomization process (like the flip of a coin) that will decide the order in which you will take the study medicines. Neither you nor the researchers will know which study medication you are taking at any time. You will be issued study medication at this visit and be instructed as to how to take it.
- Beginning at Visit 2, Day 1 and throughout the study, you will receive one of two study medications: pregabalin or placebo (a sugar pill). Neither you nor the study team will know which medication you are taking at any time; however, if you experience side-effects requiring medical treatment, the study team will be able to identify which medication you are taking. The study medication will be self-administered in the morning and evening of each study period day. You will be contacted by phone to monitor any side-effects you may be experiencing and if necessary will be asked to start taking a new pack of medication that will contain a reduced dose.

If for any reason you do not continue into the visit after screening, the data collected about you during screening will be de-identified and kept in the anonymous research database. The protections for security and confidentiality described in section 9 of this consent form will be applied to this database and to your de-identified information.

Visit 3, Day 8:

- Give a urine sample to test for drugs of abuse.
- Conduct a urine test for ongoing drug safety.
- Collect pain diaries and issue new diaries.
- Collect information on any medicines you may be routinely taking and any side-effects you may be feeling with the study medication prior to having a functional MRI (fMRI) scan.
- Collect information about your pain using questionnaires.
- Dispense new study medication and collect any unused study drug.
- A Pressure Pain Tenderness procedure. You will feel a series of different pressures of 5 second duration and varying intensities to your right thumbnail. Some pressures will feel very light to

you, like touch, while others will feel heavier and painful to you. You will be asked to rate the intensity of the pressure on a pain rating scale. Based on your range of tolerable pressures from this test, a second test will apply the pressures to your thumbnail randomly.

- Ask you to have an fMRI scan that will last approximately 80 minutes. During these scans, you will receive varying pressures on your left thumbnail. You will rate the discomfort of these sensations on visual scales. You also will be lying at rest during part of the fMRI scan. Following these tests we will use a different MRI method, called Magnetic Resonance Spectroscopy (MRS), to estimate brain metabolite levels. You will also be asked to perform a visual task while you are in the scanner; this task requires looking at a checkerboard pattern while lying. Both the fMRI and the MRS scans are performed with the same MRI scanner. You will not feel anything different between the two kinds of scans, except you will not feel thumb pressures during MRS.
- A Magnetic Resonance Imaging (MRI) scan to get a basic picture of your brain anatomy while you lie still. This scan will last about 3 minutes.

Telephone Call 1, Day 18:

A telephone call will be made to all subjects approximately 10 day after visit 3. Side effects and concomitant medications will be recorded from this call.

If experiencing side effects and if necessary, will be asked to start taking a new pack of medication that will contain a reduced dose.

Visit 4, Day 22

- Collect pain diaries and issue new diaries
- Collect information on any medicines you may be routinely taking and any side-effects you may be feeling with the study medication prior to having a functional MRI (fMRI) scan
- Collect information about your pain using questionnaires
- Dispense new study medication and collect any unused study drug.
- A Pressure Pain Tenderness procedure. You will feel a series of different pressures of 5 second duration and varying intensities to your right thumbnail. Some pressures will feel very light to you, like touch, while others will feel heavier and painful to you. You will be asked to rate the intensity of the pressure on a pain rating scale. Based on your range of tolerable pressures from this test, a second test will apply the pressures to your thumbnail randomly.
- Ask you to have an fMRI scan that will last approximately 80 minutes. During these scans, you will receive varying pressures on your thumbnail. You will rate the discomfort of these sensations on visual scales. You also will be lying at rest during part of the fMRI scan. Following these tests we will use a different MRI method, called Magnetic Resonance Spectroscopy (MRS), to estimate brain metabolite levels. You will also be asked to perform a visual task while you are in the scanner; this task requires looking at a checkerboard pattern while lying. Both the fMRI and the MRS scans are performed with the same MRI scanner. You will not feel anything different between the two kinds of scans, except you will not feel thumb pressures during MRS.
- A Magnetic Resonance Imaging (MRI) scan to get a basic picture of your brain anatomy while you lie still. This scan will last about 3 minutes.
- A blood sample will be taken to measure the amount of study drug present in your blood.

Visit 5, Day 37

- Give a urine sample to test for drugs of abuse and pregnancy, if applicable.
- Conduct a urine test for ongoing drug safety and urine pregnancy test.
- Collect pain diaries and issue new diaries.
- Collect information on any medicines you may be routinely taking and any side-effects you may be feeling with the study medication prior to having a functional MRI (fMRI) scan.
- Collect information about your pain using questionnaires.
- Dispense new study medication and collect any unused study drug.
- A Pressure Pain Tenderness procedure. You will feel a series of different pressures of 5 second duration and varying intensities to your right thumbnail. Some pressures will feel very light to you, like touch, while others will feel heavier and painful to you. You will be asked to rate the intensity of the pressure on a pain rating scale. Based on your range of tolerable pressures from this test, a second test will apply the pressures to your thumbnail randomly.
- Ask you to have an fMRI scan that will last approximately 80 minutes. During these scans, you will receive varying pressures on your thumbnail. You will rate the discomfort of these sensations on visual scales. You also will be lying at rest during part of the fMRI scan. Following these tests we will use a different MRI method, called Magnetic Resonance Spectroscopy (MRS), to estimate brain metabolite levels. You will also be asked to perform a visual task while you are in the scanner; this task requires looking at a checkerboard pattern while lying. Both the fMRI and the MRS scans are performed with the same MRI scanner. You will not feel anything different between the two kinds of scans, except you will not feel thumb pressures during MRS.
- A Magnetic Resonance Imaging (MRI) scan to get a basic picture of your brain anatomy while you lie still. This scan will last about 3 minutes.

Telephone Call 2, Day 47:

A telephone call will be made to all subjects approximately 10 day after visit 5. Side Effects and concomitant medications will be recorded from this call. If experiencing side effects and if necessary, will be asked to start taking a new pack of medication that will contain a reduced dose.

Visit 6, Day 51:

- Collect pain diaries.
- Collect information on any medicines you may be routinely taking and any side-effects you may be feeling with the study medication prior to having a functional MRI (fMRI) scan.
- Collect information about your pain using questionnaires.
- Dispense new study medication and collect any unused study drug.
- A Pressure Pain Tenderness procedure. You will feel a series of different pressures of 5 second duration and varying intensities to your right thumbnail. Some pressures will feel very light to you, like touch, while others will feel heavier and painful to you. You will be asked to rate the intensity of the pressure on a pain rating scale. Based on your range of tolerable pressures from this test, a second test will apply the pressures to your thumbnail randomly.

- Ask you to have an fMRI scan that will last approximately 80 minutes. During these scans, you will receive varying pressures on your thumbnail. You will rate the discomfort of these sensations on visual scales. You also will be lying at rest during part of the fMRI scan. Following these tests we will use a different MRI method, called Magnetic Resonance Spectroscopy (MRS), to estimate brain metabolite levels. You will also be asked to perform a visual task while you are in the scanner; this task requires looking at a checkerboard pattern while lying. Both the fMRI and the MRS scans are performed with the same MRI scanner. You will not feel anything different between the two kinds of scans, except you will not feel thumb pressures during MRS.
- A Magnetic Resonance Imaging (MRI) scan to get a basic picture of your brain anatomy while you lie still. This scan will last about 3 minutes.
- A blood sample will be taken to measure the amount of study drug present in your blood.

Follow-up Visit 7, Day 58-65:

- Your height and weight, blood pressure and pulse, urine and blood tests will be taken to assess your general health.
- A urine pregnancy test will be performed if applicable.
- Collect information on any medicines you may be routinely taking and any side-effects you may be feeling with the study medication.
- Collect any unused study drug.

4.2 How much of my time will be needed to take part in this study?

The estimated time for the study is as follows:

Visit 1 (Screening Visit):	2 hours
Visit 2 (MRI Familiarization):	5 hours
Visit 3 (Scanning Visit):	5 hours
Visit 4 (Scanning Visit):	5 hours
Visit 5 (Scanning Visit):	5 hours
Visit 6 (Scanning Visit):	5 hours
Visit 7 (Follow-up Visit):	2 hours

4.3 When will my participation in the study be over?

The study from the Screening Visit through the Follow-up Visit will be completed within approximately 65 days (9-10 weeks).

5. INFORMATION ABOUT RISKS AND BENEFITS

5.1 What risks will I face by taking part in the study? What will the researchers do to protect me against these risks?

The known or expected risks are:

- Functional MRI and Magnetic Resonance Spectroscopy:
 - There are known risks to the magnet's ability to pull metal objects toward it. This pull can cause metal objects in the body (e.g., surgical clips or staples) to move, causing bleeding or disruption of surrounding tissue. If you carry or wear metal objects (e.g., jewelry, hair clips, tools), these objects can be pulled toward the magnet; if they are free to fly through the air there is the danger that you or someone else could get hurt if the moving object struck them. The MRI can cause pacemakers or stimulators implanted in the body to malfunction. There is also a risk that metallic objects in or on your body, including transdermal patches, may be heated by the radio waves, possibly causing burns.
 - The MRI scanner is tunnel-shaped and has a diameter of about one and one-half-feet. There is a minor risk of discomfort or anxiety from being in the confined space of the MRI scanner. The MRI is known to produce a rhythmic and loud noise. It is extremely important that you lie still throughout the MRI procedure.
 - Some studies, like this one, have the potential to cause "peripheral nerve stimulation" (PNS). PNS is a light touching sensation on the skin surface, lasting only for a few seconds. It may cause mild discomfort, but is not harmful to you.
 - There is the potential that a MRI scan may reveal an abnormality that is already in your brain, such as a cyst or tumor. However, these scans will not be read by a radiologist, and it is not within the scope of this study to clinically locate, identify, or diagnose such unexpected brain findings. If a finding such as this requires additional study or treatment, this will not be paid for by the investigators, the sponsor, or the University of Michigan.
 - No adverse effects from the static magnetic field have been reported in people. However, there could be unknown risks. In particular, because the risk to the fetus is not known, women who are pregnant or think they may be pregnant are excluded from the study.
- Tender Point Exam: The tender point exam may cause discomfort at the testing sites. You may stop this test at any time if it becomes too uncomfortable.
- Questionnaires: Some questions may be probing or involve sensitive issues. This may cause discomfort and you may choose to leave some questions blank if you do not want to answer them. You will not be required to submit any personal identifying information on the questionnaires; questionnaires will only be identified by anonymous study ID. The link between study ID and personal identifying information, and the protections applied to this link are discussed in detail in section 9 of this consent form.
- Thumbnail Pressure Sensitivity: You might feel discomfort at the places where we apply pressure; your thumb will not be harmed as a result of this testing even if the pressure feels painful to you. You may stop these tests at any time if you decide you are too uncomfortable.
- Blood draw: Your blood will be analyzed to confirm your eligibility to participate in this study and for drug safety purposes for use of pregabalin. There is a small chance of pain, infection or bleeding into the area from which the blood was taken. If persisting pain or redness in the area is noted, this may require medical or surgical treatment. Withdrawing blood may also induce lightheadedness or fainting. If you have an unusual blood test result, the researchers will discuss

this with you. If this happens, you will be monitored closely by the researchers, or you may need to stop the study drugs and end your participation.

- **Medications:** Known side effects for each of the study drugs are listed below. You may or may not feel any of these side effects. However, for your safety, a complimentary taxi may be used to take you to the research MRI facility during the days you are taking medication.

1) **Pregabalin:** Pregabalin is a medication approved by the FDA for use in pain relief and seizure relief as well as fibromyalgia. The researchers will give you instructions for when and how to take the drug, warnings about the drug and a list of side-effects that you might experience. These side-effects include:

- eyesight problems, including blurred vision
- dizziness
- sleepiness
- trouble concentrating
- euphoria (feeling “high”)
- weight gain
- dry mouth
- swelling of hands and feet
- unexplained muscle problems, such as muscle pain, soreness, or weakness

Because of the possibility of drowsiness or dizziness, you should be careful that you do not engage in any dangerous activities such as driving or operating machinery until after you are certain that the drug is not making you too sleepy or dizzy. You should also avoid alcohol, as well as other drugs that might make you even more sleepy or dizzy, or could impair your ability to think.

Pregabalin may cause serious allergic reactions. Call your doctor right away if you think you have any of the following symptoms of a serious allergic reaction: swelling of the face, mouth, lips, gums, tongue or neck; or have trouble breathing. Other allergic reactions may include rash, hives and blisters.

2) **Placebo (sugar pill):** The placebo in this study is a like sugar pill or a pretend treatment (with no drug in it) that is compared to the other drug in this study to test if the other drug has a real effect. You may or may not feel any side effects from the placebo.

Note for all study drugs: Neither you nor the researchers will know which study drug you are taking at any given time. As such, you will be asked about side effects you may feel and other medications you are taking, if any, while you are taking part in this study.

Pregnancy:

- **Women volunteers of child bearing potential must not be pregnant.** There could be risks to an unborn child in this study. If you are pregnant or become pregnant during the study, these risks could affect you or the unborn child. Women will agree to use birth control during the

study. You must continue using birth control for one month after the study is over. The study doctor must approve the form of birth control.

- Before the study, a pregnancy test is done for all women. This test might not detect an early pregnancy. Pregnancy tests may be repeated during the study. If you think you are pregnant, tell the study doctor immediately.
- Pregnancy will be a reason to stop study treatment. **If you become pregnant during the study, you may be discontinued from study participation for safety reasons. If you become pregnant within 28 days after you have stopped taking study drug, we ask that you contact your study doctor for safety monitoring. In either case, please make your obstetrician aware of your study participation. Your study doctor will ask that you, or your obstetrician, provide updates on the progress of your pregnancy and its outcome. The study doctor will make this information available to the study sponsor for safety monitoring follow-up.**

As with any research study, there may be additional risks that are unknown or unexpected.

The researchers will try to minimize these risks by:

- Functional MRI:
 - To ensure your safety for the MRI procedure you will be asked to bring or wear clothing without metal fasteners, and remove jewelry and any other metal objects from your body. We will also assess whether metallic objects that may be implanted (e.g., surgical clips or staples) are hazardous or acceptable.
 - We will provide pads and blankets to make you as comfortable as possible while lying in the scanner. Additionally, you will wear foam earplugs to reduce the loud noises made by the scanner.
 - If you experience any sort of discomfort during the MRI procedure at any time, you can stop the scan. You will be able to talk to us throughout the protocol, and you will be able to let us know right away if you want to stop the procedure and get out of the scanner. You will be able to end the pain testing session at any time by saying 'Stop'. The investigators will be sitting in the control room and in the MRI-suite, present at all times.
 - The MRI machine is operated within FDA guidelines so the potential for inducing PNS is low.
 - Your heart rate and breathing will be monitored while you are in the scanner. Your breathing will be monitored by a plethmograph belt which wraps around your lower chest and expands and contracts as you breathe. Your heart rate is measured by a peripheral pulse device that fits over your middle finger and uses an infrared light source to measure blood flow
 - If you are a female of childbearing potential, you will be required to use an appropriate and effective method of birth control during your participation in this study given the unknown risk of the magnet to the fetus. These methods may be discussed with your physician. Women of childbearing potential will be required to take a urine pregnancy test the day of fMRI testing. If you do not wish to take the pregnancy test, you will be excluded from any further aspects of the study.
 - *Pressure Pain Testing:* While lying in the MRI scanner, you may stop the pressure test at any time by speaking with the investigators.

- **Questionnaires:** You may refuse to answer any question on the questionnaires or surveys that may be uncomfortable.
- **Tender Point / Dolorimeter Exams:** Researchers have been educated in how to perform these tests safely. You may stop either test at any time if the testing becomes too uncomfortable.
- **Blood drawing:** Only individuals skilled in the process of blood drawing will be used to take your blood sample. Pressure will be applied to the site to reduce the risk of bruising. Sterile technique will be used to reduce the risk of infection.
- **Medications:** You may or may not feel any side effects to study medications. However, for your safety, a complimentary taxi may be requested that will take you to the research fMRI facility during the days you are having fMRI scans.
- **Data Collection:** As mentioned in Section 9 of this consent form, we will not identify data collected during your participation in this study with personal identifying information. Data collected during this study will be kept either in a locked file cabinet or a password-protected database.
- **Pregnancy Test:** If applicable, a blood serum and additional urine pregnancy tests will be done through out the study.

As with any research study, there may be additional risks that are unknown or unexpected.

5.2 What happens if I get hurt, become sick, or have other problems as a result of this research?

The researchers have taken steps to minimize the risks of this study. Even so, you may still have problems or side effects, even when the researchers are careful to avoid them. Please tell the researchers listed in Section 10 about any injuries, side effects, or other problems that you have during this study. You should also tell your regular doctors.

If you experience a research injury, The Chronic Pain and Fatigue Research Center will provide or arrange for medical treatment at no cost to you. Pfizer will cover the costs of this treatment. A research injury is any physical injury or illness caused by your participation in the study. Payment for such things as lost wages, expenses other than medical care, or pain and suffering is not available. To help avoid injury, it is very important to follow all study directions.

5.3 If I take part in this study, can I also participate in other studies?

Being in more than one research study at the same time, or even at different times, may increase the risks to you. It may also affect the results of the studies. You should not take part in more than one study without approval from the researchers involved in each study.

5.4 How could I benefit if I take part in this study? How could others benefit?

You may not receive any personal benefits from being in this study. Data from this study may provide information that can be used to better treat symptoms of fibromyalgia in the future.

5.5 Will the researchers tell me if they learn of new information that could change my willingness to stay in this study?

Yes, the researchers will tell you if they learn of important new information that may change your willingness to stay in this study. If new information is provided to you after you have joined the study, it is possible that you may be asked to sign a new consent form that includes the new information.

6. OTHER OPTIONS

6.1 If I decide not to take part in this study, what other options do I have?

Your participation is voluntary. Should you decide not to be in the study, there are options if you need treatment: routine medical care for FM consists of some combination of medications (prescribed based on your symptoms and level of tolerance), exercise, and physical therapy. None of these treatments are included in this study. Further, pregabalin is currently FDA-approved for treatment of fibromyalgia. If you decide not to participate, or once you have ended your study participation, pregabalin will not be available to you from the study sponsor for further treatment.

7. ENDING THE STUDY

7.1 If I want to stop participating in the study, what should I do?

You are free to leave the study at any time. If you leave the study before it is finished, there will be no penalty to you. You will not lose any benefits to which you may otherwise be entitled. If you choose to tell the researchers why you are leaving the study, your reasons for leaving may be kept as part of the study record. If you decide to leave the study before it is finished, please tell one of the persons listed in Section 10 "Contact Information" (below).

Procedures completed prior to your withdrawal will be analyzed as planned. Data collected about you prior to your withdrawal will be de-identified and kept in the anonymous research database.

7.2 Could there be any harm to me if I decide to leave the study before it is finished?

You may exit the study at any time without any penalty or danger to yourself or others. We will ask you to complete a follow-up visit if you exit the study before its end.

7.3 Could the researchers take me out of the study even if I want to continue to participate?

Yes. There are many reasons why the researchers may need to end your participation in the study. Some examples are:

- ✓ The researcher believes that it is not in your best interest to stay in the study.
- ✓ You become ineligible to participate.
- ✓ Your condition changes and you need treatment that is not allowed while you are taking part in the study.
- ✓ You do not follow instructions from the researchers.
- ✓ The study is suspended or canceled.
- ✓ You become pregnant, intend to become pregnant or are nursing a child during this study.

8. FINANCIAL INFORMATION

8.1 Who will pay for the costs of the study? Will I or my health plan be billed for any costs of the study?

The study will pay for research-related items or services that are provided only because you are in the study. If you are not sure what these are, see Section 4.1 above or ask the researchers for a list. If you get a bill you think is wrong, call the researchers' number listed in section 10.1.

Pfizer will cover the cost of all examinations, tests, treatment, and procedures listed in this consent document. You may need to receive medical care that is not listed in this document. Pfizer will not cover the costs of that care unless it is needed to treat a research injury (see the discussion of research injury, above).

You or your health plan will pay for all the things you would have paid for even if you were not in the study, like:

- Health care given during the study as part of your regular care
- Treatment of complications not covered by the sponsor
- Deductibles or co-pays for these items or services.

If you do not have a health plan, or if you think your health plan may not cover these costs during the study, please talk to the researchers listed in Section 10 below or call your health plan's **medical reviewer**.

By signing this form, you do not give up your right to seek payment if you are harmed as a result of being in this study.

8.2 Will I be paid or given anything for taking part in this study?

Yes, you will be compensated a total of \$1,500 upon completion of the study. Taxi rides are complimentary between your home, Domino's Farms, and the UM North Campus MRI facility on each Scanning Day outlined above in section 4.2. If you leave the study, or if the study staff or study sponsor stops your participation, you will be paid for all completed procedures. For example, you will be paid \$100 for completion of all screening procedures and \$350 for each of the scanning periods, including study termination/follow-up as outlined in sections 4.1 and 4.2

8.3 Who could profit or financially benefit from the study results?

The company whose product is being studied: Pfizer

The researchers conducting the study: Dr. Harris's salary is supported, in part, by Pfizer, Inc. to conduct this study.

Dr. Harris and Dr. Clauw are consultants for Pfizer and members of the Pfizer Scientific Advisory Board.

9. CONFIDENTIALITY OF SUBJECT RECORDS AND AUTHORIZATION TO RELEASE YOUR PROTECTED HEALTH INFORMATION

The information below describes how your privacy and the confidentiality of your research records will be protected in this study.

9.1 How will the researchers protect my privacy?

We will put the information collected about you during the study into a research record. This research record will not show your name, but will have codes entered into it that will allow the information to be linked to you. However, we shall keep your research record confidential to the extent provided by federal, state and local law. Research records will be kept in a separate research file that does not include names, registration numbers or other information that is likely to allow someone other than the researchers to link the information to you. We will not allow anyone to see your record other than people who have a right to see it. You will not be identified in any reports on this study.

9.2 What information about me could be seen by the researchers or by other people? Why? Who might see it?

Signing this form gives the researchers your permission to obtain, use, and share information about you for this study, and is required in order for you to take part in the study. Information about you may be obtained from any hospital, doctor, and other health care provider involved in your care, including:

- Hospital/doctor's office records, including test results (X-rays, blood tests, urine tests, etc.)
- Mental health care records (except psychotherapy notes not kept with your medical records)
- Alcohol/substance abuse treatment records
- Your AIDS/HIV status
- All records relating to your fibromyalgia, the treatment you have received, and your response to the treatment
- Billing information

There are many reasons why information about you may be used or seen by the researchers or others during or after this study. Examples include:

- The researchers may need the information to make sure you can take part in the study.
- The researchers may need the information to check your test results or look for side effects.

- University, Food and Drug Administration (FDA), and/or other government officials may need the information to make sure that the study is done in a safe and proper manner.
- Study sponsors or funders, or safety monitors or committees, may need the information to:
 - Make sure the study is done safely and properly
 - Learn more about side effects
 - Analyze the results of the study
 - In addition to using it for this study, the sponsor may reanalyze the study data at a later date or combine your information with information from other studies for research purposes not directly related to this study. The goal of any such research would be to learn more about drugs or diseases or to help design better studies in the future.
- Insurance companies or other organizations may need the information in order to pay your medical bills or other costs of your participation in the study.
- The researchers may need to use the information to create a databank of information about your condition or its treatment.
- Information about your study participation may be included in your regular UMHS medical record.
- If you receive any payments for taking part in this study, the University of Michigan accounting department may need your name, address, social security number, payment amount, and related information for tax reporting purposes.
- Federal or State law may require the study team to give information to government agencies. For example, to prevent harm to you or others, or for public health reasons.
- Foreign regulatory agencies that oversee research.

The results of this study could be published in an article, but would not include any information that would let others know who you are.

9.3 What happens to information about me after the study is over or if I cancel my permission?

As a rule, the researchers will not continue to use or disclose information about you, but will keep it secure until it is destroyed. Sometimes, it may be necessary for information about you to continue to be used or disclosed, even after you have canceled your permission or the study is over. Examples of reasons for this include:

- To avoid losing study results that have already included your information
- To provide limited information for research, education, or other activities (This information would not include your name, social security number, or anything else that could let others know who you are.)
- To help University and government officials make sure that the study was conducted properly

As long as your information is kept within the University of Michigan Health System, it is protected by the Health System's privacy policies. For more information about these policies, ask for a copy of the University Of Michigan Notice Of Privacy Practices. This information is also available on the web at <http://www.med.umich.edu/hipaa/npp.htm>. Note that once your information has been shared with others as described under Question 9.2, it may no longer be protected by the privacy regulations of the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA).

9.4 When does my permission expire?

Your permission will not expire unless you cancel it. You may cancel your permission at any time by writing to the researchers listed in Section 10 "Contact Information" (below).

10. CONTACT INFORMATION

10.1 Who can I contact about this study?

Please contact the researchers listed below to:

- Obtain more information about the study
- Ask a question about the study procedures or treatments
- Talk about study-related costs to you or your health plan
- Report an illness, injury, or other problem (you may also need to tell your regular doctors)
- Leave the study before it is finished
- Express a concern about the study

Principal Investigator: Richard Harris, Ph.D.
Mailing Address: UM/Chronic Pain and Fatigue Research Center
Box 385, Lobby M, Domino's Farms
Ann Arbor, Michigan 48106
Telephone: 734-998-6996

Study Coordinator: Kathy Scott, RN
Mailing Address: UM/Chronic Pain and Fatigue Research Center
Box 0385, Lobby M, Domino's Farms,
Ann Arbor, Michigan 48106
Telephone: 734-998-7022

You may also express a concern about a study by contacting the Institutional Review Board listed below, or by calling the University of Michigan Compliance Help Line at 1-888-296-2481.

University of Michigan Medical School Institutional Review Board (IRBMED)
Argus I
517 W. William
Ann Arbor, MI 48103-4943

Telephone: 734-763-4768
Fax: 734-615-1622
e-mail: irbmed@umich.edu

If you are concerned about a possible violation of your privacy, contact the University of Michigan Health System Privacy Officer at 1-888-296-2481.

When you call or write about a concern, please provide as much information as possible, including the name of the researcher, the IRBMED number (at the top of this form), and details about the problem. This will help University officials to look into your concern. When reporting a concern, you do not have to give your name unless you want to.

11. RECORD OF INFORMATION PROVIDED

11.1 What documents will be given to me?

Your signature in the next section means that you have received copies of all of the following documents:

- This "Consent to be Part of a Research Study" document. *(Note: In addition to the copy you receive, copies of this document will be stored in a separate confidential research file and may be entered into your regular University of Michigan medical record.)*

EXPERIMENTAL SUBJECT'S BILL OF RIGHTS

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 the 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

12. SIGNATURES

Research Subject:

I understand the information printed on this form. I have discussed this study, its risks and potential benefits, and my other choices with _____. My questions so far have been answered. I understand that if I have more questions or concerns about the study or my participation as a research subject, I may contact one of the people listed in Section 10 (above). I understand that I will receive a copy of this form at the time I sign it and later upon request. I understand that if my ability to consent for myself changes, either I or my legal representative may be asked to re-consent prior to my continued participation in this study.

Signature of Subject: _____ Date: _____

Name (Print legal name): _____

Patient ID: _____ Date of Birth: _____

Legal Representative (if applicable):

Signature of Person Legally Authorized to Give Consent _____ Date: _____

Name (Print legal name): _____ Phone: _____

Address: _____

Check Relationship to Subject:

Parent Spouse Child Sibling Legal Guardian Other: _____

If this consent is for a child who is a ward of the state (for example a foster child), please tell the study team immediately. The researchers may need to contact the IRBMED.

Reason subject is unable to sign for self: _____

Principal Investigator (or Designee):

I have given this research subject (or his/her legally authorized representative, if applicable) information about this study that I believe is accurate and complete. The subject has indicated that he or she understands the nature of the study and the risks and benefits of participating.

Name: _____ Title: _____

Signature: _____ Date of Signature: _____

Witness (optional):

I observed the above subject (or his/her legally authorized representative, if applicable) sign this consent document.

Name: _____

Signature: _____ Date of Signature: _____