RUSH

Subject Information Sheet and Consent Document

Varenicline for the treatment of postural and gait dysfunction in Parkinson's Disease

Investigator: **Deborah A. Hall, MD PhD**

Contact Information: **Rush University Medical Center**
1725 W. Harrison St. Suite 755
Chicago, IL 60612
312-563-2900

Sponsor: **Section of Movement Disorders**
Rush University Medical Center

Introduction

This form provides you with information so you can understand the possible risks and benefits of participating in this study; so that you can decide whether or not you want to be a part of this research study. Before deciding whether to participate in this study, you should read the information provided on this document and ask questions regarding this study. Once the study has been explained and you have had all your questions answered to your satisfaction, you will be asked to sign this form if you wish to participate.

Parkinson's disease (PD) involves the loss of dopaminergic neurons in the substantia nigra located in the brain stem. This loss of dopamine causes the common symptoms of PD including tremor, rigidity, and slowness of movement that respond well to treatment with dopaminergic drugs. Another common symptom, postural instability (a forward or backward lean which can result in a fall as the body cannot keep a stable or balanced position) does not respond as well to these drugs. Researchers believe that balance and postural instability may be secondary to loss of non-dopaminergic neurons including cholinergic neurons. These cholinergic neurons have been targeted with different types of therapy including nicotine and other cholinergic drugs with mixed results. Varenicline (Chantix™) targets a specific class of these neurons that are located in the brain near where degeneration of neurons is known to occur in PD. Because of this, varenicline has the potential to improve this difficult to treat symptom that affects many PD subjects.

Why are you invited to participate in this study?

You are being asked to take part in this study because you have Parkinson's disease and your balance instability may benefit from this medication.

Research studies include only people who choose to take part. Please take your time to make your decision and discuss it with your friends, family and/or physician. Remember that your participation is completely voluntary. There is no penalty if you decide not to take part in this study or decide later that you want to stop participating in this research study. Your care at

Rush University Medical Center will not be affected if you decide not to participate.

What is the purpose of this study?

The purpose of this study is to test the drug varenicline to see if it can improve balance instability in study subjects with PD. Varenicline is approved by the US Food and Drug Administration (FDA) as an aid to stop smoking, and will be used for a non-approved use in this study. Varenicline directly and indirectly works on receptors in the brain that interact with dopamine and acetylcholine, two neurotransmitters that are thought to play a role in the development and progression of the symptoms of PD.

How many people are expected to take part in the study?

This research study is only being conducted at Rush University Medical Center. We expect to enroll and evaluate 42 subjects in this study at Rush University Medical Center.

What will you be asked to do?

If you meet the study requirements, you will be asked to read this subject information sheet and attached HIPAA Authorization form for Research. The information sheet describes how varenicline will be studied for its potential to improve balance in PD patients. After reading the information, you will be encouraged to ask questions and your questions will be answered to your satisfaction. If you are interested in participating in this study you will be asked to sign and date this form and the HIPAA Authorization for Research Form.

After you provide signed consent to participate in this study, you will be scheduled to undergo a baseline visit where your PD symptoms will be evaluated. You will be asked to complete questionnaires about your balance instability in various situations, about your level of depression, and about possible feelings of suicide. You will have a neurological exam and also be evaluated to assess your balance, walking ability, impression of parkinsonism, your memory, and thinking. You will also be asked to provide a sample of blood for safety testing (i.e. blood count, blood chemistries, and liver functions). Approximately 3 tablespoons (or 15cc) of blood will be taken from a vein in your arm by a person trained and experienced in drawing blood. You will have an electrocardiogram (ECG or EKG) done to evaluate the electrical activity of your heart.

At least 2 weeks later, if you qualify for treatment in this study, you will then be randomized (selected by chance, like the flip of a coin) to receive either varenicline or a placebo. A placebo looks just like the active drug, but does not contain any active ingredients. You will begin taking the study drug (varenicline or placebo). You will begin by taking the study drug twice daily for three days, then twice daily for four days) after which your dose will be increased, and still taken twice daily for the remaining eight weeks of the study treatment.

Five weeks into the study, you will be called and evaluated for depression and suicidal thoughts over the phone.

At the end of nine weeks, you will be asked to return to the Movement Disorders Clinic for another visit. At this time, you will undergo the same evaluations that were done at baseline (questionnaires, rating scales, and blood tests). Approximately 3 tablespoons of blood will be taken from a vein in your arm by a person trained and experienced in drawing blood.

How long will you be in the study?

Your active participation in this study will last for approximately 9 weeks.

You may be removed from this study without your consent for any of the following reasons: the study doctor decides that continued participation in the study will be harmful to you, you will need a treatment not allowed on the study, your disease becomes worse, you are unable to take the treatment as indicated, or the study is canceled.

What are the possible risks of the study?

The most frequently reported side effects in studies with varenicline include nausea, insomnia (inability to sleep), abnormal dreams, headache, constipation, fatigue (tiredness), gas, dry mouth, and upset stomach. Varenicline may make you drowsy, dizzy, lose consciousness, or have difficulty concentrating. There have been reports of traffic accidents, near-miss accidents, and other types of injuries in people who were taking varenicline. Do not drive a car or operate machinery until you know how this medication affects you. Since varenicline has been approved and used, there have been reports of mood changes, anxiety, agitation, panic, behavioral changes, depression, hostility, psychosis (loss of contact with reality), hallucinations (seeing or hearing things that aren't there), paranoia (a thought process heavily influenced by anxiety or fear), delusions (thinking things that are not true or real), homicidal (killing of someone else) thoughts, suicidal thoughts, and suicide. In smokers, adverse events also include chest pain, nonfatal heart attack, need for procedures to increase blood flow to the heart, and new diagnosis or admission for peripheral vascular disease.

If you or a caregiver feel that you are agitated, depressed, have a change in behavior or thinking that are not typical, or experience thoughts of suicide, the study drug should be stopped and contact a member of the study staff immediately.

You will also be asked to have your blood drawn twice during the study. Drawing blood may result in pain or discomfort, and/or bleeding, and bruising at the needle entry site. In rare cases, fainting or infection may occur.

There may be risk of allergy to one or more of the drug used in this study. Signs of an allergic reaction may include redness, itching, swelling or (in rare cases) difficulty with breathing, and lightheadedness. Severe allergic reactions may result in death. If you feel that you are experiencing a severe allergic reaction, first seek treatment and then call **Dr. Deborah Hall** at **312-563-2900**. This number is available 24 hours a day.

Are there any anticipated pregnancy risks?

Women

If you are pregnant or breastfeeding, you cannot take part in this study. A pregnancy test may be required and will be given the beginning of the study if you have not yet undergone menopause. You are responsible for using an effective birth control method such as birth control pills, barrier method (such as condoms or diaphragms), intrauterine device (IUD), hormone implants or surgical sterility while you are taking part in this study. Once you have completed treatment, you may discontinue birth control 1 month after completion of the study treatment. If you become pregnant, you must notify the study doctor immediately.

Varenicline has been shown to have an adverse effect on the fetus in animal reproduction studies.

There are no adequate and well-controlled studies in pregnant women.

Men
You are responsible for using an effective birth control method, such as the ones listed above. If you are a male and your female partner becomes pregnant, you must notify your study doctor immediately. Once you have completed treatment, you may discontinue birth control after 1 month after completion of treatment.

Are there benefits to taking part in the study?

There may be no direct benefit to you for participating in this study**.** However, it is possible that you may experience improvement in your PD related balance instability.

What other options are there?

Instead of participating in this study, you may choose another form of treatment such as physical therapy. Varenicline is available in the US for smoking cessation only and is not approved specifically for PD. The other alternative to participating in this study is not to participate.

What about confidentiality of your information?

Records of participation in this research study will be maintained and kept confidential as required by law.

In order to conduct the study, the study doctor, Deborah A. Hall, MD PhD, will use and share personal health information about you. This includes information already in your medical record, as well as information created or collected during the study. Examples of the information that may be shared include your medical history, exams, evaluations and laboratory test results. The study doctor will use this information about you to complete this research. The Food and Drug
Administration (FDA) may have access to data if needed. All identifying information from your chart will be removed before the data is shared.

Confidentiality and disclosure of your personal information is further described in the attachment to this form. The attachment is entitled HIPAA Authorization to Share Personal Health Information in Research (2 pages).

Your identity will not be revealed on any report, publication, or at scientific meetings. You may be asked to be videotaped which will possibly be used for data collection purposes as well as for publication results.

The Rush Institutional Review Board (IRB) will have access to your files as they pertain to this research study. The IRB is a special committee that reviews human research to check that the rules and regulations are followed.

What are the costs of your participation in this study?

All costs that are part of your usual medical care, such as costs of drugs you are already taking for Parkinson's disease or other medical conditions, or the cost of regular routine visits with your doctor will be charged to you or your insurance company. You will be responsible for all costs that are not paid by your insurance company. You should check with your insurance

company before you enroll in this research study.

The cost of the study visits for this study and all the study procedures and assessments (including testing) will be performed at no cost to you. The study drug will be provided by its manufacturer, Pfizer, Inc. You will be offered a ticket to pay for the cost of parking if you park in the Rush University Medical Center visitor parking structure.

Will you be paid?

You will not be paid to participate in this study.

What happens if you experience a research related injury?

If you experience any injury or illness as a direct result of your participation in this research study, immediate treatment will be provided. However, the cost of that treatment will be billed to you or your insurance company.

If you have any medical problems during the study, please contact the study doctor, they will explain your treatment options to you or tell you where you can get treatment.

Rush University Medical Center does not have a program for financial compensation or other forms of compensation for injuries which you may incur as a result of participation in this study.

What happens if you need emergency care?

If you need emergency care while you are participating in this study, it is important that you inform emergency personnel of your participation in this study.

Whom do you call if you have questions or problems?

Questions are encouraged. If there are any questions about this research study or if you experience a research related injury, please contact: Dr. Hall at 312-563-2900. Questions about the rights of research subjects may be addressed to the Rush Research & Clinical Trials Administration Office at 312-942-5498.

By signing below, you are consenting to participate in this research study. You have read the information given or someone has read it to you. You have had the opportunity to ask questions, which have been answered satisfactorily to you by the study personnel. You do not waive any of your legal rights by signing this consent document. You will be given a copy of the signed and dated consent document for your records.

SIGNATURE BY THE SUBJECT:

_____	_____	_____
Name of Subject	Signature of Subject	Date of Signature

SIGNATURE BY THE WITNESS:

I observed the signing of this consent document.

Signature of Witness | Date of Signature

SIGNATURE BY THE INVESTIGATOR/INDIVIDUAL OBTAINING CONSENT:
I attest that all the elements of informed consent described in this document have been discussed fully in non-technical terms with the subject. I further attest that all questions asked by the subject were answered to the best of my knowledge.

Signature of Individual Obtaining Consent | Date of Signature

Signature of the Principal Investigator if different from above | Date of Signature

Rush University Medical Center

AUTHORIZATION TO SHARE PERSONAL HEALTH INFORMATION IN RESEARCH

Name of the Research Study: Varenicline for the treatment of postural and gait dysfunction in Parkinson Disease

Name of Principal Investigator: Deborah A. Hall, MD PhD

The word "you" means both the person who takes part in the research, and the person who gives permission to be in the research. The word "we" refers to Rush University Medical Center, its employees and affiliates, including the study doctor and his/her research staff. You will be asked to sign this form along with the attached research consent form.

We are asking you to take part in the research described in the attached consent form. To do this research, we need to collect health information that identifies you. Some of this information may come from results of tests, procedures, questionnaires and interviews. We may also collect information from your medical record. We will only collect information that is needed for the research. This information is described in the attached consent form.

If you sign this form, we will collect your health information until the end of the research. We may collect some information from your medical records even after your direct participation in the research project ends. We may keep the information forever, in case we need to look at it again for this research study.

Your information may also be useful for other studies. We can only use your information again if a special committee in the hospital gives us permission. This committee may ask us to talk to you again before doing the research. But the committee may also let us do the research without talking to you again if we keep your health information private.

This study is considered a "blinded study", which means that the researcher is asking you to accept one of several drugs or treatments, without knowing exactly which one you are being given. Therefore, the researcher may not be able to let you know which drug or treatment you are being given at any that point in the study except in case of emergency. We cannot do the research if you do not agree to let the researcher hold back this information until the time listed below. You have the right to request to see your records after the study is completed.

- What blinded drugs or treatments are offered? Varenicline or Placebo
- When (in weeks from the start of the study, or as a date) will you be told about the specific drug or treatment that you were given? You will be told you study drug treatment assignement by December 2012
- **If you sign this form, you are giving us permission to collect, use, and share your health information.**

You do not have to sign this form. If you decide to NOT sign this form, you cannot be in the research study. We cannot do the research if we cannot collect, use and share your health information.

If you change your mind later and do not want us to collect or share your health information, you need to send a letter to the researcher listed above. The letter needs to say that you have changed your mind and do not want the researcher to collect and share your health information. If we cannot collect and share your health information, we may decide that you cannot continue to be part of the study. We may still use the information we have already collected. We need to know what happens to everyone who starts a research study, not just those people who stay in it.

If you sign this form, we may continue to share the health information collected for this study with the people listed in the Confidentiality section, without any time limit, unless you withdraw your authorization. This authorization does not expire.

CONFIDENTIALITY

We may share your information with people who help with the research. Some of these people may be other researchers outside of the hospital or are in charge of the research, pay for or work with us on the research. Some of these people make sure we do the research properly. Some of these people may share your information with someone else. If they do, the same laws that Rush must obey may not protect your health information. For this study, we will share information with:

- U.S. Food and Drug Administration

If your information is transferred outside of the United States, different privacy laws may apply. Additionally, if one of the companies or institutions listed above merges with, or is purchased by, another company or institution, this authorization to use and disclose protected health information in the research will extend to the successor company or institution.

If you have any questions, please ask the researcher or his/her staff. Their phone numbers appear in the attached consent form. You can also call 1-800-876-0772 at Rush with general questions about your rights and the research use of your health information. The researcher will give you a signed copy of this form.

SIGNATURE, DATE, AND IDENTITY OF PERSON SIGNING

The health information about _____ can be collected and used by the researchers and staff for the research study described in this form and the attached consent form.

Signature: _____ Date: _____

Print name: _____ Legal authority: _____