CONSENT BY SUBJECT FOR PARTICIPATION IN A RESEARCH PROTOCOL

Protocol Number: 10681A Name of Subject: _____
Medical History Number: _____

STUDY TITLE: **Immune function in multiple sclerosis patients**

Doctors Directing Research:
Anthony Reder, Barry Arnason, and Adil Javed
Address: Dept. of Neurology, MC-2030, 5841 S. Maryland Avenue, The University of Chicago
Telephone Number: 773-702-6204 (AT Reder)

You are being asked to participate in a research study. A member of the research team will explain what is involved in this study and how it will affect you. This consent form describes the study procedures, the risks and benefits of participation, as well as how your confidentiality will be maintained. Please take your time to ask questions and feel comfortable making a decision whether to participate or not. This process is called informed consent. If you decide to participate in this study, you will be asked to sign this form.

WHY IS THIS STUDY BEING DONE?

The purpose of this study is to investigate the immune system in multiple sclerosis.

This research is being done because the immune system attacks the brain in MS. The cause is unknown and current treatments at best only slow down the disease. Understanding the immune system should eventually lead to treatment of the disease.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

About 4000 people will take part in this study at the University of Chicago.

WHAT IS INVOLVED IN THE STUDY?

You have been asked to participate in this research study because you were diagnosed with multiple sclerosis. The purpose of this study is to determine how the immune system is different in patients with MS compared to those individuals who do not have MS (controls).

We will be studying proteins and RNA (genetic material that makes proteins) in white blood cells, changes in DNA that is circulating in the blood, and how all of these change during therapy of MS. White blood cells are thought to have a role in the attacks and progression of MS. White blood cells control some immune responses and may control the severity of MS. DNA is released when cells break down. Sometimes the DNA has been modified within the cells before they release it. By studying these white blood cells and their proteins, RNA, and DNA, we hope to determine what causes MS and use this knowledge to design potential therapies for MS patients in the future.

We will study the effects of drugs that affect the immune system in MS, including interferons (Avonex, Betaseron/Extavia, Rebif, Plegridy), glatiramer acetate (Copaxone), statins (such as Lipitor, Zocor), myelin peptides (such as MBP82-98), sphingosine receptor activators (such as FTY720, fingolimod), dimethyl-fumarate (Tecfidera), natalizumab (Tysabri), daclizumab (Zynbrita), teriflunomide (Aubagio), ACTH, rituximab (Rituxan) and ocrelizumab (Ocrevus), and others, and their interaction with the many approved drugs used to treat MS and its symptoms (aspirin, 4-AP, antidepressants).

This study may involve genetic testing to determine if there is a mutation in a gene that controls the function of a protein. Your blood cells will be stored and used for future research studies. The results of these tests will not be shared with you because the results need to be confirmed in other patients and by other labs before we can state that any changes will affect MS. The doctors directing this study will receive the results of these tests and will use this information for the purposes of this

research only. Your de-identified sample (containing no information that can identify you) may be shared with Drs. R Balabanov, Bruce Cohen, and colleagues at Northwestern University and Dr. Victor Levenson and colleagues at Rush University, Jason Monroe, Affymetrix, and Dr. Dan Wynn, Consultants in Neurology who will assist Dr. Reder.

If you agree to participate, blood will be drawn from your arm during your regularly scheduled clinic visit. Clinic visits are typically 3 to 12 months apart. If you are in a clinical trial, visits are typically every 2 to 6 months. We will follow you for 3 years or as long as you are a patient in the Neurology Clinic. The amount of blood to be drawn is up to 50 cc, which is approximately 4 tablespoons. In some cases instead of drawing blood, we will obtain DNA by scraping the inside of your mouth with a swab, or we will use other fluids (*e.g.,* spinal fluid) or tissues obtained for other reasons *e.g.,* skin biopsy). Fluids or tissues will be taken for clinical or research purposes, and leftover portions of these samples may be used for this study.

We will compare results of your immune studies with the duration, type, and severity of your MS and your response to therapy. You may refuse at any time.

During this study, Dr. Anthony Reder and his research team will collect information about you for the purposes of this research. Data will be derived from your medical record and form questions in clinic. The data includes the type and severity of your disease, lab tests, family history of MS and related diseases and toxin exposures, your prior therapeutic drug use, your name, age, sex, and phone number in order to contact you with more questions or updates about MS treatments. Since the cause and treatment of MS is unknown, all of these factors may be relevant in understanding the disease.

HOW LONG WILL I BE IN THE STUDY?

We think you will be in the study for your lifetime or until we develop a cure for MS. You will be evaluated during your yearly clinic visits, and updated about our research results in clinic.

WHAT ARE THE RISKS OF THE STUDY?

Potential Risks: The potential risks of drawing blood include a bruise at the site of the vein puncture; this happens occasionally. Very rarely, inflammation of the vein and infection have been reported. Care will be taken to avoid these complications.

Privacy: Your name and medical record number will be kept in a locked room on a password-protected computer and will not be listed in publications.

ARE THERE ANY BENEFITS TO TAKING PART IN THE STUDY?

Although this blood drawing will not benefit you directly, it may lead to information regarding the cause(s) of MS which could then help identify future treatment(s).

We hope the information learned from this study will benefit other people with MS in the future.

WHAT OTHER OPTIONS ARE THERE?

Instead of being in this study, you may choose not to participate.

The decision whether or not you wish to participate in this study will not affect your care at the University of Chicago Medical Center

WHAT ARE THE COSTS?

Clinical services provided during a clinical trial are either related to the research or to your usual medical care. *Research-related services* are done to complete the research. These costs are not the responsibility of you or your insurance. Costs considered research-related for this study include blood drawing and immunology lab tests. *Usual medical care costs* are for services considered medically necessary. Costs for this usual, ongoing medical care are the responsibility of you or your insurance.

If you suffer an unanticipated injury as a direct result of this research and require emergency medical treatment, the University of Chicago Medical Center will provide such treatment at the University of Chicago Medical Center at no cost to you. You must notify Dr. Reder as promptly as possible after your injury in order to receive this care. An injury is "unanticipated" if it is not one of the known effects of a study drug, medical device or procedure, and is not the result of your disease or

condition. The costs of any non-emergency care for such an injury will be billed to you or your insurance or the study sponsor in the ordinary manner. If you think that you have suffered a research related injury, you must let Dr. Reder know right away.

WILL I BE PAID FOR MY PARTICIPATION?

You will not be paid.

WHAT ABOUT CONFIDENTIALITY?

Study records that identify you will be kept confidential.

Your name and medical record number will be kept in a locked room on a password-protected computer and will not be listed in publications. The data will be accessible by Dr Reder, and people directly working with him on his laboratory studies. Your identity will not be known or available to anyone outside Dr. Reder's laboratory. This information will not be part of your medical record.

The data collected in this study will be used for the purpose described in the form. By signing this form, you are allowing the research team access to your medical records, which include Protected Health Information. Protected Health Information (PHI) consists of any health information that is collected about you, which could include your medical history and new information collected as a result of this study. The research team includes the individuals listed on this consent form and other personnel involved in this study at the University of Chicago.

As part of the study, Dr. Reder and his research team may report the results of your study-related procedures and tests explained above to Dr. Reder's collaborators at Acorda (producer of ACTHAR), Affymetrix, Bayer (Betaseron), Biogen (Avonex, Plegridy, Tecfidera, Tysabri, Zynbrita), BioMS (MBP82-98), Genentech (Ocrevus, Rituxan), Genzyme (Aubagio), Novartis (Excelon, Extavia, Gilenya), Pfizer (Aricept, Lipitor), Serono (Rebif), TEVA (Copaxone), The National MS Society, and the National Institutes of Health.

This information would include data from Dr. Reder's lab experiments along with relevant factors related to your MS history such as name, address, date of birth, sex, and type of MS, plus relevant lab tests such as MRI scans and blood count. This information is being sent to study connections between these lab values and your immune function, in order to understand the cause and treatment of MS. Please note that these individuals may share your health information with someone else. If they do, the same laws that the University of Chicago must obey may not protect your health information.

Your records may be reviewed by federal agencies whose responsibility is to protect human subjects in research including the Food and Drug Administration (FDA) and Office of Human Research Protections (OHRP). In addition, representatives of the University of Chicago, including the Institutional Review Board, a committee that oversees the research at the University of Chicago, may also view the records of the research. If your research record is reviewed by any of these groups, they may also need to review your entire medical record.

The results from tests and/or procedures performed as part of this study will not be part of your medical record. However, if there are significant immune abnormalities, Dr. Reder will contact you and discuss any necessary evaluation.

During your participation in this study, you will have access to your medical record. Dr. Reder is not required to release to you research information that is not part of your medical record.

This consent form will be kept by the research team for at least six years. The study results will be kept in your research record and be used by the research team until the research ends, or forever.

Data from this study may be used in medical publications or presentations. Your name and other identifying information will be removed before this data is used. If we wish to use identifying information in publications, we will ask for your approval at that time.

WHAT ARE MY RIGHTS AS A PARTICIPANT?

Taking part in this study is voluntary. If you choose not to participate in this study, your care at the University of Chicago/University of Chicago Medical Center will not be affected.

You may choose not to participate at any time during the study. Leaving the study will not affect your care at the University of Chicago/University of Chicago Medical Center.

If you choose to no longer be in the study and you do not want any of your future health information to be used, you must inform Dr. Reder in writing at the address on the first page. Dr. Reder may still use your information that was collected prior to your written notice.

We will tell you about significant new information that may affect your willingness to stay in this study.

You will be given a signed copy of this document. This consent form document does not have an expiration date.

IS THERE ANYTHING ELSE I SHOULD KNOW?

Dr. Reder receives money for consulting and clinical trials from the corporate sponsors listed in the section on Confidentiality, page 3. These companies will receive results from this study. You should ask your doctor about this if you have any questions.

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

You have talked to Dr. Anthony Reder about this study and you had the opportunity to ask questions concerning any and all aspects of the research. If you have further questions about the study, you may call Dr. Reder at 773-702-6204.

If you have a research related injury, you should immediately contact the Neurology Resident on call at 773-702-6800.

If you have any questions concerning your rights in this research study you may contact the Institutional Review Board, which is concerned with the protection of subjects in research projects. You may reach the Committee office between 8:30 am and 5:00 pm, Monday through Friday, by calling (773) 702-6505 or by writing Institutional Review Board, University of Chicago, 5841 S. Maryland Ave, MC7132, I-625, Chicago, Illinois 60637.

CONSENT

SUBJECT:

The research project and the procedures associated with it have been explained to me. The experimental procedures have been identified and no guarantee has been given about the possible results. I have received a signed copy of this consent form for my records.

I agree to participate in this study. I am aware that my participation is voluntary and that I do not have to sign this form if I do not want to be part of this research study.

Signature of Subject: _____

Date: _____ Time: _____ AM/PM (Circle)

PERSON OBTAINING CONSENT

I have explained to _____, the nature and purpose of the study and the risks involved. I have answered and will answer all questions to the best of my ability. I have given a signed copy of the consent form to the subject.

Signature of Person Obtaining Consent: _____

Date: _____ Time: _____ AM/PM (Circle)

INVESTIGATOR/PHYSICIAN:

Signature of Investigator/Physician _____

Date: _____ Time: _____ AM/PM (Circle)