

PHARMACOGENETIC EVALUATION OF TREATMENT RESPONSE

CONSENT FORM TO PARTICIPATE IN A SUBSTUDY of  
Vicriviroc in Combination Treatment With an Optimized ART Regimen in HIV-Treatment  
Experienced Subjects (VICTOR-E4)

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24 Hour Emergency Number (215) 662-6059 Ask for the Immunodeficiency Program Doctor on call

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This consent form may contain words that you do not understand. Please ask the study doctor or a member of the study staff to explain any words that you do not know or any information that is unclear or confusing.

**INTRODUCTION**

You have already agreed to take part in the main research study and have signed the consent form. In the main research study we will investigate the potential benefits, as well as side effects, of vicriviroc therapy.

You are also being invited to participate in a sub-study that will investigate whether there may be a genetic or inherited reason for differences in how patients respond to vicriviroc. The information below will help you decide whether you want to participate in the sub-study.

If you participate, this would require you to give two extra blood samples. Taking part in this genetic research is completely voluntary. Your decision to be in this sub-study or not will not impact your ability to take part in the main study.

**PURPOSE OF SUBSTUDY**

The purpose of this sub-study is to find out whether there are differences in the way that different people respond to drugs. Many differences in the way an individual responds to drugs can be learned by studying differences in genes, which are found in your DNA. For example, with certain medications it is known that there are differences in genes that can change how long a medication may stay in the body. This has not been well studied for all drugs. By studying patients being treated with our drug we hope to identify genetic markers that are associated with a greater or lesser chance of developing side effects, or a better or worse chance of responding to our therapy.

Scientists are also learning more about differences in genes that may predict whether a patient will be at risk for disease. The more that is learned about these differences in genes will help to improve our understanding and treatment of patients.

By studying DNA from your blood sample, researchers may find the differences in genes that cause disease or altered responses to therapy.

IRB APPROVAL DATE: 11/13/07  
EXPIRATION DATE: 12/10/07

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Schering-Plough P04889 - Site #28/ VICTOR-E4 Study

CONSENT FORM TO PARTICIPATE IN A RESEARCH STUDY

**DESCRIPTION OF THE STUDY**

**SAMPLE FOR CCR5 GENOTYPING**

Schering-Plough is interested in studying a gene, CCR5 that may impact how individuals respond to vicriviroc, the drug studied in the main clinical trial.

One teaspoon of your blood will be collected, your DNA will be extracted from your blood, and a test will be performed to determine the status of your CCR5 gene. The blood sample for CCR5 genotyping will be obtained at the same time that you require other blood samples for the main research study at Visit 1 (or later if it cannot be done at Visit 1), and thus no extra venipunctures will be needed. Your blood will be shipped to a central laboratory (Covance, Indianapolis, IN) where your DNA will be extracted from your blood. DNA taken from your blood will then be shipped to a research laboratory for CCR5 genotyping. Any DNA left over after this test is performed will be destroyed, and the destruction of the sample will be documented. Your DNA will not be retained for any future analysis.

The results of your CCR5 status will be forwarded to your study doctor at the end of the study if you request Schering-Plough to do so, but will not be entered into your medical record. The results of this CCR5 analysis are for research purposes only.

**SAMPLE FOR BIOREPOSITORY**

A second component for this sub-study involves obtaining a single blood sample (approximately two teaspoons of blood), which will be used for future research on genes that cause disease or altered response to therapy. This additional blood sample will be obtained at the same time that you require other blood samples for the main research study at Visit 1 (or later if it cannot be done at Visit 1), and thus no extra venipunctures will be needed. Your blood will be shipped to a central laboratory (Covance, Indianapolis, IN) where your DNA will be extracted from your blood. DNA taken from your blood will then be shipped to the Schering-Plough designated facility and stored under strict supervision in a limited access facility which operates to assure the integrity of the samples for future analysis.

This DNA sample will be used to study various genetic causes for how patients may respond to a drug. This DNA sample will be stored to provide a resource for future studies conducted by Schering-Plough focused on the study of genes responsible for how a drug enters and is removed by the body, how a drug works, other pathways a drug may interact with, or other aspects of the disease. All samples will be used by Schering-Plough or designees and research will be monitored and reviewed by a committee of our scientists and clinicians. Your blood cells will not be made to grow forever in the laboratory.

This DNA sample will be stored for future testing for up to 20 years from the time the sample is obtained, or until the sample is gone. When (or before) the 20-year period ends, your DNA sample will be destroyed and its destruction will be documented. Your samples may be stored for longer than these specified periods if a Health Authority has active questions that are being answered. In this special circumstance, samples will be stored until Health Authority questions have been adequately addressed.

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If any future testing is performed using your sample, no additional informed consent will be obtained from you and you will not be notified.

**DISCLOSURE OF RESEARCH RESULTS**

*For Samples Obtained for CCR5 Testing*

The results of the CCR5 gene tests performed on your sample will not be included in the overall clinical trial database, but will be maintained as de-identified data in a separate sample database. If you request to know the status of your CCR5 gene, this de-identified data will be reintegrated with the clinical database by the entrusted keyholder, and your results will be forwarded to your study doctor at the end of the study. However, this requested data will not be entered into your medical record.

The results of variations (also known as polymorphisms) in the CCR5 gene will not be reported back to you, your family, or the medical staff as the clinical meaning of variations in the CCR5 gene is currently unknown.

*For Samples Obtained for the Biorepository*

Many genetic studies are exploratory research studies and may not yield information that will be clinically useful to patients for some time. Therefore, no information obtained from research studies will be disclosed to you, your family or the medical staff. Research information from this sub-study will not become part of your medical records.

If there are research findings discovered while you are still actively participating in the main research study that will be critical safety findings for the patients enrolled in our clinical trial, Schering-Plough will publish the results, contact all study doctors, and offer to pay for patients enrolled in the clinical trial to have clinical diagnostic testing performed. If important research findings are discovered after subjects have concluded participation in the clinical trial, Schering-Plough will publish results, present results in national meetings, and post results on our website in order to rapidly disseminate this information to doctors and patients.

To further protect your participation, information obtained from research studies will not be linked to your medical record and will be maintained separately from all clinical information obtained during the course of the main research study. Any data that can be used to uniquely identify you will not be included in the sample database.

**RISKS OF PARTICIPATION**

The blood sample will be drawn at the same time a routine blood test is obtained and therefore will not be an additional risk for you. The amount of blood taken for the study will not be harmful to you. There is a potential risk that genetic information can be used to limit access to health insurance or employment.

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**BENEFITS OF PARTICIPATION**

You will receive no direct benefit from participating in this study. However, patients treated in the future with this drug or with the same clinical diagnosis may benefit from information learned from your participation.

The research data collected during this study will be used to learn more about the study drug and to help develop new medical treatments and tests. The sponsor does not intend to provide you with ownership or financial benefits that may result from this study.

**COMPENSATION**

If you decide to participate in the substudy, you will be given \$10 as compensation.

**ALTERNATIVES**

The alternative to participating in this trial is to not participate. Your participation in the main clinical trial will not change should you decide not to participate in this study.

**PERSONAL INFORMATION**

As part of this sub-study, a total of 14.5 mL (approximately 3 teaspoons) of blood will be taken for CCR5 genotyping 6 mL (approximately one teaspoon) and future genetic analysis 8.5 mL (approximately two teaspoons). Any genetic information derived from these analyses will be added to a computer database. This database will not be linked to the results from the main clinical trial. This information will only be linked to clinical trial results by the entrusted keyholder who is under strict procedures for this data reintegration. The clinical trial results only contain a subject number instead of your name and are being used for research purposes consistent with the main study consent, this sub-study consent and any related consent to use personal health information. All reports from the entrusted keyholder will be anonymized for release to researchers.

Results from study of this compound involving many subjects may be used for medical and scientific research in the future. Health authorities may request this information for further analysis in order to assess the safety and efficacy of this drug.

Patients will not be recontacted with information learned from the banked specimens.

**CONFIDENTIALITY**

All identifying information collected in this study will be kept strictly confidential, except as may be required by law or regulatory authority request. If any publication results from this research, you will not be identified by name. It is possible that, if people who are not involved in this research know your genetic information, there might be problems with your employment or insurance. The chance that taking part in this research will harm you is very small.

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**CONSENT FORM TO PARTICIPATE IN A RESEARCH STUDY**

To protect your privacy we will only use a subject number, instead of your name, on your blood sample. The only clinical information linked to your blood sample is that a sample was obtained. Your name will not be disclosed outside of the research clinic and will not be known by the Sponsor. We have set up study records to keep your participation and all your test results separate and confidential. No genetic test results will be kept in your medical record. When your DNA is extracted and sent to the storage facility designated by Schering-Plough, a different unique number will be applied to your sample. The “key” that will link the sample stored at the Schering-Plough designated facility with the number used on your blood sample taken at the clinic will be maintained in a secure system under strict supervision and security by authorized personnel and will not be released to clinicians or researchers.

Although all identifying information will be removed from your DNA sample before it is analyzed and stored, it is possible that members of a Health Authority or other persons required by law may have to see your study information. The study sponsor cannot absolutely guarantee that your genetic test results could never be linked to you. Any report published as a result of this study will not identify you by name.

**TERMINATION OF PARTICIPATION**

If, at any time, you should choose to withdraw from participation in the sample repository, all samples maintained within the repository will be destroyed and all records linked to the samples will be deleted. However, data obtained from samples prior to withdrawal of consent will not be deleted.

**SIGNIFICANT NEW DEVELOPMENTS**

Any significant new developments during the course of this research that might influence your willingness to continue to participate will be reported to you.

**QUESTIONS**

You are encouraged to ask any questions related to this research. All of your questions should be answered to your satisfaction before you consent to participate in this study.

**INJURY COMPENSATION**

If you have a medical emergency during the study you may contact the Principal Investigator or Emergency contact listed on page one of this form. You may also contact your own doctor, or seek treatment outside of the University of Pennsylvania. Be sure to tell the doctor or his/her staff that you are in a research study being conducted at the University of Pennsylvania. Ask them to call the telephone numbers on the first page of this consent form for further instructions or information about your care.

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In the event of any physical injury resulting from research procedures, medical treatment will be provided without cost to you, but financial compensation is not otherwise available from the University of Pennsylvania. If you have an illness or injury during this research trial that is not directly related to your participation in this study, you and/or your insurance will be responsible for the cost of the medical care of that illness or injury.

Like all needle pricks, you may experience discomfort or pain related to the blood draw procedure. In the event you are injured as a direct result of this procedure, the study sponsor will pay reasonable medical costs (doctor's fees and medical expenses) needed to treat the injury. The treatment must be authorized by the study doctor except in the event of an emergency in which case the study doctor should be notified as soon as possible.

**VOLUNTARY CONSENT**

You are free to withdraw or refuse your consent for participation in this sub-study at any time without jeopardizing your continuing participation in the main clinical trial. Data obtained or published from the use of this sample prior to withdrawal of consent will not be destroyed.

**AGREEMENT**

I confirm that I have read and understand the information sheet and have had the opportunity to ask questions. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason and without my medical care or legal rights being affected. I understand that I can participate in the Clinical Study P04889 even if I do not agree to the above genetic testing. I understand that any information or specimens (such as blood samples) collected during this study may be used in the research and development of the study drug. I also understand that I will not own any part of, or benefit financially from the research or future commercial products.

\_\_\_\_\_  
Subject/Legal Representative Signature

\_\_\_\_\_  
Date: (DD-MMM-YYYY)

\_\_\_\_\_  
Subject Name/Legal Representative (Print)

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Consent Form Administered By Signature

\_\_\_\_\_  
Date: (DD-MMM-YYYY)

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Consent Form Administered By (Print)