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 University of Pittsburgh
 Institutional Review Board
 IRB #001047

CONSENT TO ACT AS A SUBJECT IN A CLINICAL STUDY

Title of Proposal: Screening for Drug Metabolism Enzyme Studies

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To Persons Who Agree To Participate In This Study:

The following information is provided to inform you about the research project and your participation in it. Please read this form carefully. Any questions you may have about this study will be answered. Please feel free to ask any questions you may have about this study and/or about the following information.

Description:

You are being asked to provide your consent to be screened for future participation in research studies to investigate if patients with chronic liver disease are different from subjects without chronic liver disease in their ability to eliminate drugs that are metabolized (break down) by the liver. We are also investigating the different pattern of proteins found in your blood stream and how these patterns do or do not change with time. Both hereditary factors with which you were born and environmental factors can influence the way drugs break down in your body. Liver disease may also contribute to change. If you agree to participate in this screening study, you will have a medical history, a physical examination, as well as have a urine sample collected and blood samples drawn (total of 49 ml or approximately 10 teaspoons) for routine blood work, genetic testing of your drug metabolizing enzymes, analysis of protein patterns in your blood and measurement of baseline cytokine levels. If the results of these tests indicate that you are a suitable candidate for future studies, you confirm that you are willing to have these studies explained to you and at that time make up your mind whether you wish to take part.

This screening study is purely for research and not part of your routine clinical care. Approximately 1500 men and women, 18 years of age or older, will participate in this study. The screening visit will take approximately 1 hour and will be done on the General Clinical Research Center (GCRC) at Montefiore Hospital. You will have a routine medical assessment that will include blood tests, a urine sample to check kidney function and, for women of child-bearing potential, a urine pregnancy test. The blood tests (three teaspoons) will be collected to measure your blood, kidney and liver function using standard laboratory tests. Approximately three teaspoons of blood will be taken from you to analyze the drug metabolizing and DNA repair enzymes and your DNA and mRNA (genetic information). An additional 2 teaspoons will be taken to analyze the pattern of proteins present in your body and approximately 1 teaspoon will be taken to measure baseline cytokine levels.

The DNA and mRNA will be used to screen for differences in the metabolizing enzymes, which break down drugs and for differences in the enzymes which repair changes in your DNA. Individuals vary in the level of these enzyme activities due to both genetic and environmental factors. No other testing will be done or information obtained using your DNA and mRNA. Information from the DNA and mRNA contained in the blood sample will not provide any immediate benefit to you. Therefore, you will not be informed of results of any genetic testing. The results of this study are valid for research purposes only and should not form the basis for subsequent lifestyle or medical decisions. The results of the DNA and mRNA blood sample will be stored indefinitely in Dr. Marjorie Romkes' laboratory.

We will also study your blood samples to better understand the pattern of proteins present in your blood serum and how these patterns do or do not change with time. These studies are being undertaken to learn more about the range of variation we observe in blood proteins in individual donors, and between people, over time. These results will help us better evaluate and understand the differences in the patterns of proteins we observe between healthy people and patients with liver disease and cancer.

We will also study your blood samples to measure baseline cytokine levels which are markers of immune response(your ability to fight off diseases) which can be altered in some disease states. Your levels will then be compared to patients who are enrolled in other similar studies at the Center for Clinical Pharmacology.

The total volume of blood to be drawn is 49 ml or (approximately 10 teaspoons).

Risks and Benefits:

The risks include a small risk of bruising, discomfort and/or infection at the site of your blood sample, lightheadedness or fainting while having blood samples drawn, providing your confidential medical information, and providing information in your genetic material. Information from the DNA and mRNA contained in the blood sample will not provide any immediate benefit to you. Therefore, you will not be informed of results of any gene testing. It is hoped that this study will help to explain the processes in the body that are responsible for the elimination of drugs and other chemicals. It may also help to develop a simple way to assess activity of these processes.

There is a potential for breach of confidentiality which could impact future insurability, employability, or reproduction plans, or have a negative impact on family relationships, and/or result in paternity suits or stigmatization.

There is no personal benefit to you.

New Information:

You will be promptly notified if any new information develops during the course of this study which may cause you to change your mind about continuing to participate.

Costs and Payments:

Participation in this study is voluntary. If you decide to participate in this study, all procedures performed will be at no cost to you. Upon successful completion of the requirements of the study, you will be paid the sum of \$25 for your participation.

Your blood sample and its DNA and mRNA used in this research study may contribute to new inventions or products. In some instances, these inventions or discoveries may be of commercial value and may be sold, patented, or licensed by the investigators and the University of Pittsburgh for use in other research or the development of new products. There are currently no plans to share with you any money or other rewards that the investigators, the University of Pittsburgh, or their agents may realize from the blood sample and its DNA and mRNA or their use in this research study. If you agree to participate in this research study, you voluntarily and freely give your blood sample and its DNA and mRNA to the investigators and the University of Pittsburgh. If you agree to participate in the research project, use of your biological samples and genetic material will be under the control of the principal investigator of this research project. You retain the right to have your blood samples and its DNA and mRNA destroyed should you decide to withdraw from this research study.

Confidentiality:

Any information about you obtained from this research will be kept as confidential (private) as possible. All records related to your involvement in this research study will be stored in a locked file cabinet in the Center for Clinical Pharmacology for 5 years after completion of the study. In addition, your research records will be stored in a computerized filing cabinet that is secured and password protected with access only by the research administrators, faculty, and staff. Your research records at times can be directly linked with your identity, but

this link will only be viewed by the principal investigator and research coordinator. Your identity on your research records will be indicated by a code number rather than by your name. A code number will also indicate your identity on donated blood samples and mRNA. Your stored blood specimens may be made available to investigators who are not listed on this research protocol. Your blood samples will not contain your identity, although specific information from your database (age, gender, race, smoking status) will be required in some instances.

You will not be identified by name in any publication of the research results unless you sign a separate consent form giving your permission (release).

This research study will involve the recording of past and current identifiable medical information from your hospital and/or other health care provider (e.g., physician office) records. The information that will be recorded will be limited to information concerning past medical history, physical status, symptoms, lab tests and medication regimen.

In addition to the investigators listed on the first page of this consent form and their research staff, the following individuals will or may have access to identifiable information (which may include your identifiable medical record information) related to your participation in this research study:

Authorized representatives of the University of Pittsburgh Research Conduct and Compliance Office may review your identifiable research information (which may include your identifiable medical record information) for the purpose of monitoring the appropriate conduct of this research study.

In unusual cases, the investigators may be required to release identifiable information (which may include your identifiable medical record information) related to your participation in this research study in response to an order from a court of law. If the investigators learn that you or someone with whom you are involved is in serious danger or potential harm, they will need to inform, as required by Pennsylvania law, the appropriate agencies.

Authorized representatives of the sponsor of this research study will review and/or obtain identifiable research information related to your participation in this research study for the purpose of monitoring the accuracy and completeness of the research data and for performing required scientific analyses of the research data. While the study sponsor understands the importance of maintaining the confidentiality of your identifiable medical record information, the UPMC Health System and the University of Pittsburgh cannot guarantee the confidentiality of this information after it has been obtained by the study sponsor.

The investigators involved in the conduct of this research study may receive funding from the sponsor to perform the research procedures and to provide the sponsor with identifiable medical record information related to your participation in this study.

Authorized representatives of the U.S. Food and Drug Administration may review and/or obtain your identifiable research information related to your participation in this research study for the purpose of monitoring the accuracy and completeness of the research data. While the U.S. Food and Drug Administration understands the importance of maintaining the confidentiality of your identifiable research information, the UPMC Health System and the University of Pittsburgh cannot guarantee the confidentiality of this information after it has been obtained by the study sponsor.

Authorized representatives of the UPMC Health System hospitals or other affiliated health care providers may

have access to identifiable information (which may include your identifiable medical record information) related to your participation in this research study for the purpose of (1) fulfilling orders, made by the investigators, for hospital and health care services (e.g., laboratory tests, diagnostic procedures) associated with research study participation; (2) addressing correct payment for tests and procedures ordered by the investigators; and/or (3) for internal hospital operations (i.e. quality assurance).

The investigators may continue to use and disclose, for the purposes described above, identifiable information (which may include your identifiable medical record information) related to your participation in this research study for a minimum of 5 years and for as long (indefinite) as it may take to complete this research study.

Right to Participate or Withdraw from Participation: Your participation in this research study, to include the use and disclosure of your identifiable information for the purposes described above, is completely voluntary. (Note, however, that if you do not provide your consent for the use and disclosure of your identifiable information for the purposes described above, you will not be allowed, in general, to participate in the research study.) Whether or not you provide your consent for participation in this research study will have no affect on your current or future medical care at a UPMC Health System hospital or affiliated health care provider or your current or future relationship with a health care insurance provider.

Your doctor is involved as an investigator in this research study. As both your doctor and a research investigator, s/he is interested both in your medical care and the conduct of this research study. Before agreeing to participate in this research study, or at any time during your study participation, you may discuss your care with another doctor who is not associated with this research study. You are not under any obligation to participate in any research study offered by your doctor.

You may withdraw, at any time, your consent for participation in this research study, to include the use and disclosure of your identifiable information for the purposes described above. (Note, however, that if you withdraw your consent for the use and disclosure of your identifiable information for the purposes described above, you will also be withdrawn, in general, from further participation in this research study.) Any identifiable research or medical record information recorded for, or resulting from, your participation in this research study prior to the date that you formally withdrew your consent may continue to be used and disclosed by the investigators for the purposes described above.

To formally withdraw your consent for participation in this research study you should provide a written and dated notice of this decision to the principal investigator of this research study at the address listed on the first page of this form.

Your decision to withdraw your consent for participation in this research study will have no affect on your current or future relationship with the University of Pittsburgh. Your decision to withdraw your consent for participation in this research study will have no affect on your current or future medical care at a UPMC Health System hospital or affiliated health care provider or your current or future relationship with a health care insurance provider.

Compensation for Illness or Injury:

University of Pittsburgh investigators and their associates who provide services at the UPMC Health System (UPMC HS) recognize the importance of your voluntary participation to their research studies. These individuals

and their staffs will make reasonable efforts to minimize, control, and treat any injuries that may arise as a result of this research.

If you believe that you are injured as the result of the research procedures being performed, immediately call the following number 412-565-8326. After hearing a beep, please dial the phone number including the area code in which you want to be reached. This phone number is the Emergency Beeper of the Center for Clinical Pharmacology and will be answered by one of the following investigators: Robert A. Branch, Yvonne Cannon, or Louise DeRiso. Emergency medical treatment for injuries solely and directly related to your participation in this research will be provided to you by hospitals of the UPMC HS.

It is possible that the UPMC HS may bill your insurance provider for the costs of this emergency treatment, but none of these costs will be charged directly to you. If your research-related injury requires medical care beyond this emergency treatment, you will be responsible for the costs of this follow-up care unless otherwise specifically stated below. You will not receive monetary payment for, or associated with, any injury that you suffer in relation to this research.

If you have a question:

If at any point in the study you wish to discuss any aspect of the study with the investigators, you can contact them at:

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L. DeRiso, MSN, CRNP	100 Technology Drive, Suite 450	412-648-1939
A. Steele, RN	Kaufmann Med. Bldg, Suite 900	412-802-3160

Voluntary Consent:

All of the above has been explained to me and all of my current questions have been answered. I understand that I am encouraged to ask questions about any aspect of this research study during the course of this study, and that such future questions will be answered by the researchers listed above. I certify that I have read the preceding, or it has been read to me, and I understand its contents. Any questions I have concerning my rights as a research participant will be answered by the Human Subjects Protection Advocate of the IRB office, University of Pittsburgh (1-866-212-2668).

By signing this form, I agree to participate in this research study. A copy of this consent form will be given to me.

I give my permission to be re-contacted to obtain my consent if there is a desire to use information or genetic material collected in this research, with personal identifiers, in other research projects.

Yes _____ No _____

Participant's Signature

Date and Time

Participant's Printed Name

Certification of Informed Consent:

I certify that I have explained the nature and purpose of this research study to the above-named individual, and I have discussed the potential benefits and possible risks of study participation. Any questions the individual has about this study have been answered, and we will always be available to address future questions as they arise.

Printed Name of Person Obtaining Consent

Role in Research Study

Signature of Person Obtaining Consent

Date and Time