Research Consent Form
Marshfield Clinic Research Foundation
A Division of Marshfield Clinic
1000 N Oak Avenue, Marshfield, WI 54449
SP Code: BRI10412 PI: Murray Brilliant, PhD

Title: Incorporation of Pharmacogenomics into the Electronic Medical Records (PGx)

Why are you being asked to take part in this research study?

You have been asked to participate in this research because you are over the age of 50, you receive your healthcare at Marshfield Clinic and you may someday be prescribed a medication of interest to our research project. There are 7 sites involved with the eMERGE research network, https://www.mc.vanderbilt.edu/victr/dcc/projects/acc/index.php/Main_Page, and the goal is to enroll about 750 people for this research project at each site.

Why is this research study being done?

This research is being done to better understand how genetic information can affect medical care of patients. You are invited to take part in a research study funded by the National Human Genome Research Institute (NHGRI), Pharmacogenomics Research Network (PGRN) and the Marshfield Clinic Research Foundation. The purpose of this research project is to establish a group of 750 people seen at Marshfield Clinic who will contribute to a research effort to help us learn more about genetics and response to medications known as Pharmacogenomics.

Pharmacogenomics is the study of how an individual's genetics (DNA) affects the body's response to drugs. It is the hope that drugs might one day be chosen for individuals based on each person's genetic makeup. Environment, diet, age, lifestyle, and state of health all can influence a person's response to medicines. However, understanding an individual's genetic makeup is thought to be key to prescribing drugs that work better and are safer for you.

The future hope is for doctors to analyze a patient's genetic profile and prescribe the best available drug therapy. Not only will this take the guesswork out of finding the right drug, it will speed recovery time and increase safety as the likelihood of adverse reactions is reduced. Pharmacogenomics has the potential to dramatically reduce the estimated 100,000 deaths and 2 million hospitalizations each year in the United States as the result of negative drug response.

Taking part in this study is voluntary. Whether you decide to take part in this research is completely up to you. Read the following information carefully before you make a decision. In writing this consent form, some technical words were necessary. Please ask for an explanation of any you do not understand. Ask the study doctor or staff as many questions as you wish about this consent form and what will happen to you as part of this research.

What will happen if you agree to be in this research study?

If you agree to be in this research study, you will be asked to do the following:

You will be asked to meet with a research coordinator to discuss the project in depth. This will be in person at Marshfield Clinic. We will discuss the Informed Consent and explain why we are conducting this project, the risks, benefits, alternatives and responsibilities. We will answer all your questions about the project. If you choose to participate, we will require a signed HIPAA Privacy form and an Informed Consent.

You will be asked to complete a short questionnaire. This questionnaire will help us understand how people look at and feel about genetics. This will also help researchers understand how genetics (your genes) influence the way specific drugs may work for you and for other people. A follow-up questionnaire may be sent to you in the future to complete.

You will be asked for a blood sample. A trained Marshfield Clinic Phlebotomist will draw 2 vials (2 tablespoons) of blood. The DNA, or genetic part, will be taken from your blood and sent to a clinically certified (CLIA) laboratory at Marshfield Clinic or off-site for analysis. About 84 genes will be genotyped or looked at. These genes are considered high impact pharmacogenetic genes. This means variants or variations in these genes are either known or thought to be important in drug effectiveness, drug dosing or adverse outcomes. We will add certain information about your DNA genetic results in your medical records.

We will add this clinically important genetic information regarding these variants into your medical records. We will work with your Marshfield Clinic physician with the goal of having your doctor use this information for medications if they are someday prescribed to you. This knowledge will be very beneficial to your doctor with regards to dosing, efficacy and potential adverse problems.

Initially, this data will be limited to 3 drugs: Plavix (medication for heart stents), Warfarin (blood thinner) and Simvastatin (cholesterol lowering medication). As we improve knowledge and ability to link more genetic variants with other drugs, data will be expanded to include other drugs that may affect your healthcare and prescribing of these other medications. This information will include genetic variants recognized by the FDA or other experts regarding specific drugs. We will store the rest of your genetic information in the research warehouse for future use. These data may be used for additional pharmacogenetic research. Periodically, when new FDA warnings are discovered, we may update your medical record with information on how you may react to different drugs.

This study may find you have one or more genetic risk factors that we were not looking for. These conditions may be treatable, therefore you and your healthcare provider should know about them. An example of such a clinically relevant variant is a condition called malignant hyperthermia. This condition is more common in Wisconsin, and can result in serious complications if certain types of anesthesia are given prior to surgery. If one of these variants is noted to be present in your genetic make-up, we will inform you and your healthcare provider. This information will be placed in your medical record.

Clinical and Scientific experts will help decide which genetic variants may require clinical attention. If any such variants are found in your DNA, you and your primary health care provider will be sent a letter informing you of these results. However, you and/or your insurance provider will be responsible for any costs associated with clinical follow-up related to this genetic information. It is important that you notify study staff and/or your primary care provider if your contact information changes.

Research staff will have access to your medical record. Selected information from your medical record will be used to learn more about genetic variants and pharmacogenomics. Your medical record will be used to help us look at medication use and the effects it has on different people. This will continue throughout the project. Clinically important information may be added to your medical record during this project.

What are the possible risks or discomforts from being in this study?

Blood Draw Risks: There is always a risk when having blood taken from a vein. This blood draw will not be any different than the blood draw for normal clinical labs. Risks associated with blood draws include the potential for minor pain and slight bruising. There is a very small chance of infection at the site where the blood was drawn. Some people may faint when their blood is drawn.

Genetic Testing: Risks of learning genetic test results may include emotional upset or insurance or job discrimination.

Confidentiality Risk: Clinically relevant genetic information will be put into your medical record. This information will be treated the same as other medical information in your medical record. All records and materials that identify you will be treated as confidential.

Remaining genetic information that will not currently be used outside of your medical records will be stored on a secure computer system. A limited number of approved researchers and staff have access to the database. Few individuals will have access to the codes that link your identity to the data and all people working with your data are required to protect your privacy.

Although remote, there is a risk that information about your genetic make-up may be accidentally released to you or others. Researchers will take steps outlined in this consent form to protect your genetic information. However, only selected clinically relevant genetic information will be placed in your medical records for medication use and dosage.

This research may also involve risks or discomforts that are now not known.

What are possible benefits from being in this research study?

This study may not improve your health. However, the information added to your medical record from this research project may help your health care provider make better prescription drug choices for you. This may help you avoid some prescription drug-related side effects or complications. You may never need any of the medications we are studying and this information may provide no benefit to you.

Will you be paid for taking part in this research study?

You will not receive compensation or reimbursement for participation in this project.

How long will you be in this research study?

There is no specific end time since this study will build resources at Marshfield Clinic to incorporate genetic information into clinical care. This information will be placed in your medical records for your doctor to use for your future medical care. Therefore, there is no intention to end the study. You are agreeing to be part of ongoing research surrounding genetic and drug related information at Marshfield Clinic. At some point in time, Marshfield Clinic Pharmacy and medical professionals may determine that use of specific genetic variants related to prescription drugs is part of regular clinical care. At that time, your genetic information may no longer be considered part of research, but instead, part of clinical care.

You will be told of any new findings regarding this research that may affect your willingness to be in this study.

Will there be a cost to you to take part in this research study?

Neither you nor your insurance company will get billed for study-related procedures.

Who will have access to my data?

Your Marshfield Clinic primary doctor will have access to the clinically important information added to your medical records. The goal is having your doctor use this information for medications if they are someday prescribed to you.

Approved researchers and staff will have access to your research data.

Your coded research data may be shared with researchers outside of the Marshfield Clinic. Outside researchers could include other hospitals, medical schools, universities, research institutions and companies. Drug companies may use this to study how their drugs work and how different people respond. This shared information will have a coded number and will not include your name or any other identifying information. Researchers will be able to see selected medical information about you but will not have any way of knowing your name.

Databases are being developed to help further medical research. We will share coded data with these types of databases. One example of this type of database is called "dbGaP" (short for "Database Genotype and Phenotype"). This database has been set up by the National Institutes of Health.

The Marshfield Clinic Research Foundation's Institutional Review Board could review this research project. They may see sections of research records with your name or other identifiers. We may be required to provide summary information to workers or contractors of the United States Government for reviewing or evaluating Federally-funded projects. They are required by law to keep the information private.

Researchers may also present data using combined subject information at scientific meetings and in scientific publications. These results will not identify you.

How will information about you and your participation be kept confidential?

Your medical, hospital, or other billing records and research material that would identify you will be held confidential and protected by Marshfield Clinic confidential policies. Medical records that identify you and the consent form signed by you, may be inspected by the following agencies:

- National Institutes of Health (NIH)
- Other governmental regulatory (or health) agencies
- Marshfield Clinic Research Foundation's Institutional Review Board
- Medical professionals who need to access your medical record for your continuing care.

Because of the need to release pertinent sections of information to these parties, all efforts will be made to maintain confidentiality. These people must also keep the information confidential. Your name will not be given to anyone not associated with the study unless required by law.

Results of this study may be presented at scientific meetings or in scientific publications. However, your identity will not be made known.

Federal and state laws exist which provide individuals with a variety of protections against genetic-based discrimination either by employers or by health insurers.

Wisconsin state law was enacted in 1991 and applies to employers, labor unions, employment agencies, licensing agencies, health insurers and self-funded insurance plans sponsored by local government. These groups may not require or even request that you obtain a genetic test; or if a genetic test is obtained, disclose the fact that a test was taken or ask for test results

The Genetic Information Non-discrimination Act (GINA) applies to health insurance companies and group health plans, and employers with 15 or more employees. Under the terms of the act, these groups may not:

- Request genetic information collected as part of research; or
- Use your genetic information when making decisions regarding your insurance eligibility or premiums; or
- Use genetic information that is obtained from research when making a decision to hire, promote, or fire an individual, or when setting the terms of employment.

Be aware that neither GINA nor the comparable Wisconsin State laws protect against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. These laws also do not stop employers or health insurers from discriminating against someone on the basis of a pre-existing or apparent genetic disease or disorder.

As part of this research, your genotype and phenotype data will be de-identified and shared with the National Institutes of Health (NIH) GWAS data repository. From this repository it will be available to other researchers conducting research with NIH funds. The information that is shared will not include direct identifiers.

What happens if you become ill or injured from this study?

If you become ill or injured from this study, medical care is available at Marshfield Clinic or the health care provider of your choice. You or your health insurer would be responsible for this cost.

What do you do if you want to withdraw from this study?

Taking part in this research is voluntary and you do have the right to stop taking part. If you withdraw, your remaining DNA will be destroyed. We will not use your information in future studies. If your samples have already been used in research it would not be possible to remove any of the information that may have been learned prior to your request to withdraw. We will document your decision on a form,

and ask you to sign the form. Information placed in your medical records may not be removed. If you wish to withdraw please call us at **715-387-9141** or **1-800-782-8581** ext **7-9141**.

Who can I contact for more information on this research?

For more information about this research or to report injuries or side effects, you may contact Dr. Murray Brilliant, Marshfield Clinic at **1-800-782-8581** ext. **1-6469**.

What are my rights if I take part in this research?

Being in this study is voluntary. Refusing to participate or discontinuing participation at any time will involve no penalty or loss of benefits to which you are otherwise entitled. If you choose not to sign this consent form, your relationship with your doctor and this institution will not change.

You are not giving up any legal rights by signing this consent document and taking part in this research study.

If you have any questions about your rights as a research subject, you may contact Marshfield Clinic Research Foundation's Institutional Review Board (IRB) at 1-800-782-8581 ext. 9-3022. The IRB is responsible for helping protect human research subjects.

Collection/Banking of Human Biological Material for Future Research:

As a part of this study, you will have a blood sample collected. DNA will be extracted from the blood sample and research staff would like to store some of this DNA for future research.

You will likely gain no personal benefit by allowing your sample to be stored and used for future research. Society in general may benefit by learning more about certain medications, and how an individual's genetics affects a body's response to drugs. DNA sampling involves the same risks and protections regarding your genetic information as indicated in the "Confidentiality" section of this form.

Participation in this DNA banking is completely voluntary. Your decision will not affect your care. You can participate in the original study without participating in the storage and use of your DNA for future research. You can change your mind at any time about storage and future use of your DNA. Please read the two options below, think about your choice, check "Yes" or "No," and sign and date below.

1) My DNA may be stored for possible use in different future research projects to learn about prevention, treatment, or cures through Pharmacogenomics and clinically relevant variants. Clinically important information may be added to my medical record. I understand that the investigator will be required to obtain approval from an Institutional Review Board for other uses of my DNA.

☐ Yes ☐ No

2) My DNA may be stored for possible use in research about other genetic health problems (for example, diabetes, Alzheimer's, Huntington's, mental illness, etc.). I understand that the investigator will be required to obtain approval from an Institutional Review Board for future use of my DNA.

☐ Yes ☐ No

What does signing the consent form mean?

A signature indicates that:

- You have read this document.
- You have freely decided to take part in the research study as describe above.
- The study's general purposes, details of involvement and possible risks and discomforts have been explained to you.

You will receive a signed copy of this consent form.

Statement of Consent

I have read the consent form or it has been read to me. I have freely decided to take part in the research study described. The reason(s) for doing the research, procedures, possible risks and benefits, and my non-research options have been explained to me.

_____ _____

Signature of Date of Signature

- ❑ Subject
- ❑ Subject's Activated Power of Attorney for Healthcare

(*Check appropriate title*)

_____

Printed Name of Subject

_____

Printed Name of Signatory (if other than subject)
(if applicable)

_____ _____

Signature of Presenter Date Presented

_____

Printed Name of Presenter