UNIVERSITY of MARYLAND
THE FOUNDING CAMPUS

RESEARCH CONSENT FORM

Protocol Title:	Pharmacogenetics of Glucagon-Like Peptide 1 Receptor (GLP1R) Inhibitors
Study No.:	HP-00067574
Principal Investigator:	Simeon Taylor, M.D. Phone: 410-706-7103
Sponsor:	American Diabetes Association

We are asking you to take part in a research study. Your participation is voluntary. Please read this consent form and ask any questions before you decide if you want to take part.

Background Information
Until recently, drugs have been made with the idea that each drug works pretty much the same in everybody. The field of pharmacogenetics has changed that "one size fits all" approach. Pharmacogenetics uses information about a person's genes to choose the drugs and drug doses that are likely to work best for that particular person. Genes are pieces of DNA that have the instructions needed to make our bodies work. DNA stores these instructions in the form of a code. This is the code that you inherit from your parents and that you pass on to your children.

This is a study to look at how two drugs called **exenatide and sitagliptin** work in different people. Exenatide and sitagliptin are FDA approved drugs that are used to treat type 2 diabetes. Diabetes is a disease that causes a person to have high amounts of sugar in the blood. Exenatide is in a class of drugs called glucagon-like peptide 1 receptor (GLP1R) analogs. Sitagliptin is in a class of drugs called dipeptidyl peptidase 4 (DPP4) inhibitors. GLP1R analogs and DPP4 inhibitors work by stimulating the release of insulin to help lower blood sugar.

You have been asked to be in this study because you have participated in an Amish Research Clinic study before and you carry a gene variation that may affect the way exenatide or sitagliptin works.

What is the purpose of this study?
The purpose of this study is to see if a person's genes affect how well exenatide and/or sitagliptin lower blood sugar in healthy people who do not have diabetes. There will be up to 80 adult Amish participants in this study.

What will happen if I join the study?

Screening Visit

The screening visit will last about 1 hour. We will ask you questions about your health and your family's health. We will measure your height, weight, pulse and blood pressure. We will draw about 3 teaspoons of blood from a vein in your arm. Your blood will be tested to make sure you do not have diabetes, significant kidney, liver, thyroid problems or low blood cell count. If you meet the study requirements, you will have up to four study visits at the Amish Research Clinic spaced 5 days – 4 weeks apart. You will be in the study for up to 16 weeks. Your participation will include 3 or 4 of these study visits depending on your availability.

Clinic Visits

For each visit, you will arrive at the clinic after a 12 hour fast. We will measure your height, weight, waist and hip circumference, pulse and blood pressure. If you are female of child-bearing potential, you will provide a urine sample at the visit or in the week prior to make sure you are not pregnant. At your first visit only, blood will be drawn for cholesterol testing, DNA, and samples to be stored for future research. About 5 teaspoons of blood will be drawn for these tests.

Intravenous Glucose Tolerance Test (IVGTT)

At two of the visits, you will have an intravenous glucose tolerance test. This test is done to see how your body processes glucose (sugar). During this test you will rest comfortably on a cot. A small plastic tube (IV catheter) will be placed in a vein in each arm.

Before the test, you will be given either **exenatide** OR **salt water** in an injection (a shot) under the skin on your arm or abdomen. You will be given exenatide at one of the visits and the salt water at the other visit. The dose of exenatide is the same as the dose approved by the FDA for diabetic patients.

You will be then be given glucose (sugar) through the IV tube in one arm vein. Blood samples will be drawn through the IV tube in your other arm at frequent intervals for three hours. We will then remove the IV tubes and you will be given lunch. About 24 teaspoons of blood will be drawn during this 3 hour test.

Oral Glucose Tolerance Test (OGTT)

At the other two visits, you will have an oral glucose tolerance test. This test is done to see how your body processes glucose. 2 hours before the first test, you will take **a "sugar" pill** and 2 hours before the second test you will take sitagliptin 100 mg. The dose of sitagliptin is the same as the dose approved by the FDA for diabetic patients. You will take these at home before coming to the clinic. Other than taking the pill, you will continue your 12 hour fast. When you arrive at the clinic, an IV tube will be placed in a vein in one arm. You will be given a sugary beverage to drink. Blood samples will be drawn through the IV tube in your arm every ½ hour for three hours. We will then remove the IV tube and you will be given lunch. About 16

teaspoons of blood will be drawn during this 3 hour test. At one of the visits we will also collect about 4 teaspoons of blood to store for future research.

Future Use of Blood and Information

Your blood samples, genetic data and health information will be stored for future research use. Your samples will be stored with a code so that your name cannot be readily identified. Your samples and information may be shared with other researchers. This may include researchers from University of Maryland as well as from other universities, the government, and drug- or health related companies. Researchers may study your genes and other substances using your samples. Researchers may do a wide range of genetic tests, from those on a single gene to whole genome sequencing, which looks at your entire genetic code. Information from your stored samples, along with your health information, may be used by other researchers to help understand the cause of diseases and how to treat or prevent them. Your samples will not be used to develop cell lines. Your samples will not be sold or given to third parties. Information that might identify you personally will NOT be provided to other researchers. Results of research tests done with your samples **will not** be reported to you or put in your medical record. Any future research using your samples or health information will be reviewed and approved by an Institutional Review Board (IRB), which is a special Committee that oversees research studies to protect the rights and welfare of research participants. If at any time you wish to have your samples removed from the study and destroyed you may do so by contacting Dr. Simeon Taylor by phone at 410-706-7103 or by mail at 685 W. Baltimore Street, MSTF Room 357, Baltimore, MD 21201.

- You can use the information and blood samples collected from me for future studies of drug response or other disorders or health conditions.

  Please mark and initial your choice: YES ____ NO ____ Initials _____

In the future, we may want to ask you if you want to take part in other research studies. Once you hear the details of the study, you can decide then to take part or not take part.

- You can contact me in the future to ask me to take part in other studies.

  Please mark and initial your choice: YES ____ NO ____ Initials _____

Sharing Data in Large Scientific Databases

To do more powerful research, it is helpful for researchers to share test results from studying human samples. They do this by putting it into one or more scientific databases, where it is stored indefinitely along with information from other studies. There are different kinds of databases. Some databases are open to the public and some are restricted. Anyone on the Internet can look at databases open to the public. Only researchers who apply and are approved can use restricted databases. Databases may be maintained by the University of Maryland, the federal government (for example, National Institutes of Health), or by private companies. Some of your genetic and health information could be placed into one or more of these open or restricted

databases. Your name and other information that could directly identify you (such as address or social security number) **will never** be placed into any scientific database.

Are there any risks to me?

Exenatide: Common side effects of exenatide include nausea, vomiting, diarrhea, headache, dizziness, or redness or swelling at the injection site. Very rarely, exenatide can cause severe allergic reaction with rash, itching or swelling, dizziness, trouble breathing. There is a risk of acute pancreatitis. If you experience symptoms of severe abdominal pain or nausea, seek immediate medical attention. The chance of having side effects is reduced because you will only take one dose of exenatide at the lowest recommended dose.

Sitagliptin: Common side effects of sitagliptin include upper respiratory infection or headache. Very rarely, sitagliptin can cause pancreatitis, serious allergic reactions, kidney injury, and severe joint pain. The chance of having side effects is reduced because you will only take one dose of sitagliptin.

Blood Drawing: Blood drawing can cause pain, swelling, or bruising at the needle puncture site. Occasionally, blood drawing can cause feeling faint or even fainting. Rarely irritation of the vein or infection may occur. To lower these risks, only trained staff will draw your blood. The total amount of blood drawn for the entire study will be about 92 teaspoons (460 ml.).

Intravenous glucose tolerance test: In addition to the risks described above for blood drawing, IV administration of glucose may sometimes result in lightheadedness or tingling in the arm or shoulder. Rarely, giving glucose solution can cause irritation of the vein or if it "leaks" out of the blood vessel, irritation of the surrounding tissue. We will instruct you to tell us if you feel any discomfort during the glucose infusion. There is a very slight chance that some people may have a drop in blood sugar towards the end of the test and feel symptoms such as sweating, weakness, and light-headedness. If this occurs, we will have you remain in bed until you are given a sugary drink or something to eat.

Oral glucose tolerance test: In addition to the risks described above for blood drawing, you may experience nausea after drinking the sugary beverage. There is a very slight chance that some people may have a drop in blood sugar towards the end of the test and feel symptoms such as sweating, weakness, and light-headedness. If this occurs, we will have you remain in bed until you are given a sugary drink or something to eat.

Pregnancy: Because exenatide may be harmful to a pregnant woman and the unborn child, you should not become pregnant while you are in this study. A urine pregnancy test will be done at or before each clinic visit if you are able to bear children. Women who are breast feeding cannot be in this study.

Confidentiality: There is a small risk that your private medical or genetic information could be revealed or discovered by mistake. If the information suggested something serious about your

health, it could be misused. In the unlikely event this happens, this may cause you to experience feelings of anger, worry or embarrassment. The information could be used to try to make it harder for you to get or keep a job or health insurance. There are laws against using genetic information this way. They may not give full protection for life, long-term care, or disability insurances. We believe that the chance these things will happen is very small, but we cannot promise that this will not happen. We will do our best to protect your study information. The steps we will take to keep your information private are described below under the section "How will you keep my information safe?"

We do not think that there will be further risks to your privacy and confidentiality by sharing your genetic information with large scientific databases. However, we cannot predict how genetic information will be used in the future. There is a risk that someone could link the information in a scientific database back to you, because even without a name or other information, genetic information is unique to each person. We believe the chance that someone will figure out the sample is yours is very small.

There may be risks in this study which are not yet known. You will be told of any significant new findings which develop during the study which may affect your willingness to participate in the study.

Will being in the study help me?
You may or may not benefit by taking part in this study. A direct benefit cannot be guaranteed from your participation in this study. Your blood pressure measurements, screening blood test results, and cholesterol results will be shared with you. You may share your results with your doctor, who may make recommendations regarding your health. The knowledge gained from this study will improve our understanding of how genes affect people's response to medications for the treatment of diabetes. This may lead to the design of more effective medications and better patient care in the future.

What are my options?
This is not a treatment study. Your alternative is not to join the study. If you choose not to join, your healthcare at University of Maryland, Baltimore will not be affected. If you are an employee or student, your employment status or academic standing at UMB will not be affected by your participation or non-participation in this study.

Will it cost me anything to be in this study?
It will not cost you anything to take part in this study, including your transportation to and from the clinic.

Will I get paid?
You will be paid $10 for the Screening Visit and $125 for each Clinic Visit completed for a total of up to $510. A check will be mailed to you about 4 weeks after completion of your study visits.

If you do not complete the study, you will be paid for the portion of the study that you complete. Your transportation costs to and from the clinic will be paid, or reimbursed to you.

How will you keep my information safe?
Efforts will be made to limit access to your personal information, including research study and medical records to people who need to review this information. We cannot promise complete secrecy. Here are just a few of the steps we will take to protect your information:

- We will remove your name and other identifiers from your study information and specimens, and replace them with a code number. We will keep the list that links the code number to your name separate from your study information. Only a few of the study staff can see the list that links the code number to your name.
- We will store your information in locked cabinets and on password-protected computers.
- The data from the study may be published. However, you will not be identified by name.
- Organizations that may inspect and copy your information from this study include the IRB, other representatives of the University of Maryland, the American Diabetes Association, the Food and Drug Administration and of the Office of Human Research Protections (OHRP). This is necessary to make sure the research findings are true. They also protect your safety and wellbeing.
- Everyone using study information will work to keep your information confidential. Your personal information will not be given out unless required by law.

What if I no longer want to be in the study?
Being in this study is voluntary. You can say no now, or leave the study at any time later. There are no penalties, loss of benefits, or negative consequences if you choose not to take part or to leave the study. If you leave the study, data already collected will not be removed from the study database. If you decide to stop taking part, if you have questions, concerns, or complaints, or if you need to report a medical injury related to the research, please contact Dr. Simeon Taylor at 410-706-7103.

Can I be removed from the research?
The person in charge of the research study can remove you from the research study without your approval. Possible reasons for removal include if the doctor in charge decides that the research study is no longer in your best interest. The study doctor will tell you about this and you will have the chance to ask questions if this were to happen.

UNIVERSITY STATEMENT CONCERNING RESEARCH RISKS
The University of Maryland, Baltimore (UMB) is committed to providing participants in its research the rights due them under State and federal law. You give up none of your legal rights by signing this consent form or by participating in the research project. This research has been reviewed and approved by the Institutional Review Board (IRB). Please call the Institutional Review Board (IRB) if you have questions about your rights as a research subject.

Participating in research may result in an injury, as explained above. If you suffer an injury directly related to your participation in this project, UMB and/or one of its affiliated institutions or health care groups will help you obtain medical treatment for the specific injury and provide referrals to other health care facilities, as appropriate. UMB and/or its affiliated institutions or health care groups will not provide you with financial compensation or reimbursement for the cost of care provided to treat a research-related injury or for other expenses arising from a research-related injury. The institution or group providing medical treatment will charge your insurance carrier, you, or any other party responsible for your treatment costs. If you incur uninsured medical costs, they are your responsibility. The study staff can give you more information about this if you have a study injury.

By signing this Consent Form, you are not giving up any legal rights. If this research project is conducted in a negligent manner and you are injured as a direct result, you may be able to recover the costs of care and other damages from the individuals or organizations responsible for your injury.

If you have questions, concerns, complaints, or believe you have been harmed through participation in this research study as a result of researcher negligence, you can contact members of the IRB or the Human Research Protections Office (HRPO) to ask questions, discuss problems or concerns, obtain information, or offer input about your rights as a research participant. The contact information for the IRB and the HRPO is:

University of Maryland Baltimore
Human Research Protections Office
620 W. Lexington Street, Second Floor
Baltimore, MD 21201
410-706-5037

Signing this consent form indicates that you have read this consent form (or have had it read to you), that your questions have been answered to your satisfaction, and that you voluntarily agree to participate in this research study. You will receive a copy of this signed consent form.

If you agree to participate in this study, please sign your name below.

_____	_____
Participant's Signature	Investigator or Designee Obtaining Consent Signature

Date:_____ Date:_____