UNIVERSITY OF MICHIGAN

CONSENT TO BE PART OF A RESEARCH STUDY

1. KEY INFORMATION ABOUT THE RESEARCHERS AND THIS STUDY

Study title:

Vancomycin Dose Optimization in Obesity

Company or agency sponsoring the study:

This study is funded by the United States Food and Drug Administration

Names, degrees, and affiliations of the principal investigator and study coordinator (if applicable):

Principal Investigator: Manjunath Pai, PharmD, FCP

Study Coordinator: Aleksas Matvekas, BS

1.1 Key Study Information

You may be eligible to take part in a research study. This form contains important information that will help you decide whether to join the study. Take the time to carefully review this information. You should talk to the researchers about the study and ask them any questions you have. You may also wish to talk to others such as your family, friends, or other doctors about joining this study. If you decide to join the study, you will be asked to sign this form before you can start study-related activities. Before you do, be sure you understand what the research study is about.

A research study is different from the regular medical care you receive from your doctor. Research studies hope to make discoveries and learn new information about diseases and how to treat them. You should consider the reasons why you might want to join a research study or why it is not the best decision for you at this time.

Research studies do not always offer the possibility of treating your disease or condition. Research studies also have different kinds of risks and risk levels, depending on the type of the study. You may also need to think about other requirements for being in the study. For example, some studies require you to travel to scheduled visits at the study site in Ann Arbor or elsewhere. This may require you to arrange travel, change work schedules, find childcare, or make other plans. In your decision to participate in this study, consider all these matters carefully.

This research is studying a drug called vancomycin that is already approved by the Food and Drug Administration (FDA) to treat infections. Researchers are studying a group of people to continue to learn information about the best way to dose this drug in patients who are overweight. This research will compare the dosing of this drug based on body weight versus an estimate of kidney function. This study involves a process called randomization. This means that the vancomycin dose that you receive in the study is not chosen by you or the researcher. The study design divides study participants into separate groups, based on chance (like the flip of a coin), to compare different treatments or procedures. If you decide to be in the study, you need to be comfortable not knowing whether you are randomized to body weight dosing, which is the current standard, or kidney function-based dosing, which is what we are studying.

This study requires 2 visits that include a screening visit (about 1 hour), and a study procedures visit (up to 14 hours), detailed information about these tests will be provided later in this document.

During the screening visit, you will be asked to submit a single blood sample which will be used to determine your kidney function and to check that you are healthy based on two common blood tests. Your weight and height will also be recorded to calculate your body mass index (BMI). If you are a female of childbearing potential, we will

perform a urine pregnancy test to make sure that you are not pregnant before any procedures. Meeting the screening criteria will confirm your eligibility in this research study.

If you are eligible, you will be scheduled for the study procedures visit. Then, a thin tube (intravenous catheter) will be inserted into a vein in your arm. This tube will be used to infuse vancomycin and to collect the blood at different time points so that we can measure the concentrations of vancomycin in your body. More detailed information on the procedures of this study will be provided later in this document.

There can be risks associated with joining any research study. The type of risk may impact whether you decide to join the study. For this study, some of these risks may include a rash, itching, swelling, dizziness, or trouble breathing. Vancomycin can sometimes affect the kidneys especially if you already have kidney issues, we will check your kidney function before you participate. In rare cases, especially with long-term use, vancomycin can cause hearing loss or ringing in the ears. More detailed information will be provided later in this document.

This study may offer some benefit to you now by providing you with a free estimate of your kidney function, and assessment of your body composition, all of which will be given to you after completion of the study. Furthermore, we expect the results of this study may benefit others in the future by providing a better way to dose this antibiotic in patients who are overweight. More information will be provided later in this document.

We expect the amount of time you will participate in the study will be no more than 15 hours across the study visits.

Even if you decide to join the study now, you are free to leave at any time if you change your mind.

More information about this study continues in Section 2 of this document.

2. PURPOSE OF THIS STUDY

2.1 Study purpose:

It is important to select the right dose of an antibiotic to cure infections and prevent side effects. Vancomycin is a commonly used antibiotic that is dosed on body weight. Body weight does not always reflect a person's body composition or kidney function. We believe that kidney function is more important than body weight to select vancomycin doses. This research study is being conducted to see if dosing vancomycin on estimated kidney function is better than dosing on weight in healthy volunteers who are overweight.

3. WHO MAY PARTICIPATE IN THE STUDY

Taking part in this study is completely **voluntary**. You do not have to participate if you don't want to. You may also leave the study at any time. If you leave the study before it is finished, there will be no penalty to you, and you will not lose any benefits to which you are otherwise entitled.

3.1 Who can take part in this study?

Adult volunteers who meet the requirements listed below may be eligible to participate in this study.

It is important that you provide complete and accurate information about your health condition/medical history to ensure that you are a safe and appropriate candidate for participation in this study.

You can participate in this study if:

1. You weigh 80 kilograms (176 pounds) or more
2. You are between 18 to 50 years old
3. Your kidney function is in the normal range

You cannot participate in this study if:

1. You are pregnant or breastfeeding a child
2. You have been sick for any reason within the past 3 weeks
3. You have a history of severe allergic diseases including drug allergies, with the exception of seasonal allergies
4. You have any medical condition that in the opinion of the study physician puts you at a higher risk for side effects from participating in this study
5. You have a history of drug addiction or alcohol abuse within the past 12 months
6. Your lab values are not in the normal range during screening
7. You are unwilling or unable to receive vancomycin by intravenous infusion
8. You have a history of psychiatric or neurological illness, including seizure disorders
9. Your blood pressure is not within a normal range
10. Your heart rate is not within a normal range
11. You previously had a bad reaction or side effect to vancomycin, cetirizine, or famotidine
12. You have a history of hearing loss
13. You are taking a medication that might increase the risk of hearing loss

3.2 How many people are expected to take part in this study?

A total of 24 people are expected to take part in this study. The study will be conducted at the Michigan Clinical Research Unit (MCRU), located at Frankel Cardiovascular Center, 1500 E Medical Center Dr
Ann Arbor, MI 48109

4. INFORMATION ABOUT STUDY PARTICIPATION

4.1 What will happen to me in this study?

Before any study activities take place, you will be asked to read and sign this informed consent.

If you agree to take part and are determined by the study doctor to be eligible, you have certain responsibilities such as ensuring that you arrive at all your scheduled appointments on time, follow all requirements and instructions, and report any adverse reactions you may have during the study.

The study activities will occur at the Michigan Clinical Research Unit (MCRU).

Visit 1 (Screening)
During this visit, we'll check if you meet the requirements for the study. We'll only gather basic medical information and measure your height and weight to confirm if you're eligible and make sure it's safe for you to participate. We'll take a small blood sample from your arm, about two teaspoons, to run tests checking your kidney function and to make sure you are healthy.

If you're able to get pregnant, we'll also do a urine test to check if you're pregnant. You can't join the study if you are.

During this visit we'll do a DEXA scan, which is a painless and safe test used to measure body composition and bone density. During the scan, you'll lie down on a special table while a big scanning arm passes over your body. You will be provided with instructions, and this takes about 15 minutes.

Based on these tests and results, we'll decide if you can continue with the rest of the study. If we find any issues or signs of illness, we'll let you know and suggest you see your own doctor for treatment. If you're eligible to continue, we'll schedule your next visit.

Visit 2 (Study Procedures Visit, lasting up to 14 hours)
A study team member will contact you to make an appointment for this visit. At the specified appointment time, you will arrive at the Michigan Clinical Research Unit (MCRU) at Frankel's Cardiovascular Center, where the study procedures will take place. You will not be allowed to bring any food items and/or drinks from outside, except for water. Bottled water will be available and provided to you inside the unit room. We will provide you with meals during the study. Upon arrival, a study staff member will ask to confirm your personal information including name, date of birth, and age. Your vital signs (height and weight) will then be recorded. If you have a uterus and can get pregnant, we will also perform a urine pregnancy test.

Next, we'll explain the timeline of the study procedures to you. We will ask you to take an antihistamine combination of cetirizine (commonly known as "Zyrtec") and famotidine (commonly known as "Pepcid") by mouth to prevent vancomycin infusion reaction like a rash and itchiness. An intravenous catheter, which is a thin tube, will be inserted into a peripheral vein of your arm by a clinical staff member for vancomycin administration and to collect blood samples, so that we can measure vancomycin concentrations in your body. After catheter placement, one blood sample (10 mL, the equivalent of two teaspoons) will be collected prior to the administration of the study drug. You will be asked to use the bathroom so that we can collect your urine. After the collection of this blood and urine sample, vancomycin will be administered through the catheter over 3 to 5 hours followed by saline (salt water) flushes. The dose that you receive will either be the current weight-based method (Control) or the kidney-function based dose (Test). After the study drug is infused, blood samples (6 mL/or about 1 teaspoon per sample) will then be taken at 0.5-, 1-, 2-, 3-, 4-, and 8-hours time points. After the 8-hour sample collection, the intravenous catheter will be removed.

You will be discharged from the research unit after the last blood sample is collected from you. You will receive a follow-up phone call within a day of Visit 2 to ask about any side effects or problems since that visit.

4.2 How much of my time will be needed to take part in this study?

This study involves 2 visits. Each visit will take about:

- Screening Visit: about 1 hour
- Visit 2: about 14 hours.

4.3 When will my participation in the study be over?

You may choose to leave the study at any time. However, finishing the study involves successful completion of the screening visit, and study procedures visit

5. INFORMATION ABOUT STUDY RISKS AND BENEFITS

5.1 What risks will I face by taking part in the study? What will the researchers do to protect me against these risks?

The known or expected risk related to vancomycin administration:

- Most common side effects (occurring in less than 10% of people who received IV vancomycin) are:
  - Pain (related to injection)
  - Rash
  - Itchiness
  - Dizziness

- Rare side effects (less than 1% of people who received the study agent) are:
  - Serious allergic reactions

- Ringing in the ears
- Confidentiality: All research studies have some potential for a breach in confidentiality

The known or expected risk related to Cetirizine administration:

- Most common side effects (occurring in 5-15% of people who received cetirizine) are:
  - Drowsiness
  - Feeling Tired
  - Dry Mouth

The known or expected risk related to Famotidine administration:

- Most common side effects (occurring in less than 10% of people who received famotidine) are:
  - Headache
  - Dizziness
  - Constipation
  - Diarrhea

DEXA scans are commonly performed and considered safe. During the scan, you are exposed to a very low amount of radiation. The amount of radiation is less than one tenth of the amount used during a normal chest X-ray and equivalent to one day of exposure to natural background radiation. The amount of radiation used during a DEXA scan is considered safe for adults but can cause damage to unborn babies.

The researchers will try to minimize these risks by:

To minimize these risks this study will only administer a single dose of the drug at a rate of infusion that lowers the risk of a reaction. We will also ask you to take an antihistamine combination before the infusion to further lower the risk of a reaction. During each study visit, you will be observed for the development of potential side effects. Side effects will be immediately evaluated by the study doctor and appropriate treatments will be performed. A pregnancy test will be done before the DEXA scan to make sure you are not pregnant. Additionally, there may be a risk involving loss of confidentiality or privacy. For example, if individuals outside this study were to discover that you were a participant in this research, or if any collected identifiable genetic or health information were disclosed to unauthorized persons, there is a risk of discrimination by employers or insurance providers. The researchers have adopted privacy and confidentiality procedures to help prevent such disclosures. See Section 9 of this document for more information on how the study team will protect your confidentiality and privacy.

As with any research study, there may be additional risks that are unknown or unexpected.

5.2 What happens if I get hurt, become sick, or have other problems as a result of this research?

The researchers have taken steps to minimize the risks of this study. Even so, you may still have problems or side effects, even when the researchers are careful to avoid them. Please tell the researchers listed in Section 10 about any injuries, side effects, or other problems that you have during this study. You should also tell your regular doctors or any other provider or hospital you visit**.**

5.3 If I take part in this study, can I also participate in other studies?

Being in more than one research study at the same time, or even at different times, may increase the risks to you. It may also affect the results of the studies. You should not take part in more than one study without approval from the researchers involved in each study.

5.4 How could I benefit if I take part in this study? How could others benefit?

You may not receive any personal benefits from being in this study. However, others may benefit from the knowledge gained from this study.

Some subjects may potentially benefit from the kidney function screening and measurements and assessment of their body composition. Measurements associated with this study will be provided to participants at the end of the study. These measurements of kidney function and body composition are for your knowledge only and shouldn't be used to inform clinical care.

5.5 Will the researchers tell me if they learn of new information that could change my willingness to stay in this study?

Yes, the researchers will tell you if they learn of important new information that may change your willingness to stay in this study. If new information is provided to you after you have joined the study, it is possible that you may be asked to sign a new consent form that includes the new information.

6. ALTERNATIVES TO PARTICIPATING IN THE STUDY

6.1 If I decide not to take part in this study, what other options do I have?

Your participation in this study is completely voluntary. You have the option to not participate. If you choose to not take part in this study, your healthcare at the University of Michigan will not be affected. If you are an employee or student, your employment status or academic standing at University of Michigan campus will not be affected by your participation or non-participation in this study.

7. ENDING THE STUDY

7.1 If I want to stop participating in the study, what should I do?

You are free to leave the study at any time. If you leave the study before it is finished, there will be no penalty to you. You will not lose any benefits to which you may otherwise be entitled. If you choose to tell the researchers why you are leaving the study, your reasons for leaving may be kept as part of the study record. If you decide to leave the study before it is finished, please tell one of the persons listed in Section 10 "Contact Information".

7.2 Could there be any harm to me if I decide to leave the study before it is finished?

Tell us if you are thinking about stopping or decide to stop. It is important to tell us if you are thinking about stopping so any risks can be evaluated by the researchers. We will also tell you how to stop safely and discuss what follow-up care and testing could be most helpful for you. If you decide to leave the study before it is finished, please tell one of the researchers listed in Section 10 "Contact Information" (below).

You are free to end your participation partially or completely in the study. An example of partially ending your participation would be to discontinue receiving study intervention, while still allowing continuation of study follow-up procedures.

Please note that any information collected before you withdraw will be kept and used to complete the research.

Please note that even if you withdraw consent for further follow-up or contacts, if the study doctor becomes aware of additional safety information this will be reported to the sponsor to comply with legal or regulatory requirements.

7.3 Could the researchers take me out of the study even if I want to continue to participate?

Yes. There are many reasons why the researchers may need to end your participation in the study. Some examples are:

- The researchers believe that it is not in your best interest to stay in the study.
- You become ineligible to participate.
- Your condition changes and you need treatment that is not allowed while you are taking part in the study.
- You do not follow instructions from the researchers.
- The study is suspended or canceled.

8. FINANCIAL INFORMATION

8.1 Who will pay for the costs of the study? Will I or my health plan be billed for any costs of the study?

This is not a treatment study. The study will pay for research-related items or services that are provided only because you are in the study. If you are not sure what these are, see Section 4.1 or ask the researchers for a list. If you get a bill, you think is wrong, call the researchers listed in Section 10.
If you are injured or in the event of a medical emergency, dial 911 or visit your nearest Emergency Room. If you believe the study has made you sick or caused you injury, contact one of the people listed in section 10 of this document (Contact Information). If taking part in the study makes you sick or causes you injury, you or your insurance provider will be billed for all costs of treatment as the study does not provide compensation for sickness or injury caused by the study. It is possible that your insurance will not cover these costs.
If you are injured due to a study procedure and require more than a first aid, you or your health plan will pay for all the things you would need for the treatment like:

- Health care given during the study as part of your regular care
- Monitoring for side effects or other problems
- Deductibles or co-pays for these items or services

If you do not have a health plan, or if you think your health plan may not cover these costs during the study, please talk to the researchers listed in Section 10 or call your health plan's medical reviewer.

By signing this form, you do not give up your right to seek payment if you are harmed because of being in this study.

8.2 Will I be paid or given anything for taking part in this study?

You will be compensated for completing study procedures and your time/travel, as outlined below:

Study Visit	**Payment**
Visit 1: Screening visit (1 hour)	$50
Visit 2: Study procedures visit (14 hours)	$350
Total potential compensation for completing screening visit 1, and visit 2	$400

If you withdraw during Visit 2, a payment will be calculated based on the last sample collection time-point. Your time will be prorated at $25/hour.

You will be paid once all study procedures are completed and will not be able to obtain an advance payment. Even if you withdraw early, your payment will be processed around the time you would have completed the study. The process can take about 3-4 weeks.

8.3 Who could profit or financially benefit from the study results?

It is unlikely that anyone will financially benefit from this study. Neither the company whose product is being studied, nor the researchers conducting the study, nor the University of Michigan have financial interest in this study.

9. CONFIDENTIALITY OF PARTICIPANT RECORDS AND AUTHORIZATION TO RELEASE YOUR PROTECTED HEALTH INFORMATION

The information below describes how the confidentiality of your research records will be protected in this study, and any sub-studies described in this document.

9.1 How will the researchers protect my information?

Your participation will occur at Michigan Medicine. Your data will be kept confidential, to the extent permitted by applicable laws, in the following manner:

- Your name will not be used in any reports about the study
- You will be identified only by a study code
- Your identifying information will be kept secure

Despite these protections, some study data may contain information that could be used (perhaps in combination with other information) to identify you (e.g., initials, date of birth).

Your research information will be stored in a secure database accessible only to the researchers. Research records will be kept in a file that does not include names, registration numbers, or other information that is likely to allow someone other than the researchers to link the information to you. Your research information will be stored in a secure database accessible only to the researchers. This secure database, REDCap (Research Electronic Data Capture), is an open-source, secure, web-based application designed to support data capture for research studies. (See attached detailed description of RedCap).

The federal Genetic Information Nondiscrimination Act (GINA) generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. Under this law:

- Health insurance companies and group health plans may not request your genetic information that we obtain from this research
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums
- Employers with 15 or more employees may not use your genetic information that we obtain from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment

GINA does not apply to the following groups; however, these groups have policies in place that provide similar protections against discrimination:

- Members of the US Military receiving care through Tricare
- Veterans receiving care through the Veteran's Administration (VA)
- The Indian Health Service
- Federal employees receiving care through the Federal Employees Health Benefits Plans

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. This means that we cannot release or use information, documents, or samples that may identify you in any action or suit except as

described below. This protection includes federal, state, or local civil, criminal, administrative, legislative, or other legal proceedings. An example of a situation in which the Certificate would apply would be a court subpoena for research records.

There are some important things that you need to know:

- The Certificate does not stop reporting or information-sharing that you agreed to in this consent document. For example, we may share information with appropriate authorities if we think you may harm yourself or others. We may also share your information with other researchers.
- The Certificate cannot be used to stop a sponsoring United States federal or state government agency from checking records or evaluating programs.
- The Certificate does not stop disclosures required by the federal Food and Drug Administration (FDA).
- We may also release information about you to others when you say it is okay. For example, you may give us permission to release information to insurers, medical providers, or anyone else.
- The Certificate of Confidentiality does not stop you from personally releasing information about your involvement in this research if you wish.

More information about Certificates of Confidentiality and the protections they provide is available at https://www.era.nih.gov/erahelp/CoC_Ext/Content/A-Introduction/Introduction.htm

This trial will be registered and may report results on www.ClinicalTrials.gov, a publicly available registry of clinical trials.

9.2 What protected health information (PHI) about me could be seen by the researchers or by other people? Why? Who might see it?

Signing this form gives the researchers your permission to obtain, use, and share information about you for this study, and is required for you to take part in the study.

Medical information and billing records are protected by the privacy regulations of the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA). This type of information is called protected health information (PHI). PHI about you may be obtained from any hospital, doctor, and other health care provider involved in your care, including:

- Hospital/doctor's office records, including test results (X-rays, blood tests, urine tests, etc.)
- Alcohol/substance abuse treatment records
- Demographic information
- Personal identifiers

There are many reasons why information about you may be used or seen by the researchers or others during or after this study. Examples include:

- The researchers may need the information to make sure you can take part in the study.
- The researchers may need the information to check your test results or look for side effects.
- University, Food and Drug Administration (FDA) and/or other government officials, auditors, and/or the IRB may need the information to make sure that the study is done in a safe and proper manner and for quality improvement purposes.
- Study sponsors or funders, or safety monitors or committees, may need the information to:
    - Make sure the study is done safely and properly

  - Learn more about side effects
  - Analyze the results of the study

- Insurance companies or other organizations may need the information to pay your medical bills or other costs of your participation in the study.
- The researchers may need to use the information to create a databank of information about your condition or its treatment.
- Information about your study participation may be included in your regular Michigan Medicine medical record.
- If you receive any payments for taking part in this study, the University of Michigan finance department will need your name and address for tax reporting purposes. In a calendar year if: 1) your payments total greater than $400 for this study or 2) if you receive payments of greater than $400 for being in more than one study, the University of Michigan finance department will also require your Social Security Number for tax reporting purposes. If you do not wish to provide your Social Security Number, you may continue to participate in research studies, but you will not be able to receive payment for the remainder of the calendar year.
- Federal or State law may require the study team to give information to government agencies. For example, to prevent harm to you or others, or for public health reasons.

The results of this study could be published in an article, but would not include any information that would let others know who you are.

9.3 What happens to information about me after the study is over or if I cancel my permission to use my PHI?

As a rule, the researchers will not continue to use or disclose information about you, but will keep it secure until it is destroyed. Sometimes, it may be necessary for information about you to continue to be used or disclosed, even after you have canceled your permission or the study is over.

Examples of reasons for this include:

- To avoid losing study results that have already included your information
- To provide limited information for research, education, or other activities. (This information would not include your name, social security number, or anything else that could let others know who you are.)
- To help University and government officials make sure that the study was conducted properly

If your information is kept within the University of Michigan Health System, it is protected by the Health System's privacy policies. For more information about these policies, ask for a copy of the University of Michigan "Notice of Privacy Practices". This information is also available on the web at http://www.uofmhealth.org/patient+and+visitor+guide/hipaa. Note that once your information has been shared with others as described under Question 9.2, it may no longer be protected by the privacy regulations of the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA).

9.4 When does my permission to use my PHI expire?

Your permission does not expire unless you cancel it. You may cancel your permission at any time by writing to the researchers listed in Section 10 "Contact Information" (below). If you withdraw your permission, you may no longer be eligible to participate in this study.

10. CONTACT INFORMATION

10.1 Who can I contact about this study?

Please contact the researchers listed below to:

- Obtain more information about the study
- Ask a question about the study procedures or treatments
- Talk about study-related costs to you or your health plan
- Report an illness, injury, or other problem (you may also need to tell your regular doctors)
- Leave the study before it is finished
- Express a concern about the study

Principal Investigator: Manjunath Pai, PharmD
Mailing Address: The University of Michigan College of Pharmacy, 428 Church Street Ann Arbor, MI 48109-1065
Telephone: (734) 647-0006

Study Coordinator: Aleksas Matvekas, BS
Mailing Address: Pai Lab, The University of Michigan College of Pharmacy, 428 Church Street Ann Arbor, MI 48109-1065
Telephone: (734) 510-8183

You may also express a question or concern about a study by contacting the Institutional Review Board listed below:

University of Michigan Medical School Institutional Review Board (IRBMED)
2800 Plymouth Road
Building 520, Room 3214
Ann Arbor, MI 48109-2800
Telephone: 734-763-4768 (For International Studies, include the appropriate calling codes.)
Fax: 734-763-1234
e-mail: irbmed@umich.edu

If you are concerned about a possible violation of your privacy or concerned about a study you may contact the University of Michigan Health System Compliance Help Line at 1-866-990-0111.

When you call or write about a concern, please provide as much information as possible, including the name of the researcher, the IRBMED number (at the top of this form), and details about the problem. This will help University officials to look into your concern. When reporting a concern, you do not have to give your name unless you want to.

11. RECORD OF INFORMATION PROVIDED

11.1 What documents will be given to me?

You will receive a copy of the signed and dated informed consent document.

Your signature in the next section means that you have received a copy of the following document(s):

- This "Consent to be Part of a Research Study" document. (*Note: In addition to the copy you receive, copies of this document will be stored in a separate confidential research file and may be entered into your regular University of Michigan medical record.)*
- A copy of your kidney function result and body composition after study completion.

12. STORAGE, USE, AND SHARING OF SPECIMENS AND INFORMATION COLLECTED OR GENERATED IN THE STUDY DESCRIBED ABOVE

The information that follows applies to information and specimens collected and used in both the main study and the sub-study, as well as to unspecified future use of your information and samples.

12.1 What is meant by the storage, future research use, and sharing of study participants' medical information and leftover samples (sometimes referred to as biospecimens) taken from me?

Individual researchers, the University of Michigan, and companies that design and sponsor studies often want to keep subjects' medical information and leftover samples such as blood, tissue, saliva, and cells to use in future research. These future research uses take different basic forms, which are described below. The medical information and leftover samples may also be shared with other researchers so that they can use it in their studies.

The purpose of storing, using, and sharing participants' medical information and leftover samples is to promote more research that might lead to useful medical discoveries.

In some cases, researchers need your consent to store, use, and share your medical information and leftover samples; in other cases, they can store, use and/or share it without your consent. Whether or not researchers need your consent depends on if the stored information and samples would still be identifiable as yours or whether the researchers would first remove all information connecting them back to you.

12.2 Types of storage, future research use, and sharing in this study

For purposes of this research study, your coded private information will be shared with the study sponsor, the United States Food and Drug Administration (FDA). While coded data will be shared, the key/link to re-identify subjects in this dataset will not be shared with the FDA. In addition, after any remaining identifiers are removed from your coded private information, the information could be used for future research studies and shared with other researchers without your additional informed consent.

You can take part in the main study even if you decide not to let us keep your identifiable blood and medical information for future research.

If you give us your permission, we will use your identifiable blood and medical information for future research. Even if you give us permission now to keep some of your identifiable blood and study information collected in the study, you can change your mind later and ask us to destroy it. If you do change your mind, we will attempt to get your information and biospecimens back from the other researchers we've shared them with. However, there may be times we cannot. For example, if we are unable to tell which information and biospecimens came from you, we will not be able to get them back. Additionally, any information that has been added to your medical record cannot be deleted. Also, keep in mind that once we have analyzed your blood, we may not be able to take the information out of our research study.

We may share your blood and medical information with other researchers, so that they can use it in their research. Their research may be similar to this study or may be completely different. Once we have shared your blood and medical information with other researchers, we will not be able to get it back.

Although we will do our best to protect your information and specimens, both during storage and when sharing them with others, it's possible that someone may be able to identify you from them. It's also possible that unauthorized people might gain access to your information and blood. To try to minimize both of these risks, we will assign your information and specimens a random code before sharing them with other researchers. The principal investigator will securely store the code key that links your coded information and specimens to you. Future use of your identifiable data or blood will be conducted in compliance with applicable regulatory requirements.

You will not find out the results or benefit directly from future research on your blood. Sharing your information and specimens may contribute to research that helps others in the future.

13. SIGNATURES

Consent/Assent to Participate in the Research Study

I understand the information printed on this form. I have discussed this study, its risks and potential benefits, and my other choices with [NAME OF STUDY TEAM MEMBER OBTAINING CONSENT] _____. My questions so far have been answered. I understand that if I have more questions or concerns about the study or my participation as a research subject, I may contact one of the people listed in Section 10 (above). I understand that I will receive a copy of this form at the time I sign it and later upon request. I understand that if my ability to consent or assent for myself changes, either I or my legal representative may be asked to re-consent prior to my continued participation in this study.

Print Legal Name: _____

Signature: _____

Date of Signature (mm/dd/yy): _____

Principal Investigator or Designee

I have provided this participant and/or his/her legally authorized representative(s) with information about this study that I believe to be accurate and complete. The participant and/or his/her legally authorized representative(s) indicated that he or she understands the nature of the study, including risks and benefits of participating.

Printed Legal Name: _____

Title: _____

Signature: _____

Date of Signature (mm/dd/yy): _____

We would also like your permission to keep some of your identifiable blood and medical information collected in the main study, so that it may be studied in future research. The future research may be similar to this study or may be completely different.

You can take part in the main study even if you decide not to let us keep your identifiable blood and medical information for future research.

Consent/Assent to Collect for Unspecified Future Research
This project involves the option to allow the study team to keep your identifiable specimens/data for use in future research. I understand that it is my choice whether to allow future use of my specimens. I understand that if my ability to consent or assent for myself changes, either I or my legal representative may be asked to re-consent prior to my continued participation in this study.

_____ Yes, I agree to let the researchers keep my specimens for future research (signature required below).

_____ No, I do not agree to let the researchers keep my specimens for future research (no signature).

Print Legal Name: _____

Signature: _____

Date of Signature (mm/dd/yy): _____

Consent/Assent to Being Contacted Regarding Future Research
The researchers would like my permission to contact me in the future about other studies they are conducting. I understand that it is my choice whether to allow the researchers to contact me.

_____ Yes, I agree to let the researchers to contact me in the future regarding other studies (signature required below).

_____ No, I do not agree to let the researchers contact me in the future regarding other studies (no signature).

Print Legal Name: _____

Signature: _____

Date of Signature (mm/dd/yy): _____

APPENDIX:

INFORMED CONSENT TO A SUB-STUDY

Besides the information about the main study, the following information is specific to an optional sub-study. We would like your permission to study your medical information and blood for genetic analysis to estimate your biological age. You can take part in this study even if you decide not to let us analyze your blood to find out your biological age.

Even if you give us permission now to keep some of your blood and medical information, you can change your mind later and ask us to destroy it. Keep in mind, however, that once we have analyzed your blood, we may not be able to take the information out of our research. Also, if we have shared some of your blood and medical information with other researchers, we will not be able to get it back. Proper systems are in place to ensure privacy and security of your genetic information, including the genetic information nondiscrimination act (GINA) which makes it illegal for employers to discriminate against individuals based on genetic information. More information on this GINA law is in section 9 above.

You will not receive the results of the analysis of your blood. Allowing us to study your blood and medical information to find out your biological age will not benefit you directly.

If you give us your permission, we will use your identifiable blood and medical information for future research. Even if you give us permission now to keep some of your identifiable blood and study information collected in the study, you can change your mind later and ask us to destroy it. If you do change your mind, we will attempt to get your information and biospecimens back from the other researchers we've shared them with. However, there may be times we cannot. For example, if we are unable to tell which information and biospecimens came from you, we will not be able to get them back. Additionally, any information that has been added to your medical record cannot be deleted. Also, keep in mind that once we have analyzed your blood, we may not be able to take the information out of our research study.

We may share your blood and medical information with other researchers, so that they can use it in their research. Their research may be similar to this study or may be completely different. Once we have shared your blood and medical information with other researchers, we will not be able to get it back.

Although we will do our best to protect your information and specimens, both during storage and when sharing them with others, it's possible that someone may be able to identify you from them. It's also possible that unauthorized people might gain access to your information and blood. To try to minimize both of these risks, we will assign your information and specimens a random code before sharing them with other researchers. The principal investigator will securely store the code key that links your coded information and specimens to you. Future use of your identifiable data or blood will be conducted in compliance with applicable regulatory requirements.

You will not find out the results or benefit directly from future research on your blood. Sharing your information and specimens may contribute to research that helps others in the future.

Consent/Assent for Participating in an Optional Sub-Study

This project involves optional participation in a sub-study. I understand that it is my choice whether to take part in the sub-study. I understand that if my ability to consent or assent for myself changes, either I or my legal representative may be asked to re-consent prior to my continued participation in this study.

_____ Yes, I agree to take part in this optional sub-study (signature required below).

_____ No, I do not agree to take part in this optional sub-study (no signature).

Print Legal Name: _____

Signature: _____

Date of Signature (mm/dd/yy): _____