Title: Immune Response to FMT for C.difficile

NCT 02797288

January 24, 2017

Consent of an Adult to Be in a Research Study

In this form "you" means a person 21 years of age or older who is being asked to volunteer to participate in this study.

Participant's Name_____

Principal Investigator:	Dr. William A. Petri, Box 801340, University of Virginia, Charlottesville VA 22908 Phone: 434-924-5621
Sponsor:	National Institutes of Health

What is the purpose of this form?

This form will provide you with information about this research study. You do not have to be in the study if you do not want to. You should have all your questions answered before you agree to be in this study.

Please read this form carefully. If you want to be in the study, you will need to sign this form. You will be given a signed copy of this form.

Who is funding this study?

This study is funded by the National Institutes of Health (NIH)

Why is this research being done?

The purpose of this research is to study the differences in the colon before and after fecal transplantation (otherwise known as FMT) in patients who have one or more relapse of Clostridium difficile infections. We hope to learn how fecal transplant affects the immune response in the intestines. Understanding how fecal transplant works to prevent recurrent C. difficile infection could lead to new approaches for prevention or treatment.

You are being asked to be in this study, because you have had recurrent diarrhea caused by the germ Clostridium difficile (C. diff) and will be undergoing a colonoscopy for fecal transplant (FMT) as part of your medical care.

Up to 10 people will be in this study at UVA.

How long will this study take?

After you consent to participate (Screening visit), the study will require one extra visit if you agree to participate in this part of the study (Visit 2) two months after your fecal transplant

(Visit 1). The screening visit and the first visit (Visit 1) take place at the same time as your visits for medical care. These are not extra visits.

During your colonoscopy for fecal transplant (Visit 1), the study team will collect a blood and urine sample for research and pregnancy testing if you are a woman who is able to have children . These tests will take less than 15 minutes. In addition, during your colonoscopy for fecal transplant, the study team will collect additional colon biopsies for research before the fecal transplant. The study biopsy collection will add about 4-5 minutes to the colonoscopy procedure.

Visit 2 is purely for research purposes and will include a urine pregnancy test (if you are a woman who is able to have children) and blood and urine samples for research. These procedures will take less than 15 minutes. Visit 2 also includes a sigmoidoscopy (inserting a tube about 24 inches into your lower colon through your rectum), otherwise known as a "short colonoscopy". It will take about two hours. It takes about ten minutes to complete the sigmoidoscopy and take biopsies and the rest of the time is preparation and recovery. If you opt to have sedation for the sigmoidoscopy, your recovery time will take longer because we will have to wait for your sedation to wear off before we send you home.

What will happen if you are in the study?

SCREENING VISIT (will take about 30 minutes to complete):

If you agree to participate, you will sign this consent form before any study related procedures take place. Before you can participate in the study, there will be a screening period. Study doctors will review your medical records, and the results of vital signs and physical exams performed as part of your medical care. This is done to make sure you are eligible and it is safe for you to participate. The information collected during this time will be used as part of the research.

There are no screening tests specifically required for research purposes, except for pregnancy testing for women who are able to become pregnant.

If the review of your records indicates that you are eligible, and you choose to sign this consent, then you will continue to be in the study. If you wish to have additional time to consider participation or wish to discuss with family or friends, you may take the consent home. A member of the study team will call you to determine your interest, review the consent and any questions about study participation. If you wish to participate, you may sign the consent when you return for FMT.

There may be additional tests or procedures required before the FMT as part of your medical care. Your medical doctor will give you information about both of these procedures and review potential risks and benefits. Your medical team will also prescribe any prep required for these procedures.

You will return for your colonoscopy and fecal transplant (usually within 3 days to 10 weeks) based on your particular clinical circumstances; participating in this study will not affect the scheduling of your fecal transplant.

STUDY VISIT 1: Colonoscopy and Fecal Transplant Visit:

- If you are a woman who is able to have children, a urine pregnancy test will be performed as part of the research prior to the colonoscopy. This is required as part of the research. A urine sample for research will also be collected prior to the fecal transplant.
- For the research, we will draw 1 tablespoon of blood from a vein in your arm when you come for the fecal transplant. This sample will be taken prior to your fecal transplant in the UVA Medical Laboratory.
- As part of your medical care you will undergo colonoscopy.
- Before you have the fecal transplant, we will take 8 tissue samples for research, called biopsies, from the inside wall of your intestine in addition to any biopsies that are taken for your regular medical care. Biopsy tissue is small, about the size of the end of a pen or a pencil tip. The additional research biopsies may add about 4-5 minutes to the colonoscopy procedure.
- As part of your medical care you will then undergo fecal transplant.

Study Visit 2: Flexible Sigmoidoscopy Visit

Flexible sigmoidoscopy "scope" visit at about Day 60: it will take about two hours in addition to your travel time. The flexible sigmoidoscopy is performed solely for research purposes.

- You will have a clear liquid breakfast, take one Fleet enema at home and then come to UVA Primary Care Center to register for a Flexible Sigmoidoscopy to be done by Dr. Hays. After you register, you will go to the UVA Medical Laboratory located in the Primary Care Center to provide:
- For research, a urine sample will be collected for research and for pregnancy testing (if you are a woman who is able to have children).
- For research, 1 Tablespoon of blood will be drawn.
- You will then proceed to the Digestive Health Center where your vital signs and history will be taken. The consent for flexible sigmoidoscopy will be reviewed with you; after this you will be brought into an endoscopy room similar to the one where you had your fecal transplant. Dr. Hays will insert a small pediatric-size scope (tube with a light on the end of it) into your rectum and guide it about 24 inches up into your colon. This may cause slight cramping.
    - If required, you will be given light conscious sedation as you had with the fecal transplant. Options for sedation would be the medication Versed (midazolam) given by mouth or by IV infusion. This medication causes drowsiness so you would need to stay in recovery until you are alert enough to go home, usually about 30 minutes. **You will need to bring someone with you to drive you home if you have sedation.**

- For research, eight small pieces of tissue will be obtained through the scope. This will not hurt because there are not any nerve endings on the inside of the colon. Next, the scope will be removed. You will be able to leave within 10-30 minutes after the procedure is complete depending on whether you received sedation.

A study schedule is on the next page for your convenience.

Study Schedule	**Screening Visit**	**Visit 1**	**Visit 2**
Study Week	-3 days to 10 weeks	0	8
Informed Consent	x	x*	
Review study eligibility	x		
Review of Medical History	x	x	x
Review of Vital signs	x	x	x
Review of Physical Exam	x	x	x
Sigmoidoscopy for research			x
Blood draw (research)		x	x
Colon biopsies (for research)		x	x
Urine research and pregnancy test		X	X

***consent may be obtained at screening visit or Visit 1**

What are your responsibilities in the study?

You have certain responsibilities to help ensure your safety. These responsibilities are listed below:

- Stop taking antibiotics 48 hours before the fecal transplant colonoscopy and 48 hours before the flexible sigmoidoscopy if directed by the medical and study team
- Do not take bismuth subsalicylate (Pepto-Bismol) in the 24 hours before the fecal transplant colonoscopy or the flexible sigmoidoscopy
- Stop taking anticoagulants (blood thinners) 5 days before the FMT colonoscopy and 5 days before the flexible sigmoidoscopy.
- You must be completely truthful about your health history.
- Follow all instructions given.
- You should tell the study doctor or study staff about any changes in your health or the way you feel.
- Answer all of the study-related questions completely.
- Inform the study doctor or study staff as soon as possible if you have to take any new medications, including anything prescribed by a doctor or those that you can buy without a prescription (over-the-counter), including herbal supplements and vitamins. The study doctor will let you know if you can take these medications.

Specimens

Urine

A urine pregnancy test is required for women who are able to have children. Urine will also be collected for research. The urine sample will be stored for research and tested later for metabolites (any substance produced during digestion or other bodily chemical processes).

Blood testing

We will take (or "draw") 1 tablespoon of blood before your colonoscopy and again at the Visit 2 on approximately Day 60. The total amount of blood we will take for the entire study is 2 tablespoons. The blood samples will be drawn from a vein in your arm.

Part of the blood sample is for a complete blood count (CBC), a standard blood test that gives important information about the kinds and numbers of cells in the blood. The remainder of the blood sample will be stored for research and tested later for metabolites (any substance produced during digestion or other bodily chemical processes). Once the tests are completed, the specimen will be saved indefinitely for future unspecified research.

Biopsy Specimens: Colon

We will collect 8 research biopsies from the colon at the time of colonoscopy for FMT (Visit 1) and we will collect 8 research biopsies at Day 60 (Visit 2) during the flexible sigmoidoscopy**.** The total amount of research biopsies we will take will be 16. The biopsies will be tested for immune responses in the intestines. Once the tests are completed, the specimen will be saved indefinitely for future unspecified research

If you want to know about the results before the study is done:

The urine pregnancy test is being done as part of the research protocol, however if it is positive we will inform you that you are pregnant. If you are pregnant, you will not be able to continue in this study.

During the study you are having investigational tests done on your blood, urine and colon biopsies that were collected as part of this research. The purpose of these tests is NOT to diagnose any disease or abnormality you may have. Because the tests are investigational there is no way for the study leader to understand if the results are "normal" or "abnormal". However, IF any test results are concerning, your study leader will let you know.

In addition, as the research moves forward, your study leader will keep you informed of any new findings about the research itself that may be important for your health or may help you decide if you want to continue in the study. The final results of the research will not be known until all the information from everyone is combined and reviewed. At that time you can ask for more information about the study results.

What are the risks of being in this study?

Risks related to the sigmoidoscopy and colon biopsy procedures:
If the physician performing your procedure feels that donation of additional research biopsies places you at higher risk, despite your consent, the biopsies will not be obtained for research purposes.

Likely

- Temporary abdominal pain, usually mild cramping, during or immediately after flexible sigmoidoscopy
- Temporary increase in gas or loose stool immediately after flexible sigmoidoscopy

Less Likely

- Temporary minor bleeding after biopsy. This almost always consists of mild oozing that stops by itself. This type of bleeding may show up as a small amount of blood in the stool, but otherwise does not cause problems.
- Temporary change in heart rate or rise in blood pressure before or during flexible sigmoidoscopy
- Dizziness and fainting occurs in some people after sigmoidoscopy. These would be temporary and should resolve within 30 minutes to an hour.

Rare but serious. The risks are very small for all of these risks:

- Temporary: risk of major bleeding (such as bleeding requiring hospitalization, a repeat colonoscopy, or blood transfusion) is very small.
- Perforation which is a hole in the colon that would require treatment with surgery with an ostomy or bag on your abdomen to collect bowel movements. The risk is very small.
- Temporary: infection from the biopsy or flexible sigmoidoscopy.
- Tissue burn: burn of the skin or organ if cautery required to control any bleeding
- Death

Risk of sedation ONLY for those who choose to receive light sedation for flexible sigmoidoscopy:

Likely

- Not being able to remember for some time after the procedure. This is temporary and goes away as the medication wears off
- Inability to safely operate a car or machinery for several hours after receiving sedation. FOR THIS REASON –IF SEDATION IS GIVEN YOU MUST HAVE SOMEONE ELSE DRIVE YOU HOME

Rare but serious. The risks are very small for all of these risks:

- Allergic reactions to sedation medications
- Changes in breathing

- Changes in blood pressure and heart function
- Nausea and vomiting
- Aspiration (inhaling) of stomach contents
- Brain damage
- Death

You will sign a separate consent form for the colonoscopy for fecal transplant and the biopsies taken as part of your clinical care. This consent will explain the procedure and the risks involved.

Risks of having your blood drawn and IV (IV will only be placed if IV conscious sedation is requested for flexible sigmoidoscopy at Visit 2):

Having blood drawn may cause:

- ✓ pain (common),
- ✓ a bruise (sometimes),
- ✓ fainting or passing out (not very often), and
- ✓ infection (rare).

If the people doing the study are exposed to your blood or body fluids in a way that could give them a disease, your blood may be tested. The tests might check for:

- ✓ hepatitis,
- ✓ HIV (Human Immunodeficiency Virus), or
- ✓ other infections.

You and the person exposed would be told the test results. However, your name would be kept private. If your test is positive for hepatitis or HIV or any other infection that may affect your clinical care, we will tell you the results and help you understand what the results mean for you.

Other unexpected risks:

You may have side effects that we do not expect or know to watch for now. Call the study leader if you have any symptoms or problems.

Could you be helped by being in this study?

You will not benefit from being in this study. However the information researchers get from this study may help others in the future. This study could lead to new approaches for prevention or treatment of C. difficile infection.

What are your other choices if you do not join this study?

This is not a treatment study. You do not have to be in this study to be treated for your illness or condition. You can get the usual treatment even if you choose not to be in this study. The usual treatment would include:

- Colonoscopy for fecal transplant with biopsy samples or blood samples that are collected for clinical care without donating blood, urine or biopsies for research.

If you are an employee of UVa your job will not be affected if you decide not to participate in this study. If you are a student at UVa, your grades will not be affected if you decide not to participate in this study.

Will you be paid for being in this study?

You will be paid $350 by check for finishing this study to compensate you for the extra travel, time, and discomfort associated with the extra blood samples, flexible sigmoidoscopy and biopsies.

- You will be paid $50 for participating in Visit 1.
- You will be paid $300 for participating in Visit 2.
- If the study leader says you cannot continue after Visit 1, you will be paid the full amount for the study.

You should get your payment about 6 weeks after each visit. The income may be reported to the IRS as income.

If you owe money to any Virginia state agency, the state can use the money you earn in this study to pay those debts. These state agencies include the UVa Medical Center, VCU Medical Center or a college or university. The money may be withheld to pay back debt for such things as unpaid medical bills, taxes, fines, child support. Even if this happens, the money you earn may be reported to the IRS as taxable income.

By agreeing to be in this study, you are donating your blood, bodily fluids, tissue samples for research, and giving up any property rights you may have in them. The results of this research using your donated materials may have commercial value. However, you will not receive any payments.

Will being in this study cost you any money?

The following procedures/tests, which are being done if indicated for research purposes, will be provided at no cost to you or your health insurance:

- Urine for pregnancy testing and research
- Colon biopsies for research
- Blood samples for research
- Flexible sigmoidoscopy (physician and hospital charges for the flexible sigmoidoscopy)
- IV, medication, medication administration, and monitoring for light sedation if needed for flexible sigmoidoscopy

You and/or your insurance company must pay for any tests or care given beyond what is required in this study. In addition, you and/or your health insurance may also have to pay for other drugs or treatments that are given to help you control any side effects. You will have to pay for any costs not covered by your health plan. You may be responsible for any co-payments or deductibles. You may wish to ask for an estimate of your financial costs. You may also wish to check with your insurance company before the study starts. Ask what they will cover and if they require you to get their permission before you decide to be in the study.

You will be responsible for the cost of travel to come to any study visit and for any parking costs.

What if you are hurt in this study?

If you are hurt as a result of being in this study, there are no plans to pay you for medical expenses, lost wages, disability, or discomfort. The charges for any medical treatment you receive will be billed to your insurance. You will be responsible for any amount your insurance does not cover. You do not give up any legal rights, such as seeking compensation for injury, by signing this form.

What happens if you leave the study early?

You can change your mind about being in the study any time. You can agree to be in the study now and change your mind later. If you decide to stop, please tell us right away. You do not have to be in this study to get services you can normally get at the University of Virginia.

Even if you do not change your mind, the study leader can take you out of the study. Some of the reasons for doing so may include

a) Your study physician is concerned about your health
b) Your disease gets worse
c) You do not follow your doctor's instructions
d) The study leader of sponsor closes the study for safety, administrative or other reasons

How will your personal information be shared?

The UVa researchers are asking for your permission to gather, use and share information about you for this study. If you decide not to give your permission, you cannot be in this study, but you can continue to receive regular medical care at UVA.

If you sign this form, we may collect any or all of the following information about you:

- Personal information such as name, address and date of birth
- Social Security number ONLY IF you are being paid to be in this study
- Your health information if required for this study. This may include a review of your medical records and test results from before, during and after the study from any of your doctors or health care providers. This may include mental health care records, substance abuse records, and/or HIV/AIDS records.
- Tissue, urine and blood samples for research

Who will see your private information?

- The researchers to make sure they can conduct the study the right way, observe the effects of the study and understand its results
- People or groups that oversee the study to make sure it is done correctly
- The sponsor(s) of this study, and the people or groups it hires to help perform or review this research

- Insurance companies or other organizations that may need the information in order to pay your medical bills or other costs of your participation in the study
- Tax reporting offices (if you are paid for being in the study)
- People who evaluate study results, which can include sponsors and other companies that make the drug or device being studied, researchers at other sites conducting the same study, and government agencies that provide oversight such as the Food and Drug Administration (FDA) if the study is regulated by the FDA.

Some of the people outside of UVa who will see your information may not have to follow the same privacy laws that we follow. They may release your information to others, and it may no longer be protected by those laws.

The information collected from you might be published in a medical journal. This would be done in a way that protects your privacy. No one will be able to find out from the article that you were in the study.

A description of this clinical trial will be available on *http:// www.ClinicalTrials.gov,* as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

What if you sign the form but then decide you don't want your private information shared?
You can change your mind at any time. Your permission does not end unless you cancel it. To cancel it, please send a letter to the researchers listed on this form. Then you will no longer be in the study. The researchers will still use information about you that was collected before you ended your participation.

OPTIONAL Storage of Samples and Health Information for Specimen Banking

What Sort of Research Will Be Done On Your Sample(s)?

You are being asked to provide samples of your colon tissue, urine and blood to be used for research. Along with specimens, researchers may need to collect some health information about you. Combining information from the specimen with information from your health records may be useful for this research. For this research, the following types of information could be included: health history, diagnoses, medications, treatments, laboratory test results.

In addition, if you agree, specimens collected for research will be added to a research specimen bank. The purpose of a specimen bank is to process, and store samples until researchers need them for future research. The long term goals of the samples collected in this bank will be mainly used for research on C. difficile for the development of new treatments for C. difficile infection or to understand more about how fecal transplant impacts the intestine. It is not possible, however, to list every research project that will include the samples because we

cannot predict all of the research questions that will be important over the coming years. As we learn more, new research questions and new types of research may be done.

What will you have to do to give samples for research?

As previously described, the study doctor will obtain a total of 16 colon biopsies, 6 tablespoons of urine and 2 tablespoons of blood from you for research. These will be collected at study visits 1 and 2 if you participate in both visits.

How Will Your Sample(s) Be Labeled for the specimen bank?

Your sample(s) will not be labeled with your name or other information that would identify you directly. Instead, it will have a unique code that allows for it to be linked to some of your health information. This link means that your specimen can be identified but only indirectly. We can find out if we need to know which sample is yours in the event you wish the sample to be removed at a later date.

How Will Your Sample(s) Be Stored for Specimen Banking?(if applicable)

Dr. William Petri will be responsible for storing your samples and for protecting your privacy.

This research specimen bank is located at the University of Virginia under the leadership of Dr. Petri. There is no set limit to the number of people who will provide samples to this bank.

Which researchers can use your samples and what information about you can they have?

Your coded sample may be shared with researchers at the University of Virginia and at other institutions. Dr. Petri will not give your name to other researchers who want to use your sample, but will only give them information like your age and what disease/condition you have. Those who would see the information would include researchers and the others listed under "Who will see your private information?" section of this consent document.

Some of the people who receive your information may not have to follow the privacy laws and may share or release your information because they do not have to follow the privacy laws.

What Are the Benefits To Donating Your Sample(s) For Specimen Banking?

The specimen banking that is done with your sample is not meant to help you. But, doctors hope that in the future it will help people who have other diseases or conditions.

It is very unlikely that any future research (specimen banking) performed using your specimen(s) would benefit you directly, but it may provide important medical knowledge that could help other patients with your medical condition or other medical problems in the future.

What Are The Risks of Donating Your Sample(s) For This Study?

Risks to Privacy from Specimen Banking:

The main risk of allowing us to store and use your samples and certain limited health information for research is a potential loss of privacy. One of the risks to you is the release of information from your health records. The University of Virginia will do its best to protect your records so that facts about you and your health will be kept private. The chance that information identifying you will be given to someone else is very small. However, we cannot *guarantee* it will be safe. To further safeguard your privacy, information obtained from future research will not be placed in your medical record.

Will You Find Out the Results of the Research on Your Sample(s) for Specimen Banking?

Neither you, your health care provider**,** nor anyone in your family, will receive the results of any research done on your sample(s). The results will not be put in your health records. Therefore, results from any research done on your sample(s) will not affect your medical care. This helps protect you and other members of your family from harm that might be caused by this information.

What If You Change Your Mind About Donating Your Sample(s) for Specimen Banking?

If you decide now that your sample(s) can be kept for specimen banking, and later change your mind, you can simply withdraw the sample(s) at that time. To withdraw you will need to write to the Principal Investigator listed on the first page of this form. We will then destroy any of your tissue that has not already been used. Unless you withdraw from the study, permission for researchers to use your tissue and to use and share your private health information for this study will never end.

Will You Be Paid For Donating Your Sample(s) for Specimen Banking?

You will not be paid to donate your samples for specimen banking.

Will Donating Your Sample(s) Cost You Any Money?

There is no cost to you to have your samples collected or used for genetic research and/or specimen banking.

Specimen Banking Options:

You do not have to participate and agree for specimens to be collected for specimen banking in order to be in the main part of this study. No matter what you decide to do, your decision will not affect your medical care. You can tell us your choice by placing your initials in one of the options below:

SPECIMEN BANKING:

Please indicate your choice by placing your initials below (if applicable):

___ YES **Your sample(s) may be saved for <u>future research and stored in a specimen bank.</u>**

___ NO **Your sample(s) may not be saved for <u>future research and stored in a specimen bank.</u>**

<u>VISIT 2</u>

Please indicate your choice by placing your initials below:

___ YES You agree to return at Visit 2 for a flexible sigmoidoscopy with collection of biopsies, blood and urine for research

___ NO You do not agree to return at Visit 2 for a flexible sigmoidoscopy with collection of biopsies, blood and urine for research

Please contact the researchers listed below to:

- Obtain more information about the study
- Ask a question about the study procedures or treatments
- 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: William Petri
Address: Box 801340, University of Virginia, Charlottesville VA 22908
Telephone: (434)924-5621

What if you have a concern about this study?

You may also report a concern about this study or ask questions about your rights as a research subject by contacting the Institutional Review Board listed below.

University of Virginia Institutional Review Board for Health Sciences Research
PO Box 800483
Charlottesville, Virginia 22908
Telephone: 434-924-9634

When you call or write about a concern, please give as much information as you can. Include the name of the study leader, the IRB-HSR Number (at the top of this form), and details about the problem. This will help officials look into your concern. When reporting a concern, you do not have to give your name.

Signatures

<u>What does your signature mean?</u>

Before you sign this form, please ask questions about any part of this study that is not clear to you. Your signature below means that you have received this information and all your

questions have been answered. If you sign the form it means that you agree to join the study. You will receive a copy of this signed document.

Consent From Adult

_____	_____	_____
PARTICIPANT (SIGNATURE)	PARTICIPANT (PRINT)	DATE

To be completed by participant if 18 years of age or older.

Person Obtaining Consent

By signing below you confirm that you have fully explained this study to the potential subject, allowed them time to read the consent or have the consent read to them, and have answered all their questions.

_____	_____	_____
PERSON OBTAINING CONSENT (SIGNATURE)	PERSON OBTAINING CONSENT (PRINT)	DATE

Consent from Impartial Witness

If this consent form is read to the subject because the subject is blind or illiterate, an impartial witness not affiliated with the research or study doctor must be present for the consenting process and sign the following statement. The subject may place an X on the Participant Signature line above.

I agree the information in this informed consent form was presented orally in my presence to the **identified individual(s)** who has had the opportunity to ask any questions he/she had about the study. I also agree that the **identified individual(s)** freely gave their informed consent to participate in this trial.

Please indicate with check box the identified individual(s):

☐ Subject

_____	_____	_____
IMPARTIAL WITNESS (SIGNATURE)	IMPARTIAL WITNESS (PRINT)	DATE