Title of Research Study: ***Capsule Fecal Microbiota Transplant for Active Ulcerative Colitis***

Investigator Team Contact Information: ***Byron Vaughn, MD***

For questions about research appointments, the research study, research results, or other concerns, call the study team at:

Investigator Name: Byron Vaughn, MD
Investigator Departmental Affiliation: Medicine – Division of Gastroenterology
Phone Number: 612-301-8294
Email Address: bvaughn@umn.edu

If your doctor is also the person responsible for this research study, please note that he is interested in both your clinical care and the conduct of this research study. You have the right to discuss this study with another person who is not part of the research team before deciding whether to participate in the research.

Key Information About This Research Study

The following is a short summary to help you decide whether or not to be a part of this research study. More detailed information is listed later on in this form.

What is research?

Doctors and investigators are committed to your care and safety. There are important differences between research and treatment plans:

- The goal of research is to learn new things in order to help groups of people in the future. Investigators learn things by following the same plan with a number of participants, so they do not usually make changes to the plan for individual research participants. You, as an individual, may or may not be helped by volunteering for a research study.
- The goal of clinical care is to help you get better or to improve your quality of life. Doctors can make changes to your clinical care plan as needed.

Research and clinical care are often combined. One purpose of this informed consent document is to provide you clear information about the specific research activities of this study.

Why am I being asked to take part in this research study?

We are asking you to take part in this research study because you have been diagnosed with ulcerative colitis.

What should I know about a research study?

- Someone will explain this research study to you.
- Whether or not you take part is up to you.
- You can choose not to take part.
- You can agree to take part and later change your mind.
- Your decision will not be held against you.
- You can ask all the questions you want before you decide.

Why is this research being done?

It is widely unknown if the gut bacteria (microbiota) in UC is dysfunctional and therefore perpetuates inflammation, or if the ongoing inflammation shapes the microbiota. Early studies of using FMT in UC patients showed an improvement in UC symptoms, but other studies have shown mixed results, suggesting specific donor microbiota profiles should be studied to better understand the impact on UC patients. The goal of this research is to see how a donor microbiota can change the microbiota of people with UC.

How long will the research last?

We expect that you will be in this research study for 12-24 weeks, depending on your treatment decision, with safety follow up 3 months and 6 months after your last dose of FMT capsules.

- Screening for the study will take a maximum of 30 days to confirm eligibility for the study.
- Once confirmed for the study, you will be active with study visits and sample collection for 12

weeks, with safety follow up at 3 months and 6 months after your last dose. This will be approximately 8 months total of study involvement.

- If you decide to continue with additional FMT capsules through Path A, you will be involved in the study for an additional 12 weeks, with safety follow up at 3 months and 6 months after your last dose. This will be approximately 11 months of study involvement.

What will I need to do to participate?

You will be asked to come to 5 study visits at the University of Minnesota campus (or complete virtual visits), take FMT capsules daily for 8 weeks, and collect weekly stool samples for 12 weeks. Note, if you do complete virtual visits, you will still need to drop off certain stool samples, specifically at the start of the study, and at weeks 4, 8 and 12. Stool samples can be dropped off at the University of Minnesota or Indiana University.

During your study visits, or virtual visit, you will meet with study staff to review your current medications, measure your height, weight, body temperature and blood pressure, undergo a physical exam, and provide dietary information. These study visits are estimated to take about 1-2 hours.

More detailed information about the study procedures can be found under ***"What happens if I say yes, I want to be in this research?"***

Is there any way that being in this study could be bad for me?

Risk of Gastrointestinal Symptoms

Gut microbiota constitute an integral part of the gastrointestinal tract. They can potentially play a role in a variety of gastrointestinal disorders, including irritable bowel syndrome (IBS) and inflammatory bowel disease (IBD).

Common side effects associated with FMT include: fever, abdominal cramping, diarrhea, constipation, nausea, and bloating.

More detailed information about the risks of this study can be found under ***"What are the risks of this study? Is there any way being in this study could be bad for me? (Detailed Risks)"***

Will being in this study help me in any way?

We cannot promise any benefits to you or others from your taking part in this research. However, possible benefits include a potential improvement in your ulcerative colitis symptoms.

What happens if I do not want to be in this research?

You do not have to participate in this research. Instead of being in this research study, your choices may include: continuing or pursuing treatment of your ulcerative colitis with your physician.

Detailed Information About This Research Study

The following is more detailed information about this study in addition to the information listed above.

How many people will be studied?

We expect about 24 people will be in this research study here at the University of Minnesota.

What happens if I say "*Yes, I want to be in this research*"?

Screening Visit

- Review eligibility criteria
- Review of your demographic information, medical history, and current medication usage
- Complete a Partial Mayo Score Assessment for UC activity
- Measure your height and weight
- Measure your vitals, including body temperature and blood pressure
- Physical examination or review of systems if virtual visit
- Nutritional assessment
- Provide stool collection kits
- Discuss methods of documenting adverse events through the study

Visit 1 (Baseline)

- Women of child-bearing age will undergo a urine pregnancy test
- Review medications
- Measure your height and weight, or self report your most recent values if virtual
- Measure your vitals, including body temperature and blood pressure, or measure your temperature if virtual visit.
- Physical examination or review of systems if virtual visit.
- Collect stool sample(s). If virtual visit, this can be done locally at the University of Minnesota or Indiana University.
- Dispense 2 weeks of FMT or placebo capsules and review instructions
- Review adverse events

Days 1- 7 (Phone call from study staff)

- Review adverse events

Visit 2 (2 weeks +/- 5 days)

- Dispense 2 weeks of FMT or placebo and review instructions

Visit 3 (4 weeks +/- 5 days)

- Review medications
- Measure your height and weight, or self report your most recent values if virtual
- Measure your vitals, including body temperature and blood pressure, or measure your temperature if virtual visit.
- Physical examination or review of systems if virtual visit.
- Nutritional assessment
- Collect stool sample(s). If virtual visit, this can be done locally at the University of Minnesota or Indiana University
- Dispense 2 weeks of FMT or placebo capsules and review instructions
- Review adverse events

Visit 4 (6 weeks +/- 5 days)

- Dispense 2 weeks of FMT or placebo and review instructions

Visit 5 (8 weeks +/- 5 days)

- Review medications

- Complete a Partial Mayo Score Assessment for UC activity
- Measure your height and weight, or self report your most recent values if virtual
- Measure your vitals, including body temperature and blood pressure, or measure your temperature if virtual visit.
- Physical examination or review of systems if virtual visit.
- Nutritional assessment
- Collect stool sample(s). If virtual visit, this can be done locally at the University of Minnesota or Indiana University
- Review adverse events

Visit 6 (12 weeks +/- 5 days)

- Review medications
- Complete a Partial Mayo Score Assessment for UC activity
- Nutritional assessment
- Collect stool sample(s). If virtual visit, this can be done locally at the University of Minnesota or Indiana University
- Review adverse events

Visit 7 (3 months after last FMT dose +/- one week)

- Phone call follow up
- Review adverse events

Visit 8 (6 months after last FMT dose +/- one week)

- Phone Call Follow Up
- Review adverse events, serious adverse events, and the onset of any new chronic medical conditions possibly related to FMT

The experimental treatment you get will be chosen by chance, like flipping a coin. Neither you nor the study doctor will choose what experimental treatment you get. You will have a 50% chance of being given either experimental treatment.

Neither you nor the study doctor will know which experimental treatment you are getting.

Optional Open Label Extension

After the completion of study visit 4, you will have the option of repeating another round of daily FMT capsules for 8 weeks. You would immediately repeat exam visits 1-6 again and then continue on to visits 7 & 8. This option will not include placebo; you will receive FMT capsules, as part of an open-label extension. You will not be compensated for this part of the study.

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

- Follow the instructions you are given.
- Come to all study visits with the study doctor or study staff.
- Tell the study doctor or study staff about any changes in your health or the way you feel.
- Tell the study doctor or study staff if you want to stop being in the study at any time.
- Not start any new medications or change your medications without approval from the study doctor.

What happens if I say "Yes", but I change my mind later?

You can leave the research study at any time. You can leave the research study at any time and no one will be upset by your decision. If you decide to leave the research study, you will resume treatment of your ulcerative colitis with your doctor.

Choosing not to be in this study or to stop being in this study will not result in any penalty to you or loss of benefit to which you are entitled. This means that your choice not to be in this study will not negatively affect your right to any present or future medical care, your academic standing as a student, or your present or future employment.

If you stop being in the research, information about you that has already been collected may not be removed from the study database. You will be asked whether the investigator can collect information from your routine medical care, such as your medical records. If you agree, this information will be handled the same as the information obtained for the research study.

What are the risks of being in this study? Is there any way being in this study could be bad for me? (Detailed Risks)

Risks from FMT: In a randomized controlled trial of FMT for UC, adverse events occurred at a similar rate versus placebo. The most common reported adverse events (>5% in treatment arm) along with placebo are presented in table below:

Event	FMT	Placebo
Infection related adverse events	24%	35%
Upper respiratory tract infection	17%	15%
Abdominal pain	29%	28%
Colitis flare	24%	23%
Flatulence	24%	20%
Bloating	20%	28%
Headache	10%	5%
Dizziness	7%	8%
Fever	7%	5%
Rash	7%	0
Nausea	5%	13%
Alanine aminotransferase elevation	5%	5%
Chills	5%	5%
Vomiting	5%	3%
Back pain	5%	0

Other potential FMT Risks are unknown but are mitigated whenever possible, as explained below.

Potential Infectious Risk - Rare

Gut microbiota are generally non-pathogenic since their well-being depends on the well-being of the host. Some pathogens known to cause chronic infections, e.g., hepatitis viruses, can be shed in the fecal material. However, the donors supplying fecal material for transplantation are screened for the presence of these organisms and cannot donate material unless they test negative for the pathogens of concern. If any suspected or confirmed pathogens are transmitted from the FMT capsules to any participant within the study, the Investigator will impose a study-wide halt to all subjects until medical safety monitoring has been completed.

Multi-Drug Resistant Organisms (MDRO) - Rare

The transmission of microbes can cause an infection or carry antibiotic resistance genes that can be passed to other microbes and make it difficult to treat infections. The donors supplying fecal material for transplantation are screened for multiple MDROs per FDA requirements and cannot donate material unless they test negative for these MDROs. If suspected or confirmed MDROs are transmitted from the FMT capsules to any participant within the study, the Investigator will impose a study-wide halt to all subjects until medical safety monitoring has been completed.

Metabolic Risk - Rare

All donors in the program are lean (BMI ≤ 30.0 kg/m^2). Any single feature of metabolic syndrome (BMI, hypertension, abnormal lipid panel, abnormal fasting glucose, abnormal liver function tests) excludes donor candidates from participation. However, clinical donor indicators may not be perfectly predictive of metabolic potential of their microbiota, and it is possible that an opposite from desired effect could result from the intervention.

Risk of Gastrointestinal Symptoms - Common

Gut microbiota constitute an integral part of the gastrointestinal tract. They can potentially play a role in a variety of gastrointestinal disorders, including irritable bowel syndrome (IBS) and inflammatory bowel disease (IBD). FMT can trigger exacerbations of existing IBD. However, FMT has also been reported to be successful in treatment of both IBS and IBD.

Common side effects associated with FMT include: fever, abdominal cramping, diarrhea, constipation, nausea, and bloating.

Risk of Autoimmunity – Unknown Risk

The role of the gut microbiota in the function of a mature immune system is unknown. There is a risk that some form of immune disorder can be triggered by a new composition of gut microbiota in a recipient. This includes allergic disorders, serological evidence of autoimmunity, or autoimmune disorders.

Risk of Colorectal Cancer - Rare

Gut microbiota may cause colon cancer, although the link between microbiota and colon cancer development has not been proven. This risk is mitigated by eliminating potential donors of fecal microbiota considered at increased risk for colon cancer, e.g., significant family history or positive

screening test.

Risk of COVID-19

It is possible that SARS-CoV-2, the coronavirus that causes COVID-19, can spread through FMT. To decrease this risk, the manufacturer tests their donors for COVID-19 using a nasopharyngeal (back of the nose) swab test for the SARS-CoV-2 virus before using their stools in the FMT capsules. However, it is still possible for SARS-CoV-2 virus to be passed on through the stool of an infected donor who may not have symptoms of COVID-19 and may have a negative nasopharyngeal swab for SARS-CoV-2 virus.

To minimize the risks of receiving a transplant, all donors in this study will be thoroughly screened by the study doctor before they are accepted as donors. After they are accepted they will continue to be screened on an ongoing basis. Importantly, fecal microbiota is very complex biological material. We acknowledge that our tests are not perfect and can miss important information about individual or groups of microbes present in the preparation.

Other Study Risks

Stool Collection

You will be asked to collect your own stool weekly for 12 weeks, which may require storage of your stool for a period of time. This may be discomforting to you. Risk of discomfort with human waste and risk of improper storage.

Risks for Women of Child-Bearing Potential

Participation in this the study may involve unknown risks to a pregnant woman, unborn baby or nursing infant. You must not take part in this study if you are pregnant, plan to become pregnant during the research study period, or are breast-feeding a baby.

Loss of Confidentiality

There is the possibility of a breach of confidentiality.

The records of this study will be kept private and study data will not be included in your medical records. In any publications or presentations, you will not be identified by name or other recognizable way on any records, results or publications relating to the project. Research records will be kept in a locked file, and all electronic information will be coded and secured using a password protected file. Your stool specimen(s) and data will be assigned a unique identifier. Only research staff members will have access to your personally identifiable information.

In addition to these risks, this research may hurt you in ways that are unknown. These might be minor or be severe as to cause death.

What do I need to know about reproductive health and/or sexual activity if I am in this study?

You should not be or become pregnant while on this research study.

If you are sexually active, both men and women should use at least one effective means of birth control

while participating in this research study. According to the World Health Organization and the United States Center for Disease Control and Prevention, the most effective forms of birth control include complete abstinence, surgical sterilization (both male and female), intrauterine devices (IUDs), and the contraceptive implant. The next most effective forms of birth control include injectables, oral contraceptive pills, the contraceptive ring, or the contraceptive patch. Acceptable, but least effective, methods of birth control include male condoms (with or without spermicide) and female condoms.

If you or your partner become pregnant while participating in this research study, it is important that you tell the study doctor or other research team member immediately. You might be required to stop participation in this study; however, other clinical care options will be discussed with you at that time if necessary.

If you or your partner [are/is] considered to be postmenopausal, you are not required to use contraception while participating in this research study. Postmenopausal women rarely become pregnant. If you or your partner become pregnant while participating in this research study, it is important that you tell the study doctor or other research team member immediately. You may be required to stop participation in this study; however, other clinical care options will be discussed with you at that time if necessary.

Will it cost me anything to participate in this research study?

Taking part in this research study will not lead to any costs to you.

You and your insurance company will be charged for the health care services that you would ordinarily be responsible to pay. In some cases, insurance will not pay for services ordinarily covered because these services are performed in a research study. You should check with your insurance to see what services will be covered by your insurance and what you will be responsible to pay.

Will being in this study help me in any way? (Detailed Benefits)

We cannot promise any benefits to you or others from your taking part in this research. However, possible benefits include a potential improvement in your ulcerative colitis symptoms.

What happens to the information collected for the research?

Efforts will be made to limit the use and disclosure of your personal information, including research study and medical records, to people who have a need to review this information. We cannot promise complete confidentiality. Organizations that may inspect and copy your information include the Institutional Review Board (IRB), the committee that provides ethical and regulatory oversight of research, the U.S. Food and Drug Administration or other regulatory authorities, and other representatives of this institution, including those that have responsibilities for monitoring or ensuring compliance.

Your information may also be transmitted and/or reviewed by University of Minnesota (UM), University of Minnesota Physicians (UMP) and University of Minnesota Medical Center, Fairview personnel who monitor research and UM, UMP and Medical Center personnel who need access to the information to complete the program.

Data or Specimens Collected

Stored Stool Samples

Your stool samples collected for this study will be stored by Dr. Vaughn to allow for the characterization of microbial communities. Dr. Vaughn will be the custodian of the samples and will be stored by your unique identifier, which will not include any identifying data about you.

The microorganisms in the samples may be examined using genetic techniques. No human genetic testing will be performed on these samples.

Samples may be stored for 5 years or more and you may be contacted in the future regarding research on stored samples. Specimens will be disposed of following the University of Minnesota's Biohazardous and Pathological Waste Management Plan. Study records will be retained for 3 years after study closure. Destruction of electronic data and paper records will follow the University of Minnesota's Media Sanitization Standard.

If identifiers are removed from your identifiable private information or identifiable samples that are collected during this research, that information or those samples could be used for future research studies or distributed to another investigator for future research studies without your additional informed consent.

The sponsor, monitors, auditors, the IRB, the University of Minnesota Research Compliance Office and other University compliance units, the US Office of Research Integrity (ORI), the US Office for the Protection of Human Research Protections (OHRP), the US Food and Drug Administration (FDA) may be granted direct access to your medical records to conduct and oversee the research. By signing this document you are authorizing this access. We may publish the results of this research. However, we will keep your name and other identifying information confidential.

A description of this clinical trial will be available at 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.

Will I receive research test results?

Most tests done on samples in research studies are only for research and have no clear meaning for health care. The investigator(s) will not contact you or share your individual test results.

Whom do I contact if I have questions, concerns or feedback about my experience?

This research has been reviewed and approved by an IRB within the Human Research Protections Program (HRPP). To share feedback privately with the HRPP about your research experience, call the Research Participants' Advocate Line at 612-625-1650 (Toll Free: 1-888-224-8636) or go to z.umn.edu/participants.You are encouraged to contact the HRPP if:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You want to talk to someone besides the research team.
- You have questions about your rights as a research participant.

- You want to get information or provide input about this research.

Will I have a chance to provide feedback after the study is over?

The HRPP may ask you to complete a survey that asks about your experience as a research participant. You do not have to complete the survey if you do not want to. If you do choose to complete the survey, your responses will be anonymous.

If you are not asked to complete a survey, but you would like to share feedback, please contact the study team or the HRPP. See the "Investigator Contact Information" of this form for study team contact information and "Whom do I contact if I have questions, concerns or feedback about my experience?" of this form for HRPP contact information.

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: becoming pregnant during participation in the study or if you have a severe flare of your disease.

What happens if I am injured while participating in this research?

In the event that this research activity results in an injury, treatment will be available, including first aid, emergency treatment and follow-up care as needed. Care for such injuries will be billed in the ordinary manner, to you or your insurance company. If you think that you have suffered a research related injury let the study physicians know right away.

Will I be compensated for my participation?

If you agree to take part in this research study, we will pay you a total of $50 for your time and effort. You will receive $25 after completion of the week eight study visit and an additional $25 after completion of the week twelve study visit.

Payment you receive as compensation for participation in research is considered taxable income. If payment to an individual equals or exceeds $600 in any one calendar year, the University of Minnesota is required to report this information to the Internal Revenue Service (IRS). Research payments to study participants that equal or exceed $600 during any calendar year will result in a FORM 1099 (Miscellaneous Income) being issued to you and a copy sent to the IRS.

Use of Identifiable Health Information

We are committed to respect your privacy and to keep your personal information confidential. When choosing to take part in this study, you are giving us the permission to use your personal health information that includes health information in your medical records and information that can identify you. For example, personal health information may include your name, address, phone number or social security number. Those persons who get your health information may not be required by Federal privacy laws (such as the 1099 Rule) to protect it. Some of those persons may be able to share your

information with others without your separate permission. Please read the HIPAA Authorization form that we have provided and discussed.

The results of this study may also be used for teaching, publications, or for presentation at scientific meetings.

Optional Elements:

The following research activities are optional, meaning that you do not have to agree to them in order to participate in the research study. Please indicate your willingness to participate in these optional activities by placing your initials next to each activity.

Yes, I agree	**No, I disagree**	
_____	_____	The investigator may contact me in the future to see whether I am interested in participating in other research studies by Byron Vaughn, MD.

If yes, provide the following contact information:

Email Address: _____

Phone Number: _____

Your signature documents your permission to take part in this research. You will be provided a copy of this signed document.

_____ _____
Signature of Participant Date

_____
Printed Name of Participant

_____ _____
Signature of Person Obtaining Consent Date

_____
Printed Name of Person Obtaining Consent