Weill Cornell Medicine NewYork-Presbyterian

IRB Protocol #: 19-04020045
IND #: 19087
NCT03998488
INFORMED CONSENT FORM

A randomized, placebo-controlled clinical trial examining the efficacy of Fecal Microbiota Transplantation (FMT) and subsequent dietary fiber in patients with moderate ulcerative Colitis

Version Date: 10/13/2022

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WEILL CORNELL MEDICAL COLLEGE

Informed Consent and HIPAA Authorization for Clinical Investigation

Project Title: A randomized, placebo-controlled clinical trial examining the efficacy of Fecal Microbiota Transplantation (FMT) and subsequent dietary fiber in patients with moderate ulcerative colitis

IRB Protocol #: 19-04020045

Principal Investigator: Dr. Randy Longman

Subject Name or number: _____

MRN: _____

Institution: **Weill Cornell Medical College**

KEY INFORMATION ABOUT THIS RESEARCH STUDY	
We are asking you to choose whether to volunteer for a research study about mild to moderate Ulcerative Colitis (UC) disease response to human fecal microbiota transplantation (FMT) of the investigational study drug, FMP250, and the efficacy of the FMT if combined with supplemental psyllium fiber. Subjects will be randomized to the double-blinded, placebo-controlled study to determine whether they will receive FMP250 or placebo first in an endoscopic procedure and if they are randomized to take supplemental psyllium fiber. Subjects will also provide blood, fecal and mucosal biopsy samples throughout the course of the study. This page is designed to give you key information to help you decide whether to participate. We have included detailed information after this page. Ask the research team questions. If you have questions later, the contact information for the research investigator in charge of the study is below.	
Purpose: **What is the study about and how long will it last?**	The purpose of this interventional study is to gather information on the safety and effectiveness of the investigational drug, FMP250 when combined with supplemental psyllium fiber for patients with mild to moderate UC. For detailed descriptions, use the Consent Document. Your participation in this research will last about one year.
Benefits: **Key reasons you might choose to volunteer**	We cannot and do not guarantee that you will receive any benefits from this study. We hope the information learned from this study will benefit other patients with ulcerative colitis in the future.
Risks: **Key reasons you might choose NOT to volunteer**	The study is associated with risks to receiving the stool transplant, which is obtained from a donor. This can include fevers, abdominal cramping, bloody diarrhea, and serious blood-stream infections (rare). An additional risk of the stool transplant includes the transmission of various infectious organisms (bacterial, viral, fungal) contained in the stool. For a complete description of possible transmissible infectious organisms, refer to the Consent Document below.

	If you are randomized to receive supplemental psyllium fiber, the main concern is the risk of choking. Rare side effects may include abdominal discomfort, nausea, mild abdominal cramps, griping, and faintness. Providing blood samples may cause discomfort, bleeding, bruising, and infection at the site of blood withdrawal (rare). Additional research biopsies pose the same risks as standard of care biopsies. These include small risk of bleeding and rare risk of infection. Due to the unknown risks of stool transplants to pregnant women, unborn babies, or nursing infants, 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. For a complete description of risks, refer to the Consent Document below. Alternative treatments including standard medical therapy alone or surgery exist**.** For a complete description of alternate treatment/procedures, refer to the Consent Document below.
Voluntary Participation: **Do you have to take part in the study?**	Participation is optional. If you decide to take part in the study, it should be because you really want to volunteer. You will not lose any services, benefits or rights or access to you would normally have if you choose not to volunteer.
What if you have questions, suggestions, or concerns?	The person in charge of the study is Dr. Randy Longman [PI]. If you have questions, suggestions, or concerns regarding this study or you want to withdraw from the study his contact information is**:** 212-746-5077. If you have any questions, suggestions or concerns about your rights as a volunteer in this research, contact staff in the Weill Cornell Medicine Institutional Review Board (IRB) between the business hours of 9am and 5pm EST, Monday-Friday at 646-962-8200 or send an e-mail to irb@med.cornell.edu.
This overview does not include all the information you need to know before deciding whether to take part in the study. Much additional detail is given in the full consent document, which can be found on the pages that follow. Be sure to review the rest of this consent form before deciding about participation.	

INTRODUCTION

You are invited to consider participating in a research study. You were selected as a possible participant in this study because you carry a diagnosis of ulcerative colitis and according to your medical provider have symptoms consistent with inadequately controlled disease. Please take your time to make your decision. It is important that you read and understand several general principles that apply to all who take part in our studies:

a. Taking part in the study is entirely voluntary.

b. Personal benefit to you may or may not result from taking part in the study, but knowledge gained from your participation may benefit others.

c. You may decide not to participate in the study or you may decide to stop participating in the study at any time without loss of any benefits to which you are entitled.

The purpose and nature of the study, possible benefits, risks, and discomforts, other options, your rights as a participant, and other information about the study are discussed below. Any new information discovered which might affect your decision to participate or remain in the study will be provided to you while you are a participant in this study. You are urged to ask any questions you have about this study with members of the research team. You should take whatever time you need to discuss the study with your physician and family. The decision to participate or not to participate is yours. If you decide to participate, please sign and date where indicated at the end of this form.

The research study is being funded by Weill Cornell Medical College. Crohn's Colitis Foundation and The National Institutes of Health (NIH) is providing a research grant for this study. Dr. Randy Longman is the primary investigator.

The study will take place at facilities of New York Presbyterian Hospital where the investigators are members of the medical staff. New York-Presbyterian Hospital is neither a sponsor nor an investigator for this study.

WHY IS THE STUDY BEING DONE?

Ulcerative Colitis (UC) is a disease that causes diarrhea and lower abdominal pain. The current standard treatments for UC includes medicines that help to reduce the inflammation of your intestines or change your immune system, including steroids. Biologic therapies may also be used, but they work in different ways to also help reduce inflammation in your intestines. Although there are numerous medications available for the management of UC, patients commonly become steroid dependent and/or intolerant to medical management.

Human fecal microbiota transplantation (FMT) is also known as a stool transplant and is an emerging treatment for UC, however, its clinical efficacy is variable. This is done by delivering the study drug, FMP250, by fecal transplantation (FMT) ideally at the ileum. This procedure is used to treat severe or chronic Clostridium difficile colitis and, in this case, it will be investigated in ulcerative colitis with the intention of introducing normal bacterial flora from a healthy donor to a diseased colon.

The purpose of this study is to determine the efficacy of investigational FMT (FMP250) and to determine if the efficacy of FMT is increased when taken with supplemental psyllium fiber for patients with mild to moderate ulcerative colitis.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

Participants in the study are referred to as subjects.

135 subjects will be recruited at this site.

WHAT IS INVOLVED IN THE STUDY?

This is a randomized, double-blind, placebo-controlled study done to test the role of supplemental psyllium fiber in the enhancement of efficacy of the investigational Fecal Microbiota Transplantation (FMT) done with the study drug, FMP250.

If you decide to participate in this study, you will be "randomized" at a 1:1:1 ratio into one of the following 3 research intervention groups provided all the inclusion and exclusion criteria are met:

Group 1: Investigational FMT
- Subject will receive investigational FMP250 once at day 0 colonoscopy
- Subject will receive placebo FMP250 once at week 8 flexible sigmoidoscopy
- Observed for 12 weeks

Group 2: Investigational FMT + psyllium fiber
- Subject will receive investigational FMP250 once at day 0 colonoscopy
- Fiber supplementation of 1 teaspoon 2x/day (morning and night) for 8 weeks
- Subject will receive placebo FMP250 once at week 8 flexible sigmoidoscopy
- Observed for 12 weeks

Group 3: Placebo FMT with or without psyllium fiber
- Subject will receive placebo FMP250 once at day 0 colonoscopy
- Half of subjects will be randomized to receive fiber supplementation of 1 teaspoon 2x/day (morning and night) for 8 weeks
- Subject will receive investigational FMP250 once at week 8 flexible sigmoidoscopy
- Observed for 12 weeks

Randomization means that you are put into a group by chance. It is like flipping a coin. Neither you, the research team, nor treating clinician will choose what group you will be in. You will have an equal chance of being placed in any group, 2 in 3 chances of receiving investigational FMT with a 1 in 3 chance of receiving placebo (which looks exactly like study drug but does not contain active ingredient).

This is a blinded research study; therefore, neither you nor the clinician will know which research intervention will be given to you at the day 0 colonoscopy or week 8 flexible sigmoidoscopy. Blinding subjects and clinicians is done to ensure the results of the research are not influenced by anyone. It is important to note that even though you may be randomized to one of the research intervention groups receiving the study drug, the final eligibility criterion is determined by endoscopic evaluation during the day 0 colonoscopy. There is a chance that you may not receive the study drug at all if you do not meet this final endoscopic criterion. The randomized assignment will not be made known to you or the study physician until all week 8 evaluations have been completed for all study participants. Therefore, if you were blindly randomized to receive placebo at the day 0 colonoscopy, you will be given the investigational FMT (FMP250) during your week 8 flexible sigmoidoscopy and if you were blindly randomized to receive investigational FMT (FMP250) at the day 0 colonoscopy, you will be given the placebo FMT during your week 8 flexible sigmoidoscopy In the case of a medical emergency, the randomized intervention you received may be revealed by the study coordinator to the study doctor upon request.

Please advise the researchers of any medications you are taking. In addition, if you are taking any over-the-counter drugs or herbal supplements, which you have obtained, from the drug store, grocery store, etc., you should advise the researchers.

Study Procedures/Assessments

You will have the following tests and procedures as a part of this research study:

Study Procedures	Screening Period	Screening Colon-oscopy	Phone Call	Phone Call	Clinic Visit	Phone Call	Clinic Visit	Phone Call	Clinic Visit	
Study Timeline	Day -28 to -3	Day 0	Day 1	Wk 2	Wk 4	Wk 6	Wk 8	Wk 10	Wk 12	Off Study[d]

Informed consent	X									
Demographics	X									
Medical history	X									
Concurrent medication	X---------- X									
Intervention Randomization	X									
Physical exam	X				X		X		X	
Vital signs + Height + Weight	X				X		X		X	
B-HCG (serum pregnancy test) (research purposes)	X									
Urine Pregnancy Test (standard of care and research purposes)		X[c]					X			
CRP: C-Reactive Protein (standard of care)	X*						X			
ESR: Erythrocyte Sedimentation Rate (standard of care)	X*						X			
CBC[a] (standard of care)	X*						X			
CMP[b] (standard of care)	X*						X			
Blood: HIV screen (standard of care)	X*									

Blood: Hepatitis A B C Profile (standard of care)	X*									
Blood: RPR (*Treponema pallidum*) (research purposes)	X									
Blood: CMV IgM (standard of care)	X*									
Blood: Quantiferon-TB (standard of care)	X*									
Fecal Calprotectin (standard of care)	X*						X			
Stool: Ova &parasites (standard of care)	X*									
Stool: *Clostridium Difficile* Toxin PCR (standard of care)	X*									
Stool: Gastrointestinal Pathogen PCR Panel[e] (standard of care)	X*									
Screening Colonoscopy (standard of care)		X								
Blinded (Investigational or Placebo) FMP250 Intervention		X								
Follow-up Flex sigmoidoscopy (standard of care)							X			
Blinded Investigational FMP250 at week 8 (research purposes)							Placebo FMP250 group only			
Blinded Placebo FMP250 at Week 8 (research purposes)							Investigational FMP250 group only			
Mucosal Biopsy Collection (research purposes)		X					X			
Blood and Stool Collection (research purposes)	X ------- X				X		X		X	
Follow-Up Phone calls (research purposes)			X	X		X		X		X

Diet Recall with Clinical Nutritionist or study MD (research purposes)	X									
Psyllium Fiber Supplements (research purposes)	X---------- X									
Adverse event evaluation	X---------- X									

*: These standard of care laboratory tests are required to be conducted during the screening period. However if you consent below on page 5, this study may instead use recent laboratory results you had conducted within 2 weeks of signing consent.

a: Complete Blood Count (WBC count, RBC count, Hb, Hct, platelet count)

b: Comprehensive Metabolic Panel (glucose, calcium, sodium, potassium, CO_2, chloride, BUN, Creatinine)

c: Urine pregnancy test (women of childbearing potential) as standard of care for colonoscopy

d: Off-study evaluation for the following year.

e: Gastrointestinal Pathogen GI Panel (Campbylobacter species, *Plesiomonas Shigelloides*, *Salmonella* Species, *Vibrio* Species, *Vibrio cholerae*, *Yersinia Enterocolitica*, Enteroaggregative *E. coli* (EAEC), Enterpathogenic *E. coli* (EPEC), Enterotoxigenic *E. coli* (LT/ST), Shigalike toxin producing *E.coli* I (STX/ST2), *Cryptosporidium*, *Cyclospora caretanensis*, *Entamoeba Cayetanensis*, *Giardia*, *Adenovirus* F 40/41, *Astrovirus*, *Norovirus* GI/GII, *Rotavirus* A, *Sapovirus*, GID PCR INTERP)

1. Screening Visit

Once the informed consent document has been signed, the research study will be initiated by a screening visit. This is intended to ensure that you meet all criteria for this study.

During this visit, the clinician will ask about your medication and medical history and will also conduct a physical exam. Additionally, you will meet with a registered dietician or your study physician during the screening period (days -28 to -3), either by an in-person or phone call consult, for research purposes to assess what you normally eat on a regular weekday by going through a 24-hour diet recall.

Standard of care blood and stool testing will be conducted, if not done within 2 weeks of signing this consent form, in addition to a few other tests for research purposes to further determine eligibility. More details on these specific tests can be found in the **Study Procedures/Assessments** section.

Please check "Yes" if you consent to having your recent blood and stool laboratory results to be used to determine your eligibility into this study. These laboratory tests must have been collected within 2 weeks of signing this consent form. If you check "No" you will be asked to do all standard of care blood and stool testing after signing this consent form.

❑ Yes ❑ No

Once you have met all the eligibility criteria during the screening visit and the study clinician has reviewed your lab results, only then can you be randomized and evaluated at your upcoming standard of care colonoscopy.

Evaluation of your disease severity during the colonoscopy is the final measure assessing your eligibility for this study. Your disease activity score will be evaluated during the colonoscopy and will determine if you are eligible to receive the active or placebo FMP250; there is a chance that you may not receive the study drug at all.

If you do not meet the requirements to be included in this study, your clinician will explain why and should detail other appropriate therapeutic alternatives.

2. Day 0 Colonoscopy and study drug administration

You will undergo **bowel prep** and food fasting as of midnight of the procedure date, as you do for your usual standard of care colonoscopies with biopsies. 1-2 hours prior to the colonoscopy procedure, you will receive an **anti-diarrheal agent(s)** (e.g. loperamide and/or diphenoxylate/atropine) to help with the retention of the fecal transfer for research purposes.

The colonoscopy will be performed in the NYP Endoscopy suite using standard of care practices, and you will be monitored post-procedure using standard practices. The study clinician will evaluate and score your disease activity to determine if you are eligible to receive the study drug. If you are eligible, you will blindly receive either the active or placebo FMP250 for research purposes based on your randomization. The fecal suspension will be delivered by 60cc syringes via the colonoscope to the deepest level of insertion (ideally the ileum). Therefore, up to 250cc of the fecal suspension will be administered in aliquots of 60cc. You will be asked to retain the fecal transfer for as long as possible, ideally greater than 4 hours. Your randomized intervention will not be made known to you or the medical provider conducting the procedure until after an evaluation by flexible sigmoidoscopy at week 8.

Mucosal Biopsies for research

A mucosal biopsy is the removal of a small piece, approximately the size of the tip of a pen, of your tissue from your intestine during an endoscopy procedure. Intestinal tissue biopsies may be tested to understand the effect of FMP250 and/or psyllium fiber, to predict who may respond to this intervention in the future, and to learn more about UC.

During your colonoscopy, biopsies will be taken for diagnostic purposes. Additionally, 2 biopsies of the rectal tissue and 2 biopsies of the sigmoid tissue will be taken prior to the fecal microbiota transfer for research purposes. You will also undergo a flexible sigmoidoscopy with biopsies for standard of care at week 8. The same 4 biopsies from the rectal and sigmoid tissue will additionally be taken during this procedure for research purposes.

Blood and Stool samples for research

Collection 1:

Prior to the day of your colonoscopy or if applicable, the initiation of psyllium husk, you will be asked to provide a pre-FMT stool sample for research purposes. You will also be asked to provide a blood sample and it will be drawn via venipuncture (the puncture of a vein with a needle to withdraw blood) and approximately 2.5 teaspoons of blood will be collected.

Collection 2:

You will be asked to provide a stool and blood sample on the day of your post-FMT week 4 clinic visit.

Collection 3:

You will be asked to provide a stool and blood sample on the day of your post-FMT week 8 clinic visit.

Collection 4:

You will be asked to provide a stool and blood sample on the day of your post-FMT week 12 clinic visit.

Pharmacodynamic blood testing

Blood samples will also be drawn and used to test for certain proteins that may identify how your body is responding to the study drug, these proteins are called protein biomarkers.

Pregnancy Testing
If you are a female who can have children, you will provide a blood sample at the screening visit for research purposes, and then a urine sample for the colonoscopy as per standard of care protocol and at the week 8 clinic visit for research purposes to see if you are pregnant. A positive pregnancy result will disqualify you from being in the study.

Stool Sample testing
The standard of care stool samples taken at the screening visit will predominantly be tested to measure active gut inflammation and to ensure you do not have any intestinal viral or bacterial infections. Another stool sample will be collected at the week 8 clinic visit as standard of care to again test for active inflammation. All other stool samples collected throughout the course of the study are for research purposes. These will be immediately stored and eventually used to investigate the effect of FMT and/or psyllium fiber, to predict who may respond to this type of intervention in the future, and to learn more about UC.

Follow-Up
Phone Consults: 2, 4, 6 and10 weeks after the FMT

- You will receive follow-up phone calls for evaluation of adverse effects and ulcerative colitis activity for research purposes. You will continue to receive follow-up phone calls every 6 months for the next year for research purposes.

Importantly, you will follow up with your gastroenterologist as clinically indicated, and they will also ask you questions regarding your symptoms from the time of stool transplant, as well as perform further studies, as they feel is indicated by normal standards, such as colonoscopy, endoscopy, etc.

HOW LONG WILL I BE IN THE STUDY?

We think you will be in this study for a year. The research intervention visits along with clinical visits will occur over a 12-week period; however, you will receive follow up phone calls every 6 months for the following year so that we can evaluate how you respond to this therapy long-term.

You can stop participating at any time. However, if you decide to stop participating in the study, we encourage you to talk to the researcher and your regular doctor first. There will be no consequences of sudden withdrawal from the study. If you choose to not participate in the study or to leave the study, your regular care will not be affected nor will your relations with WCMC, New York-Presbyterian Hospital, your physicians, or other personnel. In addition, you will not lose any of the benefits to which you are entitled.

Withdrawal by investigator, physician, or sponsor

The investigators, physicians or sponsors may stop the study or take you out of the study at any time should they judge that it is in your best interest to do so, if you experience a study-related injury, if you need additional or different medication, or if you do not comply with the study plan. They may remove you from the study for various other administrative and medical reasons. They can do this without your consent.

WHAT ARE THE RISKS OF THE STUDY?

For trials of drugs and procedures, there may be risks. These risks will be discussed with you by the research doctor.

Risks and side effects related to the stool transplant we are studying include: Risks from donor stool, such as serious blood-stream infection (rare) or fevers, abdominal cramping, bloating, diarrhea, and bloody stool (less likely). Complications may include but are not limited to the following:

a. Transmission of infectious organisms (bacterial, viral, fungal) contained in the stool
    a. Multi-Drug Resistant Organisms (MDROs)
        i. A potential risk of fecal microbiota transplantation (FMT) is the transmission of antibiotic-resistant bacteria. These are bacteria that are resistant to some antibiotics. These bacteria could be transmitted through FMT and could cause serious invasive infection or death.
        ii. The study drug, FMP250, that will be delivered by FMT is provided by OpenBiome, a universal stool bank where donors who provide stool for FMT undergo regular screening for certain antibiotic-resistant bacteria. Each FMT is only made available when these screens do not detect antibiotic-resistant bacteria in the donor before and after the stool donation. Donors also undergo regular clinical assessments for any risk factors associated with carrying antibiotic-resistant bacteria, such as recent use of antibiotics, visiting certain healthcare facilities, or certain travel activities.
    b. Shiga Toxin-Producing E. Coli (STEC) and Enteropathogenic E. Coli (EPEC)
        i. A potential risk of fecal microbiota transplantation (FMT) is the transmission of STEC and EPEC. STEC is a type of E. coli that can produce a toxin called Shiga toxin. Shiga toxin can be transmitted through FMT and can cause symptoms like abdominal pain, diarrhea (often bloody), vomiting, and mild fever. Most people develop symptoms within 3-4 days of acquiring the bacteria, and most get better within 5-7 days. EPEC is another type of E. coli that can be transmitted through FMT and is generally carried asymptomatically but can sometimes cause transient watery diarrhea, similar to traveler's diarrhea. Symptoms typically resolve in a matter of days.
        ii. The study drug, FMP250, that will be delivered by FMT is provided by OpenBiome, a universal stool bank where donors who provide stool for FMT undergo regular screening for these bacteria. Each FMT is only made available to delivery when these stool screenings do not detect EPEC or STEC in the donor before and/or after the stool donation.
    c. SARS-CoV-2 Infection
        i. A potential risk of fecal microbiota transplantation (FMT) is the transmission of SARS-CoV-2, a novel coronavirus that causes the disease COVID-19. Infection with SARS-CoV-2 may be transmitted through stool and may cause serious illness or death. It is possible for healthy, asymptomatic stool donors to potentially be infected with SARS-CoV-2.
        ii. The FMT you will receive is provided by OpenBiome, a universal stool bank where donors who provide stool for FMT undergo regular stool, blood, and nasal screenings for many different infectious agents, including SARS-CoV-2, the virus that causes the illness called COVID-19. However, not all infectious agents are screened for and some infectious agents are as yet undiscovered. Each FMT unit is only made available for use when these screens do not detect the infectious agents for which we test. Donors also undergo regular in-person clinical assessments for any risk factors, including risk factors associated with carrying SARS-CoV-2, such as visiting certain healthcare facilities, or other behaviors that may increase the risk of exposure. However, because COVID-19 is so widespread, donors may be exposed or infected without having an identified risk factor for exposure. They may also have no symptoms of infection. OpenBiome continually updates its screening

guidelines and procedures as additional data, tests, and information become available.

iii. If the FMT that you receive was made from stool donated after December 1st, 2019, either the donor's stool was tested for the presence of SARS-CoV-2 using a viral RNA test, or the stool donor was tested for the presence of SARS-CoV-2 using a nasopharyngeal swab at least every 14 days. Both kinds of test looks for the specific genetic material that makes up the virus. If a donor tests positive for SARS-CoV-2, OpenBiome destroys any FMT units made from that donor in the 4 weeks (28 days) before their positive test result. The donor is also disqualified from providing stool donations for at least 8 weeks. To be re-instated in the stool donation program after 8 weeks, the donor must pass all screens.

iv. Although we cannot be absolutely certain, it is unlikely that SARS-CoV-2 is present in stool donations that were provided to OpenBiome on or prior to December 1st, 2019. For this reason, testing on donors prior to December 1st has not been performed.

v. Though these precautions are taken to minimize the risk of SARS-CoV-2 transmission via FMT, the scientific and clinical community continues to learn more about SARS-CoV-2 and COVID-19. There are limits to the detection levels of laboratory tests, including those for SARS-CoV-2. Even with current screening and testing strategies, there may be additional risks that are unknown at this time. Although the donor screening tests we perform are likely to prevent you from receiving FMT from a donor who is infected with SARS-CoV-2, we cannot be absolutely certain that the stool you receive has not been contaminated with the SARS-CoV-2 virus.

d. Monkeypox Infection

i. A potential risk of fecal microbiota transplantation (FMT) is the transmission of monkeypox. Infection can cause symptoms including rash, fever, fatigue, myalgia, and respiratory symptoms which may be severe especially in immunocompromised patients. Studies have documented the presence of monkeypox virus DNA in rectal swabs and/or stool from infected individuals, but it is unknown whether monkeypox can be transmitted through stool or from asymptomatic infected individuals.

b. Missed polyps, cancer, or other lesion (infusing donor stool interferes with visualization of colonic mucosa)
c. Allergic reaction to antigens in donor stool
d. Enhanced ulcerative colitis activity
e. Theoretical increased risk of developing disease which may be related to donor gut bacteria (i.e. obesity, metabolic syndrome, autoimmune conditions, allergic/atopic disorders, neurologic disorders, and/or malignancy)

Risks from colonoscopy and sigmoidoscopy, such as perforation (serious but less likely), abdominal discomfort during or after the procedure (common but mild), and risks related to sedation (less likely). The incidence of risk associated with biopsies taken as standard of care does not increase with additional biopsies taken for research. These risks include bleeding, intestinal perforation, and / or infection. Bleeding associated with biopsy generally resolves spontaneously, however, in the unlikely event of persistent bleeding, clips and / or cautery can be applied to stop the bleeding.

Risk from Medical Record Review: Subjects will be asked about their medical history, usage of birth control, concurrent medication. There is a risk associated with the loss of privacy or confidentiality due to the probing of information. For example, if your identity as a participant in this study or your

identifiable health information were disclosed to unauthorized persons, there is the possible risk of discrimination by employers or insurance providers.

Risk from Blood Draws: Drawing blood from a vein may cause local pain, bruising, occasional lightheadedness, fainting, and very rarely, infection at the site of the blood draw. Rarely, blood clots may form and infections may occur. If you feel faint, you should lie down right away to avoid falling down. You should let your study doctor or staff know if you have any of these problems.

Risk from Placebo: In this research study, you may receive a placebo (inactive substance). If you receive the placebo, your condition may not change or may worsen.

Risk from Psyllium Husk: The main concern with psyllium husk is the risk of choking, specifically if the product is not consumed with sufficient liquid. Our research physicians also hypothesize bloating may occur. The following rare side effects may be of concern for older adults: abdominal discomfort, nausea, mild abdominal cramps, griping, and faintness.

Risk from Anti-Diarrheal Agents: Healthy adults usually don't experience side effects from antidiarrheal medicines. But side effects may be a concern if you are older or have health problems. Side effects of diphenoxylate/atropine may include: drowsiness, dizziness, headache, tiredness, restlessness, blurred vision, dry mouth, nausea, vomiting, upset stomach, loss of appetite, skin rash, or itching. Unlikely but serious side effects of diphenoxylate/atropine including: stomach or abdominal pain or swelling, severe nausea or vomiting, mental/mood changes (e.g., confusion, depression), or numbness and tingling of arms or legs. Side effects of loperamide may include: dizziness, drowsiness, tiredness, constipation, stomach pain, skin rash, or itching. Unlikely but serious side effects may also include severe constipation/nausea/vomiting, stomach or abdominal pain, or uncomfortable fullness of the stomach or abdomen.

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.

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

If you are sexually active, you 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 become pregnant while participating in this research study, it is important that you tell the study doctor or other research team member immediately. You will be required to stop receiving procedures and blinded FMT interventions for this study; however, other clinical care options will be discussed with you at that time if necessary and you will continue to complete the AE phone calls, week 4 clinic visit, and week 12 clinic visit as originally planned. The only difference will be that your week 8 assessment will be changed from a standard of care flexible sigmoidoscopy procedure into a clinic visit. This means you will do all other assessments, such as standard of care labs, research collection of blood and stool, physical exam, vital signs, height and weight measurements, etc. Therefore, the week 8 will no longer include a procedure, FMT blinded treatment, and biopsy collection for research.

If you are considered to be postmenopausal, you are not required to use contraception while

participating in this research study. Postmenopausal women rarely become pregnant.

There may also be side effects, other than listed above that we cannot predict. Other drugs may be given to make side effects that occur less serious and less uncomfortable. Many side effects go away shortly after the stool transplant is stopped, but in some cases side effects can be serious, long lasting or permanent

For more information about risks and side effects, ask the researcher or contact Dr. Randy Longman at 212-746- 5077.

ARE THERE ANY BENEFITS TO TAKING PART IN THE STUDY?

We cannot and do not guarantee that you will receive any benefits from this study. We hope the information learned from this study will benefit other patients with ulcerative colitis in the future.

WHAT OTHER OPTIONS ARE THERE?

Instead of being in this study, you have these options:

- You may choose not to participate in this study
- You may choose to take standard medical therapy alone (for example, topical 5-ASA medications or topical steroids, oral steroids, immune modulators, and anti-TNF medications) or even surgery depending on what is recommended by your primary gastroenterologist.

WHAT ABOUT CONFIDENTIALITY?

Efforts will be made to protect your medical records and other personal information to the extent allowed by law. However, we cannot guarantee absolute confidentiality. Records of study participants are stored and kept according to legal requirements and may be part of your medical record. You will not be identified personally in any reports or publications resulting from this study. Organizations that may request to inspect and/or copy your research and medical records for quality assurance and data analysis include groups such as:

- Weill Cornell Medical College and New York-Presbyterian Hospital
- The Institutional Review Board (IRB)
- The Office of Human Research Protection (OHRP)
- Department of Health and Human Services and National Institutes of Health
- The Food and Drug Administration (FDA) and/or their representatives

By signing this consent form, you authorize access to this confidential information. You also authorize the release of your medical records to Weill Cornell Medical College and New York-Presbyterian Hospital by any other hospitals or institutions where you might receive medical care of any kind while you are participating in this study.

If information about your participation in this study is stored in a computer, we will take the following precautions to protect it from unauthorized disclosure, tampering, or damage by requiring a unique ID and password to log into the database: All tissue, blood, or stool samples will be labeled with a unique alphanumeric identifier that does not link the specimen to the subject or the subjects' demographics. The samples are physically hand delivered to Dr. Longman's lab at WCMC by the PI and/or the research team. Identifiable samples are not sent to Dr. Longman's lab. A password protected database file will be maintained that links the samples with the subject. Only the study investigators will have access to this file. It will be stored in a password protected computer in a locked office. In addition, only personnel who are associated with the study will have access to the study specific records in the database.

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.

Genetic Information Nondiscrimination Act (GINA)

To the extent permitted by law, under no circumstances will any information linking you to specific test results be disclosed to any individual or organization without your written consent. A Federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that we get 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 get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.

Be aware that this new Federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. Nor does this Federal law prohibit discrimination on the basis of an already manifest genetic disease or disorder.

HIPAA AUTHORIZATION TO USE/DISCLOSE PROTECTED HEALTH INFORMATION FOR RESEARCH

Purposes for Using or Sharing Protected Health Information: If you decide to join this study, WCMC researchers need your permission to use your protected health information. If you give permission, Weill Cornell Medical College (WCMC) and/or New York-Presbyterian Hospital (NYPH) researchers may use your information or share (disclose) information about you for their research that is considered to be protected health information.

Voluntary Choice: The choice to give WCMC and/or NYPH researcher's permission to use or share your protected health information for their research is voluntary. It is completely up to you. No one can force you to give permission. However, you must give permission for WCMC and/or NYPH researchers to use or share your protected health information if you want to participate in the study. If you decline to sign this form, you cannot participate in this study, because the researchers will not be able to obtain and/or use the information they need in order to conduct their research. Refusing to give permission will not affect your ability to get usual treatment, or health care from WCMC and/or NYPH.

Protected Health Information To Be Used or Shared: Government rules require that researchers get your permission (authorization) to use or share your protected health information. Your medical information may be disclosed to authorized public health or government officials for public health activities when required or authorized by law. If you give permission, the researchers could use or share with the entities identified above any protected health information related to this research study from your medical records and from any test results, which includes HIV testing, hepatitis testing, additional blood tests (RPR, CMV IgM antibody, ESR, CRP), stool studies (routine stool culture for enteric GI pathogens: *E. coli, Salmonella, Shigella, Yersinia, Campylobacter, Cryptosporidium, Giardia, Vibrio, H. pylori, Plesiomonas Shigelloides, Cylospora*, *Entamoeba*, *Adenovirus*, *Astrovirus*, *Norovirus, Rotavirus*, *Sapovirus*), Ova and parasites, *Clostridium difficile* toxin by PCR, urine pregnancy test, colonic biopsies during colonoscopy, genetic testing (genetic sequencing of bacteria) from research only stool and biopsy

specimens, and immune cells taken from blood research samples.

Other Use and Sharing of Protected Health Information: If you give permission, the researchers could also use your protected health information to develop new procedures or commercial products. They could share your protected health information with the study sponsor the WCMC Institutional Review Board, inspectors who check the research, government agencies and research study staff.

The information that may be shared with the sponsor and/or government agencies could include your medical record and your research record related to this study. They may not be considered covered entities under the Privacy Rule and your information would not be subject to protections under the Privacy Rule.

RESEARCH REPOSITORY

What is a Research Repository?

A research repository (database) is a collection of information from the health and medical records of many individuals and can sometimes include identifiable specimens (like your tissue). The repository (database) may share the information with researchers who study medical conditions and diseases.

The repository (database) includes codes that identify each person whose information is collected. However, the repository does not share information with researchers unless the researchers promise to keep the information confidential.

RESEARCH PARTICIPANT: Please check the box below that describe your wishes. :

- ☐ The WCMC Repository may keep my protected health information and/or specimens and share it with qualified researchers studying the research described above. If information goes to an outside entity then the Privacy Rule may not apply.

- ☐ The WCMC Repository may keep my protected health information and/or specimens and share it with qualified researchers studying the research described above **AND** for unspecified research to be done in the future. I understand that the samples will be stored for 20 years and will be destroyed after the research is completed. If information goes to an outside entity then the Privacy Rule may not apply.
- ☐ The WCMC Repository may not keep my protected health information for a research repository.

By signing this consent form, you agree to give these samples to WCMC for research purposes.

CANCELING AUTHORIZATION

Canceling Permission: If you give the WCMC and/or NYPH researchers permission to use or share your protected health information, you have the right to cancel your permission whenever you want. However, canceling your permission will not apply to information that the researchers have already used or shared.

If you wish to cancel your permission, you may do so at any time by writing to:

Privacy Officer
1300 York Avenue, Box 303
New York, NY 10065

If you have questions about this, call (646) 962-6930 or e-mail: privacy@med.cornell.edu

End of Permission: Unless you cancel it, permission for WCMC and/or NYPH researchers to use or share your protected health information for their research will never end.

ACCESS TO RESEARCH RECORDS

During the course of this study, you will not have access to see or copy specific sections of your protected health information that contains research information as described in this authorization form, in accordance with Weill Cornell Medical College (WCMC) and/or New York-Presbyterian Hospital (NYPH) policies. This is done to prevent knowledge of study results affecting the reliability of the study. The part of your private information that you will not have access to is: **which arm of the study you are randomized to** or any other information that is "blinded" (that is, kept secret during the study to prevent bias). Your information will be available should an emergency arise that would require the treating physician to know this information in order to best treat you. Your right to access this information will be reinstated **after the completion of your week 8 visit**. If you wish to appeal this temporary suspension at any time, please write to the Privacy officer at the address provided on this form. By signing this form, you are agreeing to this temporary suspension of your rights to assess protected health information.

CERTIFICATE OF CONFIDENTIALITY

A Certificate of Confidentiality has been granted by the Department of Health and Human Services (DHHS). This Certificate will protect the investigators (research/study staff) from being forced to release any research data in which the subject is identified even under a court order or subpoena. This protection is not absolute. For instance, it does not override any state requirement to report child abuse to the appropriate authorities.

WHAT ARE THE COSTS?

The study will pay for any related procedures that are not considered standard care for patients with your disease. You will not have to pay for the study drug (fecal microbiota transplantation), psyllium dietary supplements, blood and stool sample collection for research purposes, or the loperamide and/or diphenoxylate/atropine provided for stool retention at the day 0 colonoscopy. These services will be provided for research purposes by Weill Cornell Medicine at no cost.

The physical examinations, standard laboratory tests, and diagnostic procedures, such as the colonoscopy and flexible sigmoidoscopy, are considered part of the standard care for patients with your disease who have had a change in clinical symptoms. The costs associated with each test will be charged to you or your insurance provider in the same manner as if you were not part of this research study. You or your insurance company will be charged for continuing medical care and/or hospitalization that are not a part of the study. The costs of all of the other medications and the administration of these medications that you receive during this study will be charged to you or your insurance provider. If unsuspected, incidental findings are noted during blood or stool testing or during colonoscopy and further medical tests and/or treatments are considered, such tests and/or treatments are no longer considered part of the study and therefore would be billed to you or your insurer. You should expect no compensation or reimbursement for these costs or any risks and anxieties associated with any such follow up care. Therefore, you or your insurance provider will need to assume responsibility for these costs. You will be billed for all costs or co-payments that are not paid by your insurance provider.

Taking part in this study may lead to added costs for you or your insurance company. Please ask about any expected added costs or potential insurance problems. You may wish to consult with your insurance company in advance about whether insurance will pay for these costs.

POLICY/PROCEDURES FOR RESEARCH RELATED INJURY

The Policy and Procedure for Weill Cornell Medical College are as follows:

We are obligated to inform you about WCMC's policy in the event injury occurs. If, as a result of your participation, you experience injury from known or unknown risks of the research procedures as described, immediate medical care and treatment, including hospitalization, if necessary, will be available at the usual charge for such treatment. No monetary compensation is available from WCMC or New York-Presbyterian Hospital. Further information can be obtained by calling the Institutional Review Board at (646) 962-8200.

COMPENSATION FOR PARTICIPATION

You will not receive compensation for participating in this study. You should not expect anyone to pay you for pain, worry, lost income, or non-medical care costs that occur from taking part in this research study.

COMMERCIAL INTEREST

Materials or data obtained from you in this research may be used for educational or commercial purposes. It is the policy of WCMC, New York-Presbyterian Hospital not to provide financial compensation to you should this occur.

WHAT ARE MY RIGHTS AS A PARTICIPANT?

Taking part in this study is voluntary. You may choose to not take part in the study or to leave the study at any time. If you choose to not participate in the study or to leave the study, your regular care will not be affected nor will your relations with the Weill Cornell Medical College, New York-Presbyterian Hospital, your physicians, or other personnel. In addition, you will not lose any of the benefits to which you are entitled.

A Data Safety and Monitoring Board, an independent group of experts, will be reviewing the data from this research throughout the study. We will tell you about new information that may affect your health, welfare, or participation in this study.

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

For questions about the study, a research-related injury, any problems, unexpected physical or psychological discomforts, or if you think that something unusual or unexpected is happening, call Dr. Randy Longman at 212- 746-5077 or the Department of Gastroenterology. Be sure to inform the physician of your participation in this study.

If you have questions about your rights as a research participant, contact the WCMC IRB Office.
Direct your questions to: Institutional Review Board
Address: 1300 York Avenue, Box 89, New York, New York 10065
Telephone: (646) 962-8200

Consent for Research Study

Project Title: A randomized, placebo-controlled clinical trial examining the efficacy of Fecal Microbiota Transplantation (FMT) and subsequent dietary fiber in patients with moderate ulcerative colitis

Principal Investigator: Dr. Randy Longman, MD PhD

RESEARCHER'S STATEMENT

I have fully explained this study to the subject. As a representative of this study, I have explained the purpose, the procedures, the benefits and risks that are involved in this research study. Any questions that have been raised have been answered to the individual's satisfaction.

_____	_____	_____
Signature of person obtaining the consent (Principal Investigator or Co-investigator)	Print Name of Person	Date

SUBJECT'S STATEMENT

I. I_____ (patient name) authorize the performance of fecal transplantation (stool transplant) procedure to be performed by Dr. Randy Longman, M.D Ph.D., and his assistants or designees.

II. I understand that fecal transplantation may be performed through colonoscopy, but fecal transplant is neither intended nor adequate to screen for colorectal cancer. Instead, fecal transplantation is a procedure that has been used to treat severe or chronic *Clostridium difficile* colitis and in my case its use will be investigated in ulcerative colitis by introducing normal bacterial flora from a healthy donor to the diseased colon.

III. I also acknowledge that residents and assistants designated by my physician may participate in the procedure and there may be other observers or vendors present.

IV. I, the undersigned, have been informed about this study's purpose, procedures, possible benefits and risks, and I have received a copy of this consent. I understand that donors are screened and undergo testing for many common communicable diseases to ensure that the procedure is done as safely as possible, but that it is not possible to test donors for all possible organisms and some infections may be undetectable. I understand that a solution of donor stool is infused into the colon. The alternative treatment(s), including antibiotics, 5-ASAs, immune-modulators, steroids, surgery, or no treatment at all and the risks and benefits of those alterative treatment(s) have been explained to me and I understand that my condition could worsen, improve or stay the same with fecal transplant or any other alternative treatments. Patients critically ill with ulcerative colitis, have a risk of dying from this condition regardless of what treatment is used and fecal transplant may not be successful. The risks related to the use of colonoscopy and sigmoidoscopy have been explained, and I have signed a form entitled, "Acknowledgement of Consent for Surgical or Other Procedure."

V. The risks of a fecal transplantation procedure have been discussed with me. I understand that complications may arise as a result of a fecal transplant. Complications may include but are not limited to the following:
   a. Transmission of infectious organisms (bacterial, viral, fungal) contained in the stool
   b. Missed polyps, cancer, or other lesion (infusing donor stool interferes with visualization of colonic mucosa)
   c. Allergic reaction to antigens in donor stool
   d. Enhanced ulcerative colitis activity
   e. Theoretical increased risk of developing disease which may be related to donor gut bacteria (i.e. obesity, metabolic syndrome, autoimmune conditions, allergic/atopic disorders, neurologic disorders, and/or malignancy)

VI. I understand that this is NOT a complete list, and that unforeseen risks do exist which may not have

been discussed with me.

VII. I understand that the above, as well as other complications, sometimes require additional procedures or operations and they have been discussed with me. I consent to such additional procedures which my physician deems necessary.

VIII. I hereby consent to the taking of photographs, videotapes, and/or illustrations of my operation and other medical procedures for clinical purposes.

IX. I, the undersigned, have been informed about this study's purpose, procedures, possible benefits and risks, and I have received a copy of this consent. I have been given the opportunity to ask questions before I sign, and I have been told that I can ask other questions at any time. I voluntarily agree to participate in this study. I am free to withdraw from the study at any time without need to justify my decision. This withdrawal will not in any way affect my future treatment or medical management and I will not lose any benefits to which I otherwise am entitled. I agree to cooperate with Randy Longman, M.D. Ph.D. and the research staff to inform them immediately if I experience any unexpected or unusual symptoms.

_____	_____	_____
Signature of Subject	Print Name of Subject	Date

OPTIONAL GENETIC TESTING

In addition to the study, you have the option to allow further experimental studies with your samples as explained below. Your participation is optional and you do not have to agree to participate in the additional studies in order to participate in the main study.

Blood, stool, and tissue samples obtained for research purposes throughout the study may be used to perform genetic tests (tests on cells which look for changes in your genetic makeup, like DNA or RNA). These tests will not tell if your UC is inherited and will not involve members of your family.

The researchers will study how changes in cells' genetic information might affect the disease's response to study treatment and the course of disease.

The test results may not be helpful to you at this time and are research-grade only. However, this data may make it possible to better understand UC and other diseases and for the potential development of companion diagnostics and to know how to diagnose and treat UC in the future. This knowledge may also be useful for future clinical studies.

The samples will be retained at the study site or at a secure storage facility in case there is a need to re-test them. The samples will be destroyed within twenty years after the end of the trial or earlier if required by law. If you decide to withdraw your consent, you can request that all retained identifiable samples be removed from any future genetic testing. If you make this decision, you must notify the study doctor in writing.

The results of the tests may not be available to you via your doctor because the tests are research-grade only and may not have been done by the end of your study duration. These results must not be used to

diagnose your disease and/or make treatment decisions.

☐ I have read this informed consent and AGREE to participate in the optional genetic testing.

☐ I have read this informed consent and DO NOT WISH to participate in the optional genetic testing.

_____

Research Subject's Name (Print)

_____ _____

Research Subject's Signature Date of Signature