INFORMED CONSENT FORM

Sponsor / Study Title:	**Rebiotix Inc. / "A Phase 3 Open-Label Clinical Study to Evaluate the Safety and Tolerability of Rebiotix RBX2660 (microbiota suspension) in Subjects with Recurrent Clostridium difficile Infection"**
Protocol Number:	**2019-01**
Principal Investigator: (Study Doctor)	**Donald Poretz, MD**
Telephone:	**703-560-4821 (24 Hours)**
Address:	**Clinical Alliance for Research and Education - Infectious Diseases, LLC** **3289 Woodburn Rd, Suite 250** **Annandale, VA 22003**

You are being asked to be in a medical research study. You may choose to be involved or not; it is completely voluntary. To allow you to make an informed decision about if you want to be part of this study, the possible risks and benefits of the study are described in this Form. This Form describes the purpose, procedures, possible benefits and risks, the information that will be collected and used and who will see information about you. You will receive a copy of this Form to review at home. You are encouraged to talk to family and friends before you decide whether to participate in the study. This process is known as informed consent.

Your study doctor has determined that you have a medical problem called recurrent *Clostridium difficile* infection (CDI), which is an ongoing infection in your intestines. This infection causes severe diarrhea, called *Clostridium difficile*-associated diarrhea, or CDAD. RBX2660 (microbiota suspension) is an investigational new drug used in this study to prevent recurrent CDI. It is manufactured by Rebiotix Inc, the sponsor of this study. More information about RBX2660 and this study is found in this Form.

If you have any questions about the study or you don't understand something in this Form, you should ask the study doctor. You should not sign this Form unless all of your questions have been answered, and you decide that you want to be a part of this study.

Being in a study is not the same as getting regular medical care and does not replace your regular medical care. When you are involved in a study, you are called a "study subject" which is a term you will see in this Form.

Initials _____ Date _____

WHAT IS THIS RESEARCH STUDY ABOUT?

You are invited to take part in this study because you have recurrent CDI that has not resolved using standard treatments, including several courses of antibiotic treatments.

Clostridium difficile infection (CDI) is a bacterial infection of the gut (intestine) that infects over 500,000 people and kills about 15,000-20,000 people each year in the United States. Many people who have CDI are successfully treated with antibiotics but this doesn't work for everyone. For some people, CDI occurs over and over again even if it is temporarily relieved with a new course of antibiotics. This type of CDI is called "recurrent CDI."

It is believed that CDI is caused by a disruption of the normal, healthy balance of microorganisms (tiny living cells) in the intestine (gut or bowel) after taking antibiotics. Many people with CDI are cured with a course of antibiotics, but many people develop chronic (ongoing) CDI. They have repeated episodes of severe diarrhea that resolve while the person is taking antibiotics. But, the diarrhea typically returns when the antibiotics are stopped.

For over 50 years, doctors have treated people with recurrent CDI with a solution made of stool (poop or feces) from healthy people. The goal of this treatment is to prevent additional episodes of diarrhea from occurring by introducing a healthy mix of microorganisms (tiny living cells) to the intestine. This therapy is called "fecal transplant." Although no controlled clinical studies have been performed, doctors believe that a fecal transplant may help to prevent recurrent CDI.

This study involves an investigational new drug called RBX2660 (microbiota suspension) that may prevent recurrent CDI, like a fecal transplant. A microbiota suspension is a biologic product (a product made from living cells). A microbiota suspension is thought to prevent recurrent CDI by restoring the normal balance of microorganisms in the intestines through the transplant of live, beneficial microorganisms. An investigational new drug is a product that is tested in people and has not been approved for sale by the United States Food and Drug Administration (FDA) or by Health Canada.

Rebiotix has developed RBX2660 to help prevent CDI infections in people with recurrent CDI. RBX2660, is made from stool collected from healthy people, and is manufactured in a different way than fecal transplant products. Similar to fecal transplant products, RBX2660 is given as an enema.

The purpose of this study is to learn about the safety of RBX2660 in patients with recurrent CDI. This study will take place in up to 80 hospitals or clinics in the United States and Canada. Up to 600 people will be treated in this study.

If you decide to be in this study, you might have to stop taking your regular medication(s) or supplement(s) during the entire study.

WHO IS PAYING FOR THIS RESEARCH STUDY?

Rebiotix Inc is the sponsor of the study and pays the study centers and study doctors to conduct this study. In addition to the study doctor there are other study staff that will be involved in the study and data collection (we call these people the study team).

Initials _____ Date _____

HOW LONG WILL I BE IN THE RESEARCH STUDY?

If you are in the study, you will be followed by the study team for approximately 9 months. At a minimum, you will come to the study center 4 times during the study and have 3 telephone contacts. The screening visit and enema administration visit will require longer visits, approximately 2 hours each. The amount of time required at the in-office follow-ups visits will be about 30-45 minutes. The telephone calls are expected to take less than 30 minutes. Extra visits may be required if your CDI returns while you are participating in the study.

ARE THERE REASONS WHY YOU SHOULD NOT TAKE PART IN THE STUDY?

If you are pregnant or breastfeeding, you cannot participate in this study. It is not known how this study drug will affect an unborn child. If you are a person who could become pregnant, you will need to have a urine test to ensure you are not pregnant before you start the study and during the study before receiving an enema. If you are a sexually active person, you will be asked to agree to take precautions to avoid the possibility of impregnation. If you become pregnant during this study or impregnate your partner, you will need to notify the study doctor as soon as possible.

Additional items that may exclude you from this study will be reviewed with you by your study doctor and/or their staff prior to your participation in this study. Some reasons may include:

- A past medical condition that, in the opinion of the study doctor, prevents you from participating
- Uncontrolled diarrhea despite current antibiotic treatment
- You had treatment with CDI monoclonal antibodies in the past 12 months
- You currently have a colostomy
- You had intraabdominal surgery in the last 60 days
- You have a planned surgery requiring the use of antibiotics within 8 weeks of study treatment
- Illegal drug use within the past 90 days (marijuana use is allowed)
- You are currently participating in another clinical study

WHAT WILL HAPPEN DURING THIS RESEARCH STUDY?

Being in a study is not the same as getting regular medical care and does not replace your regular medical care. There are screening tests to see if you qualify to continue in the study. None of the screening tests are investigational or experimental. Not everyone who is screened will continue in the study and receive the study enema. All testing is described below.

If your study doctor thinks you might be a good candidate for this study, a member of the study team will talk to you about your recurrent CDI condition and the benefits, risks, and responsibilities you will have as a study participant. If you agree to be part of the study, you will sign this Form, undergo screening tests and an evaluation by the study team to confirm you meet all the requirements of this study.

Initials _____ Date _____

This is a single arm study, meaning that all subjects will receive the same investigational drug, RBX2660. This type of study is called an open-label study. This type of study is commonly used to assess the safety of an investigational drug.

If your diarrhea returns within 8 weeks after receiving the enema and you have a positive stool test for *C. difficile* from the study's central laboratory, you may be eligible to receive a second enema of RBX2660. If you do not want to receive the second RBX2660 enema, your study doctor will discuss alternative treatment options with you. If you do not receive the second treatment of RBX2660 you will remain in the study through the 6-month study visit.

Study Visits

Your participation in the study will end after you complete the 6-month phone call after your final study enema.

None of the tests you will undergo as part of this study are investigational or experimental.

Visit 1 Screening: After you agree to participate in this study by signing this Form, you will be asked to complete the following screening activities:

- You must be taking antibiotics prescribed for you to control your CDAD, which is standard of care for someone with recurrent CDAD.
    - You must stop taking the antibiotics 24-72 hours before your study enema.
- Record your health history and any medications or supplements you are taking
- Record your demographics: gender, ethnicity, race, date of birth
- A physical exam
- Measure vital signs including: height, weight, blood pressure, pulse, breathing rate and temperature
- Blood sample to assess your general health (about 3 teaspoons)
- Urine pregnancy test (for people of child bearing potential)
- The C. diff 32 Questionnaire: a series of 32 questions that assess how recurrent CDI affects your life. There are no right or wrong answers and it is very important you answer truthfully every time.
- You will be asked about your employment status.
- Review instructions to complete the Subject Diary from the date you sign this form through 7 days following the study enema
- You must agree to not take the following medications through the Week 8 visit unless specifically needed to treat a recurrence of CDI: oral vancomycin, metronidazole, fidaxomicin, rifaximin, nitazoxinide, bezlotoxumab, and intravenous immunoglobulins (IVIG)
    - *NOTE: Use of IVIG for treating a disease other than CDI is allowed*
- You must agree to not take non-dietary probiotics (including over-the-counter and prescription) through 8 weeks after receiving the last study enema

Initials _____ Date _____

- You must not delay receiving your study enema after you stop your antibiotics, or your diarrhea may come back and you may not be allowed to receive the study drug or to continue in the study.

Visit 2 Baseline, Enema Administration: If you are eligible to continue in the study, as determined by the results of your Screening visit, then you will be scheduled for Visit 2. This visit will be scheduled no more than 21 days from your Screening visit. At this visit, you will receive your study enema. You will also complete the following activities:

- Collect information about health events and medication changes
- Measure vital signs including: blood pressure, pulse, breathing rate and temperature
- Collection of stool sample for the main study (previously collected at home or at the visit prior to receiving the enema)
- Review of the completed Subject Diary pages
- Review instructions for completion of the Subject Diary for approximately 7 more days
- Blood sample to assess your general health as well as HIV, Hepatitis A, B & C (viruses that infect the liver) and Treponema antibody (test for syphilis – a bacterial infection) (about 2 ½ teaspoons). The study doctor or study staff will tell you if the HIV test results are positive. If required by state law, the study doctor or study staff may report a positive test result for HIV, hepatitis, or syphilis to the local health department.
- Urine pregnancy test – for people of child bearing potential.
    - The study doctor or study staff will tell you if the pregnancy test results are positive.
    - The results of the pregnancy testing must be negative in order for you to be in the study.
- Enema administration (about 2/3 cup or 150 milliliters; see below for details)

The study drug will be given to you as an enema by a trained study doctor or study staff member. An enema is a common procedure that is used to deliver fluids into the lower intestine through your anus and rectum (bottom or butt). You will be asked to either lie on your left side or crouch on the exam table with your elbows and knees almost touching. The administrator will uncover your bottom, gently insert a lubricated tube into your anus, and allow the enema solution (about 2/3 cup or 150 milliliters of liquid) to flow into your rectum. You will be asked to stay in this position for approximately 15 minutes, but if the procedure causes you to have a bowel movement; you will be allowed to get up and go to the bathroom if necessary.

After you receive your enema, the study team will monitor how you are feeling and check your temperature, blood pressure, heart rate, and breathing for at least an hour afterwards. It is very important that you let the study team know of any problems you are having right away. Afterward, you will go home and be told to contact the study doctor if CDI symptoms reoccur. You will continue to complete the Subject Diary and return it at your 1-week visit.

Initials _____ Date _____

In-Office Assessments (Weeks 1 & 8): You will return to the clinic as instructed by the study team at the following intervals after you receive your study enema to talk about how you are feeling: 1-week and 8-weeks. You will complete the following activities:

- Collect information about health events like new medical conditions, recurrence of CDI, other events and medication changes
- Collect your current weight
- Staff will review your Subject Diary at the 1-week visit only
- The C. diff 32 Questionnaire
- You will be asked about your employment status (at week 8 only).
- Optional stool sample: Reminder to collect and send a stool sample to Rebiotix

Telephone Assessments (Week 4): You will receive a phone call from the study team on week 4 after receiving your study enema to check on how you are feeling and discuss the following:

- Collect information about health events like new medical conditions, recurrence of CDI, other events and medication changes
- Collect your current weight, self-reported
- Optional stool sample: Reminder to collect and send a stool sample to Rebiotix

Telephone Assessments (Months 4 & 6): You will receive phone calls from the study team at months 4 & 6 after receiving your study enema to check on how you are feeling and discuss the following:

- Collect information about health events like new medical conditions, recurrence of CDI, other events and medication changes
- Collect your current weight, self-reported
- Complete C. diff 32 Questionnaire and mail it to the study center.
- You will be asked about your employment status.
- Optional stool sample: Reminder to collect and send a stool sample to Rebiotix

Return of CDI: At any time during the study you feel that your CDI diarrhea has returned, please call the study doctor right away. If the study doctor thinks your recurrent CDI has returned, you will need to return to the office and complete the following:

- Collect information about health events like new medical conditions, recurrence of CDI, other events and medication changes
- Provide a stool sample to the clinic be sent to the central laboratory for *C. difficile* testing
- Your temperature, blood pressure, heart rate and breathing will be measured
- Complete C. diff 32 Questionnaire
- Optional stool sample: Collect and send a separate stool sample to Rebiotix

Initials _____ Date _____

If you experience a confirmed CDI before the Week 8 visit, and you and your study doctor agree, you can receive a second RBX2660 enema.

- This enema will be administered in the same manner as your previous enema, including a prior urine pregnancy test for people of child-bearing potential. After the enema, you will wait for an hour so that the study team can monitor your temperature, blood pressure, heart rate and breathing.
- If you decide to receive a second RBX2660 enema, your follow-up is completed by telephone assessments at 1-Week, 4-Weeks, 8-Weeks and 6 Months. The study team will ask how you are feeling and discuss the following:
    - if you have had any illnesses or injuries
    - Collect information about health events like new medical conditions, recurrence of CDI, other events and medication changes
    - Collect your current weight
    - Optional stool sample: Reminder to collect and send a stool sample to Rebiotix
- If your recurrent CDI returns within 8 weeks of your second RBX2660 enema, you will stay in the study until you've completed the 6-month phone call as described above, but you and your study doctor will consider a new plan for you.

Optional Stool Samples:

To help scientists understand more about the microorganisms in the human gut and how RBX2660 might work, you will be asked to provide stool samples to Rebiotix for testing and storage. Participating in the collection of these stool samples is optional, and is a separate activity from the stool samples collected in the main part of the study. At the end of this form you will indicate if you want to provide these extra stool samples. Optional stool sample collections may occur at 6 timepoints. The stool samples will be collected at your home at the following study timepoints:

- Visit 1 (Screening)
- 1-Week
- 4-Weeks
- 8-Weeks
- Month 4
- Month 6

If you have a confirmed recurrence of CDI, you will be requested to collect stool samples at your home at the following study timepoints:

- Time of recurrence
- 1-Week

Initials _____ Date _____

- 4-Weeks
- 8-Weeks
- Month 6

You will collect your samples at home in special, pre-labeled containers given to you by the study team, and send them as directed in prepaid, pre-addressed packages. Your stool samples will only be identified by the label on the container that will include your study subject number and date/time of the sample collection. It will not contain any personal information that would identify you. These optional stool samples may be stored for about five years.

The stool samples will be used for research about the microorganisms in the human gut. Some of the testing will include testing for microorganisms (*Clostridium difficile* and vancomycin-resistant enterococcus) both before and after receiving the study enema. Comparing the type of microorganisms present in stool before and after receiving the study enema may show differences in the type of microorganisms that live in the gut. This may help explain how RBX2660 works. Differences may also help to identify people at risk for recurrent CDI, and who might benefit from RBX2660. The results of the research may be shared with the scientific community, but will not contain any information that would identify you.

If you change your mind later, no additional stool samples will be collected. Any samples already submitted to the sponsor will not be able to be destroyed. These samples will not contain any information that will identify you. You can ask the study doctor or study staff about this.

About blood samples

Your blood samples will only be used for the tests identified in this consent form and will be discarded after the testing is complete. Blood samples will not be stored as part of this study. Your samples will not be labeled with your name or other directly identifying information.

WHAT ARE MY RESPONSIBILITIES AS A STUDY SUBJECT?

You have certain responsibilities as a study subject. While in the study you have the responsibility to:

- Follow the instructions you are given by the study doctor or study team
- Be truthful regarding your health and medications, including your medical history
- Complete the study questionnaires and Subject Diary to the best of your ability
- Come to the study center, on time, for all visits with the study team
- Participate in assessments made over the phone with the study team

Initials _____ Date _____

- Report all injuries, illnesses, doctor visits, hospitalizations, emergency room visits, symptoms or complaints to the study team as soon as possible even if you don't think they are related to your CDI, enema product or the enema procedure.
- Call your study team as soon as possible if your CDI returns to discuss further treatment
- Tell the study doctor or study team if you want to stop being in the study at any time

ARE THERE RISKS, DISCOMFORTS, OR INCONVENIENCES TO ME IF I AM IN THIS RESEARCH STUDY?

There are risks, discomforts, and inconveniences to being in this study which are listed below. There is always a chance that a study drug can harm you, and the investigational drug in this study is no different. In addition to the risks listed below, you may experience a previously unknown risk or side effect, which includes your CDAD getting worse. Ask the study doctor if you have questions about the signs or symptoms of any side effects that you read about in this consent form.

RBX2660 Risks: RBX2660 is made from human donors' stool and there is a very small risk that you might receive a serious disease from RBX2660 if the donor had a disease that was not or could not be detected by the donor health screening, donation testing, or donor blood testing that is routinely conducted which can then be passed to you.

To help ensure you don't become ill from the donor, Rebiotix carefully and rigorously screens and tests all donors before they can donate stool. Rebiotix obtains a detailed health and lifestyle history from the donor and tests for harmful organisms and diseases in the donor's blood and stool donations. The donor's blood is also re-tested approximately every 45 days for other potential organisms and diseases to ensure the donor's continued health. Healthy, asymptomatic stool donors may potentially be infected with SARS-CoV-2 (the coronavirus that causes the disease COVID-19) despite screening and testing strategies. If you are receiving RBX2660 that was collected from a donor after the start of SARS-CoV-2, screening and testing strategies have been implemented to minimize the risk of transmission of SARS-CoV-2, but unknown transmission risks may still exist.

If you are receiving RBX2660 collected from a donor after the start of SARS-CoV-2, the following testing has been done:

> The donor screening included checking for any symptoms or potential exposure to disease and testing for SARS-CoV-2 (COVID-19) virus. Testing requirements include at least two negative test results no greater than 14 days prior to donation and 2 more negative test results following the date of donation. Testing is performed using FDA-authorized tests to detect the SARS-CoV02 virus. The results of all tests and screening requirements are confirmed to be negative before you may receive RBX2660 manufactured from the stool donation.
>
> As new information is learned about SARS-CoV-2, new testing continues to be developed. In addition to frequent testing of the donor for the SARs-CoV-2 (COVID-19)

Initials _____ Date _____

virus, the donor's blood is also re-tested approximately every 45 days for other potential organisms and diseases to ensure the donor's continued health.

Rebiotix implements donor and stool screening and testing procedures that meet the FDA's requirements.

Rebiotix tests the donors' stool or blood for the following diseases that could potentially be transmitted from donor stool to you including HIV (the virus that causes AIDS), hepatitis, syphilis, and diseases from the stool such as those that cause contaminated food illnesses (such as Salmonella) or from organisms in the stool including Giardia, Listeria, Norovirus, or a multi-drug resistant organism (MDRO). There have been two reports of transmission of an MDRO to immunocompromised patients who received a fecal transplant that developed into an invasive infection, one of which resulted in death. It is not known if these diseases can be transmitted to you by RBX2660. The full risk of disease transmission from a fecal transplant is unknown and may not be known for many years.

RBX2660 may cause mild intestinal conditions, including:

- gas (flatulence)
- burping
- abdominal distension or bloating
- increased diarrhea
- abdominal cramping or pain
- constipation, colitis (inflamed intestine)
- fever greater than or equal to 37.8° C (100.0°F)
- fatigue
- chills
- abnormal test results (changes to your blood or stool test results)

While some of these risks have occurred in people who have received a fecal transplant, many of the problems are mild, temporary and resolve without medical treatment.

It is possible that receiving RBX2660 may change how your regular medications, vaccines, or supplements work. It is important that you tell the study doctor about any medications, supplements, or vaccines.

Please tell the study doctor or study staff right away if you have any side effects. Please tell them if you have any other problems with your health or the way you feel during the study, whether or not you think these problems are related to the study.

<u>If I stop my regular medication what are the risks?</u>

If you stop your regular medication to be in the study, your CDI symptoms might come back or get worse. Please tell the study doctor or study staff right away if you have any problems when you stop or change your regular medication.

Initials _____ Date _____

Pregnancy Risks

It is not known if there are risks to your baby if you are breastfeeding while participating in this study. You are advised to discuss with your study doctor the potential risks of participating in the study if you are pregnant, become pregnant during the study, or if you are nursing a baby. If you are a man, or a woman who could become pregnant, you are asked to use an effective form of contraception (pregnancy prevention) while you are in this study. If you are a person who could become pregnant, you will take a urine pregnancy test when you enter the study and on the day of an enema procedure before receiving the enema to make sure that you are not pregnant.

If you think you are or your partner becomes pregnant during the study, you must tell the study doctor or study staff immediately. The study doctor or study staff may ask for information about the pregnancy and the child's health at birth and may share this information with the sponsor.

Blood Collection Risks:

A total of 5 ½ teaspoons of blood will be drawn for this study: 3 teaspoons for Visit 1, and 2 ½ teaspoons for Visit 2). Withdrawal of blood for laboratory analysis may cause the site to become red and tender to the touch. You may have some pain, soreness, bruising, or bleeding when blood samples are taken during the study. Rarely does infection occur where you were stuck with the needle. You may also feel light-headed or faint when the blood is being drawn.

Enema Risks: An enema carries a very small risk of anal discomfort or irritation, rectal bleeding, nausea, vomiting, low blood pressure, and very rarely, irritation or puncture of the intestine.

Other Risks

Filling out the questionnaires could lead you to feel uncomfortable or upset. Please tell the study doctor or study staff if you feel uncomfortable or upset while filling out a questionnaire. You have the right to refuse to answer any questions.

There is a risk of loss of confidentiality of your information. You will read more about the protection of your information later in this form. Please ask the study doctor or study staff if you would like to know more about how your information will be protected while you are in this study.

WILL BEING IN THIS RESEARCH STUDY HELP ME?

There is no guarantee that you will get any benefit from taking part in this study. You may or may not personally benefit from being in this study. The potential benefit of the study drug is resolution of your recurrent CDI, but this benefit may or may not happen for you. Your willingness to take part in this study may, in the future, help doctors better understand and/or treat others who have your condition. Your participation in this research study may contribute information that may benefit the development of a new drug to treat recurrent CDI.

Initials _____ Date _____

WHAT IS MY ALTERNATIVE TO BEING IN THIS RESEARCH STUDY?

You do not have to be in this study to get help for your recurrent CDI. The study doctor will talk to you about treatments for your recurrent CDI, including the important risks and benefits related to the treatment options before you decide to be in this study. Treatments include taking different types of antibiotics or trying different doses of antibiotics you've already taken. In addition, you may discuss your options with your regular health care provider.

WHO WILL USE AND SHARE INFORMATION ABOUT MY BEING IN THIS RESEARCH STUDY?

Your participation in this study is confidential, but if you decide to participate in the study, Rebiotix and their contractors may see your health information and relevant personal information. This Form includes another document called an Authorization to Use and Disclose Health Information (Authorization Form), which discusses how your information is used and who may see your information. Rebiotix will keep your information confidential in accordance with all applicable laws and regulations.

The Authorization Form describes how your information may be used and/or disclosed by the study doctor, the hospital or clinic and their respective staff, Rebiotix, study monitors, auditors and other researchers.

Information that may be collected as part of this study includes, but is not limited to, your birth date, dates of visits to your regular doctor, your health history and status during the study, previous and current medications. This information is important to the conduct of the study and to ensure you are eligible to be in the study. Due to the COVID-19 pandemic, Rebiotix is utilizing a secure portal (computer website) for the study site to provide your health information to Rebiotix. This is to allow for Rebiotix to review the data collected for study participation remotely for your study participation. Typically, this review would take place at the study site, but due to COVID-19 the monitor cannot always travel and visit the site. Your health information will not be shared with anyone other than Rebiotix and their contractors and it will be deleted from the secure portal after remote monitoring is complete. Use of this portal is based on the site's discretion. Your health information may also be shared with Rebiotix by other electronic means such as email, if this method is used Rebiotix has instructed the study site to block out personal identifying information from records such as your name, medical record number and insurance information prior to sending. However, if such information is accidentally shared with Rebiotix, Rebiotix will keep your information confidential according to all applicable laws and regulations.

The results of this study may be published or reported. Any reports or publications about the study will not include your name or any personal identifying information about you. Rebiotix may use your study information and stool samples not only for this study's research, but for additional purposes as well. These purposes include overseeing and improving the performance of its products, new medical research, proposals for developing new medical products or procedures, and other business purposes.

Initials _____ Date _____

The United States Food and Drug Administration's regulations as well as other applicable laws control Rebiotix's work in developing and ensuring the safety and quality performance of its products. Rebiotix may be required to disclose information about your participation in the study to the FDA and foreign government authorities responsible for assessing the effectiveness and safety of medical products in other countries. Your name and other identifying information is not routinely required to be given; however, on rare occasions, disclosure to third parties may be required by law. Rebiotix may also disclose your health information to Advarra IRB (a group of people who review research studies to protect the rights and welfare of research participants) and other organizations that are required to watch over the effectiveness and safety of medical products and therapies and the conduct of research. In addition, Rebiotix, the FDA, and other regulatory or government authorities, and Advarra IRB, will be granted access to your research records, including direct access to your original medical records to inspect and verify study procedures and information to the extent permitted by applicable laws and regulations.

In the event of a study-related injury and you are on Medicare, Rebiotix may be required to notify the Center for Medicare and Medicaid (the government agency that manages Medicare) that such an injury has occurred. In this situation, the study center may need to release personal information about you to Rebiotix, such as your name and Social Security number, so it can make the proper reports to the U.S. government if you are on Medicare. This specific information will only be collected on the rare occasion it is needed to file a claim for Medicare in the event of a study-related injury; the study site will notify you in advance that it is releasing this information to Rebiotix for reporting to Medicare.

With your approval, your personal doctor may be informed of your participation in this study.

WILL IT COST ME ANYTHING TO BE IN THIS RESEARCH STUDY?

There are no direct costs to you to participate in this study. All the study related research costs for the required study visits, phone calls, examinations, laboratory procedures, supplies and the enema study drug(s) will be provided by Rebiotix, the sponsor of the study.

While you are in the study, you may still need to receive regular medical care from your primary care doctor. You and/or your medical insurance will pay for the costs of your regular medical care in the ordinary manner that is not a part of this study.

If you have any questions or concerns about your potential costs, please talk with your study doctor or your health insurance company.

WHAT IF I GET HURT OR SICK FROM THIS RESEARCH STUDY?

If you get hurt or sick as a direct result of being in this study, medical treatment will be available, including first aid, emergency treatment, and follow-up care as needed. You are expected to pay for the medical treatment or seek reimbursement from your health insurance company. Always tell all other doctors that you are in this study and let your study doctor know as soon as possible if you have any illness or injury while in this study.

Initials _____ Date _____

By signing this Form, you are not giving up any of your legal rights or benefits.

Be aware that your health care payer/insurer might not cover the costs of study-related injuries or illnesses.

WILL I BE PAID IF I AM IN THE RESEARCH STUDY?

You will be compensated $50 for each completed in-office visit (screening/Visit 1, baseline/Visit 2, in-office assessments at Weeks 1 and 8) and $50 for each monthly telephone assessment (Week 4, 4-months and 6-months) for a maximum of $350.

If you are a confirmed treatment failure and receive a second RBX2660 enema, you will receive $50 for second enema and the following compensation for the telephone assessments at 1-week, 4-week, 8-week and 6 months: $50 (totaling $250 for a treatment course for recurrence).

Payment will be made via distribution of dedicated debit card issued per participant or by check. Every effort will be made to issue payment within 24 hours of visit completion.

Although future research that uses your stool samples may lead to the development of new products, you will not receive any payments for these new products.

DO I HAVE TO BE IN THIS RESEARCH STUDY?

Your participation in this study is voluntary. You may refuse to participate. If you decide to take part in the study you still have the right to decide at any time that you no longer want to continue. There will be no penalty to you and you won't lose any benefits.

If you decide to withdraw, please notify the study team right away. You will not be treated differently if you decide to stop taking part in the study. If you stop being in the study, any information already collected about you will still be shared with Rebiotix and used as described in this Form. You may be asked to respond to phone calls from the study team about any health problems you may experience after leaving the study. Any additional health information collected after your decision to stop participating in the study will not be shared with Rebiotix.

The study doctor or Rebiotix may remove you from the study without your consent at any time for any of the following reasons:

- You are unable to follow the study procedures;
- Medical events occur that could impact your safety if you continue your participation;
- You decide not to continue in the study after being told of changes in the research that may affect you;
- The entire study is put on hold or stopped early;
- Or for any other reason.

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.

Initials _____ Date _____

What if I work for the study center? What if I am a family member of someone who works for the study center?

Study center employees and their family members do not have to be in this study. No one should influence or pressure you to be in this study. An employee's or his/her family member's decision to be in the study, or to leave the study early, will not affect the employee's job or job benefits.

WHAT IF NEW INFORMATION BECOMES AVAILABLE ABOUT THE STUDY?

If the researcher learns of any new information about this study that might change your willingness to stay in this study, the information will be provided to you. You may be asked to sign a new informed consent if the information is provided to you after you have joined the study.

WHOM TO CONTACT ABOUT THIS STUDY

During the study, if you experience any medical problems, suffer a research-related injury, or have questions, concerns or complaints about the study, please contact the Investigator at the telephone number listed on the first page of this consent document. If you seek emergency care, or hospitalization is required, alert the treating physician that you are participating in this research study.

An institutional review board (IRB) is an independent committee established to help protect the rights of research subjects. If you have any questions about your rights as a research subject, and/or concerns or complaints regarding this research study, contact**:**

- By mail:
  Study Subject Adviser
  Advarra IRB
  6100 Merriweather Dr., Suite 600
  Columbia, MD 21044
- or call **toll free**: 877-992-4724
- or by **email**: adviser@advarra.com

Please reference the following number when contacting the Study Subject Adviser: Pro00035155.

Initials _____ Date _____

SUBJECT'S STATEMENT:

I have read this Consent Form and I have been able to ask questions about this study. The study team has talked with me about this study. They have answered my questions and I voluntarily agree to be in this study. I have received a copy of this Consent Form.

By signing this Form, I have not given up any of my legal rights as a study subject which I otherwise have.

The stool samples that you collect at home and ship in pre-labeled packages are an optional part of this study. Please initial below to indicate whether you wish to provide these samples:

_____ Yes

_____ No (You can still be in the main study)

_____

Printed Name of Participant

_____ _____

Signature of Participant Date

I attest that the individual providing consent had enough time to consider this information, had an opportunity to ask questions, and voluntarily agreed to participation in this study.

_____

Printed Name of Person Explaining Consent

_____ _____

Signature of Person Explaining Consent Date

Initials _____ Date _____

AUTHORIZATION TO USE AND DISCLOSE HEALTH INFORMATION

The Authorization Form describes how your information may be used and/or disclosed by the study doctor, the hospital or clinic and their respective staff, Rebiotix, and other researchers. You agree to allow access to and use of your information in accordance with this Informed Consent and Authorization Form.

1. The health information that may be used and disclosed includes:

- All information collected during the research described in the Informed Consent Form above, and
- Health information in your medical records that is relevant to the Research such as:
    - Date of birth
    - Ethnicity & race
    - Vital Signs
    - CDI history & treatments
    - Blood & stool test results
    - Medical history
    - Medications

2. The Providers may disclose protected health information in your medical records:

- To the Researchers and to the sponsor of the Research, Rebiotix Inc and its agents and contractors (together "Rebiotix"); and
- As required by law and to representatives of government organizations (such as the FDA) in the U.S. or other countries, Advarra IRB, and other persons who are required to watch over the effectiveness and safety of medical products and therapies and the conduct of research.
- Your protected health information may be shared with a public health authority that is authorized by law to collect or receive such information for the purpose of preventing or controlling disease, injury, or disability, and conducting public health surveillance, investigations, or interventions.

Initials _____ Date _____

3. The Researchers may:

- Use and share your protected health information among themselves and with other participating researchers to conduct the Research;
- Disclose your protected health information to Rebiotix; and
- Disclose your protected health information as required by law and to representatives of government organizations, review boards, and other persons who are required to watch over the effectiveness and safety of medical products and therapies and the conduct of research.

4. Rebiotix may:

- Use and share your protected health information as described in the Informed Consent Form.
- Use your protected health information for future research.

5. Once your protected health information has been disclosed to a third party:

- It may be subject to further disclosure by recipients, and federal privacy laws may no longer protect it from further disclosure.

6. Please note that:

- You do not have to sign this Authorization, but if you do not, you will not be allowed to participate in the Research.
- You may change your mind and cancel this authorization at any time. To cancel this Authorization, you must write to the study doctor at the address on the first page of this form. However, if you revoke this Authorization, you will no longer be allowed to participate in the Research. Also, even if you revoke this Authorization, the information already obtained by the Researchers and Rebiotix may be used and disclosed as permitted by this Authorization and the Informed Consent Form.
- While the research is in progress, you may not be allowed to see your health information that is created or collected in the course of the research. After the research is finished, however, you may see this information as described in the clinical trial site's Notice of Information practices.

Initials _____ Date _____

7. This Authorization expires in 50 years.

8. You will be given a copy of this Authorization after you have signed it.

_____ _____

Signature of Participant Date

Initials _____ Date _____