INFORMED CONSENT FORM
and
AUTHORIZATION TO USE AND DISCLOSE PROTECTED HEALTH INFORMATION

Sponsor / Study Title:	**Crestone, Inc. / "A PHASE 2, RANDOMIZED, DOUBLE-BLIND, COMPARATOR-CONTROLLED, MULTICENTER STUDY TO EVALUATE THE SAFETY AND EFFICACY OF CRS3123 COMPARED WITH ORAL VANCOMYCIN IN ADULTS WITH CLOSTRIDIOIDES DIFFICILE INFECTION"**
Protocol Number:	**19-0021**
Principal Investigator: (Study Doctor)	**«PiFullName»**
Telephone:	**«IcfPhoneNumber»**
Address:	**«PiLocations»**

This form is for use in a research study that may involve subjects who may or may not have the capacity to consent to take part in the study. When the subject cannot legally consent to take part, pronouns "you" and "your" should be read as referring to the subject rather than the person (legally authorized representative) who is signing and dating this form for the subject. In cases where the subject's representative gives consent, the subject should be informed about the study to the extent possible given his/her understanding. During the course of the study, if the subject regains the capacity to consent, informed consent will be obtained from the subject and the subject offered the ability to leave the study if desired.

KEY INFORMATION

The purpose of this research study is to test if an investigational study drug (not approved by the United States Food & Drug Administration) (CRS3123) is a safe and effective study treatment of an infection due to a bacteria called Clostridioides difficile. This infection is sometimes referred to as CDI which is short for Clostridioides difficile infection (CDI). ***Crestone, Inc.*** is the company sponsoring this research study with support from the National Institutes of Health, National Institute of Allergy and Infectious Diseases (NIH/NIAID).

The study will test two different doses of CRS3123 compared to a standard antibiotic treatment for this infection called vancomycin. CRS3123 is a drug with a new way of attacking the bacteria that causes Clostridioides difficile infection. It is effective against many types of

bacteria that cause CDI. If enrolled, you will be asked to complete up to 5 outpatient study visits over 70 days.

The study has a screening period to determine if you meet the required criteria to enroll in the study. During the study treatment period, each subject will receive capsules of study drug (containing CRS3123, vancomycin, or placebo) four times a day (at approximately 6-hour intervals) for 10 days. The study treatment will last 10 days. Then there will be a follow-up period from day 11 through day 70.

Since CRS3123 has only been tested in healthy subjects, the side effects are relatively unknown in patients with CDI. The healthy volunteers who received either a single dose or multiple doses had the following most reported adverse events including:

- Headache
- Abdominal pain
- Upset stomach
- Diarrhea
- Taste disturbance
- Some changes in laboratory tests including decreased hemoglobin, liver function, decreased blood calcium, and blood tests that may indicate altered function of the pancreas.

Your participation in this research study is completely voluntary, meaning that you may or may not choose to participate. To decide whether or not you want to be part of this research, the risks and possible benefits of the study are described in this form so that you can make an informed decision. This consent form describes the purpose, procedures, possible benefits and risks of the study. This form explains how your medical information will be used and who may see it. You may have a copy of this form to review at your convenience or to ask advice from others before signing and dating it.

Please read this form carefully. Take your time to ask the Investigator or study staff as many questions about the study as you would like. The Investigator or study staff can explain words or information that you do not understand. Reading this form and talking to the Investigator or study staff may help you decide whether to take part in the study or not. If you decide to take part in this study, you must sign your name at the end of this form and date it.

BACKGROUND AND PURPOSE

You are being invited to participate in this research study because you have primary episode or first recurrence of Clostridioides difficile (C. difficile) infection referred to as CDI. This means it is your first episode or that you have been treated for this infection in the past no more than one time before this current infection you have now.

C. difficile is a type of bacteria, which lives in the intestines of many people and animals and is also present in the environment in places such as soil and water. Diarrhea, the most common symptom of CDI, may be caused by the use of some antibiotic therapies causing a change to the normal balance of the microflora (a complex community of naturally occurring bacteria that live in your intestines). When the intestinal microflora is out of balance, the C. difficile bacteria begin to grow and produce toxins causing diarrhea and other symptoms such as abdominal pain or tenderness, loss of appetite, low-grade fever, nausea and vomiting. Sometimes CDI can become severe causing bloody diarrhea and even death. It is for this reason that new treatments are being discovered and tested.

The purpose of this research study is to:

- Test the safety and effectiveness of the 2 dosages of the study drug***, CRS3123,*** compared with vancomycin.
- Test the amount of CRS3123 in your blood; this tells researchers how much time it takes for the study drug to be absorbed.
- To see how well this study treatment is impacting your symptoms and the quality of your life by using a Health-related quality of life (HRQoL) questionnaire.

This is a research study to test a new investigational drug (CRS3123). An investigational drug is one that is not approved by the United States Food and Drug Administration (FDA). It is being compared to vancomycin; this study drug may be available by prescription for CDI.

A total of 30-36 subjects are planned per study treatment type, for a total of ***90-108*** total subjects for the study.

WHAT WILL HAPPEN DURING THE STUDY

Your participation in this study will last approximately ***70 days*** and will include approximately up to ***5*** study visits to the study center.

The sponsor anticipates that the total amount of blood taken for study assessments will not exceed 129 mL (milliliters), or about half a cup.

Screening:

Before any study-related tests and procedures are performed, you will be asked to read and sign and date this consent document. The following screening tests and procedures will then be performed to determine if you qualify to take part in this study:

- An interview to collect information on your current and past medical history; current and recent medications you take; and information about your CDI.
- You will be asked to have your temperature, blood pressure, heart rate, breathing rate, weight and height taken.

- A complete physical examination evaluation will be performed and includes evaluation of the head, eyes, ears, nose, and throat, neck, lungs, heart, chest, abdomen, extremities, neurological status, and skin.
- You will be asked to have an electrocardiogram (ECG) done, which is a recording of the electrical activity of your heart.
- Blood and urine samples will be collected to test the function of your major organ systems. These tests will be compared to the same blood tests that are done at a later visit, after taking study drug.
- Urine pregnancy testing will be done for all women of childbearing potential. Women who are post-menopausal less than one year will have a urine pregnancy test.
- You will receive your Daily Diary that will capture details for each of your bowel movements, any missed doses of the study drug, other new medications, and the questions about your CDI symptoms. The study staff will train you on how to use that paper booklet every day.
- A stool sample will be collected at screening to determine if you have the infection and the type of CDI you have. The stool sample will also be sent for cultures and analysis at a designated lab.

If you qualify to take part in this study and go on to receive the study treatment, then the following will happen:

Study Treatment:

During the study treatment period, each subject will receive capsules of study drug (containing CRS3123, vancomycin, or placebo) four times a day (at approximately 6-hour intervals), by mouth, for 10 days. Everyone will get an active study drug (either vancomycin or CRS3123). No one will receive placebo alone.

If you agree to participate in this study, you will be randomly assigned (like the flip of a coin) to receive one of the following study treatments:

- Arm A: CRS3123 200 milligram dose (400 mg/day) given orally at approximately 6-hour intervals for 10 days.

or

- Arm B: CRS3123 400 milligram dose (800 mg/day) given orally at approximately 6-hour intervals for 10 days.

or

- Arm C: Vancomycin 125 milligram dose (500 mg/day) given orally at approximately 6-hour intervals for 10 days.

This random assignment to a study treatment is called “randomization.” The study treatment randomization will be in a 1:1:1 ratio, which means there is a 1 out of 3 chance of being randomized to any of the 3 arms.

This is a “double-blind study” which means that you and your Investigator will not know which

study treatment you are receiving. In case of an emergency, however, the Investigator can get this information.

Due to the difference in dosing schedules between CRS3123 (twice a day) and the standard of care vancomycin (four times a day) and appearance of study drugs used in the 3 Arms, placebo will be used to match the total number of capsules in each arm. A placebo study treatment is designed to appear very similar to the active study drug treatment being tested. In this study, the placebo looks exactly like the real study drug, but it does not have any active ingredients in it. When we talk about "study drug" or "study treatment" we are talking about both the placebo and the active study drug.

You will have the following study visits and undergo the following procedures:

Day 1 (Before taking Study Drug)

- Vital signs including temperature, pulse rate, respiratory rate, and blood pressure.
- Review of your current medications: you will be asked to list any medications that you have taken since your last visit.
- You will be asked to give a stool sample. Part of the stool sample will be stored for future analyses.
- Blood samples will be collected for pharmacokinetic (PK) tests. PK tests are research tests done to see how long the study drug remains in your body.
- Randomization - all inclusion and exclusion criteria need to be met before randomization to a study treatment arm. All participants will be randomized by a computer system.

Day 1 (After taking Study Drug)

- Routine blood tests to check your overall health.
- You will be asked to give a stool sample. Part of the stool sample will be stored for future analysis.
- Blood samples will be collected for pharmacokinetic (PK) tests. PK tests are research tests done to see how long the study drug remains in your body. The samples will be taken approximately 1 hour and 3 hours after taking the study drug.
- You will receive your Daily Diary that will capture details for each of your bowel movements, date and time of study drug dosing, concomitant medications, and the questions about your CDI symptoms and how much of a burden they are to you. The study staff will train you on how to use that paper booklet every day.
- The study staff will review clinical observations during your study site visit.
- You will be given enough study drug at enrollment for all ten days of dosing. You will take your dose with water approximately every 6 hours as instructed by the study site staff.

Day 2, Day 5, Day 7, Day 8, and Day 9

- Complete your Daily Diary as instructed by the study site staff.

- You will take your study drug approximately every 6 hours with water and you will record if you missed any of the study drug in your Daily Diary.

Day 3 and Day 6 – phone contact

- The study site staff will contact you on the phone to capture an update on your symptoms, new or ongoing health problems.
- Complete your Daily Diary as instructed by the study site staff.
- Study drug will be taken approximately every 6 hours with water and any doses missed will be recorded in your Daily Diary.

Day 10/day of last dose - clinic visit

- Blood samples will be collected for pharmacokinetic (PK) tests. PK tests are research tests done to see how long the study drug remains in your body. The samples will be taken pre-dose, about 2-hours post-dose, and about 4 hours post-dose.
- You will be asked to have your temperature, blood pressure, heart rate, and breathing rate taken.
- An interview to capture an update on your symptoms, new or ongoing health problems.
- You will be asked to have an electrocardiogram (ECG) done, which is a recording of the electrical activity of your heart.
- Daily Diary completion and review with study site staff.
- Routine blood tests to check your overall health (about 10.5 mL [about 2 teaspoons] of blood will be drawn for these tests).
- You will be asked to give a stool sample pre-dose and another pre-dose or post-dose. Part of the stool sample will be stored for future analysis.
- You will return your empty study drug wallets or unused study drug to the study site staff.

After Study Treatment:

Because this is a research study, the study drug will be given to you only during this study and not after the study is over.

Follow Up Visit-1, two days after last dose- clinic visit

Height and weight will be measured

- You will be asked to have your temperature, blood pressure, heart rate, and breathing rate taken.
- A complete physical examination evaluation will be performed and include evaluation of the head, eyes, ears, nose, and throat, neck, lungs, heart, chest, abdomen, extremities, neurological status, and skin.
- An interview to capture an update on your symptoms, new or ongoing health problems.
- Daily Diary completion and review with study site staff. This is the final day the diary will be completed unless there is suspected reoccurrence of CDI during the follow up period.

- Routine blood test to check your overall health.
- You will be asked to give a stool sample. Part of the stool sample will be stored for future analysis.

Day 20 and Day 27 – phone contact

- The study site staff will contact you on the phone to capture an update on your symptoms, new or ongoing health problems.

Follow Up Visit-2, Day 40 - clinic visit

- You will be asked to have your temperature, blood pressure, heart rate, and breathing rate taken.
- A complete physical examination evaluation will be performed and include evaluation of the head, eyes, ears, nose, and throat, neck, lungs, heart, chest, abdomen, extremities, neurological status, and skin.
- An interview to capture an update on your symptoms, new or ongoing health problems.
- Routine blood tests to check your overall health.
- Urine pregnancy testing will be done for all women of childbearing potential. Women who are post-menopausal less than one year will have a urine pregnancy test.
- You will be asked to give a stool sample. Part of the stool sample will be stored for future analysis

Follow Up Visit-3, Day 70 – phone contact

- The study site staff will contact you on the phone to capture an update on your symptoms, new or ongoing health problems.

Unscheduled Visit, Suspected Recurrence

If signs and symptoms of CDI recurrences are suspected at any point in the study prior to Follow up Visit-3 on Day 70, you will be asked to return for an unscheduled clinic visit.

- You will be asked to have your temperature, blood pressure, heart rate, and breathing rate taken.
- A complete physical examination evaluation will be performed and include evaluation of the head, eyes, ears, nose, and throat, neck, lungs, heart, chest, abdomen, extremities, neurological status, and skin.
- An interview to capture an update on your symptoms, new or ongoing health problems.
- Daily Diary completion and review with study site staff.
- Routine blood tests to check your overall health.
- You will be asked to give a stool sample. Part of the stool sample will be re-tested for *C. difficile,* and part will be stored for future analysis.

EXPECTATIONS

If you participate in this study, you will be expected to:

- Complete a Daily Diary that will capture details for each of your bowel movements, date and time of study drug dosing, concomitant medications, and the questions about your CDI symptoms.
- Take your study drug as directed by the Investigator or his/her designee. Return to the study site for all study procedures. Continue taking all other medications as told to you by your doctor.
- Call the study site if you are hospitalized, visit an emergency room or urgent care, your diarrhea returns for more than one day, or you do not feel well.
- Refrain from consuming non-dietary probiotics include capsules, powders, or liquids that are nutraceutical probiotics [primary ingredient is bacteria or yeast]. Yogurt, kombucha, kimchi, kefir, brine pickles, cheese, and other foods that are considered "dietary probiotics" are permitted.)
- Refrain from consumption of grapefruit and its juices as well as nutraceutical supplements containing curcumin (i.e., turmeric) until 24 hours after the last dose of study medication
- Females: if of childbearing potential and sexually active use 2 methods of birth control from the screening period until 60 days after taking last dose of study drug.
- Males: use highly effective method of birth control if female partner is of childbearing potential and refrain from sperm donation for 2 months after your last dose of the study drug.

RISKS, SIDE EFFECTS, AND/OR DISCOMFORTS

For *CRS3123:*

CRS3123 and placebo were tested in normal healthy volunteers who received either a single dose or multiple doses and the most common reported adverse events included:

- Headache
- Abdominal pain
- Upset stomach
- Diarrhea
- Taste disturbance
- Some changes in laboratory tests including deceased hemoglobin, liver function, and decreased blood calcium function of the pancreas

As with any drug, allergic reaction is possible which can sometimes be severe or potentially life-threatening. This is a possibility but, to date, no reports of allergic reactions have occurred. Some symptoms of allergic reactions are rash, wheezing, difficulty breathing, dizziness, fainting, swelling around the mouth or throat or eyes, a fast pulse, and sweating. Please seek treatment immediately and tell the Investigator and study staff if you have any of these symptoms, or any other side effects, during the study.

For Vancomycin
Vancomycin capsules have been approved by the US Food and Drug Administration for the planned use and at the planned dose in this study. In studies done in humans, the most common side effects, occurring in at least 5% of people treated included:

- Nausea
- Stomach Pain
- Vomiting
- Diarrhea
- Flatulence
- Fever
- Swelling of the legs
- Tiredness
- Urinary Tract Infection
- Low blood levels of potassium
- Back pain
- Headache

In people over the age of 65 years, there is a chance that the kidneys can be injured. This may be as serious as kidney failure; it may also be milder kidney impairment or just an increase in the blood level of creatinine, a substance that is an indicator of how the kidneys are working.

There have also been cases of hearing loss or loss of balance and infections caused by bacteria that are resistant to vancomycin.

As with any drug, allergic reaction is possible which can sometimes be severe. While this is possible, it is not common with vancomycin.

RISKS OF STUDY PROCEDURES

- **Blood samples:** Possible side effects from blood drawing include faintness, inflammation of the vein, pain, bruising, or bleeding at the site of puncture. There is also a slight possibility of infection.
- **Electrocardiogram (ECG):** Skin irritation is rare but could occur during an ECG from the electrodes or gel that is used.
- **Stool Sample:** When you need to take a stool sample at home, there may be a possibility that you soil your skin with stool from the collection container if you do not handle your stool collection according to the instructions.

If you are taking antidiarrheals you will be asked to stop taking these medicines (washout period) from randomization until after Follow up Visit 3 (day 70). During this time, your symptoms may not improve or may get worse. If your symptoms get worse, tell the Investigator immediately.

UNFORESEEN RISKS

Since the study drug is investigational, there may be other risks that are unknown. Additionally, there may be unknown risks to a pregnancy or unborn child if you or your female partner become pregnant.

CRS3123 may interfere with how some medications are processed by your body. If you are taking medications, it is important to inform your doctor to discuss if these medications might be impacted by CRS3123. He or she might make adjustments to your medication.

BIRTH CONTROL RESTRICTIONS

Taking the study drug may involve risks to a pregnant woman, an embryo, fetus (unborn baby) or nursing infant. Therefore, if you are pregnant, planning to become pregnant, planning to father a child, or are breastfeeding a child, you cannot participate in this study.

Females:

- In order to reduce the risk of pregnancy, you should use an effective method of birth control while you are participating in this study and for 2 months after your last dose of the study drug. Acceptable methods of birth control for use in this study are Abstinence, Oral contraceptives ("the pill") or other prescription hormonal contraceptive method, Birth control injections, Birth control patch, Intrauterine device, Double-barrier method (condoms, diaphragm, or cervical cap plus spermicidal foam, cream, or gel), or if female, male partner sterilization. The Investigator or study staff will discuss this with you. The use of contraception does not apply if the male partner has been vasectomized at least 6 months prior to dosing.

If you become pregnant while you are participating in this study or within 2 months after you have stopped taking the study drug, tell your Investigator or study staff immediately. The study drug will be stopped and your participation in this study will be ended. The Investigator will ask to follow the pregnancy to its outcome and for up to 6-8 weeks after delivery.

Males:

In order to reduce the risk of pregnancy, you should use an effective method of birth control while you are participating in this study and for ***2 months*** after your last dose of the study drug. Acceptable methods of birth control for use in this study are complete abstinence, male vasectomy, or double barrier method (condoms plus spermicidal foam, cream, or gel). The Investigator or study staff will discuss this with you.

If your female partner becomes pregnant while you are participating in this study or within 2 months after you have stopped taking the study drug, tell your Investigator or study staff immediately. The Investigator will ask for permission to follow up with your partner and, with her consent, will follow the pregnancy to its outcome and for up to 6-8 weeks after delivery. Your partner will be provided with a consent form for this pregnancy follow-up.

ALTERNATIVES TO PARTICIPATION

You do not have to be in this study to receive treatment for your CDI. Your options may include:

- There may be other clinical research studies available to you.
- Standard antibiotic treatment with Vancomycin, Fidaxomicin, or Metronidazole or treatment with Microbiota Restoration Therapy.

Please talk to the Investigator about your options before you decide whether or not you will take part in this study.

NEW FINDINGS

Any new important information that is discovered during the study and which may influence your willingness to continue participation in the study will be provided to you by the Investigator or study staff.

BENEFITS

You may benefit as a result of your participation in this study. There is, however, no guarantee that you will benefit from your participation in this study. Information learned from the study may help other people in the future.

COMPENSATION FOR PARTICIPATION

«Compensation»

You will be paid up to a total of $_____ if you complete this study. You will be paid for the visits you complete according to the following schedule:

- $_____ for Visits Day 1, Day 10, Follow up Visit 1, Follow up Visit 2, and Follow Up Visit 3.
- $_____ for Visits Day 3, Day 6, Day 20, and Day 27

If you do not complete the study, for any reason, you will be paid for each study visit you do complete.

You will be paid _____ *["after each visit," "at the end of study participation," etc.]*.

Transportation assistance to and from clinical visits may be available to you. If you have any questions regarding your compensation for participation, please contact the study staff.

CONFIDENTIALITY

Records of your participation in this study will be held confidential except when sharing the information is required by law or as described in this informed consent. The Investigator, the sponsor or persons working on behalf of the sponsor, and under certain circumstances, the United States Food and Drug Administration (FDA) and the Institutional Review Board (IRB) will

be able to inspect and copy confidential study-related records which identify you by name. This means that absolute confidentiality cannot be guaranteed. If the results of this study are published or presented at meetings, you will not be identified.

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.

Certificate of Confidentiality

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. This means that the researchers cannot release or use information, documents, or samples that may identify you in any action or suit unless you say it is okay. They also cannot provide them as evidence unless you have agreed. This protection includes federal, state, or local civil, criminal, administrative, legislative, or other proceedings. An example would be a court subpoena.

There are some important things that you need to know. The Certificate DOES NOT stop reporting that federal, state or local laws require. Some examples are laws that require reporting of child or elder abuse, some communicable diseases, and threats to harm yourself or others. The Certificate CANNOT BE USED to stop a sponsoring United States federal or state government agency from checking records or evaluating programs. The Certificate DOES NOT stop disclosures required by the U.S. Food and Drug Administration (FDA). The Certificate also DOES NOT prevent your information from being used for other research if allowed by federal regulations.

Researchers may release information about you when you say it is okay. For example, you may give them permission to release information to insurers, medical providers or any other persons not connected with the research. The Certificate of Confidentiality does not stop you from willingly releasing information about your involvement in this research. It also does not prevent you from having access to your own information.

COMPENSATION FOR INJURY

If you become ill or are injured while you are in the study, get the medical care that you need right away. You should inform the healthcare professional treating you that you are participating in this study. If you tell the study staff that you think you have been injured, then they will help you get the care you need.

If you are injured as a result of taking the study drug(s) or from procedures done for the purpose of this study, the sponsor will pay for those medical expenses necessary to treat your injury that are not covered by your medical insurance or any other third-party coverage. You will not lose any of your legal rights or release the sponsor, the Investigator, the study staff, or study site from liability for mistakes by signing this consent document. To pay medical expenses, the sponsor will need to know some information about you like your name, date of

birth, and Medicare Beneficiary Identifier (MBI). This is because the sponsor has to check to see if you receive Medicare and if you do, report the payment it makes to Medicare.

In general, no long-term medical care or financial compensation for research-related injuries will be provided by the NIH or the Federal Government.

COSTS

There will be no charge to you for your participation in this study. The study drug, study-related procedures, and study visits will be provided at no charge to you or your insurance company.

FUTURE RESEARCH STUDIES

Identifiers will be removed from your identifiable private information or identifiable biospecimens collected during this study and **could then be used for future research studies or distributed to another investigator for future research studies**. You may change your mind about secondary research and withdraw consent for the storage and use of your coded samples or information at any time. You will need to contact the Investigator using the contact information listed on page 1 of this form. We will do our best to follow your wishes but cannot promise that we will always be able to destroy your samples or data. For example, if your samples were already used, we would not be able to destroy them.

Blood and urine specimens remaining after clinical safety assessments are performed will not be stored for future use.

Excess/leftover blood and fecal specimens remaining after pharmacokinetic tests may be stored for up to 5 years for future analyses.

No human genetic (DNA) tests will be done on these samples. The results of any future testing will be kept confidential in the same way as the results of other testing done for this study.

_____ **YES**, you may store my excess/leftover blood and fecal samples for up to 5 years and use them for future research.

_____ **NO**, you may not store my excess/leftover blood and fecal samples for up to 5 years and use them for future research.

COMMERCIAL PROFIT

Your biospecimens collected during this study may be used for commercial profit (even if identifiers are removed) and **you will not share in this profit**.

CONFLICTS OF INTEREST

The policy of the NIH is to evaluate investigators at least yearly for any conflicts of interest. You may review the system for assessing conflicts of interest by checking the web site link:

http://ethics.od.nih.gov/forms/Protocol-Review-Guide.pdf. Copies of the standards may also be requested by research subjects. Crestone, Inc., the company that makes CRS3123 and NIH are providing funding for this study.

CLINICALLY RELEVANT RESULTS

Research results that are clinically relevant, including individual research results, **will not be disclosed to you.**

GENOME SEQUENCING

Researchers will only look at the genetic information of the microbes found in your stool sample. The research **will not include study of any of your genetic information** by sequencing, or "reading," every letter in your DNA (your genome).

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 Drive, 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: Pro00046367.

VOLUNTARY PARTICIPATION / WITHDRAWAL

Your decision to participate in this study is voluntary. You may choose to not participate, or you may withdraw from the study for any reason without penalty or loss of benefits to which you are otherwise entitled and without any effect on your future medical care. However, please note that the FDA requires that any information collected up to the point of your withdrawal cannot be removed from the study.

For participants who discontinue prematurely during the study treatment period, an end of study treatment visit will be conducted as soon as possible after discontinuation of study and

the Investigator and study staff will subsequently perform all assessments as specified for follow up visits.

The Investigator or the sponsor can stop your participation at any time without your consent for the following reasons:

- If it appears to be medically harmful to you;
- If you fail to follow directions for participating in the study;
- If it is discovered that you do not meet the study requirements;
- If the study is canceled; or
- For administrative reasons.

If you leave the study for any reason, the Investigator may ask you to have some end-of-study tests for your safety.

PRIMARY HEALTH CARE PROVIDER NOTIFICATION OPTION

I consent to having my family doctor or primary health care provider notified by the study site of my participation in this study and/or any significant findings related to my health (please check yes or no).

❒**YES** (If yes, please complete the information below)
❒**NO**

Name and address of family doctor or primary health care provider:	Name: Address:
Telephone and Fax Number:	Tel: Fax:

CONSENT

I have read and understand the information in this informed consent document. I have had an opportunity to ask questions and all of my questions have been answered to my satisfaction. I voluntarily agree to participate in this study until I decide otherwise. I do not give up any of my legal rights by signing and dating this consent document. I will receive a copy of this signed and dated consent document.

_____
Subject's Printed Name

_____ _____
Subject's Signature Date

Printed Name of the Person Conducting the Consent Discussion

Signature of the Person Conducting the Consent Discussion Date

AUTHORIZATION TO USE AND DISCLOSE PROTECTED HEALTH INFORMATION

If you decide to be in this study, the Investigator and research team will use and share health data about you to conduct the study. Health data may include:

- Your name.
- Address.
- Phone number.
- Date of birth.
- Medical history.
- Information from your study visits, including all test results.

Health data may come from your study records or from existing records kept by your doctor or other health care workers.

For this study, the research team may share health data about you with authorized users. Authorized users may include:

- Representatives of **Crestone, Inc**.
- Representatives of **InClin.**
- Representatives of **National Institutes of Health (NIH).**
- Representatives of Division of Microbiology and Infectious Disease (DMID).
- Representatives of Advarra IRB (an Institutional Review Board that reviews this study).
- The United States Food and Drug Administration (FDA) and other U.S. federal and state agencies.
- Governmental agencies of other countries.
- Outside individuals and companies, such as laboratories and data storage companies, that work with the researchers and sponsor and need to access your information to conduct this study.
- Other research doctors and medical centers participating in this research, if applicable.
- A data safety monitoring board which oversees this research, if applicable.

Your health data will be used to conduct and oversee the research, including for instance:

- To see if the study drug works and is safe.

- To compare the study drug to other drugs.
- For other research activities related to the study drug.

Once your health data has been shared with authorized users, it may no longer be protected by federal privacy law and could possibly be used or disclosed in ways other than those listed here.

Your permission to use and share health data about you will end in 50 years unless you revoke it (take it back) sooner.

You may revoke (take back) your permission to use and share health data about you at any time by writing to the Investigator at the address listed on the first page of this form. If you do this, you will not be able to stay in this study. No new health data that identifies you will be gathered after your written request is received. However, health data about you that has already been gathered may still be used and given to others as described in this form.

Your right to access your health data in the study records will be suspended during the study to keep from changing the study results. When the study is over, you can access your study health data.

If you decide not to sign and date this form, you will not be able to take part in the study.

STATEMENT OF AUTHORIZATION

I have read this form and its contents were explained. My questions have been answered. I voluntarily agree to allow study staff to collect, use and share my health data as specified in this form. I will receive a signed and dated copy of this form for my records. I am not giving up any of my legal rights by signing and dating this form.

_____

Printed Name of Subject

_____ _____

Signature of Subject Date

Printed Name of the Person Obtaining the Authorization

Signature of the Person Obtaining the Authorization Date