Study Title: An Experimental Infection Study of Dermally-Applied *Necator americanus* Hookworm Larvae in Hookworm-Naïve Adults

Principal Investigator: David Diemert, MD

You have been asked to participate in a research study. Before you decide whether you want to participate in the study, you have a right to the following information:

1. The nature and purpose of the study.
2. The investigational product that will be used in the study.
3. The procedures that will be performed in the study.
4. Risks and discomforts that can reasonably be expected from the study.
5. Benefits that can reasonably be expected from the study.
6. Alternatives to participating in the study.
7. Availability of medical treatment should you become injured as a result of the study.
8. The opportunity to ask questions about the study.
9. The right to stop participating in the study at any time without any penalty.
10. A copy of this signed and dated written consent form for you to keep.

INFORMED CONSENT FOR A NEW RESEARCH STUDY

Study Title: An Experimental Infection Study of Dermally-Applied *Necator americanus* Hookworm Larvae in Hookworm-Naïve Adults

Principal Investigator: David Diemert, MD

Study Sites: George Washington Medical Faculty Associates,
George Washington University School of Medicine & Health Sciences

24-Hour Telephone Number: (202) 270-2393

We are inviting you to take part in a research study. This research study is sponsored and being paid for by the Baylor College of Medicine (Houston, TX). The person in charge of this study will be Dr. David Diemert of the George Washington University. Please take as much time as you need to read this consent form. You may want to talk about it with your family, your friends, or your personal health care provider. You may find parts of this form hard to understand. If you do, please ask questions. Participation in this research study is voluntary. If you choose to join the study, you will be asked to sign this form. We will give you a copy of the signed form to keep.

WHY ARE WE DOING THIS STUDY?

We are doing this study to find out the amount of hookworm larvae (baby worms) that is safe to give to healthy adults, and that leads to an infection with adult hookworms in the intestine (gut). This will help us to test hookworm vaccines in future studies. A vaccine is something that is used to prevent an infection or disease. Researchers from the Baylor College of Medicine and the George Washington University are trying to make a new vaccine for hookworm because right now there is NO vaccine for this important disease.

Hookworm is a parasitic worm that can live for several years in the intestine (gut) of humans if they do not receive any treatment with an anti-worm medication. Hookworms feed on the blood of the people they infect, which can cause anemia (low blood counts) and other illness if not treated. People get infected with hookworm when their skin comes into contact with tiny larvae (baby worms) that live in soil that has been contaminated with human feces that has not been properly treated. After penetrating the skin, the larvae travel through the body until they reach the gut where they develop into adult worms that are about half an inch long.

Hookworm infection does not happen in the United States, but it is very common in poor parts of South America, Africa and Asia. Over 500 million people in the world are living with hookworm infection right now. We hope that this study will give us information that can be used to test the hookworm vaccines that the Baylor College of Medicine is developing. In future studies, we plan to vaccinate people with the hookworm vaccine and then given them hookworm larvae to see if the vaccine can prevent (stop) the larvae from developing into adult worms. However, in this study, you will NOT receive a vaccine. You will only receive the hookworm larvae.

You will be infected with hookworm if you participate in this study. This infection may lead to adult worms in your gut (intestine). However, we can cure this infection by giving you an anti-worm medication. This medication will be given to you at the end of the study. We will do tests to make sure that this medication has killed all of the adult worms in your gut.

You can take part in this study if you are a **HEALTHY MAN OR WOMAN** between the ages of 18 and 45 years and live in the Washington, DC metropolitan area. Up to 30 people will take part in this study.

WHAT IS INVOLVED IN THE STUDY?

Everyone in this study will be infected with hookworm by placing hookworm larvae on their skin. Hookworm larvae are microscopic, that is, they are too small to see with the naked eye and can only be seen using a microscope. The hookworm larvae are put onto a gauze pad, which will be placed onto the skin of your arm. Different participants will have different amounts of hookworm larvae placed on their arm. Three different amounts of larvae will be used in the study. 10 participants will have 25 larvae placed on their arm, 10 participants will get 50 larvae, and 10 participants will get 75 larvae. This will allow us to see how safe different amounts of the larvae are.

We will collect fecal (stool) samples from you before you get the larvae, and at regular intervals after you get the larvae. We will test your stool to see if you have become infected with hookworm. This will tell us if the larvae have matured into adult worms.

If you agree to participate in the study, we will put you into one of 3 groups of people. Each group will have 10 people. We will assign you to a group based on the order that you join the study, kind of like being in line at a store checkout. If the first group fills up before you are registered in the study you will be asked to join the next group.

No matter which group you are in you will have hookworm larvae placed on your skin. You cannot ask to be in a specific group.

- 10 people will be in **Group 1:** 10 people will have 25 larvae placed on their arm
- 10 people will be in **Group 2**: 10 people will have 50 larvae placed on their arm
- 10 people will be in **Group 3**: 10 people will have 75 larvae placed on their arm

You will be given the larvae all at once, during a single study visit. Both you and the study staff will know the amount of larvae that was on the pad that is placed on your skin.

Your first visit (this visit) will be a screening visit. If you don't want to do everything in one visit, you can come back later to finish the screening. During screening, the following things will happen:

- You will read this informed consent form. After this you will decide if you want to participate in the study or not.
- If you want to participate, you will sign this informed consent form.

- Next, we will check if you can join the study. You have to be healthy to be in this study. We will ask you questions about your health and you will have a complete physical examination.
- We will take a blood sample (about 2 tablespoons) from your arm that will be tested for the following:
  - A complete blood count
  - Tests of your kidney and liver function
  - Tests for HIV, Hepatitis B, and Hepatitis C
- You will give a urine sample that will be tested to see if there is protein or sugar in it. If you are a woman, your urine will also be tested to see if you are pregnant.
- You will give a stool sample that will be tested for blood and parasites. If you are unable to provide a stool sample during this visit you will be asked to bring a sample to the clinical before your next visit.

We will have to wait for your blood test results to come back from the lab before we will know if you can be in the study. If your examination or blood tests show that you have an illness, or if you are not in good health, you cannot be in this study. You must have a negative pregnancy test (if you are a woman), HIV test, and Hepatitis B and C tests to be in this study. You also cannot be in the study if you have had hookworm before or if you have lived for more than 6 months in a place where people can get hookworm infection (for example, in rural parts of Africa). The study staff will tell you your results and refer you for follow-up care if needed.

If you test positive for HIV or Hepatitis B or C virus, we are required by law to notify the DC Department of Health. We will have to tell the Department of Health your name and other personal identifying information, but they will keep this information secret.

If your screening tests show that you can participate in the study, and you decide that you want to participate, you will be in the study for 6 months. You will visit the clinic 23 times (including this screening visit). The first 2 visits (the screening visit and the visit when the hookworm larvae will be placed on your skin) will last about 2 hours each. The remaining visits will last about 15-30 minutes each. The total amount of time is about 15 hours. There will be a visit 3, 7, 14 and 28 days after the visit when you will get the hookworm larvae. Then we will see you once every week for 15 weeks. We will call you about 6 months after you get the larvae to ask how you are doing.

You will receive only one application of hookworm larvae. The larvae will be put on a gauze pad and then placed onto the skin of your arm. The pad will be kept in place on your arm for 1 hour by using an adhesive (sticky) dressing.

We will take some blood from you up to 15 times during the study. The amount of blood taken each time will be between 2½ to 4 tablespoons (38 mL to 55 mL). The total amount of blood we will take during the whole study will be up to about 606 mL (about 2½ cups). During the study, we will test your blood to check your blood cell counts and your kidney and liver function to be

sure that you stay healthy. Some blood will also be used to see if your body is making antibodies (germ fighters) and other substances that help your body fight infections.

You will give us some of your stool 8 times before you receive the anti-worm medication. You will then take the anti-worm medication once a day for 3 days, starting about 3 months after the larvae are put on your arm. You will then provide stool samples 3 more times. This will allow us to make sure that you are no longer infected. We will give you toilet "hats" for collecting your stool, and containers for bringing your stool to the clinic. Study staff will explain how the hats and containers are used and will answer any questions you have.

We may also ask you to give us a urine sample at each study visit (this is optional). We will test your urine for markers of infection, to see if they change over time after you get the hookworm larvae. Urine samples will be shipped to The Netherlands for analysis.

Only hookworm larvae can cause hookworm infection in people. Touching or swallowing adult hookworms or hookworm eggs will not cause infection. Hookworm eggs must sit for several days in a warm and moist environment before they can hatch and become hookworm larvae. During the study, all of your bowel movements (stool) should be flushed down a toilet, unless you are gong to bring them into our clinic. This will stop the hookworm eggs from becoming larvae and will stop the spread of hookworm infection to other people.

If you are a woman, we will also take urine samples during the screening visit and the first study visit to see if you are pregnant. You cannot participate in the study if you are pregnant.

- **Visit 1 (Screening Visit)**
  - As described above
- **Visit 2 (Application of Hookworm Larvae)**
  - We will take a history of symptoms since your last visit
  - We will do a brief physical exam
  - We will take a blood sample from you (about 3 ¾ tablespoons)
  - You may give a urine sample
  - We will place the larvae on the skin of your arm
  - You will have to stay in the clinic for 1 hour after the larvae are placed on your arm to see if you have any reaction
- **Visit 3 (3 days after application of the larvae)**
  - We will take a history of symptoms since your last visit
  - We will do a brief physical exam
  - You may give a urine sample
- **Visits 4, 5, 6, and 7 (7, 14, 28, and 35 days after application of the larvae)**
  - We will take a history of symptoms since your last visit
  - We will do a brief physical exam
  - We will take a blood sample from you (about 2½ to 3½ tablespoons) at Visits 4, 5 and 6

  - You may give a urine sample

- **Visits 8 to 20 (once per week, 42 to 126 days after application of the larvae)**
  - We will take a history of symptoms since your last visit
  - We will do a brief physical exam
  - We will take a blood sample from you (about 3 to 3½ tablespoons)
  - You will give us a sample of your stool
  - You may give a urine sample
  - At Visit 20, we will give you one dose of the anti-worm medication to take by mouth in the clinic. If you are female, we will test your urine to make sure you are not pregnant before we give you the anti-worm pills
  - We will give you two more of the anti-worm pills to take at home
- **At Home (127 and 128 days after applications of the larvae)**
  - You will take anti-worm medication once a day for two more days
- **Visit 21 (136 days after application of the larvae)**
  - You will give us a sample of your stool
  - You may give a urine sample
- **Visit 22 (140 days after application of the larvae)**
  - You will give us a sample of your stool
  - You may give a urine sample
- **Visit 23 (143 days after application of the larvae)**
  - You will give us a sample of your stool
  - You may give a urine sample
  - We will take a blood sample from you (about 3 to 3½ tablespoons)
  - If you are female, you will give a urine sample to check for pregnancy
- **Telephone call: 6 months after application of the larvae**
  - We will call you and ask you about any symptoms since your last visit

Throughout the study, we will give you weekly diary cards and ask you to record your symptoms every day during the study.

Information about Samples Collected as Part of This Research Study:

If you do not want to have blood collected or give us stool or urine samples you will not be able to participate in the study.

Extra blood, urine and stool may be stored for future research. If you do not want your blood, urine and stool stored for future research you can still participate in the study. At the end of this consent form, we will ask you if we can keep your blood, urine and stool samples for future testing.

WHAT ABOUT PREGNANCY?

Hookworm infection during pregnancy may cause women to have anemia (low blood cell counts), and may cause an unborn baby to have a low birth weight. If you are pregnant, you cannot be in this study. If you are a woman, we will do a urine pregnancy test to make sure you are not pregnant. We will do a pregnancy test during screening and on the day that we place the larvae on your skin. If you are sexually active or plan to be during the study, you must use two effective birth control measures during the study. These are some birth control measures that you can use:

- Hormonal contraceptives (such as birth control pills, implants, or injections)
- Barrier methods (such as a condom or diaphragm) used with a spermicide
- An intrauterine device (IUD)
- Surgical sterilization (hysterectomy or tubal ligation)

It you are female, it is very important that you do not become pregnant during this study. The anti-worm medication, albendazole, is not recommended for use during pregnancy, especially during the first trimester (the first three months of pregnancy). Birth defects from albendazole have not been seen in humans. However, albendazole has been shown to cause damage to the fetus of pregnant mice and rats. We will do a urine pregnancy test before giving you the albendazole to make sure you are not pregnant. If you become pregnant during the study while infected with hookworm, we will discuss treatment options with you.

If you become pregnant during the study we will monitor you closely until the end of the pregnancy for your safety and the safety of your baby.

If you are breastfeeding and do not want to stop, you cannot take part in this study.

WHAT ARE THE POSSIBLE RISKS AND DISCOMFORTS?

In previous studies in the US, Australia, and the United Kingdom, over 90 people have been given the same type of hookworm larvae that we will use in this study. Some of these people got a skin rash (redness and itching) at the site where the larvae were placed on the skin. This rash may last up to about a month. After clearance of the rash, some people experience skin discoloration at the application site. This skin discoloration will fade over time. You may also feel that your abdomen (stomach) is bloated or that you have a lot of gas (fart or burp more than usual). You may have some abdominal pain, nausea, vomiting, or diarrhea. These will usually happen about one month after the larvae were placed on your skin. There may be other bad reactions that we don't know about yet. If we do find out about a new reaction, we will tell you.

At the end of your time on the study, we will treat the hookworm infection with anti-worm pills, a drug called albendazole. With the anti-worm pills you may feel some stomach pain, nausea, vomiting, and diarrhea.

You may also have some discomfort when we take blood from you. We will use a brand new needle to take the blood from your arm and will clean your skin with alcohol before taking the

blood. You may feel some pain and bruise at the site where we take the blood, or have some dizziness. Rarely, infection occurs where the needle enters the skin.

WILL YOUR INFORMATION BE KEPT PRIVATE?

We will keep your information private to the extent possible by law. Federal laws require that researchers and health care providers protect the privacy of information that identifies you and relates to your past, present and future physical and mental health or conditions, or the provision of health care. If you agree to take part in this study, protected health information will be used and shared with others for the purposes of the study. By signing this form, you are allowing the people and groups that are listed in the next paragraphs to use your health information for this research study. Your information will only be used or shared as explained in this informed consent form.

The use and release of protected health information is for the purpose of collecting information for this study. Protected health information to be shared includes your name, address, telephone number, birth date, diagnosis, medical history, and test results.

The study doctors and other members of the study team may get your individual health information from hospitals, clinics, health care providers, and health plans that provide care to you during the study. By signing this form, you allow the use, sharing, copying, and release of your protected health information in connection with this study by:

- The members of the research team;
- Other healthcare providers such as labs which are part of the study;
- A safety monitoring committee that will be monitoring your safety during the study;
- Institutional officials who are responsible for compliance;
- Representatives and agents of the sponsor of the study (Baylor College of Medicine);
- Representatives of federal regulatory agencies such as the U.S. Food and Drug Administration (FDA).

All of the tests we will do in this study will be done only because you are in this study. The results of these tests will not be sent to your primary doctor or included in your medical record. Once your health information has been given to others outside of the study team the information may no longer be covered by the federal regulation that protects privacy of health information.

If you don't sign this form or if you cancel your permission later, it will not affect your health care treatment outside of the study, payment for healthcare from a health plan, or ability to get health plan benefits. However, if you do not give permission to use your protected health information you will not be able to take part in this study because your protected health information is needed in order to do the study. Your permission to use and share your health information has no time limit. You may cancel your decision to share your health information at any time. If you cancel it, you will not be able to stay in this study. Once you have cancelled, no new information or new biological samples (for example, blood) will be collected from you. If you cancel, the study team will still be allowed to use the information that they have already collected from you.

To cancel your permission, you will need to send a letter to Dr. David Diemert stating that you are canceling your permission. This letter must be signed and dated and sent to this address:

Dr. David Diemert
George Washington University
2300 Eye Street NW, Ross Hall Room 524
Washington, DC 20037

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by US law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time. We may also publish the results from this study in journals or present it at scientific meetings. If we do, we will not use your name.

WHAT ARE THE POSSIBLE BENEFITS OF TAKING PART IN THIS STUDY?

There will be no direct benefit to you for taking part in this study. However, your participation will help us develop ways to test vaccines for hookworm and could help people all over the world in the future if it helps us to develop a vaccine for hookworm.

WHAT OTHER OPTIONS ARE THERE?

An alternative would be to not participate in this study. You do not have to participate in this study, and no one will be upset with you if you decide you do not want to take part.

ARE THERE ANY PAYMENTS TO YOU FOR TAKING PART IN THE STUDY?

If you decide to be in the study and are eligible, you will receive $60 for every study visit that you complete (up to 23 visits to the clinic). This will cover your time, inconvenience, and travel expenses to and from the George Washington Medical Faculty Associates. In addition, a bonus of $100 will be paid to you at the last visit if you complete all of the study visits. You will receive a maximum of $1480 if you complete all visits to the clinic in the study.

You will receive $10 for each subject that you refer and who enrolls in the study.

Your name and social security number will be reported to the appropriate George Washington University employees for purposes of making and recording the payments. You are responsible for paying income taxes on any payments provided by the study. If the payments total $600 or more, the University must report the amount you receive to the Internal Revenue Service (IRS) on the form 1099-Misc. This form tells the IRS that payment was made to you, but it does not say that you were paid for taking part in this research study. You should talk to your tax advisor regarding the proper use of this form 1099-Misc.

WHAT ARE THE COSTS?

All research tests and procedures will be paid for by the sponsor of the study (Baylor College of Medicine). Neither you nor your health insurance company will be charged for the cost of any research tests or procedures that are being done as part of this research study.

WHAT HAPPENS IF YOU GET INJURED OR NEED EMERGENCY CARE?

It is important that you tell someone on the study team if you feel that you have been injured because of taking part in this study. You can tell one of the people on the study team in person or call Dr. Diemert at 202-270-2393.

If you get hurt or sick from participating in the study we will give you any urgent medical treatment needed if the injury is reported in a timely manner. The George Washington Medical Faculty Associates will seek payment from your health insurance company or other third-party payor for any medical care or services you receive. Some health care plans may not cover the costs associated with treating an injury that may result from your participation in this research. If your health insurance plan does not pay the costs associated with treating such an injury, you will be responsible for the payment. However, the sponsor of the research study (Baylor College of Medicine) has an insurance policy that will pay for these costs if they are determined to be related to the research.

The George Washington Medical Faculty Associates, the George Washington University and the George Washington Hospital will not give you any financial payments for, or related to your injury. No financial compensation will be provided for such things as lost wages, disability or discomfort, losses claimed by spouses or family members, medical expenses due to treatment of any underlying or unrelated condition, or any expense arising from or claimed to be due to any research-related injury. However, by signing this form you have not given up any of your legal rights.

WILL YOU RECEIVE NEW INFORMATION ABOUT THIS STUDY?

During the study, we may learn new things about the risks or benefits of being in the study. If we do, we will share this information with you. You might change your mind about being in the study based on this information.

WHAT ARE YOUR RIGHTS AS A PARTICIPANT, AND WHAT WILL HAPPEN IF YOU DECIDE NOT TO PARTICIPATE?

Your participation in this study is voluntary. Your decision whether or not to take part will not affect your current or future care at the George Washington Medical Faculty Associates or the George Washington University Hospital. You are not giving up any legal claims or rights. If you decide to take part in this study, you are free to change your mind and stop being in the study at any time. If you are a student or employee at George Washington University, your academic standing/employment status will not be affected in any way should you choose not to take part or to withdraw at any time.

If you do choose to leave the study prior to Visit 20, it is very important that you return for follow-up with us so that we can treat the hookworm infection. This would involve getting the anti-worm pills and then providing stool samples so that we can make sure that your infection is cured.

CAN YOU BE REMOVED FROM THE STUDY?

You may be removed from this study without your consent if you do not follow the study team's instructions, at the discretion of the study doctors or the sponsor, or if the sponsor closes the study.

WHOM DO YOU CALL IF YOU HAVE QUESTIONS OR CONCERNS?

You may contact Dr. David Diemert at 202-270-2393 with any questions, concerns, or complaints about the research, or your participation in this study, or if you feel you have been hurt by taking part in this study. If you have questions, concerns, or complaints about the research and are unable to contact the study team, contact the George Washington University Medical Center's Institutional Review Board (IRB) Office at 202-994-2715 between the hours of 9:00 AM and 5:00 PM, Monday to Friday or by email at ohrirb@gwu.edu.

If you have any questions about your rights as a research participant, or want to talk to someone independent of the research team, you may contact the Institutional Review Board Office at the phone number or email above.

The IRB is a research review board that is made up of professionals and community members who review and monitor research studies to protect the rights and welfare of research participants.

You will get a copy of this consent form.

CHOICES FOR BLOOD, URINE AND STOOL SAMPLES COLLECTED AS PART OF THIS RESEARCH:

We would like to store blood, urine and stool samples collected from you during this study for future research as identified below. Prior to use all samples will be stored at The George Washington University.

My blood, urine and stool samples may be kept for use in future medical research related to hookworm.

☐ Yes ☐ No _____initials

My blood, urine and stool samples may be shared with other researchers conducting research related to hookworm.

☐ Yes ☐ No _____initials

AGREEMENT: I have read this information and will receive a copy of this form after I sign it. I can decide to stop being in this study at any time.

Printed Name of Participant

Signature Date Signed

AFFIDAVIT OF PERSON OBTAINING CONSENT: I certify that I have explained to the above individual the nature and purpose of the study, potential benefits, and possible risks associated with participation in this study. I have answered any questions that have been raised.

Printed Name of Person Obtaining Informed Consent	Signature	Date Signed