INFORMED CONSENT FORM FOR A NEW RESEARCH PROJECT

Title of Research Project: Phase 1 Study of the Safety and Immunogenicity of *Na*-APR-1 (M74)/Alhydrogel® Co-administered with *Na*-GST-1/Alhydrogel® in Brazilian Adults (SVI-DBL-01)

INTRODUCTION

We are asking you to participate in a research study for a new hookworm vaccine. This consent form gives you information about the study that will be discussed with you. Once you understand the study, and if you agree to join, we will ask you to sign or put your fingerprint on this form. Two equally valid copies of this document will be signed and every page will be initialed. We will give you one copy to keep and the researcher in charge will store the other one in a safe place.

First, we want you to know that:

- Your participation in this research study is optional.
- You do not have to take part in this study, or you can decide later to leave this study if you change your mind.
- If you decide to leave the study, nothing that you have received will be taken away from you.

Before you decide to be in this research study, please take as much time as you need to ask any questions and discuss this study with people on the research team, or with family, friends, or people from your community. You may also ask questions at any time after joining the study.

WHO IS SPONSORING THIS STUDY?

This research study is being sponsored by the **Sabin Vaccine Institute** located in the United States. The people responsible for the study are **Dr. David Diemert**, and Dr. Rodrigo Correa, together with Drs. Frederico Talles and Geraldo Castro from FIOCRUZ.

WHAT IS A HOOKWORM VACCINE?

Scientists at the Federal University of Minas Gerais (UFMG), at FIOCRUZ and the Sabin Vaccine Institute are doing research to make a vaccine against hookworm. This new vaccine against hookworm contains a protein – *Na*-APR-1 – that comes from a small part of the hookworm parasite. We will test this with another protein from the hookworm, called *Na*-GST-1. These two vaccines are being tested and are not yet approved for use in Brazil, the United States, or anywhere else. At this time, there is no approved vaccine for hookworm. We hope that this study will give us information that can be used to develop a hookworm vaccine that will help stop people from getting sick from this worm.

WHY ARE WE ASKING YOU TO TAKE PART IN THIS STUDY?

We are asking you to be in this study because you live in an area of Brazil where many people get worms. Hookworm is one of many types of worms that are found in the area that you live. Anyone can get hookworm if their skin touches dirt or water that is contaminated with hookworm larvae. Larvae in the dirt or water come from the feces of people who are already infected with hookworm. Sometimes you can feel sick from the worms and other times you may not know that you have them. When you have hookworms you may feel tired and weak.

We are asking you to be in this study because the researchers want to test the new vaccines against hookworm to see if the vaccines are safe, before testing them in more people or in children. Only adults

between the ages of 18 and 45 years can be in this study. The vaccines we will test in this study are only against hookworm and they will not have any effect on other kinds of worms.

WHY ARE WE DOING THIS STUDY?

In this study, we want to find out:

- If the new hookworm vaccines are safe when given to adults
- How your body reacts to the vaccines

If the vaccines are safe when given to you and the other participants in this study, the researchers will test them in children who live in the northeast region of Minas Gerais. Also, they will combine the *Na*-APR-1 and *Na*-GST-1 proteins into a single vaccine that will be tested in people.

HOW LONG WILL THIS STUDY LAST?

Your participation in this study will last for 13 months. If you have plans to move away from your community during this time, you will not be able to join this study because you need to be here for the whole study.

WHAT DO I HAVE TO DO IN THIS STUDY?

If you agree to be in this study, the first visit will be a screening visit. This visit will take about 1 -2 hours. We will ask you some questions about your health. One of the research medical doctors will examine you to see if you are in good health. A small amount of blood (around 30 mL) will be taken from your arm to do some lab tests. Your blood will be tested to check your blood cells, your liver and your kidney, and to see if you are infected with viral hepatitis B or C or HIV. You will give us a stool sample so we can check if you have a worm infection. We will ask you to give us some of your urine to see if there is blood or protein in it. If you are a woman, we will also test your urine to see if you are pregnant. Pregnant women and women who are breastfeeding cannot be in this study. The medical doctor will have to wait for your test results to come back from the lab before we will know if you can be in the study.

If your blood tests show that you have an illness, or if you are not in good health, you cannot be in this study. The researchers will discuss this with you and will make sure that you are followed up at the municipal health clinic. If you are infected with worms, you can still be in the study, but only if you agree to be treated with medication for the infection before you get any injections.

If the screening tests and the medical exam show that you can take part in this study and if you still want to be in the study, we will ask you to come to the study clinic to start the study. It is possible that we will not choose you to be in the study even though we ask you to come to the clinic. If this happens, we will ask you if you want to receive a different vaccine, like the approved tetanus or influenza vaccine, instead of being in the study.

If you are chosen to be in the study, on the first day of the study you will receive two injections: one in your right arm and one in your left arm. You will get either one injection of the new *Na*-APR-1 hookworm vaccine in one arm and one injection of salt water in the other arm, OR, one injection of *Na*-APR-1 in one arm and one injection of *Na*-GST-1 in the other arm. If you get the *Na*-APR-1 vaccine, you will get either a LOW dose of the protein, a MEDIUM dose of the protein, or a HIGH dose of the protein. We are trying to find the combination of ingredients that is safe and that gives the best chance of preventing hookworm disease. In addition, we are trying to see if adding a substance called "GLA-AF" to the *Na*-APR-1 vaccine will increase the chances of it working. The GLA-AF substance is not part of any approved vaccines in Brazil or anywhere else.

In this study, 60 people from Americaninhas will participate, divided into 6 groups:

Groups 1 and 2 (low dose vaccine)
5 people will get the **low** dose *Na*-APR-1 vaccine AND saline (salt water)
5 people will get the **low** dose *Na*-APR-1 vaccine AND the *Na*-GST-1 vaccine
5 people will get the **low** dose *Na*-APR-1 vaccine with GLA-AF AND saline
5 people will get the **low** dose *Na*-APR-1 vaccine with GLA-AF AND the *Na*-GST-1 vaccine

Groups 3 and 4 (medium dose vaccine)
5 people will get the **medium** dose *Na*-APR-1 vaccine AND saline (salt water)
5 people will get the **medium** dose *Na*-APR-1 vaccine AND the *Na*-GST-1 vaccine
5 people will get the **medium** dose *Na*-APR-1 vaccine with GLA-AF AND saline
5 people will get the **medium** dose *Na*-APR-1 vaccine with GLA-AF AND the *Na*-GST-1 vaccine

Groups 5 and 6 (high dose vaccine)
5 people will get the **high** dose *Na*-APR-1 vaccine AND saline (salt water)
5 people will get the **high** dose *Na*-APR-1 vaccine AND the *Na*-GST-1 vaccine
5 people will get the **high** dose *Na*-APR-1 vaccine with GLA-AF AND saline
5 people will get the **high** dose *Na*-APR-1 vaccine with GLA-AF AND the *Na*-GST-1 vaccine

We will put you into a group based on the order that you join the study, kind of like being in line at a store. If a group fills up before you join the study you may be asked to join the next group. You cannot ask to be in a specific group.

Once you are in a group, you, the doctors and other members of the study team will not know which vaccine combination you receive. The decision will be made by chance, like when you toss a coin and you don't know what side it will land on. There will be 3 visits where you get the vaccines. At the first vaccination visit, you will have 2 injections, one in each arm (the vaccine is injected into your upper arm muscle using a needle). The second vaccination visit will be 2 months later. You will get two injections, one in each arm. The last vaccination visit will be 2 months after the second and again you will get two injections, one in each arm. You will get the same vaccines at each of the three vaccination visits. At the end of the study, we will tell you which vaccines you got. The vaccination visit will take about 2 hours.

If you are a woman, we will test your urine before every injection to make sure that you are not pregnant. If you are pregnant, you will not be allowed to get any more injections, but we still will still follow you at the study clinic – without any cost to you – so that we can check if you and your baby stay healthy. We will follow you and your baby during all of your pregnancy, during delivery, and after delivery, and we will provide full and free medical care for as long a period as is necessary.

Every time that you get an injection, you will have to stay in the study clinic for at least one hour to make sure you do not start feeling bad. We will also examine you in the clinic or at your home 1, 3, 7, 14 and 28 days after each vaccination. At these visits we will ask you how you are feeling and examine you. These visits will take about 15-30 minutes. We will also take some of your blood (around 40 - 50 mL) on the days that you get the injections, and 7, 14 and 28 days after each injection.

We will ask you to return to the clinic for follow-up 3, 6, and 9 months following your final vaccination visit. At each follow-up visit we will ask you how you are feeling and examine you and we will take some of your blood (up to 40 mL). These visits will last about 15-30 minutes. We will ask you to give us a stool sample to check for worm infections 1 month after the last injection, and at the end of the study. If

you are infected with worms at the end of the study, we will give you medicine if you want it. There will be no charge for this medicine and we will give it to you for free. You can ask one of the research medical doctors to explain to you the risks and benefits of these medicines.

During this study, we will take blood from you 16 times, and the total amount of blood will be around 670 ml. Your blood will be tested to check the function of your blood, your liver and your kidney, and to measure how your body responds to the vaccines. More blood tests might be needed if you get sick. Some of your blood and stool will be stored at FIOCRUZ in Belo Horizonte initially for 5 years, and possibly for longer. This material may be used to do more tests on your blood if you become sick, or in future research related to worms and vaccines. Storage for longer than 5 years or use of your blood in conducting other research will only be done after getting approval from the ethics committee at FIOCRUZ.

If you stop participating in the study for any reason, we will ask you to come to the clinic for a final visit. At this visit, we will ask you questions about your health and examine you, and we may take up to 50 mL of blood from you, if you agree.

CAN I GET HURT IF I AM IN THIS STUDY?

The *Na*-APR-1 hookworm vaccine is currently being tested in 40 healthy adults in the United States. The *Na*-GST-1 hookworm vaccine has been tested in 40 healthy adults in the United States and in 96 healthy adults in Brazil, in Belo Horizonte and in your community of Americaninhas. However, this will be the first time that the *Na*-APR-1 hookworm vaccine will be given together (injected at the same time) with the *Na*-GST-1 hookworm vaccine. We do not know if the new hookworm vaccines will protect you from hookworm infection, and there is a chance that they will not work at all.

When you get the new *Na*-APR-1 hookworm vaccine (with or without the GLA-AF) or the *Na*-GST-1 vaccine, you can expect some soreness and sometimes some redness where the injections are given. You may also feel pain and itching and have purple or red spots on your skin. Some people feel a little sick for a few days after getting an injection. You could feel periods of hot and cold, headache, stomach ache, nausea and sore muscles and joints. You may have swelling or pain in your armpit due to enlarged lymph nodes. Some of this can happen several weeks after you receive the injection. It is possible that the GLA might increase the risk or the intensity of these reactions.

With any vaccine, there is a very small chance that a serious and sometimes deadly allergic reaction might happen within the first hour after the injection is given. These feelings can start with your tongue swelling, feeling lightheaded or dizzy, or having a hard time breathing. Because of this you will be watched carefully for 1 hour after each injection. There may be other bad reactions that we don't know about yet. If we do find out about a new reaction to the hookworm vaccines, we will tell you. The research doctors and nurses will take care of you if you have any problems with the injections. If you have a bad reaction to an injection, we will not give you any more injections.

The *Na*-APR-1 and *Na*-GST-1 hookworm vaccines have never been tested in pregnant women and might be dangerous for the baby. If you are a woman, are sexually active and have not had a tubal ligation or other surgery that would prevent pregnancy, to be in this study you will have to use birth control until 1 month after the last injection. However, the method that you choose to use is up to you (such as birth control pills, birth control injections, intrauterine device, condoms, or others). We can help you pick the best method, or we can send you to the health clinic to discuss the best birth control methods. We will give you the birth control that you want to use, for free. However, if you are not sexually active for religious reasons, or have sex without risk of pregnancy, you do not have to use any birth control method.

The blood tests may cause a little pain when the needle is put in the arm. Later the arm may have some bruising (purple spots) or bleeding where the needle went in, and rarely can get infected. Sometimes

drawing blood causes people to feel lightheaded and even faint.

WHAT IF I GET HURT WHILE IN THIS STUDY?
If you get hurt or sick during the study, you should tell someone on the study team right away, and we will give you medical care for free. The research doctors and nurses will make sure you get immediate treatment for any type of injury, direct or indirect, immediate or delayed, that is caused by taking part in this study, whether mentioned in this document or not. You will also receive care that is guaranteed by the sponsor of the study, without any limitation or condition and the legal right to receive payment for injury. If you get hurt during the study and the research doctors think that it might be caused by the vaccine, they may stop giving you more injections during the study.

ARE THERE ANY BENEFITS TO BEING IN THIS STUDY?
You may not directly benefit from being in this study. However, your participation may help us to develop a vaccine for hookworm and could help people in the future who are living in places like Americaninhas where many people get hookworm. Also, you will receive medical care during the study at the study clinic in Americaninhas. At the end of the study, we will tell you what vaccine you got.

DO I GET ANYTHING FOR BEING IN THIS STUDY?
You will not receive any money if you join this study. However, we will pay for all the expenses that you and your companions have that are associated with your participation in this study. We will provide transportation to the clinic for you and your companions as well as food during the study visits. Also, if you or your companions have other expenses related to visits to the clinic, we will pay for these.

DO I HAVE ANY OTHER OPTIONS BESIDES BEING IN THIS STUDY?
You do not have to be in this study, and no one will be mad at you if you decide you do not want to do it. Medical care and health exams are available at the health clinic in Americaninhas. If you decide not to be in this study it will not affect your current or future medical care at the Americaninhas health clinic or at any other place.

WHAT ARE SOME OF THE REASONS I MIGHT NOT BE ABLE TO FINISH THE STUDY?
The research doctors may decide that it is not good for you to continue receiving the study vaccinations . In this case, you will not be removed from the study, but the future vaccinations will be cancelled and we will continue to monitor your health and to give you full medical care for as long a period as necessary. However, you can be removed from the study for other reasons, for example if you do not come to the clinic when we ask you to. Finally, the study team or the sponsor might decide to stop the whole study from finishing. This will only happen after the approval of the ethical review committees that originally approved the study. However, if this happens, we will continue to give you full medical care for as long a period as necessary.

HOW WILL MY INFORMATION BE KEPT PRIVATE?

Information about you in this study will be kept at the study clinic in a secure place with restricted access. Only the study staff, the sponsor of the study, the ethics committees that have approved the study, and the Brazilian and United States regulatory agencies, may have access to your information but will not be allowed to identify you as a study participant. All of these people will keep your information private. We will not give any information that identifies you to anyone who is not working on the study.

WHO CAN I TALK TO IF I HAVE QUESTIONS?

For questions about your rights as a volunteer in research:

Research Ethics Committee:
Federal University of Minas Gerais (UFMG)

The part of UFMG that protects the welfare of individuals taking part in research done by the University
Antônio Carlos Avenue, #6627 – Unidade Administrativa II – Pampulha
2º Floor– Room 2005 – CEP: 31.270-901
Belo Horizonte, MG – Tel: (31) 3409-4592 – E-mail: coep@prpq.ufmg.br
Hours of operation: 09:00 to 11:00h and 14:00 to 16:00h

For questions about the study:
Principal Investigator: Dr. David Joseph Diemert
Escola de Enfermagem – Universidade Federal de Minas Gerais
Alfredo Balena Avenue, #190 – Santa Efigênia
CEP: 30130-100 Belo Horizonte/MG
Tel: (31) 3409-9181

For questions about the study or if you want to report an illness:
Research Manager: Renata Caldeira Diniz
Americaninha Vaccine Center
Rua Tancredo Neves s/n Povoado de Americaninha
Novo Oriente de Minas/MG
Tel: (33) 3532-7014 (available 24 hours)

I have read, discussed, and understood this informed consent form. My questions were answered. I freely consent to participate in this study.

…..…….
Volunteer's Name (printed letters)

……..……...
Volunteer's Signature/Thumbprint

Date: |__|__|/|__|__|__|/|__|__|__|__|

<u>Person Obtaining Consent</u>:

…….
Name (stamp or printed letters)

…….……..……
Signature

Date: |__|__|/|__|__|__|/|__|__|__|__|

Can the volunteer read? |__| Yes |__| No *(requires presence and signature of a witness)*

Witness (if volunteer is not able to read and understand the Informed Consent Form):
I affirm that the Informed Consent Form has been read to the volunteer and he/she understands the study and I have witnessed the volunteer's consent to participate in the study.

…….. ……..….
Name (printed letters) *Signature*

Date: |__|__|/|__|__|__|/|__|__|__|__|

Principal Investigator or Designee: Name*:* ……..……..…
(stamp or printed letters)

Signature: ……..……..

Date: |__|__|/|__|__|__|/|__|__|__|__|