Appendix II
Sample Informed Consent Form for Infant Study Participation

IMPAACT 2008
Phase I/II Multisite, Randomized, Controlled Study of Monoclonal Antibody VRC01 with Combination Antiretroviral Therapy to Promote Clearance of HIV-1-Infected Cells in Infants

Version 2.0, dated 29 May 2017
With changes from Letter of Amendment (LoA) #1, dated 14 June 2018

Your baby is being asked to participate in the research study named above.

This form gives information about the study. Please read it, or have it read to you, and ask any questions you may have. We will take as much time as you need to fully understand the study. We will ask you questions to see if we have explained the study clearly.

After you understand the study, if you decide to have your baby participate, you will be asked to sign or make your mark on this form. You will be offered a copy to keep.

About the study

The International Maternal Pediatric Adolescent AIDS Clinical Trials Network (IMPAACT) and [*insert site name*] are doing this study. The study is testing an experimental injection called **VRC01** in babies who have HIV. HIV is the virus that causes AIDS.

The study will include about 68 babies who are less than 12 weeks old from Botswana, Brazil, Haiti, Malawi, South Africa, Zimbabwe, and the United States. Babies will be in the study for about one year.

The person in charge of the study at [*insert site name*] is [*insert name of IoR*]. The United States National Institutes of Health are paying for the study.

1. The study is testing VRC01 in babies who have HIV.

The study will test the safety of VRC01 when given to babies who are starting treatment for HIV. It will also test the effect of VRC01 on the amount of HIV that can be found in babies' blood and blood cells.

VRC01 is an antibody against HIV. Antibodies are made by the immune system to fight infection. Antibodies can also be made in laboratories. VRC01 is made in a laboratory.

VRC01 has been tested in laboratory experiments and in animals and people. It has been tested in HIV-negative adults, HIV-positive adults, and babies born to HIV-positive mothers. Laboratory experiments have shown that VRC01 could help decrease the amount of HIV in the body. However, we are still in the early stages of testing VRC01 to find out what its effects may be. This will be the first study of VRC01 in babies who have HIV.

2. We do not know if VRC01 may be a useful treatment for HIV.

The study is a first step in testing VRC01 in babies who have HIV. All babies in the study will be taking anti-HIV medicines (ARVs). We do not know if VRC01 may be a useful treatment when given in addition to ARVs. The study will help us learn about that. ***While we are learning about VRC01, it is very important that babies keep taking ARVs. Taking ARVs is the best known way for people who have HIV to stay healthy.***

3. Only babies who qualify can participate in the study.

If you decide to have your baby join the study, we will first do some tests to see if your baby qualifies. More information about the tests is given in #5 (see below). If your baby qualifies, he or she will be entered in the study. If your baby does not qualify, he or she cannot be entered in the study.

4. It is your decision whether to join the study.

Deciding to have your baby join the study is voluntary (your choice). You are free to have your baby join or not join. If you decide to have your baby join, you can change your mind and take your baby off the study. Your decisions will have no effect on the medical care that your baby receives at this clinic. Your baby's access to services, and the benefits and rights he or she normally has, will not be affected.

Take your time and consider your decisions carefully. If you wish, you can talk to other people about the study before you decide. You can bring other people here to learn about the study with you.

No matter what you decide about the study, your baby should continue to receive standard medical care outside of the study. This includes childhood immunizations, ARVs, and other standard care and treatment for children with HIV. We will tell you where your baby can receive this care if needed.

Finding out if you and your baby qualify

5. We will ask questions, examine your baby, and test your baby's blood.

To find out if your baby qualifies for the study, we will:

- Review your baby's medical records.
- Ask about your baby's health and how you are feeding your baby.
- Ask about the ARVs and other medicines you (the baby's mother) and your baby have taken.
- Give your baby a physical examination.
- Draw your baby's blood (up to 6 mL or about 1 teaspoon) for tests. The tests will:
  - Check your baby's blood cells, liver, and kidneys.
  - Check your baby's CD4 and CD8 cells. These cells are part of the immune system, which is the part of the body that fights infections. HIV attacks CD4 cells, so it is important to check the number of these cells that can be found in the blood.
  - Confirm that your baby has HIV. There are certain HIV tests that are required for this study. If the required tests are not in your baby's medical records, we will do the tests that are needed.
- Talk with you about the study requirements and if your baby will be able to meet these requirements.

These procedures will take about 2 hours. The results of your baby's blood tests will then be available within several days. We will review the results and all other information to determine if your baby qualifies for the study. We will schedule your baby to come back to the clinic when the results are available.

- If your baby does not qualify, we will tell you this. Your baby will not be entered in the study and we will tell you where your baby can go for any medical care or other services your baby may need.

- If your baby does qualify, he or she will be entered in the study.

Entering the study

6. If your baby qualifies, he or she will enter the study within a specified timeframe.

There are certain timeframes for when babies can enter the study. For example, babies must be less than 12 weeks old when they enter. We will explain the timeframes to you so you know what to expect.

On the day your baby enters the study, we will:

- Review your baby's medical records and ask about:
  - Your (the baby's mother's) and your baby's ARVs.
  - Your baby's health and other medicines.
  - How you are feeding your baby.
- Give your baby a physical examination.
- Collect your baby's urine for tests to check his or her kidneys.
- Draw your baby's blood (up to 9 mL or about 2 teaspoons) for tests including:
  - A test of the amount of HIV in your baby's blood. This is called your baby's "viral load." The viral load should decrease over time as your baby takes ARVs.
  - Tests of the effects of VRC01.

7. Babies will be placed in 1 of 2 groups on the day they enter the study.

Babies placed in one group will be given VRC01. Babies placed in the other group will not be given VRC01. To test the effects of VRC01, babies given VRC01 will be compared to babies not given VRC01.

Each baby will be placed a group at random, [like flipping a coin; *sites may insert a different example if preferred*]. Each baby has a 1-in-2 or 50% chance of being placed in the group that is given VRC01. The study staff cannot choose which group each baby is placed in. Babies' parents also cannot choose.

8. Babies in the VRC01 group will be given 4 injections.

Babies in the VRC01 group will be given the first injection of VRC01 when they enter the study. The other injections will be given 2, 6, and 10 weeks later. The injections will be given in the skin of the thigh. The amount of VRC01 given will depend on the baby's weight. The largest amount given will be about 4 mL (less than 1 teaspoon). If the full amount of VRC01 cannot be given in one injection, two injections will be given. Each injection is expected to take about 10-15 minutes.

Although babies in the VRC01 group are expected to be given 4 injections, we may not give injections to babies who are sick when injections are scheduled to be given. We may stop giving injections to any baby if we determine that more injections might be harmful. Babies who miss any injections will still stay in the study.

9. Babies in the VRC01 group will be checked for reactions to the injections.

After the first injection of VRC01, babies must stay in the clinic for at least 2 hours. During this time, study staff will check for reactions to the injection. After the other injections, babies must stay in the clinic for at least one hour.

[Here and in #19, sites may modify text regarding photographs if IRBs/ECs mandate a separate form for obtaining informed consent for photographs.] If your baby has any reactions to VRC01, such as redness where VRC01 in injected, we may take a photo of the reaction. The photo will help the doctors working on the study assess the reaction.

10. All babies will have 13 scheduled visits over 1 year.

Starting 1 week after entering the study, babies will have 11 visits over 6 months. After that, babies will have 2 more visits, about 3 months apart. Each visit will take about 2 hours. At these visits, we will:

- Review your baby's medical records and ask about:
  - Your (the baby's mother's) and your baby's ARVs.
  - Your baby's health and other medicines.
  - How you are feeding your baby.
- Give your baby a physical examination.
- Collect your baby's urine for tests to check his or her kidneys.
- Draw your baby's blood for tests. The amount drawn will be up to 5 mL (about 1 teaspoon) while the baby is less than 3 months old, and up to 20 mL (about 4 teaspoons) as the baby ages to 6 and 12 months. At different visits, the tests will check your baby's:
  - Blood cells, liver, and kidneys.
  - CD4 and CD8 cells.
  - HIV viral load.

  Tests will also check the amount of VRC01 in the blood and the effects of VRC01.

Babies may have more visits if they are sick or need more tests to check on their health. Additional blood or urine may be drawn at these visits if needed.

11. Mothers or caregivers are asked to check on their babies.

After 4 of the study visits, you will be asked to take your baby's temperature and write down how your baby is doing. You will be asked to do this for 7 days after the visit when your baby enters the study, and for 7 days after the visits 2, 6, and 10 weeks later. For babies in the VRC01 group, these are the visits when VRC01 is given, but you will be asked to do this even if your baby is not given VRC01.

We will show you how to write down the information about your baby. After 3 days, we will telephone you to ask for the information you have written down. You can also come to the clinic with your baby or have a study staff member come to your home instead of having the telephone call. If your baby has any problems, you will be asked to bring him or her to the clinic.

12. If babies need a lumbar puncture, we will save spinal fluid for the study.

[here and below, sites may use locally appropriate terminology (e.g., "spinal tap") to refer to lumbar puncture]

A procedure called "lumbar puncture" is sometimes done when babies are sick. This procedure uses a needle to collect fluid from the baby's spine. The fluid is then tested to find out what may be causing the baby to be sick. No lumbar punctures will be done for this study. However, if your baby has a lumbar puncture outside of the study, we would like to save any spinal fluid that may be left over for tests. If you agree to this, the tests will look for HIV in the fluid. The tests may also look for other factors related to HIV and the immune system in the fluid.

If your baby has a lumbar puncture, and you agree to have the spinal fluid saved, we will ask you to bring your baby to the clinic. At this visit, we will:

- Review your baby's medical records
- Ask about your baby's health and medicines.
- Draw your baby's blood (2 mL or about half a teaspoon) for tests. The tests may look for HIV in the blood and blood cells. The tests may also look for other factors related to HIV and the immune system.

13. Different tests will be done at different laboratories.

We will do tests of your baby's urine, blood cells, liver, kidneys, CD4 and CD8 cells, and HIV viral load here at our laboratory. We will give you the results of these tests at the next scheduled visit or sooner if necessary. We will explain the results and give you counseling and referrals as needed.

Tests of the amount of VRC01 in the blood and of the effects of VRC01 will be done at different laboratories in the United States. Tests of spinal fluid will also be done in the United States. Some tests may be done while the study is ongoing, others after the study is completed. The results of these tests are for research purposes only. This means they are not expected to give any information relevant to your baby's health. The results will not be given to the study staff or to you.

If you agree, some of your baby's blood will be used for tests of his or her genes. Genes are passed to children from their birth parents. They affect how people look and how their bodies work. Differences in people's genes can help explain why some people get a disease while others do not. For this study, only genes related to HIV, the immune system, and the effects of VRC01 will be tested. The results of these tests are for research purposes only and will not be given to the study staff or to you.

14. We may take your baby off the study early.

Babies are expected to stay in the study for about 1 year. However, we may take your baby off the study if:

- The study is stopped for any reason.
- We determine that your baby cannot meet the study requirements (for example, if you move away and cannot come to the clinic).
- We determine that staying in the study might harm your baby.

15. Please tell us if you wish to take your baby off the study.

You are free to take your baby off the study at any time for any reason. The care that your baby receives at this clinic will not be affected, but it is important that we know your decision. We will ask you to bring your baby to the clinic for one last visit. At this visit we will:

- Ask about your (the baby's mother's) and your baby's ARVs.
- Ask about your baby's health and other medicines.
- Ask about how you are feeding your baby.
- Give your baby a physical examination.
- Draw your baby's blood (about 15 mL or 3 teaspoons) for tests. The tests will check:
  - The baby's blood cells
  - The baby's CD4 and CD8 cells
  - The baby's HIV viral load
  - The effects of VRC01

If your baby has been in the study for less than six months, we will also collect urine for tests to check his or her kidneys.

We will answer any questions you may have and tell you how to contact us in the future, if you wish.

Risks of the study

16. There is little risk from the study procedures.

Most procedures done in this study are routine medical procedures, with little risk to your baby. Drawing blood can cause pain, swelling, bruising, or bleeding where the needle is inserted. Rarely, drawing blood can cause fainting or infection.

17. VRC01 is experimental.

This means we do not know if VRC01 is safe to use in people. We also do not know if VRC01 is useful as a treatment for HIV. VRC01 is being tested in research studies to learn more about it, and this study will help us learn about VRC01 in babies who have HIV.

VRC01 will be given as an injection in the skin. This kind of injection can cause stinging, itchiness, discomfort, pain, soreness, redness, bruising, swelling, or a small cut where the needle enters the skin. Rarely, this kind of injection can cause infection.

As of January 2017, more than 800 HIV-negative and HIV-positive adults have received VRC01 in research studies in the United States, Botswana, Malawi, South Africa, Zimbabwe, and other countries. Some people had mild or moderate reactions like itchiness, redness, or swelling where VRC01 was injected. Some people felt tired or had mild body discomfort, muscle or joint pain, headache, chills, or nausea after receiving injections. Some people had hives while VRC01 was being given or soon after VRC01 was given. In some cases, the hives were severe. One person had chest discomfort and one fainted. Some people had abnormal results on tests of their blood cells, liver, or kidneys. These came back to normal after a few days or weeks.

As of January 2017, 40 babies born to mothers who have HIV have received VRC01 in a research study being done by the IMPAACT network in the United States, South Africa, and Zimbabwe. Most of these babies had redness, swelling, or a small bruise where VRC01 was injected, which lasted for a short time. No other effects thought to be caused by VRC01 have been seen, and no serious health problems have occurred.

It is possible that babies who receive VRC01 in this study could develop "resistance" to VRC01 or other antibodies like VRC01. If resistance develops, the antibodies may not be effective in helping to control the baby's HIV. In this study, the risk of resistance is minimized by giving VRC01 with ARVs.

18. Other antibodies have caused other side effects.

Other antibodies that are different from VRC01 have been given to people for other illnesses. With those antibodies, most side effects happen within the first 24 hours including fever, chills, shaking, nausea, vomiting, pain, headache, dizziness, trouble breathing, high or low blood pressure, itchiness, rash, hives, lip or face swelling, diarrhea, racing heartbeat or chest pain. Rarely, some antibodies have caused serious reactions that may be life-threatening.

One type of serious reaction may occur soon after getting an antibody. It includes difficulty breathing possibly leading to low blood oxygen, low blood pressure, hives or rash, and swelling in the mouth and face. A second type of serious reaction may occur several days to 3 weeks after getting an antibody. It includes hives or a rash, fever, big lymph nodes, muscle and joint pains, kidney problems, chest discomfort and shortness of breath. Rarely, antibodies used to treat other diseases have been linked to a blood disorder that interferes with blood clotting, cancer, damage to the heart muscle, and to the body's immune system attacking healthy cells.

These rare side effects and reactions have not been seen in other studies of VRC01. However, it is possible that babies in this study could have these types of reactions. Babies could also have other side effects or reactions that we do not yet know about.

We will closely check on babies in this study for side effects and reactions. Please contact the study staff if any of these problems or any other problems occur.

19. There could be risks of disclosure of your baby's information.

We will make every effort to keep your baby's information private and confidential. Study records and specimens will be kept in secure locations. All specimens and most records will be labeled only with a code number. However, your baby's name will be written on some records. Despite our best efforts to keep your baby's information private, it is possible that your baby's information, including information about your baby's genes, could be obtained by someone who should not have it. If this were to happen, your baby could be treated badly or unfairly.

[Sites may modify this paragraph if IRBs/ECs mandate a separate form for obtaining informed consent for photographs.] If we take photos of any reactions to VRC01, we will not photograph your baby's face. Photos will be labeled only with a code number (not with your or your baby's name). Photos will be kept securely with other information collected for the study. Photos also may be shared with other doctors working on the study. The other doctors may be here at *[site name]* or in other countries. These doctors will not be given your or your baby's name, and they will be required to keep the photos private and confidential. When the study is completed, the photos will be destroyed.

[*US sites, insert:* To help us protect your privacy, we have obtained a Certificate of Confidentiality that protects us from being forced to release information that may identify your baby, such as by the courts or police. The certificate cannot be used in all situations, but it can be used to resist demands for information that would identify your baby. The certificate does not protect against requests for information from the US federal government or from the US Food and Drug Administration. Regardless of the certificate, you can release information about your baby's participation in the study to others, if you wish.]

Benefits of the study

20. There may be no benefit from being in the study.

By joining the study, your baby will be part of the search for new treatments for babies who have HIV. However, being in the study may not benefit your baby in any way.

Your baby will have regular visits here and frequent checks on his or her health. It is possible that the examinations and tests done in the study may help your baby stay healthy. If these procedures show that your baby may need medical care that cannot be provided through the study, we will tell you where you can go for the care your baby needs.

Other information about the study

21. There are no costs to you or your baby.

There are no costs to you or your baby for the study visits, injections, or procedures.

[*Insert information about compensation/reimbursement here*, e.g., You will be reimbursed for the cost of transport to study visits. For each visit, you will be given (specify amount).]

22. Your baby's study records may be reviewed by study staff and groups that oversee the study.

Groups that oversee the study include:

- [i*nsert name of site IRBs/ECs*]
- [i*nsert name of site drug regulatory authority*]
- [i*nsert name of other site drug entities that may review records*]
- The United States National Institutes of Health and its study monitors
- The United States Food and Drug Administration
- The United States Office for Human Research Protections
- The IMPAACT Network that is coordinating the study
- Other US, local, and international regulatory entities

The study staff and these groups are required to make every effort to keep study records private and confidential. Your baby's study information may be disclosed to other authorities if required by law. The results of the study may be presented publicly or published. However, no presentation or publication will use your baby's name or identify your baby personally.

A description of this study will be available on www.ClinicalTrials.gov as required by United States Law. This website will not include any information that can identify your baby. At most, the website will include a summary of the results of the study. You can search this website at any time.

23. If your baby gets sick or injured, contact us right away.

Your baby's health is important to us. We will make every effort to minimize risks and protect your baby's well-being. It is possible, however, that your baby could have an illness or injury that is study-related. This means that the illness or injury occurred as a direct result of the study injections or other study procedures.

[Sites may modify this paragraph to reflect local institutional policies; information regarding coverage available through clinical trial insurance obtained by the site should be included if applicable; the statement regarding no program for compensation through the NIH may not be removed.] If a study-related illness or injury occurs, we will treat your baby or tell you where you can you can get the treatment your baby needs. The cost for this treatment may be charged to you or your health insurance. There is no program to pay money or give other forms of compensation for study-related illness or injury through [site name or] the United States National Institutes of Health.

Who to contact

24. If you have questions, concerns, or problems at any time, use these contacts.

- If you have questions about the study:
  [*insert name and telephone number of investigator or other study staff*].

- If you have questions about your baby's rights as a research participant or concerns about how your baby is being treated in the study:
  [*insert name and telephone number of IRB contact person or other appropriate person/organization*].

- If your baby has health or other problems that may be related to study participation:
  [*insert name and telephone number of investigator or other study staff*].

- If you want to take your baby off the study:
  [*insert name and telephone number of investigator or other study staff*].

Signatures

25. If you decide to have your baby join this study, please sign or make your mark below.

Before deciding whether to have your baby join this study, make sure you have read this form, or had it read to you, and that all of your questions have been answered. You should feel that you understand the study, its risks and benefits, and what is expected if you decide to have your baby join.

We will tell you any new information from this study or other studies that may affect your willingness to keep your baby in the study. You can ask questions or request more information at any time.

You do not give up any rights by signing this form.

[Insert initial and signature blocks as required by site IRB/EC policies. Separate consent decisions must be documented for storage of residual CSF and for genetic testing].

Please write your initials or make your mark next to your choices:

_____ I agree to have my baby join this study

For storage of leftover spinal fluid:

_____ I agree to storage of leftover spinal fluid (if my baby has a lumbar puncture outside of the study)

_____ I do not agree to storage of leftover spinal fluid (if my baby has a lumbar puncture outside of the study)

For genetic testing:

_____ I agree to testing of my baby's genes related to HIV, VRC01, and the immune system

_____ I do not agree to testing of my baby's genes

Name of Infant (print)		
Name of Mother (or Legal Guardian; print)	Signature of Mother (or Legal Guardian)	Date
Name of Witness (if applicable; print)	Signature of Witness	Date
Name of Study Staff Conducting Consent Process (print)	Signature of Study Staff	Date