Appendix G.

Research Participation Informed Consent
HIV POSITIVE CHILDREN- EXALT PHARMACOKINETIC STUDY

Protocol Title:	EXALT trial: Extended duration artemether-lumefantrine treatment for malaria in children
Funding Source:	National Institute of Child Health and Human Development (NICHD)
UCSF-CHR Number:	
SOMREC Number:	
Yale HIC Number:	
Sites of Research:	Tororo District Hospital, Tororo, Uganda; Masafu General Hospital, Busia, Uganda
Principal Investigators:	Francesca Aweeka, Pharm.D. Sunil Parikh, M.D., M.P.H. Norah Mwebaza, MBChB, DPPM, PhD.
Version/Date:	2.0, August 11th, 2017

INTRODUCTION:
You are being asked to allow your child to participate in this research study because your child is suffering from malaria. This research study is being done by Makerere University, University of California, San Francisco, and Yale University, and is sponsored by the U.S National Institute of Child Health and Human Development (NICHD). While your child is in the study, your child will receive standard of care medical treatment for malaria and receive the antimalarial medication, artemether–lumefantrine (*Coartem*®). This drug will be provided by the study and would be one of the treatments preferred for your child whether your child is in the study or not. *Coartem*® has been recommended by the Uganda Ministry of Health and is currently used for treatment of uncomplicated malaria.

This is a consent form. It gives information about this study. The study staff is available to talk more about the study. You can ask questions about this study at any time. If you agree to allow your sick child to participate, we will ask you to sign the consent form. You will get a copy of this form to keep. Participation in this study is voluntary.

Before you decide if you want your child to participate in this study, we want you to know as much as possible about the study. This consent form will explain the purpose of this study, how the study will be done, any risks and benefits to your child and what is expected of you and your child.

WHY IS THIS STUDY BEING DONE?
Malaria is a common disease in Tororo and Busia District. Studies by our group in Tororo and by other groups show that HIV-infected children taking the antiretroviral medicine efavirenz have much lower levels of the antimalarial drug, Coartem, in their blood. The information gained by this study can help us determine if those children are

receiving the best dose possible of their malaria medication by comparing the level of the antimalarial drug after 6 doses (over 3 days) or 10 doses (over 5 days).

Also, we want to know the best dose of malaria medication for children:

- To reduce the chance for new episodes of malaria.
- That does not increase the chance for side effects
- And hopefully, will reduce the risk that malaria parasites become resistant to the medicine

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY AND HOW LONG WILL THE STUDY LAST?

This study will take place at either the Tororo District Hospital or Masafu General Hospital. We want to study 160 HIV-infected children between the ages of 3 years and 10 years of age, although we expect this number to be much lower since many children should be studied for more than one episode of malaria.

Each participant will be in this study for 42 days for each episode of uncomplicated *falciparum* malaria. Through participation, this study will provide care for each child's malaria. For this study, children can participate in the study for up to a maximum of 4 episodes of malaria.

WHO CAN PARTICIPATE IN THIS STUDY?
We plan to study HIV-infected children with confirmed uncomplicated *falciparum* malaria; living within 60 km of the study clinic; who can come to clinic for all follow-up procedures for one or more episodes of malaria.

WHAT WILL HAPPEN IF I AGREE TO HAVE MY CHILD PARTICIPATE IN THE STUDY?

Please note that your child's HIV care will continue through your child's regular medical clinic and he or she will receive anti-HIV drugs through this clinic. However, we will keep a supply of antiretroviral drugs at our clinic in case of emergencies. We ask that your child continues to take his/her antiretroviral medications as usual, but that you record the time of taking the medication in a log book that will be given to you at the time of joining the study.

1) First visit (today, the total time needed for is approximately 2 hours)

Screening

If your child has symptoms such as a fever, your child will be tested immediately to see if he or she has malaria. This testing will be done either by the study doctors or by a doctor at one of the other medical clinics located in Tororo or Busia, including the Tororo District Hospital, Masafu General Hospital, or nearby referral clinics. If your child does have malaria, your child will receive treatment for malaria immediately with artemether-lumefantrine. Again, this treatment is a preferred treatment for malaria in Uganda.

If your child does have malaria and you are willing to have your child participate in this study, the following procedures will take place:

- We will read this consent form to you to explain the study. If you remain interested in having your child in the study, we will ask that you sign the consent form today to agree to have your child participate in the study. To help you decide, you may talk to people you know. In any case, your child will receive the treatment needed to treat your child's malaria.

If you have agreed and consented to have your child in the study, we will perform the following additional screening procedures to determine if your child is eligible to participate in the study.

- **Physical exam and medical history**: If you agree to have your child participate and sign the consent form, the study doctors will perform a physical examination of your child and ask you about his or her medical history.

- **Blood drawing**: Screening will also entail a drop of blood for testing of your child's hemoglobin, to see if he/she is anemic

Enrollment

If your child meets the criteria to participate in the study, the following will be done on the same initial visit

- **Blood drawing**: Tests will be done to determine your child's blood count and liver function. We will also test to determine the type and amount of malaria parasite your child is infected with. We will test to see if there is any antimalarial medication in your child's blood that may remain from the last time your child was treated with malaria.

    - The total amount of blood collected on this first day will not exceed 1 or 2 teaspoonful which will be collected by a small needle stick in one of your child's arm veins.
    - During this and subsequent blood draws, if samples can not be obtained through a needle in the vein, your child may have blood drawn through a fingerprick to obtain the necessary sample.

- If the study doctor confirms your child's participation, your child will receive a study number and study card today. At this time your child will begin his or her malaria treatment.

- Your child will receive only brand name *Coartem*® (artemether-lumefantrine made by Novartis Pharmaceuticals), so that we can make sure all children participating in this study are receiving the same formulation of the drug.

- If your child does not yet have a long-lasting insecticide treated bed net, the study will provide this as part of a basic care package.

2) Placement into one of two study arms.

Our study has two different blood draw strategies AND two different drug regimen durations that will be followed for each episode of malaria. They are summarized here:

Blood Drawing Schedules:

1. "Intensive" schedule of blood draws – during the intensive schedule, your child will have more frequent blood draws, particularly after the last dose of the antimalarial medication.

2. "Population" schedule of blood draws – during the population schedule, your child will have fewer blood draws, and more will be taken by the finger instead of placing a needle in the arm.

   Regimen durations:

   1) 3-day artemether-lumefantrine – this is the standard way that artemether-lumefantrine is given. It is usually given as 6 doses (one dose twice a day for 3 days).

   2) 5-day artemether-lumefantrine – this is the new extended regimen that we are studying. It will be given as 10 doses, (one dose twice a day for 5 days).

Your child will be assigned to one of these two regimen durations, either 3-day or 5-day regimens simply by chance (this is called by randomization). For the initial episode of malaria, your child will undergo the intensive schedule.

- If your child has another episode of malaria at a later time point, they will switch to the other regimen duration for that episode of malaria.

- If all study requirements are met, your child will undergo the intensive blood draws again for the 2nd episode of malaria. If intensive blood draws requirements are not met or you choose to not undergo the intensive blood draws again, you may decide to allow your child to undergo population blood draws

- Your child can then be enrolled later for a 3rd or even a 4th episode of malaria to complete both the intensive and population blood drawsfor both regimens. Your child can only be enrolled for a MAXIMUM of 4 episodes of malaria, 2 as intensive blood draws, and 2 as population blood draws.

- If we no longer require additional intensive blood draws participants, or your child meets population blood draws criteria, but not intensive criteria, you may be enrolled directly into the population blood draws study.

3) Schedule for the treatment of malaria in this study

Your child will receive therapy for malaria with *Coartem.*® It will be important that all doses of the drug be given with some food or whole milk. At the time your child enters the study, you will be provided with containers of whole milk or vouchers to purchase whole milk. Milk provides a certain amount of fat that can improve the absorption of *Coartem.*®

Your child will be provided a form of *Coartem*® that dissolves in water, called *Coartem*® *Dispersible.* You will be instructed on how to give this form of drug to your child. Each

tablet should be placed in approximately 2 teaspoonsful of water and the water should be stirred gently and given immediately to your child. The glass should then be rinsed with some more water which your child should drink so all the medicine is taken by your child. Each morning or daytime dose will be given to your child in the study clinic and each evening dose will be given by you to your child at home.

If your child vomits any malaria doses that are given at home, you will be given instructions as to whether or not your child should receive another dose. If your child misses a malaria dose for any other reason, you should give your child his or her dose as soon as you remember and then inform the study staff when you bring your child to the study clinic in the morning.

It is important for you to record the time of the day when your child receives his or her doses of malaria medication at home, so we will ask you to tell us the time you gave the doses to your child.

3-day *Coartem*® "Intensive" blood draws

If your child is receiving the six-dose regimen, this is the standard treatment duration and dosing for malaria. The time for when each of the 6 doses should be given to your child will be explained to you by the study doctor. The schedule for giving the doses is also provided in the table below.

Day of study	1st (Day 0)	2nd (Day1)	3rd (Day 2)	4th (Day 3)
When to give each dose	Morning or Afternoon Evening	Afternoon	Morning Evening	Morning
# Doses per Day	2	1	2	1

3-day *Coartem*® "Population" blood draws

If your child is receiving the six-dose regimen, this is the standard treatment duration and dosing for malaria. The time for when each of the 6 doses should be given to your child will be explained to you by the study doctor. The schedule for giving the doses is also provided in the table below.

Day of study	1st (Day 0)	2nd (Day1)	3rd (Day 2)
When to give each dose	Morning or Afternoon Evening	Morning Evening	Morning Evening
# Doses per Day	2	2	2

5-day *Coartem*® "Intensive" blood draws

If your child is receiving the ten-dose regimen, this is the extended treatment duration and dosing for malaria. The time for when each of the 10 doses should be given to your child will be explained to you by the study doctor. The schedule for giving the doses is also provided in the table below.

Day of study	1st (Day 0)	2nd (Day1)	3rd (Day 2)	4th (Day 3)	3rd (Day 4)	4th (Day 5)
When to give	Morning/	Afternoon	Morning	Morning	Morning	Morning

each dose	Afternoon Evening		Evening	Evening	Evening	
# Doses per Day	2	1	2	2	2	1

5-day *Coartem*® "Population" blood draws

If your child is receiving the ten-dose regimen, this is the extended treatment duration and dosing for malaria. The time for when each of the 10 doses should be given to your child will be explained to you by the study doctor. The schedule for giving the doses is also provided in the table below.

Day of study	1st (Day 0)	2nd (Day1)	3rd (Day 2)	4th (Day 3)	3rd (Day 4)
When to give each dose	Morning/ Afternoon Evening	Morning Evening	Morning Evening	Morning Evening	Morning Evening
# Doses per Day	2	2	2	2	2

4) Overview of Study Follow up

Your child will be seen in the study clinic several times during the 42 days for the study. The procedures for evaluating your child for any given day may either be the same or different depending on the study day and which study blood draws or regimen your child is currently enrolled in. You will be provided with a study card and a reminder for all visits.

If you do not bring your child to a scheduled visit for treatment of malaria, a health worker will visit you at your home. The health worker will bring you and your child to the study clinic.

The study clinic follow-up visits needed for this study are for the following reasons:

- Morning doses of *Coartem*® will be given in the study clinic for your child's malaria on study days 0, 1, 2 and 3 (4 and 5 as well, if your child is on the 10-dose regimen).

- Clinical and safety evaluation, and blood draws: Your child will be evaluated by a study doctor to see how she or he is doing on a total of 11 to 13 follow-up days in clinic. The precise schedule of follow-up will be explained by your doctor or nurse. Blood tests to measure the safety of the medication will be drawn by venipuncture on 2 of those days, just as this was done at the beginning of the study. In addition, blood tests to measure the amount of antimalarial medication in the blood will be drawn on 8-10 of those follow-up days.

- Your child may undergo additional finger prick samples in the evenings following each dose for the measurement of parasite levels.

- The total amount of blood drawn from your child over the entire 42 days will be no more than 5 to 6 teaspoons.

5) PK Blood Draws

- After each dose administered in the clinic during the day (study days 0,1 and 2 for the 3-day regimen or study days 0,1,2,3 and 4 for the 5-day regimen, two samples by finger prick will be drawn 2 and 4 hours after each dose (each sample is no more than 1/20th of a teaspoonful)

- Depending on the regimen duration or blood draw schedule, you and your child will return to the study clinic on 6 more days (day 4 or 6, 7 or 8, 14, 21, 28, 35, and 42) for more clinical and safety tests, and a small needle stick on your child's arm veins or fingerprick blood draws.

6) INTENSIVE PK STUDY ONLY: Specific Blood draw Schedule on the last day of drug treatment (following the 6th Dose or 10th dose (last dose) of *Coartem*®) Today the total time needed for this visit and the following morning is approximately 8 hours). Intensive blood draws around the last dose will not occur for the population PK studies.

- On the last day of drug treatment, your child will receive the 6th or 10th dose of *Coartem*® in the clinic. Before taking this morning dose, a small tube or catheter will be placed in an arm vein of your child so that your child does not have multiple pricks with a needle. This catheter will remain in your child's arm for the duration of blood blood draws on day 3 or 5, depending on which regimen your child is taking. This will allow us to only have to perform a single venipuncture on that day.

- The first blood sample will be collected just before your child receives the last dose of *Coartem*®*,* and your child will have 7 more small blood samples collected over the next 8 hours. Each time we collect blood, it will be a very small amount, approximately 1/10th of a teaspoonful. At approximately 2 points during these collections, we will also collect a very small amount by a finger prick (less than 1/20th of a teaspoonful). Thus, the total amount of blood taken on day 3 or 5 will be under one teaspoonful.

- You and your child will remain for this 8-hour period in a special room set up especially for this study that is located within the clinic. The room will be set up so that you and your child will be comfortable. There will be some toys for your child to play with and you and your child will be able to rest if you would like.

- After the 8-hour blood draw, the small tube that is placed in your child's arm will be removed by the study doctor. You and your child will be discharged from the study clinic so that you can return to your home.

7) Unscheduled Contact Visit

If your child becomes sick during the day while in the study, please bring your child to the study clinic. There will be someone at the study clinic every day from 8 am to 5 pm.

The clinic is open on weekends and holidays. If your child has a repeat malaria infection during the 42-day follow-up we will ask to collect an additional blood sample to measure how much malaria medication is in his or her blood (1/8th teaspoon).

If your child becomes sick after 5 pm, please bring him or her to the Tororo District or Masafu General Hospital. Please tell the staff you are part of this study and show them the card that tells them you are part of this study.

If your child became ill after clinic hours, please plan to bring your child to the study clinic on the following day. If your child becomes sick with malaria when the clinic is not open, your child will receive treatment for his or her malaria from a hospital supply at the Tororo District or Masafu General Hospital.

If your child is diagnosed with severe malaria during any time she or he is enrolled in the study, treatment will be given in the hospital using another malaria medication called quinine or artesunate. Quinine and artesunate are effective and approved for treating complicated malaria in Uganda. The length of your child's stay in the hospital will be decided by the Tororo District or Masafu General Hospital staff managing your child's illness.

If your child does not have malaria, the study doctors may refer your child to their usual medical clinic to receive the necessary care.

HOW LONG WILL MY CHILD BE IN THE STUDY?

We are asking you to let your child participate in this study for 42 consecutive days during and following treatment for each malaria episode or until you or the study doctors decide your child should stop being in the study. In the case that your child gets malaria again during the course of follow-up, your child will be eligible to be re-enrolled in the study for blood draws and follow-up as described above. Your child will only be enrolled in the study for a maximum of 4 episodes of malaria.

WHY WOULD MY CHILD BE WITHDRAWN FROM THE STUDY EARLY?

You may decide to stop your child from being in the study at any time and for any reason. For your child's safety and health, study doctors might decide he or she should stop being in the study.

Your study doctors may also take your child out of the study. These are the possible reasons:

1. If you are unable to bring your child to the scheduled study visits.
2. If your child misses the correct times for the doses of malaria medication. (In any case, your child must complete the course of treatment)
3. Any dosing of malaria medications or other medications outside study procedures.
4. Your child develops complicated malaria and requires treatment with quinine or artesunate in the hospital.
5. If the study doctors think the study is no longer good for your child
6. Stopping or missing anti-HIV medications while participating in this study
7. If you withdraw your consent to have your child stay in this study

8. The study is cancelled by the UCSF, Yale University, Uganda National Council of Science and Technology (UNCST) or Makerere University ethics committees, Ugandan Ministry of Health, the U.S. National Institute of Child Health and Human Development (NICHD), or by the U.S. Office for Human Research Protections (OHRP).

If we are unable to locate you during follow-up or you decide to withdraw from the study, follow-up will end. However, In the event that your child stops the study early, they would be eligible to reenroll in the study during a later episode of malaria. We will also make an effort to follow your child to at least 7 days after beginning treatment for malaria.

CAN I DECIDE TO STOP MY CHILD'S PARTICIPATION IN THE STUDY?

Yes. You can decide to stop at any time. Tell the study doctor or nurse if you are thinking about stopping or deciding to stop. He or she will tell you how to stop your child's participation safely. It is important that you tell the study doctor if you are thinking about stopping so that your doctor can evaluate any risks and discuss what alternative follow-up care and testing could be most helpful to your child.

WHAT WILL HAPPEN IF I OR MY CHILD'S STUDY DOCTORS DECIDE TO TAKE MY CHILD OFF STUDY?

If either the study doctors take your child off study or if you decide to stop his or her participation, your child may still get health care at the Tororo District or Masafu General Hospital or his or her regular clinic. If your child stops participating in the study for any reason, the study doctors will ask to examine your child and draw a small amount of blood (less than 1 teaspoon) for laboratory tests for the safety of your child. You have the right to not agree to the examination and tests. If your child leaves the study before finishing, if funds are available we will give your child medical care for any problems that began during the study. Your child may be taken out of the study because of a serious health problem. If the study doctors think the health problem is probably related to study treatment, they will arrange for needed follow-up tests.

WHAT SIDE EFFECTS OR RISKS CAN I EXPECT MY CHILD TO HAVE FROM BEING IN THE STUDY?

1) **Non-Study Medications and Other Clinical Studies**: There may be a risk of serious side effects when non-study medications are taken with study drugs. You must tell your doctor or study nurse about all other medicines and herbs that your child is taking before your child starts the study. You must tell the study doctor or nurse before taking any non-study therapies while your child is in the study. You must also tell your study nurse and doctor if you join any other research studies.

2) **Risks of *Coartem*®:** Coartem® is standard of care for treating malaria in Uganda and is commonly used to treat the type of malaria your child has. A standard regimen is 6 tablets (one tablet given twice a day for 3 days). We are also studying a 10-tablet regimen (one tablet twice a day for 5 days). Both regimens may cause rare side effects such as lowering of blood counts and swelling of the liver. These happen less than 1 out of 100 times the drug is used. Other side effects happen up to 1 out of 10 times the drug is used. Some of these are sleep problems, headache, dizziness, a

feeling of a rapid or irregular heartbeat, diarrhea, vomiting, pain in the abdomen, rash, itching, cough, muscle and joint aches, and fatigue. Based on our experience with Coartem®, we do not expect there to be more side effects with the 5-day regimen than with the 3-day regimen. We will be following your child closely during the course of follow-up for any side effects.

3) **Blood drawing (venipuncture, finger or heel prick) risks**: Drawing blood may cause temporary discomfort from the needle stick, bruising, fainting, and infection. The amount of blood removed will be too small to affect your child's health.

4) **Unknown Risks**: There is always the possibility of side effects that no one knows about yet. The study doctors will let you know if they learn anything that might make you change your mind about your child participating in the study.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

There are minimal direct benefits to your child for taking part in this study. Your child will receive close clinical care over 42 days for the treatment of malaria and other illnesses that may occur during this time. The information we get from this study might help Uganda and other countries to decide whether the extended 5-day/ 10 dose of artemether-lumefantrine (Coartem®) is both safe and effective for the treatment of malaria in those infected with HIV and on efavirenz.

WHAT OTHER CHOICES DO I HAVE IF MY CHILD DOES NOT TAKE PART IN THIS STUDY?

You are free to decide whether or not you want your child in this study. If you decide you do not want your child in the study or decide to stop your child from being in the study at any time and for any reason, this will not affect your child's care at Tororo District or Masafu General Hospital or any referral clinics, and they will still be able to receive care for their malaria at these locations. All of the study procedures and study medicines are available outside this study. If you decide not to take part, your child could still get medical care and could still get any of these medicines if your doctor thought they were needed. Currently, *Coartem*® is provided free at government clinics and hospitals and drugs for treating HIV are provided for free at Tororo District or Masafu General Hospital and referral clinics.

WILL MY CHILD'S MEDICAL INFORMATION BE KEPT PRIVATE?

Other people may learn that your child is part of this study because you will get medical care at the study clinic. Other people may think that your child has HIV because they see you in the study clinic more often than usual due to your child's participation in this study. However, we will not allow people who are not working for the study to see any medical information about your child. Medical information about malaria and HIV will be collected on your child, but only the people working on the study will see it. These study staff will not be allowed to discuss your child's medical information outside of the study clinic. Only study staff will be able to link your child's medical records and personal study number. The universities and research organizations running this study or making sure that the research is done properly are not allowed to let others know the identity of the people in the study. These organizations include the NIH/NICHD, U.S. Office for Human Research Protections, Committees for Human Research of the University of California,

San Francisco, Yale University, the Makerere University Faculty of Medicine Research Ethics Committee (FOM-REC), and the Uganda National Council on Science and Technology. The medical records for the study will be kept in a locked office and will only be able to be seen by study staff. Your name or your child's name will not be written in any reports based on this research.

WHAT ARE THE COSTS OF TAKING PART IN THIS STUDY?

There will be no cost for you or your child to take part in this study. We will pay for the cost of all tests or drugs prescribed by our doctors that you may have to purchase outside the clinic. Payment for visits outside the study clinic or Tororo District or Masafu General Hospital will only be possible if we have enough funds.

WILL I BE PAID FOR TAKING PART IN THIS STUDY?

You or your child will not be paid for participation in the study. We will be giving you money for transport to and from your home to the study clinic for all study visits and visits needed if your child is sick. On certain days, participants will have to be in the clinic for several hours. On those days, we will provide food and drink to participants (breakfast, dinner, and/or snacks) to ensure their well-being. If you agree for your child to be in this study, your child will be given a long-lasting insecticide - treated bed net.

WHAT HAPPENS IF MY CHILD IS INJURED BECAUSE HE OR SHE TOOK PART IN THIS STUDY?

If your child is injured or becomes ill, please contact the doctors at the study clinic. If you have questions about injuries as a result of being in the study, contact the doctors at the study clinic. You can get health care services at Tororo District or Masafu General Hospital in case of such injuries. If funds provided by the study investigators to carry out this research project are available, you will not have to pay for care for study-related injuries.

WHAT ARE MY CHILD'S RIGHTS IF HE OR SHE TAKES PART IN THIS STUDY?

You are free to decide whether or not you want your child in this study. You have the right to stop your child's participation in the study at any time without penalty or loss of benefits to which you are otherwise entitled. We will tell you about new information or changes in the study that may affect your child's health or your willingness to have your child continue in the study.

WHO CAN ANSWER MY QUESTIONS ABOUT THE STUDY?

Drs. Mwebaza, Aweeka, and Parikh, and their staff can answer questions you have about the study. You may call Dr Norah Mwebaza at 0782589889 or 0758743264 or Dr. Richard Kajubi at 0776211591. If your child has been injured or becomes ill, please contact the doctors at the study clinic at 0454448840. You may also contact Dr. Ponsiano Ocama (+256-414-530555/0701283388) at the Makerere University Faculty of Medicine - Research and Ethics Committee which approved this study for questions about participants' rights and research-related harm.

HOW WILL MY BLOOD SAMPLES BE USED AFTER THE STUDY IS COMPLETED?

We would like to keep some of these samples that are left over for future research. If you agree, these samples will be kept and may be used in research to learn more about malaria. Your child's samples may be helpful for research, and is not designed specifically to help your child. It might help people who have malaria in the future. Reports about research done with your child's samples will not be given to you and will not be put in your health record. The research will not influence your child's care.

The choice to let us keep the left-over samples for future research is up to you. No matter what you decide to do, it will not affect your child's care. If you decide now that your child's samples can be kept for research, you can change your mind at any time. Just contact us and let us know that you do not want us to use your samples. Then any samples that remains will no longer be used for research.

Your child's samples will be used only for research and will not be sold. The research done with your samples may help to develop new or improved treatments for malaria in the future.

Making Your Choice

Please read each sentence below and think about your choice. After reading each sentence, put your initials in the appropriate box. If you have any questions, please talk to your doctor or nurse, or call our research review board at IRB's phone number.
No matter what you decide to do, it will not affect your care.

☐ I give my permission for my child's or my blood to be used for future research on Malaria

☐I do not give my permission for my child's or my blood to be used for future research on Malaria

You may call Dr Norah Mwebaza at 0782589889 or 0758743264 or Dr. Richard Kajubi at 0776211591 if you decide you would no longer like to have your child's samples stored for future usage.

CONSENT: WHAT YOUR SIGNATURE OR THUMBPRINT MEANS

PARTICIPATION IN RESEARCH IS VOLUNTARY. You have the right to decline to allow your child to participate or to withdraw your child at any point in this study without penalty or loss of benefits to which your child is otherwise entitled. A copy of this consent form will be given to you. Your signature or thumbprint below means that you have had this study explained to you. Your signature or thumbprint below means you have had the opportunity to ask questions and get answers. If you wish your child to participate in this study, you should sign or place your thumbprint below.

Name of Parent or Guardian (printed)

Signature or Thumbprint * of Parent or Guardian Date

Name of Study Staff Administering Consent (printed) Position/Title

Signature of Study Staff Administering Consent Date

Name of Translator (if necessary)

Signature of Translator Date

*If the parent or guardian is unable to read and/or write, an impartial witness must be present during the consent discussion. After the written informed consent form is read and explained to the parent or guardian, and after he or she has orally consented to his or her child's participation in this study, and has either signed the consent form or provided his or her fingerprint, the witness must sign and personally date the consent form. By signing the consent form, the witness attests that the information in the consent form and any other written information was accurately explained to, and apparently understood by, the parent or guardian, and that consent was freely given.

Name of Person Witnessing Consent (printed)

Signature of Person Witnessing Consent Date

Name of Participant (printed)

Name of Study Staff Administering Consent (printed) Position/Title

Signature of Study Staff Administering Consent Date

Name of Translator (if necessary)

Signature of Translator Date

*If the participant is unable to read and/or write, an impartial witness must be present during the informed consent discussion. After the written informed consent form is read and explained to the participant, after oral consent to the participation in the trial, and after the participant has signed the consent form or provided her fingerprint, the witness should sign and personally date the consent form. By signing the consent form, the witness attests that the information in the consent form and any other written information was accurately explained to, and apparently understood by, the participant and that informed consent was freely given.

Name of Person Witnessing Consent (printed)

Signature of Person Witnessing Consent Date

Appendix H.

Research Participation Informed Consent
HIV NEGATIVE CHILDREN- EXALT PHARMACOKINETIC STUDY

Protocol Title:	EXALT trial: Extended duration artemether-lumefantrine treatment for malaria in children
Funding Source:	National Institute of Child Health and Human Development (NICHD)
UCSF-CHR Number:	
SOMREC Number:	
Yale HIC Number:	
Sites of Research:	Tororo District Hospital, Tororo, Uganda; Masafu General Hospital, Busia, Uganda
Principal Investigators:	Francesca Aweeka, Pharm.D. Sunil Parikh, M.D., M.P.H. Norah Mwebaza, MBChB, DPPM, PhD.
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INTRODUCTION:
You are being asked to allow your child to participate in this research study because your child is suffering from malaria. This research study is being done by Makerere University, University of California, San Francisco, and Yale University, and is sponsored by the U.S National Institute of Child Health and Human Development (NICHD). While your child is in the study, your child will receive standard of care medical treatment for malaria and receive the antimalarial medication, artemether–lumefantrine (*Coartem*®). This drug will be provided by the study and would be one of the treatments preferred for your child whether your child is in the study or not. *Coartem*® has been recommended by the Uganda Ministry of Health and is currently used for treatment of uncomplicated malaria.

This is a consent form. It gives information about this study. The study staff is available to talk more about the study. You can ask questions about this study at any time. If you agree to allow your sick child to participate, we will ask you to sign the consent form. You will get a copy of this form to keep. Participation in this study is voluntary.

Before you decide if you want your child to participate in this study, we want you to know as much as possible about the study. This consent form will explain the purpose of this study, how the study will be done, any risks and benefits to your child and what is expected of you and your child.

WHY IS THIS STUDY BEING DONE?
Malaria is a common disease in Tororo and Busia District. Studies by our group in Tororo and by other groups show that children have differences compared to adults in how their bodies handle antimalarial medications. Studies also show that the drugs used to treat malaria are not working as well as they have in the past. The information gained

by this study can help us determine if children are receiving the best dose possible of their malaria medication.

This study will also help us determine if the preferred drug used for malaria treatment is most effective if given for 3 days or 5 days. This information will help us determine if children are receiving the best regimen possible for their malaria medication.

Also, we want to know the best dose of malaria medication for children:

- To reduce the chance for new episodes of malaria.
- That does not increase the chance for side effects
- And hopefully, will reduce the risk of malaria parasites becoming resistant to the medicine

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY AND HOW LONG WILL THE STUDY LAST?

This study will take place at either the Tororo District Hospital or Masafu General Hospital. We want to study up to 220 HIV-uninfected children between the ages of 6 months and 10 years of age, although we expect this number to be much lower since many children should be studied for more than one episode of malaria.

Each participant will be in this study for 42 days for each episode of uncomplicated *falciparum* malaria. Through participation, this study will provide care for each child's malaria. For this study, children can participate in the study for up to a maximum of 4 episodes of malaria.

WHO CAN PARTICIPATE IN THIS STUDY?
We plan to study children with confirmed uncomplicated *falciparum* malaria; living within 60 km of the study clinic; who can come to clinic for all follow-up procedures for one or more episodes of malaria.

WHAT WILL HAPPEN IF I AGREE TO HAVE MY CHILD PARTICIPATE IN THE STUDY?

7) First visit (today, the total time needed for is approximately 2 hours)

<u>Screening</u>

If your child has symptoms such as a fever, your child will be tested immediately to see if he or she has malaria. This testing will be done either by the study doctors or by a doctor at one of the other medical clinics located in Tororo or Busia, including the Tororo District Hospital, Masafu General Hospital, or nearby referral clinics. If your child does have malaria, your child will receive treatment for malaria immediately with artemether-lumefantrine. Again, this treatment is a preferred treatment for malaria in Uganda.

If your child does have malaria and you are willing to have your child participate in this study, the following procedures will take place:

- We will read this consent form to you to explain the study. If you remain interested in having your child in the study, we will ask that you sign the consent form today to agree to have your child participate in the study. To help you decide, you may talk to people you know. In any case, your child will receive the treatment needed to treat your child's malaria.

If you have agreed and consented to have your child in the study, we will perform the following additional screening procedures to determine if your child is eligible to participate in the study.

- **Physical exam and medical history**: If you agree to have your child participate and sign the consent form, the study doctors will perform a physical examination of your child and ask you about his or her medical history.

- **HIV testing:** You will be counseled and asked to agree to have your child tested for HIV. We need to know whether children are HIV-infected and which children are not infected to understand the results of the study.

    - If your child is tested and is positive for HIV infection and this is the first time you are learning that your child is positive, you will receive counseling about your child's HIV infection. This may also have implications for your HIV status and you will be encouraged to undergo testing too.

    - In addition, if your child is infected with HIV, your child will be referred to the necessary clinic to be evaluated for whether or not he or she should begin treatment with anti-HIV medications.

    - If your child is not infected with HIV, your child will be eligible to participate in the study for this episode of malaria, provided the other criteria for study entry are met.

- **Blood drawing**: Screening will also entail a drop of blood for testing of your child's hemoglobin, to see if he/she is anemic

Enrollment

If your child meets the criteria to participate in the study, the following will be done on the same initial visit

- **Blood drawing**: Tests will be done to determine your child's blood count and liver function. We will also test to determine the type and amount of malaria parasite your child is infected with. We will test to see if there is any antimalarial medication in your child's blood that may remain from the last time your child was treated with malaria.

    - The total amount of blood collected on this first day will not exceed 1 or 2 teaspoonful which will be collected by a small needle stick in one of your child's arm veins.

- During this and subsequent blood draws, if samples can not be obtained through a needle in the vein, your child may have blood drawn through a fingerprick to obtain the necessary sample.

- If the study doctor confirms your child's participation, your child will receive a study number and study card today. At this time your child will begin his or her malaria treatment.

- Your child will receive only brand name *Coartem*® (artemether-lumefantrine made by Novartis Pharmaceuticals), so that we can make sure all children participating in this study are receiving the same formulation of the drug.

- If your child does not yet have a long-lasting insecticide treated bed net, the study will provide this as part of a basic care package.

8) Placement into one of two study arms.

Our study has two different blood draw strategies AND two different drug regimen durations that will be followed for each episode of malaria. They are summarized here:

Blood Drawing Schedules:

3. "Intensive" schedule of blood draws – during the intensive schedule, your child will have more frequent blood draws, particularly after the last dose of the antimalarial medication.

4. "Population" schedule of blood draws – during the population schedule, your child will have fewer blood draws, and more will be taken by the finger instead of placing a needle in the arm.

Regimen durations:

3) 3-day artemether-lumefantrine – this is the standard way that artemether-lumefantrine is given. It is usually given as 6 doses (one dose twice a day for 3 days).

4) 5-day artemether-lumefantrine – this is the new extended regimen that we are studying. It will be given as 10 doses, (one dose twice a day for 5 days).

Your child will be assigned to one of these two regimen durations, either 3-day or 5-day regimens simply by chance (this is called by randomization). For the initial episode of malaria, your child will undergo the intensive schedule.

- If your child has another episode of malaria at a later time point, they will switch to the other regimen duration for that episode of malaria.

- If all study requirements are met, your child will undergo the intensive blood draws again for the 2nd episode of malaria. If intensive blood draws requirements are not met or you choose to not undergo the intensive blood draws again, you may decide to allow your child to undergo population blood draws.

- Your child can then be enrolled later for a 3rd or even a 4th episode of malaria to complete both the intensive and population blood draws for both regimens. Your child can only be enrolled for a MAXIMUM of 4 episodes of malaria, 2 as intensive blood draws, and 2 as population blood draws.

- If we no longer require additional intensive blood draws participants, or your child meets population blood draws criteria, but not intensive criteria, you may be enrolled directly into the population blood draws study.

9) Schedule for the treatment of malaria in this study

Your child will receive therapy for malaria with *Coartem.*® It will be important that all doses of the drug be given with some food or whole milk. At the time your child enters the study, you will be provided with containers of whole milk or vouchers to purchase whole milk. Milk provides a certain amount of fat that can improve the absorption of *Coartem.*®

Your child will be provided a form of *Coartem*® that dissolves in water, called *Coartem*® *Dispersible.* You will be instructed on how to give this form of drug to your child. Each tablet should be placed in approximately 2 teaspoonsful of water and the water should be stirred gently and given immediately to your child. The glass should then be rinsed with some more water which your child should drink so all the medicine is taken by your child. Each morning or daytime dose will be given to your child in the study clinic and each evening dose will be given by you to your child at home.

If your child vomits any malaria doses that are given at home, you will be given instructions as to whether or not your child should receive another dose. If your child misses a malaria dose for any other reason, you should give your child his or her dose as soon as you remember and then inform the study staff when you bring your child to the study clinic in the morning.

It is important for you to record the time of the day when your child receives his or her doses of malaria medication at home, so we will ask you to tell us the time you gave the doses to your child.

3-day *Coartem*® "Intensive" blood draws

If your child is receiving the six-dose regimen, this is the standard treatment duration and dosing for malaria. The time for when each of the 6 doses should be given to your child will be explained to you by the study doctor. The schedule for giving the doses is also provided in the table below.

Day of study	1st (Day 0)	2nd (Day1)	3rd (Day 2)	4th (Day 3)
When to give each dose	Morning or Afternoon Evening	Afternoon	Morning Evening	Morning
# Doses per Day	2	1	2	1

3-day *Coartem*® "Population" blood draws

If your child is receiving the six-dose regimen, this is the standard treatment duration and dosing for malaria. The time for when each of the 6 doses should be given to your child will be explained to you by the study doctor. The schedule for giving the doses is also provided in the table below.

Day of study	1st (Day 0)	2nd (Day1)	3rd (Day 2)
When to give each dose	Morning or Afternoon Evening	Morning Evening	Morning Evening
# Doses per Day	2	2	2

5-day *Coartem*® "Intensive" blood draws

If your child is receiving the ten-dose regimen, this is the extended treatment duration and dosing for malaria. The time for when each of the 10 doses should be given to your child will be explained to you by the study doctor. The schedule for giving the doses is also provided in the table below.

Day of study	1st (Day 0)	2nd (Day1)	3rd (Day 2)	4th (Day 3)	3rd (Day 4)	4th (Day 5)
When to give each dose	Morning/ Afternoon Evening	Afternoon	Morning Evening	Morning Evening	Morning Evening	Morning
# Doses per Day	2	1	2	2	2	1

5-day *Coartem*® "Population" blood draws

If your child is receiving the ten-dose regimen, this is the extended treatment duration and dosing for malaria. The time for when each of the 10 doses should be given to your child will be explained to you by the study doctor. The schedule for giving the doses is also provided in the table below.

Day of study	1st (Day 0)	2nd (Day1)	3rd (Day 2)	4th (Day 3)	3rd (Day 4)
When to give each dose	Morning/ Afternoon Evening	Morning Evening	Morning Evening	Morning Evening	Morning Evening
# Doses per Day	2	2	2	2	2

10) Overview of Study Follow up

Your child will be seen in the study clinic several times during the 42 days for the study. The procedures for evaluating your child for any given day may either be the same or different depending on the study day and which study blood draws or regimen your child is currently enrolled in. You will be provided with a study card and a reminder for all visits.

If you do not bring your child to a scheduled visit for treatment of malaria, a health worker will visit you at your home. The health worker will bring you and your child to the study clinic.

The study clinic follow-up visits needed for this study are for the following reasons:

- Morning doses of *Coartem*® will be given in the study clinic for your child's malaria on study days 0, 1, 2 and 3 (4 and 5 as well, if your child is on the 10-dose regimen).

- Clinical and safety evaluation, and blood draws: Your child will be evaluated by a study doctor to see how she or he is doing on a total of 11 to 13 follow-up days in clinic. The precise schedule of follow-up will be explained by your doctor or nurse. Blood tests to measure the *safety* of the medication will be drawn by venipuncture on 2 of those days, just as this was done at the beginning of the study. In addition, blood tests to measure the *amount* of antimalarial medication in the blood will be drawn on 8-10 of those follow-up days.

- Your child may undergo additional finger prick samples in the evenings following each dose for the measurement of parasite levels.

- The total amount of blood drawn from your child over the entire 42 days will be no more than 5 to 6 teaspoons.

11) PK Blood Draws

- After each dose administered in the clinic during the day (study days 0,1 and 2 for the 3-day regimen or study days 0,1,2,3 and 4 for the 5-day regimen, two samples by finger prick will be drawn 2 and 4 hours after each dose (each sample is no more than 1/20th of a teaspoonful)

- Depending on the regimen duration or blood draw schedule, you and your child will return to the study clinic on 6 more days (day 4 or 6, 7 or 8, 14, 21, 28, 35 and 42) for more clinical and safety tests, and a small needle stick in one of your child's arm veins or finger prick blood draws.

12) INTENSIVE PK STUDY ONLY: Specific Blood draws Schedule on the last day of drug treatment (following the 6th Dose or 10th dose (last dose) of *Coartem*®) Today the total time needed for this visit and the following morning is approximately 8 hours). Intensive blood draws around the last dose will not occur for the population PK studies.

- On the last day of drug treatment, your child will receive the 6th or 10th dose of *Coartem*® in the clinic. Before taking this morning dose, a small tube or catheter will be placed in an arm vein of your child so that your child does not have multiple pricks with a needle. This catheter will remain in your child's arm for the duration of blood draws on day 3 or 5, depending on which regimen your child is taking. This will allow us to only have to perform a single venipuncture on that day.

- The first blood sample will be collected just before your child receives the last dose of *Coartem®,* and your child will have 7 more small blood samples collected over the next 8 hours. Each time we collect blood, it will be a very small amount, approximately 1/10th of a teaspoonful. At approximately 2 points during these collections, we will also collect a very small amount by a finger prick (less than 1/20th of a teaspoonful). Thus, the total amount of blood taken on day 3 or 5 will be under one teaspoonful.

- You and your child will remain for this 8-hour period in a special room set up especially for this study that is located within the clinic. The room will be set up so that you and your child will be comfortable. There will be some toys for your child to play with and you and your child will be able to rest if you would like.

- After the 8-hour blood draw, the small tube that is placed in your child's arm will be removed by the study doctor. You and your child will be discharged from the study clinic so that you can return to your home.

7) Unscheduled Contact Visit

If your child becomes sick during the day while in the study, please bring your child to the study clinic. There will be someone at the study clinic every day from 8 am to 5 pm. The clinic is open on weekends and holidays. If your child has a repeat malaria infection during the 42-day follow-up we will ask to collect an additional blood sample to measure how much malaria medication is in his or her blood (1/8th teaspoon).

If your child becomes sick after 5 pm, please bring him or her to the Tororo District or Masafu General Hospital. Please tell the staff you are part of this study and show them the card that tells them you are part of this study.

If your child became ill after clinic hours, please plan to bring your child to the study clinic on the following day. If your child becomes sick with malaria when the clinic is not open, your child will receive treatment for his or her malaria from a hospital supply at the Tororo District or Masafu General Hospital.

If your child is diagnosed with severe malaria during any time she or he is enrolled in the study, treatment will be given in the hospital using another malaria medication called quinine or artesunate. Quinine and artesunate are effective and approved for treating complicated malaria in Uganda. The length of your child's stay in the hospital will be decided by the Tororo District or Masafu General Hospital staff managing your child's illness.

If your child does not have malaria, the study doctors may refer your child to their usual medical clinic to receive the necessary care.

HOW LONG WILL MY CHILD BE IN THE STUDY?

We are asking you to let your child participate in this study for 42 consecutive days during and following treatment for each malaria episode or until you or the study doctors decide your child should stop being in the study. In the case that your child gets malaria again during the course of follow-up, your child will be eligible to be re-enrolled in the

study for blood draws and follow-up as described above. Your child will only be enrolled in the study for a maximum of 4 episodes of malaria.

WHY WOULD MY CHILD BE WITHDRAWN FROM THE STUDY EARLY?

You may decide to stop your child from being in the study at any time and for any reason. For your child's safety and health, study doctors might decide he or she should stop being in the study.

Your study doctors may also take your child out of the study. These are the possible reasons:

9. If you are unable to bring your child to the scheduled study visits.
10. If your child misses the correct times for the doses of malaria medication. (In any case, your child must complete the course of treatment)
11. Any dosing of malaria medications or other medications outside study procedures.
12. Your child develops complicated malaria and requires treatment with quinine or artesunate in the hospital.
13. If the study doctors think the study is no longer good for your child
14. If you withdraw your consent to have your child stay in this study
15. The study is cancelled by the UCSF, Yale University, Uganda National Council of Science and Technology (UNCST) or Makerere University ethics committees, Ugandan Ministry of Health, the U.S. National Institute of Child Health and Human Development (NICHD), or by the U.S. Office for Human Research Protections (OHRP).

If we are unable to locate you during follow-up or you decide to withdraw from the study, follow-up will end. However, In the event that your child stops the study early, they would be eligible to reenroll in the study during a later episode of malaria. We will also make an effort to follow your child to at least 7 days after beginning treatment for malaria.

CAN I DECIDE TO STOP MY CHILD'S PARTICIPATION IN THE STUDY?

Yes. You can decide to stop at any time. Tell the study doctor or nurse if you are thinking about stopping or deciding to stop. He or she will tell you how to stop your child's participation safely. It is important that you tell the study doctor if you are thinking about stopping so that your doctor can evaluate any risks and discuss what alternative follow-up care and testing could be most helpful to your child.

WHAT WILL HAPPEN IF I OR MY CHILD'S STUDY DOCTORS DECIDE TO TAKE MY CHILD OFF STUDY?

If either the study doctors take your child off study or if you decide to stop his or her participation, your child may still get health care at the Tororo District or Masafu General Hospital or his or her regular clinic. If your child stops participating in the study for any reason, the study doctors will ask to examine your child and draw a small amount of blood (less than 1 teaspoon) for laboratory tests for the safety of your child. You have the right to not agree to the examination and tests. If your child leaves the study before finishing, if funds are available we will give your child medical care for any problems that

began during the study. Your child may be taken out of the study because of a serious health problem. If the study doctors think the health problem is probably related to study treatment, they will arrange for needed follow-up tests.

WHAT SIDE EFFECTS OR RISKS CAN I EXPECT MY CHILD TO HAVE FROM BEING IN THE STUDY?

5) **Non-Study Medications and Other Clinical Studies**: There may be a risk of serious side effects when non-study medications are taken with study drugs. You must tell your doctor or study nurse about all other medicines and herbs that your child is taking before your child starts the study. You must tell the study doctor or nurse before taking any non-study therapies while your child is in the study. You must also tell your study nurse and doctor if you join any other research studies.

6) **Risks of *Coartem*®:** Coartem® is standard of care for treating malaria in Uganda and is commonly used to treat the type of malaria your child has. A standard regimen is 6 tablets (one tablet given twice a day for 3 days). We are also studying a 10-tablet regimen (one tablet twice a day for 5 days). Both regimens may cause rare side effects such as lowering of blood counts and swelling of the liver. These happen less than 1 out of 100 times the drug is used. Other side effects happen up to 1 out of 10 times the drug is used. Some of these are sleep problems, headache, dizziness, a feeling of a rapid or irregular heartbeat, diarrhea, vomiting, pain in the abdomen, rash, itching, cough, muscle and joint aches, and fatigue. Based on our experience with Coartem®, we do not expect there to be more side effects with the 5-day regimen than with the 3-day regimen. We will be following your child closely during the course of follow-up for any side effects.

7) **Blood drawing (venipuncture, finger or heel prick) risks**: Drawing blood may cause temporary discomfort from the needle stick, bruising, fainting, and infection. The amount of blood removed will be too small to affect your child's health.

8) **HIV testing risks**: Testing your child for HIV may cause anxiety regardless of the test results. A positive test indicates your child has been infected with the HIV virus, but no one knows for certain when, if ever, your child will become sick with AIDS or a related condition. Receiving positive results may make you very upset. If your child's test is negative, there is still the possibility that your child could be infected with the HIV virus during breastfeeding and test positive at some time in the future. Also, it is always possible that the test results could be wrong.

9) **Unknown Risks**: There is always the possibility of side effects that no one knows about yet. The study doctors will let you know if they learn anything that might make you change your mind about your child participating in the study.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

There are minimal direct benefits to your child for taking part in this study. Your child will receive close clinical care over 42 days for the treatment of malaria and other illnesses that may occur during this time. The information we get from this study might help Uganda and other countries to decide whether the extended 5-day/ 10 dose of artemether-lumefantrine (Coartem®) is both safe and effective for the treatment of malaria in those not infected with HIV.

WHAT OTHER CHOICES DO I HAVE IF MY CHILD DOES NOT TAKE PART IN THIS STUDY?

You are free to decide whether or not you want your child in this study. If you decide you do not want your child in the study or decide to stop your child from being in the study at any time and for any reason, this will not affect your child's care at Tororo District or Masafu General Hospital or any referral clinics, and they will still be able to receive care for their malaria at these locations. All of the study procedures and study medicines are available outside this study. If you decide not to take part, your child could still get medical care and could still get any of these medicines if your doctor thought they were needed. Currently, *Coartem*® is provided free at government clinics and hospitals.

WILL MY CHILD'S MEDICAL INFORMATION BE KEPT PRIVATE?

Other people may learn that your child is part of this study because you will get medical care at the study clinic. These study staff will not be allowed to discuss your child's medical information outside of the study clinic. Only study staff will be able to link your child's medical records and personal study number. The universities and research organizations running this study or making sure that the research is done properly are not allowed to let others know the identity of the people in the study. These organizations include the NIH/NICHD, U.S. Office for Human Research Protections, Committees for Human Research of the University of California, San Francisco, Yale University, the Makerere University Faculty of Medicine Research Ethics Committee (FOM-REC), and the Uganda National Council on Science and Technology. The medical records for the study will be kept in a locked office and will only be able to be seen by study staff. Your name or your child's name will not be written in any reports based on this research.

WHAT ARE THE COSTS OF TAKING PART IN THIS STUDY?

There will be no cost for you or your child to take part in this study. We will pay for the cost of all tests or drugs prescribed by our doctors that you may have to purchase outside the clinic. Payment for visits outside the study clinic or Tororo District or Masafu General Hospital will only be possible if we have enough funds.

WILL I BE PAID FOR TAKING PART IN THIS STUDY?

You or your child will not be paid for participation in the study. We will be giving you money for transport to and from your home to the study clinic for all study visits and visits needed if your child is sick. On certain days, participants will have to be in the clinic for several hours. On those days, we will provide food and drink to participants (breakfast, dinner, and/or snacks) to ensure their well-being. If you agree for your child to be in this study, your child will be given a long-lasting insecticide - treated bed net.

WHAT HAPPENS IF MY CHILD IS INJURED BECAUSE HE OR SHE TOOK PART IN THIS STUDY?

If your child is injured or becomes ill, please contact the doctors at the study clinic. If you have questions about injuries as a result of being in the study, contact the doctors at the study clinic. You can get health care services at Tororo District or Masafu General Hospital in case of such injuries. If funds provided by the study investigators to carry out

this research project are available, you will not have to pay for care for study-related injuries.

WHAT ARE MY CHILD'S RIGHTS IF HE OR SHE TAKES PART IN THIS STUDY?

You are free to decide whether or not you want your child in this study. You have the right to stop your child's participation in the study at any time without penalty or loss of benefits to which you are otherwise entitled. We will tell you about new information or changes in the study that may affect your child's health or your willingness to have your child continue in the study.

WHO CAN ANSWER MY QUESTIONS ABOUT THE STUDY?

Drs. Mwebaza, Aweeka, and Parikh, and their staff can answer questions you have about the study. You may call Dr Norah Mwebaza at 0782589889 or 0758743264 or Dr. Richard Kajubi at 0776211591. If your child has been injured or becomes ill, please contact the doctors at the study clinic at 0454448840. You may also contact Dr. Ponsiano Ocama (+256-414-530555/0701283388) at the Makerere University Faculty of Medicine - Research and Ethics Committee which approved this study for questions about participants' rights and research-related harm.

HOW WILL MY BLOOD SAMPLES BE USED AFTER THE STUDY IS COMPLETED?
We would like to keep some of these samples that are left over for future research. If you agree, these samples will be kept and may be used in research to learn more about malaria. Your child's samples may be helpful for research, and is not designed specifically to help your child. It might help people who have malaria in the future. Reports about research done with your child's samples will not be given to you and will not be put in your health record. The research will not effect your child's care.

The choice to let us keep the left-over samples for future research is up to you. No matter what you decide to do, it will not affect your child's care. If you decide now that your child's samples can be kept for research, you can change your mind at any time. Just contact us and let us know that you do not want us to use your samples. Then any samples that remains will no longer be used for research. Your child's samples will be used only for research and will not be sold. The research done with your samples may help to develop new or improved treatments for malaria in the future.

<u>Making Your Choice</u>
Please read each sentence below and think about your choice. After reading each sentence, put your initials in the appropriate box. If you have any questions, please talk to your doctor or nurse, or call our research review board at IRB's phone number.
No matter what you decide to do, it will not affect your care.
☐ I give my permission for my child's or my blood to be used for future research on Malaria
☐I do not give my permission for my child's or my blood to be used for future research on Malaria

You may call Dr Norah Mwebaza at 0782589889 or 0758743264 or Dr. Richard Kajubi at 0776211591 if you decide you would no longer like to have your child's samples stored for future usage.

CONSENT: WHAT YOUR SIGNATURE OR THUMBPRINT MEANS

PARTICIPATION IN RESEARCH IS VOLUNTARY. You have the right to decline to allow your child to participate or to withdraw your child at any point in this study without penalty or loss of benefits to which your child is otherwise entitled. A copy of this consent form will be given to you. Your signature or thumbprint below means that you have had this study explained to you. Your signature or thumbprint below means you have had the opportunity to ask questions and get answers. If you wish your child to participate in this study, you should sign or place your thumbprint below.

Name of Parent or Guardian (printed)

Signature or Thumbprint * of Parent or Guardian Date/Time

Name of Study Staff Administering Consent (printed) Position/Title

Signature of Study Staff Administering Consent Date/Time

Name of Translator (if necessary)

Signature of Translator Date/Time

*If the parent or guardian is unable to read and/or write, an impartial witness must be present during the consent discussion. After the written informed consent form is read and explained to the parent or guardian, and after he or she has orally consented to his or her child's participation in this study, and has either signed the consent form or provided his or her fingerprint, the witness must sign and personally date the consent form. By signing the consent form, the witness attests that the information in the consent form and any other written information was accurately explained to, and apparently understood by, the parent or guardian, and that consent was freely given.

Name of Person Witnessing Consent (printed)

Signature of Person Witnessing Consent Date/Time

Name of Participant (printed)

Name of Study Staff Administering Consent (printed) Position/Title

Signature of Study Staff Administering Consent Date

Name of Translator (if necessary)

Signature of Translator Date

*If the participant is unable to read and/or write, an impartial witness must be present during the informed consent discussion. After the written informed consent form is read and explained to the participant, after oral consent to the participation in the trial, and after the participant has signed the consent form or provided her fingerprint, the witness should sign and personally date the consent form. By signing the consent form, the witness attests that the information in the consent form and any other written information was accurately explained to, and apparently understood by, the participant and that informed consent was freely given.

Name of Person Witnessing Consent (printed)

Signature of Person Witnessing Consent Date