Title: Parent/Guardian Informed consent for minor and addendum

NCT number: NCT05567016

Date: 05/13/ 2024 (original consent form) and 04/28/2025 (addendum)

Parent/Guardian Informed Consent form

Informed Consent- Parent/Guardian Consent for Minor

Protocol Title:	Child Health and Infection with Low Density (CHILD) Malaria, a randomized controlled trial to assess the long-term health and socioeconomic impact of interventions targeting low-density malaria infection (LMI) among children in Tanzania
Funding Source:	NIH
UCSF-IRB Number:	22-36146
IHI-IRB Number:	IHI/IRB/No:08-2023
NatHREC Number:	NIMR/HQ/R.8a/Vol.IX/4202
Site of Research:	Kiwangwa and Fukayosi wards, Bagamoyo District, Tanzania
U.S. Principal Investigator:	Michelle Hsiang, MD, MSc
Tanzanian Principal Investigator:	Ally Olotu, MD, PhD
Version	6.0
Version Date:	May 13, 2024

INTRODUCTION

Your child is being asked to participate in this research study because he or she is 6 months to 10 years old. My name is _____. I am conducting the research study with Ifakara Health Institute (IHI), Bagamoyo Research and Training Centre Laboratory, The united Republic of Tanzania Ministry of Health Community Development, Gender, Elderly and Children (MoHCDGEC), University of California San Francisco (UCSF), Swiss Tropical and Public Health Institute (Swiss TPH), and Stanford University and it is sponsored by the United States National Institutes of Health/National Institute of Allergy and Infectious Diseases (NIH/NIAID). 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 is a consent form which gives information about what is involved in the screening process and participation in the research study. After screening, if it is decided that participation in a research study would be right for your child, the study staff will talk more about the study in detail for you to decide. You can ask questions about this study at any time. If you agree to participate, we will ask you to sign the consent form. You will get a copy of this form to keep.

WHY IS THIS STUDY BEING DONE?

Malaria infection can occur in the body at low levels and persist for many months. These low-level infections are not treated because the standard malaria test, namely rapid diagnostic test (RDT) that detects a protein in the malaria parasite, does not detect them. Also, the current thinking is that these infections should not be treated because they are not the cause of your child's current illness and they may boost your child's immune responses to provide protection against future malaria infections. At the same time, new malaria tests to detect low-level infections are becoming available. These tests are called PCR or molecular tests, and they are highly sensitive because they detect genetic material of the malaria parasite. Some research suggests that the low-level malaria infection could be harmful to health, cognition, and learning over time.

Therefore, we would like to learn how detection and treatment of low-level malaria infection impacts health. We are also interested to see if detection and treatment of low-level malaria infection has socioeconomic benefits (such as improved school performance, or if it saves your family and the health system money) over time.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?
About 600 children will take part in the study.

WHAT WILL HAPPEN IF MY CHILD TAKES PART IN THE STUDY?
If your child is eligible and you agree for your child to be in this study, we will perform the following procedures today:

a. We will also ask questions about your household including the materials the house is made of who lives there, your health practices, and household factors related to malaria risk (e.g. geographical location, household size, use of mosquito control measures). We will also record the location of your household so that study team can follow up with your child for study activities.
b. We will take a photograph of your child, so we can prepare a study identification card to identify your child when you visit the clinic for study procedures. The study ID card will also have contact numbers for the study team. You should have the ID card with you anytime you bring your child to the study site or to any health facility. Your child's medical information will remain secret and only some members of the trial team will have access to your child's personal information.

<u>Part 1: Enrollment (total time needed for this activity is about 1.5 hours):</u>
We will request that you bring your child to the study clinic that you will select today to complete the enrollment process. During that visit (referred to "Day 0"), the following procedures will be performed:

- We will collect information on your child's health, family and symptom history, and record the answers on a tablet.
- We will conduct a physical exam and collect height, weight, and arm measurements.
- We will collect blood from a vein in your child's arm (1-2 teaspoons) to check for any inherited blood cell conditions and measure your child's immune responses. If your child has an inherited blood cell condition, your child will be referred for further care. Other testing will be used for study analyses only and will never be used for anything else. Blood will also be saved for future testing related to malaria.
- We will ask you to collect a stool and urine sample from your child. We will look for other parasitic diseases and these results will only be for study analyses only. Note that your child will be eligible to receive standard therapy for non-malarial parasitic diseases through the government's annual deworming program, and we will provide information regarding how you can access these services for your child.
- We will give you/your child an insecticide treated bed net and some instruction on how to use it.
- We will assess your child's cognition and attention through various tests including tests of vocabulary and math. You will receive results from these tests. As part of the assessment, we will also review and collect information from your child's report card and may visit their school to collect data on their performance.
- Your child will be randomly assigned to one of three treatment arms:
    1. Control (standard of care) – In this arm, your child will receive standard of care for malaria, which includes malaria rapid diagnostic testing (RDT) if your child has fever and suspected malaria, and AL, or "Coartem," if the RDT test is positive. Your child will also receive routine

2. ACDm (active case detection using molecular testing) – In this arm, your child will receive standard of care described for Arm 1. Additionally, your child will receive malaria testing with an RDT and PCR (molecular testing) 3x/year. If your child tests positive by RDT or PCR, your child will receive AL, or "Coartem."
3. PCDm (passive case detection using molecular testing) – In this arm, your child will receive standard of care described for Arm 1. Additionally, your child will receive malaria PCR testing if your child tests RDT-negative at the time of fever and suspected malaria. If your child tests positive by molecular testing, your child will receive AL, or "Coartem."

- You, your child, and the study staff will know which treatment group your child has been assigned to.
- The procedures for the follow-up visits of the study are detailed below in Part 2. Many of the procedures are the same for all 3 study arms, but some apply to only one study arm.

<u>Part 2: Monthly follow-up visits for 24 months (total time needed for most visits is 30 minutes. The endline assessment will require about 1.5 hours)</u>:

Once enrolled, you will need to bring your child to the study clinic every other month for follow-up visits. If you are not able to easily bring your child to the clinic for these follow-up visits, we may be able to arrange for some of these visits to take place in a more convenient location such as your home or the child's school. On the alternating months, a community field worker will come to your home for follow-up visits.

At monthly follow-up visits, we will perform all or some of the following procedures:

- At each visit, we will obtain a medical history and collect information about any symptoms your child is having, as well as any sick visits since the last follow-up visit. If your child is in school, we will ask how any illness may have influenced your child's school attendance, and we will also review school records to check on your child's school attendance and whether he or she advances to the next grade each year.
- We will ask you about how many days you miss work due to any illness your child may experience and how much you had to spend in health care costs.
- At follow-up visits in the study clinic, a few drops of blood will be collected from your child in a tube by a finger prick. At months 6, 12, 18, and 24, a larger volume of blood (1-2 teaspoons) will be collected from a vein in your child's arm. Various testing related to malaria and how your body responds to malaria will be conducted. At M12, we will also conduct tests to understand non-malaria causes of fever. These tests will generally be used for study analyses only.
- A swab of your child's nose and throat will be collected at M12 for research purposes to better understand non-malaria causes of fever.
- *Arm #2 (ACDm arm) only: If your child is assigned to Arm#2 (ACDm), the following will occur:*
    - *Every 3-4 months, blood from the finger prick will also be used to conduct a malaria RDT. If the RDT show malaria, we will provide your child the antimalarial drug artemether-lumefantrine (AL, "Coartem") for treatment.*
    - *If the RDT is negative, we will use already collected blood for a test called "PCR" to determine if your child has a low-level malaria infection. The PCR test takes 0-3 days to obtain a result.*

- *If we find your child has low-level malaria infection by the PCR test, we will notify you and provide your child the antimalarial drug artemether-lumefantrine (AL, "Coartem") for treatment.*
- *Treatment administration: Our study team will explain how your child should take the medication. This medication is meant to be taken twice per day, for three total days. That will equal 6 total doses. Your child will be given the first dose during this visit. You will take the subsequent doses home and a member of the study team will coordinate to meet you at your home or other convenient location to observe your child take the subsequent doses. Your child will not be given AL if it is unsafe for them. Only the child who is participating in the study should take the medication and it is important to wait until a member of the study team is able to be with you to observe the child take each dose of the medication.*

- At Month 24, we will assess your child's cognition and attention through various tests including tests of vocabulary and math. You will receive results from these tests. To further understand the performance of your child, we will review and collect information from your child's report card and may visit their school to collect data on their performance.
- At three additional timepoints, we will ask you to collect urine and stool samples from your child. We will look for other parasitic diseases and these results will only be for study analyses only. These timepoints will likely occur at months 0, 12 and 24, however this may change as we would like to collect this sample before your child receives his or her annual deworming medication from the government. Note that your child will be eligible to receive standard therapy for non-malarial parasitic diseases through the government's annual deworming program.

Illness during the follow-up period:

If your child experiences fever or other illness at any time during the study, please come to the study clinics. If there are challenges to coming to the clinic (for example transport) or you are not sure if you should bring your child, please call the study nurse who will be available by telephone 24 hours a day, 7 days a week to discuss. If the illness is associated with fever, a standard evaluation will be performed, including RDT testing for malaria. Blood (half a teaspoon) will be collected from a vein in your child's arm for the malaria testing and for other laboratory testing for research related to malaria and other causes of fever. A swab of your child's nose and throat will also be collected for research to better understand non-malaria causes of fever. If the standard malaria test is positive, your child will receive standard antimalarial treatment with AL. Our study team will explain how your child should take the medication. This medication is meant to be taken twice per day, for three total days. That will equal 6 total doses. Your child will be given the first dose during this visit. You will take the subsequent doses home and a member of the study team will coordinate to meet you at your home or other convenient location to observe your child take the subsequent doses. Your child will not be given AL if it is unsafe for them. Only the child who is participating in the study should take the medication and it is important to wait until a member of the study team is able to be with you to observe the child take each dose of the medication. The clinic staff will also check the child for other causes of fever and appropriate steps will be taken to care for the child, including referral to the hospital if needed.

Arm #3 (PCDm arm) only: If your child is assigned to Arm#3 (PCDm), the following will occur:

- *If your child has fever and a negative malaria RDT result, we will use the blood already collected to conduct a malaria test using a method called "PCR" to determine if your child has a low-level malaria infection. The PCR test takes 0-3 days to obtain a result.*
- *If we find your child has low-level malaria infection by the PCR test, and your child was not already treated with an antimalarial drug, we will notify you and provide*

- *If we find your child has low-level malaria infection by the PCR test, and your child was not already treated with an antimalarial drug, we will notify you and provide your child the antimalarial drug artemether-lumefantrine (AL, "Coartem") for treatment.*
- *Treatment administration: Our study team will explain how your child should take the medication. This medication is meant to be taken twice per day, for three total days. That will equal 6 total doses. Your child will be given the first dose during this visit. You will take the subsequent doses home and a member of the study team will coordinate to meet you at your home or other convenient location to observe your child take the subsequent doses. Your child will not be given AL if it is unsafe for them. Only the child who is participating in the study should take the medication and it is important to wait until a member of the study team is able to be with you to observe the child take each dose of the medication.*

For sick visit associated with fever, a community field worker will come to your home or make a phone call approximately 7 days later for a follow-up visit. We ask that you bring your child back to clinic 28 days later for a follow-up visit. At these follow-up visits, we will assess your child to see if your child has improved. If your child has not improved, we will assess to see if further care is needed. This assessment may involve testing that will influence how your child's illness is managed. At the follow up visit 28 days later, we will also collect a few drops of blood from your child in a tube by a finger prick *for research purposes only. The duration of these visits associated with fever (initial visit and Days 7 and 28 visits) are expected to be 30 minutes, though they may be longer depending on the nature of your child's illness.*

Please note that HIV testing will only be offered if clinically indicated, as part of routine healthcare. If it is offered to your child, you can choose to accept or decline, and this decision will not affect your child's participation in the study or your child's receipt of routine healthcare. Any HIV testing and counseling will be as per national policy, results would be communicated privately, and per national policy, any HIV result would not be reportable.

Someone is at the clinic every day from 8:00 am to 5:00 pm. The clinic will be open on weekends and public holidays. If your child becomes sick after 5:00 pm, or has an urgent condition at any time, please contact our study team and will provide care through an on-call health worker and/or coordinate transport to Bagamoyo District Hospital if needed. If you go to the hospital on your own, you should tell the hospital staff that you are a part of this study. We will give you a study card that tells the doctors some information about your participation in the study. Please take this card with you whenever you get sick and seek care. If you choose to go to another clinic or hospital for medical care, or if you fall sick you are visiting another area, please call our study team.

Total amount of blood to be collected

Over the two years of the study, we will collect about 3 to 6 tablespoons of blood from your child. This amount of blood will not cause any problems with your child's health.

Where my samples will be tested

All lab tests needed for your child's care will be conducted within Tanzania. Some blood or stool samples may be sent to UCSF in the U.S., or Kenya Institute Medical Research Institute (KEMRI) for testing of drug levels, your child's responses to low-level malaria infections, and other studies related to malaria and neglected tropical diseases.

HOW LONG WILL MY CHILD BE IN THE STUDY?

If you agree for your child to be in this study, he/she will be in the study for 2 years from the Day 0 visit.

CAN I STOP MY CHILD FROM BEING IN THIS STUDY? WHAT OTHER CHOICES DO I HAVE?
You are free to choose whether or not to allow your child to take part in this study. If you decide to allow your child to take part, you can contact us to withdraw your child's information and/or blood samples. No matter what decision you make, there will be no penalty to you/your child in any way. You/your child will not lose any of your regular benefits, all the services you/your child receive at the clinic will continue and nothing will change. We would use the data that has been collected prior to your withdrawal. However, you can decide if you want the trial data or the samples from the trial to be destroyed if you withdraw consent for your child to participate in the study.

WHY WOULD THE DOCTOR TAKE ME OFF THIS STUDY EARLY?
The study doctor may need to take you off the study early without your permission if:

- A regulatory agency (e.g. ethics committee), the safety oversight committee, or the study investigators determine that the study would no longer be in your best interest.
- You consistently fail to follow study requirements.
- Your family and child move away from the study area.
- The study is terminated.

CAN I STOP MY CHILD FROM BEING IN THE STUDY?
Yes. You can decide to stop your child's participation 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 assess any risks and discuss other ways of follow-up care and testing could be most helpful to you.

FUTURE USE OF SPECIMENS

While your child is in this study, there may be blood (capillary and venous), stool, and urine taken from your child that may be useful for future research. We will request your consent for future use of these samples. If you do not agree, your child can still participant in the current study. If you do agree, these samples will be stored indefinitely at one of the universities or research organizations involved in this study. These are: Ifakara Health Institute (IHI), Bagamoyo Research and Training Centre Laboratory or University of California San Francisco (UCSF) in the U.S. Samples may also be shared with investigators at other institutions. We will not share your name or any other personal information that would let the researchers know who you are. We will not ask you for additional permission to share this de-identified information.

What will my child's samples be used for?
Your child's samples will be used to study malaria, the way the body responds to malaria, and we may study other diseases. The information we get from these studies will not affect your child's care.

1. These samples will be used for future research to learn more about malaria and other diseases.
2. Your child's samples will be used only for research. The information we get from these studies will not affect your child's care.
3. We may perform genetic research on these samples.

We will code your child's samples using numbers. Therefore, the study workers will not be able to easily find out your child's name. To further safeguard your privacy, we will not put information obtained from the

research (including any genetic information) into your child's medical record. We may present results from future research using your child's samples in publications and meetings. If this happens, we will not identify your child's name.

Genetic information that results from this study does not have medical or treatment importance at this time. However, there is a risk that information about taking part in a genetic study may influence insurance companies and/or employers regarding your child's health.

Taking part in future studies (including genetic studies) may also have a negative impact or unintended consequences on family or other relationships. If you do not share information about taking part in this study, you will reduce this risk. Although your child's name will not be with the sample, it will have other facts about your child such as your child's age, gender, and location of residence. These facts are important because they will help us learn if the factors that cause malaria and associated illness to occur or get worse are the same or different based on these facts. Thus, it is possible that study finding could one day help people of the same race, ethnicity, or sex as you. However, it is also possible through these kinds of studies that genetic traits might come to be associated with your group. In some cases, this could reinforce harmful stereotypes.

ARE THERE RISKS FROM TAKING PART IN THE STUDY?

Risks of study drugs: Normally, your child would not be tested and treated for low-level malaria. Therefore, if your child is assigned to the control group (Arm #1), your child will not experience additional risks. If your child is assigned to Arm #2 or #3, your child is unlikely to experience any risks. In many studies, AL has been used to treat children with low-level malaria infection and it has been shown to be very safe. Nonetheless, there is still some risk. Rare health problems that have been reported are listed below. Those listed as less likely are mild and occur in fewer than 1 in 5 patients. Those listed as rare but serious occur in less than 1 in 100 patients.

Likely and mild to moderate: No side effect is likely, but the most common is cough or fever in children.
Less Likely and mild to moderate: Generalized weakness or diminished energy, chills, dizziness, nausea, vomiting, abdominal pain, diarrhea, joint or muscle pain.
Rare but serious: hives or mouth swelling, skipped heartbeat, heart rhythm disturbance.

These mild to moderate side effects (both the likely and less likely ones) are reversible. The rare but serious ones may be irreversible if the appropriate medical care is not sought or provided.

Non-study Medications and Other Clinical Studies: You must tell your doctor or study nurse about all other medicines and herbs that you are taking to make sure that your study drugs are safe to take. You must also tell your study nurse and doctor if you join any other research studies.

Risks of Randomization: Your child will be assigned to a treatment group by chance (like the flip of a coin). The treatment group your child is assigned to may prove to be less effective or have more side effects than the other treatment group.

Risks of Blood Draws: There may be some discomfort when blood is drawn. Other risks include bleeding or bruising where the needle enters the body, or fainting. A small blood clot may form where the needle enters the body or swelling of the surrounding skin may occur. There is a rare risk of minor infection at the blood

draw site. The amount of blood taken is generally not enough to cause any problems with your child's health.

Questionnaires: Answering some questions may make you feel uncomfortable. You may refuse to answer any question or stop at any time.

Unknown risks: The experimental treatments may have side effects that no one knows about yet. The researchers will let you know if they learn anything that might make you change your mind about participating in the study.

Risks with donating my child's samples for research

There are few risks to your child from future use of his or her samples. A potential risk might be the release of information from your child's health or study records. We will not put reports about research done with your child's samples into health records. We will keep these reports with study records. We will keep study records as private and safe as possible.

If you/your child notice anything out of the ordinary or if you/your child have concerns or questions, contact the study nurse at (Tel: _____). You/your child can also come to the study clinic at any time.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

If your child takes part in this study, he or she will receive enhanced health care by having access to a study nurse and physician throughout the study.

There may be a direct benefit to your child in terms of health, cognition, and learning. But no guarantee can be made. It is also possible that your child may receive no benefit from being in this study.

The information we get from this study might help Tanzania and other countries to decide if low-level malaria infections should be detected and treated to improve the health of children. From future research on stored samples, we may learn more about malaria or other diseases. We may learn how to prevent them, how to treat them, or how to cure them.

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

You are free to decide whether or not your child should be in this study or if your child's samples can be use for future studies. If you decide you do not want your child to be in this study, or decide you do not want your child's samples to be used for future studies, or decide to stop being in the study at any time and for any reason, this will not affect your or your child's care at the local health facilities or the district hospital. All study procedures and study drugs are available outside this study. If you decide not to take part, your child may still get medical care and get any of the study drugs if your doctor thinks they are needed.

There is currently effective drug to treat malaria if your child is found to have malaria. You may protect your child by letting them sleep under an insecticide treated bed net with no holes and/or having the inside of your house sprayed with insecticide. The risk of severe illness from malaria can be reduced by seeking medical care immediately when you feel unwell, in order to receive prompt diagnosis and treatment. Please talk to your doctor about these and other choices available to you. Your doctor will explain the risks and benefits of these choices.

WILL INFORMATION ABOUT MY CHILD BE KEPT PRIVATE?
Other people may learn that your child is part of this study because your child will get medical care at the study clinic. 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 other diseases, including genetic data, will be collected on your child, but only the people working on the study will see it. Only people involved in this study will be able to link your child's medical records and your study number. The universities and research organizations running this study are not allowed to let others know the identity of the people in the study. The medical records for the study will be kept in a locked office and will only be seen by study workers. People or organizations which may review your child's records include: IHI, The united Republic of Tanzania Ministry of Health Community Development, Gender, Elderly and Children (MoHCDGEC), University of California, Swiss TPH, Stanford University, Institutional review board of UCSF, or Tanzania National Health Research Ethics Sub-Committee (NatHREC), study staff, and study monitors. Your child's name will not appear in any reports or publications.

WHERE WILL THE RESULTS OF THE STUDY BE POSTED?
This study will be registered on ClinicalTrials.gov, a registry of clinical trials run by the United States National Library of Medicine (NLM) at the NIH. Results of the study will be posted to this site within one year of study completion. No individual identities will be provided or posted.

ARE THERE COSTS OR PAYMENTS ASSOCIATED WITH TAKING PART IN THE STUDY?
The costs for all study related investigations or treatments will be covered by the study. You/your child will not be charged to take part in the study, including for the malaria and non-malaria tests. You/your child will also not be charged for donating specimens. If the data or any new products, tests or discoveries that result from this research have potential commercial value, you and your child will not share in any financial benefits.

WILL I/MY CHILD BE PAID FOR PARTICIPATING IN THE STUDY?
You/your child will not be paid for participating in the study.

If your child is enrolled in the study and you decide to travel to the study clinic for scheduled visits or sick visits, we will reimburse your transportation costs. During scheduled visits, we will compensate you for the time your child spends completing study activities. At scheduled monthly clinic visits you will receive 10,000 Tanzania shillings for your time. When our study team visits you in your home for scheduled monthly home visits, you will receive 5,000 Tanzania shillings for your time. You will not be compensated for your time when you bring your child to the clinic for sick care or when our study staff come to observe your child taking treatment for malaria.

WHAT HAPPENS IF MY CHILD IS INJURED BECAUSE OF TAKING PART IN THIS STUDY?
If your child is injured as a result of being in this study, your child will be given immediate treatment for any injuries, and will be referred for further treatment, if necessary. The project will meet the cost of treatment of injuries/harms incurred as a result of participating in this study as long the project can afford. If your child is injured by a study drug or a study clinical procedure that your child would not have been given outside this study, you will be compensated. The local Principal Investigator can provide you with information about the compensation guidelines for this sort of injury.

WHAT ARE MY RIGHTS IF MY CHILD TAKES PART IN THIS STUDY?
You are free to decide whether or not you want your child to be 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 your child is

otherwise entitled.

You are also free to talk with relatives, friends, health care providers and other people you know before you decide if you want your child to be in the study or not.

We will tell you about new information from this or other studies that may affect your child's health, welfare, or your willingness to keep your child in this study.

WHO CAN I/MY CHILD CONTACT IN CASE OF INJURY OR IF I/MY CHILD HAVE FUTURE QUESTIONS ABOUT THIS STUDY?

If your child feels unwell or experiences side effects, you should contact a Study Nurse (Tel: _____) and/or go to the study clinic or Bagamoyo district hospital.

If you have any questions about this study, your child's participation, or your child's rights as a research participant you may call Dr. Nicolaus Gutapaka (Tel: 0719512306) who is the lead study clinician, Dr. Ally Olotu (Tel+255 718 927104), who is the local Principal Investigator at IHI, or Dr. Deborah Sumari (Tel: +255 713 413331) who is the Research Manager at IHI. If you wish to contact someone other than the researchers or if you wish to voice any problems or concerns you may have about the study, please call Secretary of IHI IRB: Dr. Mwifadhi Mrisho Phone: +255 22 2774756 or Tanzania National Health Research Ethics Sub-Committee (NatHREC) (Tel: +255 22 2121400), which approved this study for questions about participants' rights and research-related harm.

CONSENT

You have been given a copy of this consent form to keep. PARTICIPATION IN RESEARCH IS VOLUNTARY. You have the right to decline to participate or to withdraw at any point without penalty or loss of benefits to which you are otherwise entitled. Your child is unable to consent for themselves because they are less than 18 years old. By signing this form or providing your thumbprint, you are giving permission for your child to participate in the study.

I consent for my child to participate in this study.	Yes [ ] No [ ]
I consent to have my child's samples stored and used for future research.	Yes [ ] No [ ]
I consent to be contacted about any follow-up studies in the future.	Yes [ ] No [ ]

Name of Child (print)

Date	Name of parent/guardian	Signature or thumbprint of parent/guardian

Date	Name of study staff obtaining consent (print)	Signature of study staff obtaining consent

If consent conducted in language other than Swahili, indicate language that consent was conducted in: _____.

Date Name of translator Signature of translator

*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 by the participant.

Date Name of witness Signature of witness

Informed Consent Form Addendum

Informed Consent- Parent/Guardian Consent for Minor

STUDY TITLE: Child Health and Infection with Low Density (CHILD) Malaria, a randomized controlled trial to assess the long-term health and socioeconomic impact of interventions targeting low-density malaria infection (LMI) among children in Tanzania.

PRINCIPAL INVESTIGATORS:

- Michelle Hsiang MD MSc (University of California, San Francisco, USA)
- Ally Olotu MD PhD (Ifakara Health Institute, Tanzania)

The purpose of this form is to tell you about new and important information we have learned since you joined this research study. The original consent form you signed is still valid except for the changes described here.

NEW INFORMATION:
Change in study follow-up: Extending participant follow-up to November 28, 2025

At the beginning of the study, we informed you that your child would participate in the study for a period of 2 years from the day your child was enrolled in the study (Day 0 visit). If you consent, we would like to extend your child's follow-up time in the study until November 28, 2025. This longer follow-up will help us to better understand how detection and treatment of low-level malaria infection impacts health and longer-term outcomes like school performance.

The study aims and procedures remain the same. We will continue to see your child monthly, either at your home or at the clinic and collect samples. Every 6 months, we will continue to collect a larger blood volume (1-2 teaspoons) to learn how your child's body responds to malaria. We will also continue gathering information on your child's school performance. However, we will not collect urine since we have not seen any parasitic diseases in the urine samples collected so far. We will also not collect nasal swabs. If your child becomes ill during

the study, he/she will continue to receive care from our study team. As we are currently doing, we will reimburse your transportation costs for visits to the clinic and for the time spent completing study activities during scheduled visits.

PARTICIPATION IN RESEARCH IS VOLUNTARY
You have the right to decline to participate or to withdraw at any point in this study without penalty or loss of benefits to which you are otherwise entitled.

WHO CAN ANSWER MY QUESTIONS?
You can contact the research team at 0719512306 (Dr. Nicolaus Gutapaka; lead study clinician, 0718 927104 (Dr. Ally Olotu; local Principal Investigator at IHI) or 0713 413331(Dr. Deborah Sumari; Research Manager at IHI) with any questions or concerns about the information provided in this form.
OR
The Secretary of the IHI-IRB Dr. Mwifadhi Mrisho Phone: +255 22 2774756 or the National Health Research ethics committee (NatHREC) (Tel: +255 22 2121400), who gave permission for this study, for questions regarding participant rights and the impact of the study on you.

The above information has been explained to me and all my questions have been answered. By signing this form or providing my thumbprint, I indicate that I have received this new information and give permission for my child to continue participating in the research study.
If I have any additional questions, I can always contact members of the research team. A copy of this document will be given to me.

I consent for my child to participate in this study. Yes [ ] No [ ]

I consent to have my child's samples stored and used for future research. Yes [ ] No [ ]

I consent to be contacted about any follow-up studies in the future. Yes [ ] No [ ]

Name of Child (print)

UCSF IRB# 22-36146

IHI IRB# IHI/IRB/No:08-2023

NatHREC NIMR/HQ/R.8a/Vol.IX/4202

Informed Consent Form Addendum #1, dated 04/28/2025

Date Name of parent/guardian Signature or thumbprint of parent/guardian

Date Name of study staff obtaining consent (print) Signature of study staff obtaining consent

If consent conducted in language other than Swahili, indicate language that consent was conducted in: _____.

Date Name of translator Signature of translator

*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 by the participant.

Date Name of witness