PROTOCOL TITLE: Minimally Invasive Tissue Sampling in Adult Populations

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*Data Use Agreements have been signed between the respective US Centers for Disease Control and Prevention and The Task Force for Global Health organizations. Listed individuals have Emory-sponsored accounts.

**Data Use Agreement has been signed by Portia Mutevedzi. Dr. Mutevedzi has an Emory-sponsored account.

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FUNDING SOURCE: Bill and Melinda Gates Foundation

REVISION HISTORY

Revision #	Version Date	Summary of Changes
1	10/30/2022	Revisions based on Emory IRB pre-review comments

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1. Study Summary

Project Title	Minimally Invasive Tissue Sampling in Adult Populations
Project Design	Multi-site, cross-sectional study targeting recruitment of adult (18 years and above) deaths in both rural and urban settings in sub-Sahara Africa and South Asia. Participants will be recruited using consecutive convenience sampling as death notifications are received by study staff. Emory University faculty and staff will not be involved in the consent process and will not interact directly with study participants. Emory faculty and staff will have access to potentially identifying health information. Emory's involvement in the study is as a data analysis and scientific advisory partner. Additionally, the prime grant for this work is with Emory University.
Primary Objective	To assess the relative contribution of malaria to death in adults (18 years and above), in a high malaria and infectious disease endemic settings in Sub-Saharan Africa and South Asia.
Secondary Objective(s)	1. To assess the relative contribution of other infectious and non-infectious disease etiologies to death in adults (18 years and above) 2. To identify the etiology of enrolled non-malarial adult deaths 3. To assess the prevalence of SARS-CoV 2 positivity among enrolled adult deaths 4. To characterize anti-microbial and anti-malarial sensitivity patterns in settings with limited routine culture and sensitivity testing 5. To describe the differences in mortality rates attributed to malaria and other infectious and

	non-infectious disease etiologies in rural vs urban settings
Research Intervention(s)/Interactions	Conduct minimally invasive tissue sampling (MITS) using standard CHAMPS protocols with laboratory testing of all specimens (microbiology, histopathology testing, etc.) Collect demographic, epidemiologic, clinical, and verbal autopsy data from enrolled adult participants
Study Population	All adult deaths (18 years and above) among residents of Child Health and Mortality Prevention Surveillance (CHAMPS) catchment areas.
Sample Size	200-300 adult deaths per site
Study Duration for individual participants	Prospective enrollment for a period of at least 14 months to include at least 2 peak malaria seasons or until target sample size is achieved
Study Specific Abbreviations/ Definitions	**Abbreviations** BMGF: Bill and Melinda Gates Foundation CDA: Complete Diagnostic Autopsies CDC: Centers for Disease Control and Prevention CHAMPS: Child Health and Mortality Prevention Surveillance COMSA: Countrywide Mortality Surveillance for Action CPL: CHAMPS Pathology Laboratory DeCoDe: Determination of Cause of Death HDSS: Demographic Surveillance System MITS: Minimally Invasive Tissue Sampling MoH: Ministry of Health PCR: Polymerase Chain Reaction PO: Program Office PPE: Personal Protective Equipment

	SBS: Social Behavioral Science TAC: TaqMan Array Cards WHO: World Health Organization **Definitions** Adult: Individual aged 18 years or above. Catchment area: Area from which hospital draws patients or defined demographic surveillance area, as appropriate for site. CHAMPS Program Office: A unit comprised of staff from the Emory Global Health Institute, the Centers for Disease Control and Prevention, The Task Force for Global Health (Public Health Informatics Institute), the International Association of National Public Health Institutes, and other stakeholders, which develops protocols and procedures for CHAMPS and provides technical assistance to sites for implementation, under the direction of the prime awardee, Emory University. Death: Irreversible cessation of all cardiorespiratory function, as certified by the attending clinician or study staff. Traumatic death: Death due to injuries, trauma-related death, and death due to a natural disaster or conflict. Notified adult death: All deaths occurring among adults (18 years or above) that are reported through CHAMPS mortality surveillance in health facilities or communities or demographic surveillance.
Funding Source (if any)	Bill and Melinda Gates Foundation

2. Objectives

General aim: To assess the role of malaria and other infectious disease etiologies in areas endemic for various infectious diseases by applying minimally invasive tissue sampling (MITS).

Primary objective: To assess the role of malaria as significant contributor to death in adults (ages 18 years and above) in disease endemic settings in sub-Saharan Africa and South Asia.

Secondary objectives:

1. To assess the relative contribution of other infectious and non-infectious disease etiologies to death in adults 18 years and above
2. To identify the etiology of enrolled non-malarial adult deaths
3. To assess the prevalence of SARS-CoV-2 positivity among enrolled deaths
4. To characterize anti-microbial and anti-malarial sensitivity patterns in settings with limited routine culture and sensitivity testing
5. To describe the differences in mortality rates attributed to malaria and other infectious and non-infectious disease etiologies in rural vs urban settings

3. Background

Malaria

In Sub-Saharan Africa and South Asia, malaria is recognized as a major cause of preventable mortality among children and pregnant women, the two populations traditionally considered vulnerable to severe disease. In such settings, and where transmission intensity remains high, continuous exposure to the infective bites of anopheles mosquitoes and infections with infectious disease agents contributes to the progressive acquisition of partial natural immunity against majority of these infections. For example, this natural immunity is the basis for the clinical tolerance to malarial infections that older children, teenagers, and adults experience. For this reason, very few clinicians practicing in malaria-endemic settings argue that malaria represents a substantial cause of mortality among adults. However, epidemiological studies using the verbal autopsy tool as the method to infer cause of death have highlighted that malaria appears to be an important contributor to adult mortality (15-20% in some age groups).[1] While verbal autopsies have repeatedly shown poor precision in determining cause of death at the individual level, the potential role of malaria as a cause of mortality in adults remains to be poorly described especially in malaria-endemic populations.

As described elsewhere,[2] MITS is a procedure that involves sampling of fluids and key body organs which are rapidly collected shortly after death by trained technicians using biopsy needles, followed by histopathological and microbiological analysis of the obtained samples with a goal of determining the cause of death when combined with clinical information of the deceased. In brief, MITS is a simplified postmortem examination technique that has shown to be an adequate approach for cause of death investigation in low-resource settings and could potentially provide data to help quantify the relative contribution of the role of malaria in adult deaths in regions where such pathogens are endemic.

Respiratory infections

Respiratory infections are a leading cause of death in Sub-Saharan Africa and South Asia; however, they have not been adequately studied in adult populations.[3, 4, 5, 6, 7] Endemic lung

infections such as pulmonary tuberculosis and bacterial infections may account for 5-20% of adults deaths yearly, including among persons living with human immunodeficiency virus (HIV).[8, 9, 10] Rising antimicrobial resistance rates disproportionately affect the lung[11, 12], and viral agents are frequently associated with endemic and seasonal epidemic patterns.[4, 5, 7] Patients with co-morbid conditions such as diabetes, HIV, cardiovascular or cerebrovascular disease are at an increased risk of death due to lung or airway infections.[6] Debilitated and immunosuppressed patients are at risk of fungal respiratory infections while rates of parasitic infections such as toxoplasmosis are unknown.[13, 14]

Ante-mortem testing of lung infections has poor yields within clinical areas because invasive sampling of the lung using bronchoscopy or other procedures are seldom conducted, particularly in resource-constrained settings.[15, 16, 17] Postmortem testing is therefore essential for diagnosis and surveillance.[18]

Minimally invasive tissue sampling (MITS)

Cause of death information is essential for improving clinical services, planning, and quality assurance in health care.[19] The complete diagnostic autopsy (CDA), where detailed examination of whole organs is performed and targeted samples taken, is the gold standard for cause of death diagnosis.[19, 20] However, in many countries in Sub-Saharan Africa and South Asia, regular conduct of CDA is not feasible to implement widely because of limited infrastructure, human resources, and laboratory capacity. In comparison, MITS consists of relatively inexpensive techniques for sampling of target tissues, has good correlation with CDA, and can be safely and reliably performed in low resource settings.[9, 18, 21]

Child Health and Mortality Prevention Surveillance (CHAMPS)

CHAMPS is a global network that aims to provide timely and accurate tracking of infectious and preventable causes of death for children under 5 years of age through a network of sites. Causes of stillbirths and deaths in children <5 years are determined after examining data from MITS specimens that undergo comprehensive microbiology and pathology testing, review of clinical records, and verbal autopsy. The data are reviewed by a panel of local experts who determine the entire causal pathway leading to death including the underlying, intermediate, and immediate causes of death. CHAMPS is currently enrolling deaths in 7 sites in Sub-Saharan Africa and South Asia and additional sites are in planning stages. This work is covered under Emory IRB 00091706. Several of the sites have high endemic rates of malaria. This provides an opportunity to leverage CHAMPS investments and methods to study adult mortality.

The first phase of the CHAMPS network focused on establishing an initial set of six sites of the CHAMPS Network over three years (June 2015 – June 2018) that would track the most preventable causes of mortality among children under five years of age, including neonates and stillbirths. A supplement was awarded in July 2017 for strengthening existing sites and adding an additional site, launching pregnancy surveillance, and establishing The Countrywide Mortality Surveillance for Action (COMSA) collaborations in two CHAMPS countries, and addressing the higher costs associated with greenfield sites. In 2019, a new supplement was

awarded for July 2019 through June 2025 to support the implementation of Phase 2 CHAMPS network activities. The primary objectives for Phase 2 included (1) continuing to generate and analyze data that characterizes the specific causes and contributors to child mortality, (2) ensuring that individuals, communities, national and global stakeholders have the skills and tools to use CHAMPS data; (3) to drive actions to reduce child mortality, and (4) strengthening network capabilities with infrastructure and tools to achieve program priorities and actions.

We propose to add a study in the context of the existing CHAMPS project to unequivocally respond to a controversial finding by several epidemiological studies (using the verbal autopsy tool as the method to infer cause of death) that malaria appears to be an important contributor to adult mortality, with a classical "U" shaped curve, according to age. We propose to conduct a set of MITS in community and hospital adult deaths to refute or confirm the hypothesis that malaria is a significant contributor to adult mortality. CHAMPS network sites aim to conduct 200-300 MITS (10-20% community deaths, 80-90% hospital deaths) at their respective site among individuals having any cause other than trauma as part of the process that led to their death (i.e., not limited to those with fever).

Social behavioral science (SBS)

Although significant amount of foundational work has been done by the CHAMPS network at each of the sites since 2015, site investigators will conduct a rapid assessment to understand community acceptance and expectation with conducting MITS in recently deceased adults. These SBS activities are covered under separate protocols at each site but a brief description is included below. Data will not be received by the Program Office at Emory University.

In brief, the SBS team will conduct the minimum set of community engagement and social science research activities required to prepare the health facilities and catchment communities for conduct of MITS in adults. These activities will build on ongoing work at CHAMPS which includes but not limited to performing qualitative Rapid Assessments that aim to probe leadership and communication structures (e.g., community perceptions on conducting MITS in adults, versus in children), rumor surveillance for duration of the project, and burial customs that may impact the MITS procedures and timelines. Once these activities are conducted, the expected outputs will guide other measures such as alignment of messages to reduce possible tension with MITS and the identification of key community leaders and community-based organizations (CBOs) that could be CHAMPS partners. A limited set of key informant interviews, focus groups and semi-structured observations may be conducted primarily as part of SBS activities within the community settings, healthcare facilities and governmental structures to assess feasibility, acceptability, and practicality of surveillance activities. The findings from these assessments will inform mortality surveillance using MITS procedure within health facilities and community as appropriate.

4. Study Endpoints

Each participating CHAMPS sites will aim to enrolled 200-300 individuals who have died from any or unknown illnesses (i.e., not limited to those with fever); deaths due to trauma or other accidental causes (e.g. drowning) will not be eligible for enrollment. Consent will be received

from family members and MITS will be conducted on all enrolled individuals. The target sample size was derived from sample size estimates showing how many subjects would be needed to show with reasonable certainty a proportion of febrile deaths determined to have died from malaria (estimated range of 10-14%) and respiratory disease (estimated 15%) in adults aged 18-69 years (Statistical Analysis Plan). A total 195 subjects would provide confidence limits of +/-5% around a point estimate of 15%. Fewer subjects are needed for point estimates 10-14%. Given geographic differences in malaria burden and in use of treatment and prevention measures, the planned sample size allows for robust estimates for each location.

5. Study Intervention/Investigational Agent

The study is observational and therefore will not be evaluating an intervention or investigational agent.

6. Procedures Involved

Study design

Multi-site, cross-sectional study

Major activities

CHAMPS Network sites:

1. Consent process
2. Direct interactions with participants and families
3. Specimen collection, testing, and archive
4. Clinical abstraction
5. Verbal autopsy
6. Data analysis and dissemination of findings to key stakeholders

CHAMPS Program Office (PO):

1. Technical assistance in adaptation and implementation
2. Data management, including data quality assurance and quality control
3. Specimen reference testing and archive
4. Data analysis and dissemination of findings to key stakeholders

Study setting and population

The study network sites in country will recruit adult mortality cases (18 years or above) in both rural and urban settings in CHAMPS catchment areas. The CHAMPS Network sites have been described in detail elsewhere.[22] Briefly, the CHAMPS network currently consists of 7 sites in Sub-Saharan African and South Asia and additional sites are currently in the planning stage. Site-specific settings and populations can be found in Appendices A and B.

Mortality Surveillance

Identification of deaths will be performed through examination of mortuary and clinical records, and from community or hospital-based staff notifying the study personnel of deaths. Therefore, deaths will be identified through passive and active surveillance in the hospital and surrounding communities and will include deaths that occurred outside the hospital that are

brought to the hospital. Deaths will be identified by study staff or informants at morgue admission through standard procedures for review of clinical summaries and death notification records. Clinical consultants and their staff will identify mortalities and notify the study team for consenting and MITS.

Study personnel will track all notified deaths and determine which are eligible for MITS based on age, death within 24-36 hours, and death not caused by trauma. Tracking deaths will allow calculation of the overall proportion of deaths identified that underwent MITS and then likely had malaria, other infectious disease agents or in which malaria and other infectious disease was in the causal chain for death.

Minimally invasive tissue (MITS) procedure

The MITS procedure will be conducted by local site personnel, under their local ethical review procedures. The CHAMPS Program Office, including Emory faculty and staff, is not involved in this procedure or consent process. The Program Office may receive tissue samples and other data collected from the procedure.

Anthropometric measurements will be collected from the deceased including height, weight, head and middle upper arm circumference. A detailed external macroscopic examination will also be conducted and the body will be digitally photographed, following a set of standard operating procedures to ensure standardized and optimal measurements and images.

Tissue specimens will be collected from the lung, heart, liver, and brain. Non-tissue specimens to be collected include blood, saliva, cerebrospinal fluid, stool, and nasopharyngeal and rectal swabs. Specimens will be aliquoted after testing, tissues processed for histopathology, and stored as part of the CHAMPS specimen archive in the local laboratory based at each of the CHAMPS sites.

Diagnostic procedures routinely undertaken by each site will include initial histopathology, bacterial culture, HIV polymerase chain reaction (PCR) testing, TB GeneXpert, malaria rapid diagnostic testing and blood smear slide analyses, and molecular diagnostics using TaqMan Array Cards (TAC). Microbiological culture (aerobic and anaerobic) will be performed on blood and cerebrospinal fluid. Multi-pathogen testing using multiplex PCR by TAC will be performed on blood, CSF, NP swab, lung tissue and rectal swabs collected through the MITS procedure. Histopathological testing using hematoxylin and eosin-stained sections will be examined by experienced pathologists for morphological diagnosis and localization/identification of infectious diseases. Special stains including tissue Gram stains and Warthin Starry for identifying bacteria, Gomori Methenamine Silver for fungal agents, and specific immunohistochemistry for infections such as influenza A, influenza B, parainfluenza, respiratory syncytial virus, adenovirus, cytomegalovirus and toxoplasmosis will be performed if warranted. In addition, specimens will be tested to assess plasmatic levels of PfHRP2 as a more reliable measure of total parasite burden, and specific malaria immunohistochemistry in tissues. Because of the known risk for severe malaria in pregnant women, women of reproductive age

will be tested for pregnancy (unless they are already known to be pregnant or recently delivered (within two weeks)).

Aliquots of formalin-fixed tissue specimens will be shipped to the CHAMPS Central Pathology Lab (CPL) based in CDC Atlanta for additional testing of infectious pathogens as warranted. The CPL will conduct a standardized telepathology review of concurrently obtained histopathologic findings with each surveillance site pathology team at least twice a month, and in certain cases may view scans with the site in real time.

The site labs performing diagnostic testing will remain enrolled in external quality assurance regimens for bacterial culture, HIV PCR testing, TB GeneXpert, and malaria rapid diagnostic testing and optic microscopy. For the purposes of quality assurance, 5-10 % of all specimens tested by TAC at site will be re-extracted and re-run-on TAC cards by the CDC laboratory or another designated laboratory.

Drug and antimicrobial resistance testing
In addition, and directly linked to our interest on assessing the contribution of malaria to mortality, CHAMPS Network sites will conduct, using standard WHO-recommended methods, molecular surveillance of known markers of antimalarial drug resistance among Plasmodia isolates recovered from study patients. This will allow us to evaluate the potential contribution of antimalarial drug resistance to mortality in our series of patients. Standard diagnostic screening with molecular testing (PCR) will be conducted to all patients to ensure RDTs and/or optic microscopy have not missed any submicroscopic parasitemia and as quality control mechanism and more sensitive screening method.

Clinical abstraction and verbal autopsy
Clinical information including medical history and physician examinations, clinical laboratory results will be abstracted for each death. Verbal autopsies will be conducted on each death.

Assignment of causes of death
Within a target of 150 days following the date of death, an expert panel (including a malariologist, an adult physician, a pathologist, a microbiologist and a public health specialist) known as the Determination of Cause of Death (DeCoDe) panel, will review and assess the combined histopathologic, clinical, epidemiologic, microbiological, and molecular findings to assign a final cause of death. Clinical data and information from verbal autopsy, will be provided to the pathology teams and DeCoDe panels in-country and at the CHAMPS Central Pathology Laboratory to enable the most accurate attribution of cause of death. Everyone involved in the DeCoDe panel will either be part of the Emory or Network site protocol, or have signed an Emory approved and countersigned Data Use Agreement if potentially identifying information is used in the DeCoDe panel.

Biosafety for Site Network Staff

1. Autopsy Facilities: Autopsy facilities are equipped with adequate ventilation as described by the World Health Organization and respective Ministries of Health (MoHs). COVID guidelines are already in use.
2. Body Handling Procedures: Bodies will be handled by trained study mortuary personnel. Sample collection will be performed within 6-24 hours after death and refrigerated at 2-7 degrees prior to autopsy. Prior to autopsy, bodies will be placed on the autopsy table. Bodies will be removed from body bags, clothes removed, and bodies photographed.
3. MITS procedures: These will be performed according to the standard CHAMPS MITS protocol by three trained MITS personnel (Appendix C). These will include the MITS technician and two assistants.
4. Body Handling after MITS procedures: The body will be cleaned by the MITS personnel and placed in a fresh body bag or wrapped in a mortuary sheet. These will be returned to cold storage or released to the next of kin following the usual (hospital) processes. Ongoing formative research by the SBS team will help guide community preferences and expectations, and the CHAMPS SOPs will be adapted accordingly.
5. Personal Protective Equipment (PPE): Strict adherence to biosafety rules will include proper PPE use as defined by the national and institutional infection prevention and control and COVID prevention guidelines. Personnel handling bodies and performing MITS will wear full coveralls, goggles, face shields, N95 masks and double gloves.
6. Occupational Health Care: All study personnel will be required to undergo medical follow-up. These will include vaccination for hepatitis B, Influenza, tetanus and pertussis. Regular COVID-19 testing will be performed as defined by national guidelines and those who test positive will undergo isolation as defined by national guidelines. Personnel will receive regular grief counselling and debrief. They will be encouraged to maintain social distancing and adhere to COVID-19 prevention regulations

7. Statistical Analysis Plan

Sample size determination

Our sample size determination method was adopted from a method which has been detailed elsewhere.[24] In brief, below is our sample size estimates:

$$n=(Nz^2p(1-p)/((N-1)\ d^2+z^2p(1-p))$$

n = minimum sample size
N = Number of adult mortalities, per year (32,000)
Z = z value 1.96 at 5% type 1 error, 95% confidence level
p = prevalence of adult respiratory disease mortality (estimated at 15% of all adult mortalities)
d = margin of error taken as 0.05

The minimum sample size needed for respiratory disease mortality is 195. The estimated prevalence of adult malaria mortality is 10-14% per site, which will require a smaller target sample size (n=138 at 10% prevalence). This study plans to enroll 200 or more adults at each site.

Interim analysis

A preliminary evaluation of data will be conducted by each site after 25-50 deaths with completed MITS. Case demographics and malaria test results will be assessed to determine whether criteria for enrollment needs to be adjusted (e.g. representation of likely malaria deaths, rural-urban residence, gender balance, community versus hospital deaths). The CHAMPS site study team (in collaboration with the CHAMPS PO) will analyze the initial data on deaths at each site in order to recommend measures aimed at making deaths selected for MITS as representative as possible within resource constraints, and/or to recommend differential sampling of certain age groups and/or types of deaths in order to optimize the resources allocated for MITS. A similar interim analysis will be conducted after 100 deaths.

Purpose: To identify issues that will affect our approach to the primary analysis. Specifically:

1. To assess the distribution of age groups and malaria positivity by different testing methods
2. To summarize the amount of missing data for key variables
3. To examine the distributional characteristics of key variables in order to detect potential data entry/reduction errors

Methods**:** Relevant approaches may include:

1. Tabulation of descriptive statistics for key variables including missing observations
2. Histograms and other data visualizations

Analysis plan for primary objective

Purpose: To assess the relative contribution of malaria and other infectious disease etiologies to death in adults 18 years and above, in each CHAMPS site

Methods: Relevant approaches may include:

1. Descriptive analysis to examine the distribution of deceased cases with malaria, infectious and non-communicable disease etiologies
2. Descriptive analysis to examine key demographic and clinical characteristics

8. Data and/or Specimen Banking

CHAMPS datasets captured at each CHAMPS site will be maintained at each site in a local secure data repository as well as mirrored in a secure global data repository maintained by the CHAMPS Project Officer based at Emory University. Any physical data collection instruments containing unique identifiers will be stored in closed, locked filing systems with restricted access at CHAMPS study offices at sites, where each site will be the custodian of their respective site study data. The CHAMPS Network global data repository will be a centralized, web-accessible, composite database of CHAMPS Network data from all participating sites that will provide data visualizations and analyses.

Where indicated, defined specimens will be shipped to the CHAMPS CPL in Atlanta, Georgia, USA, for confirmatory testing and bio banking. This will be the site for quality assurance and shipment of specimens will be guided by approved material transfer agreements and batch shipment requests, with strict adherence to MoHs and local CHAMPS site regulations on shipment of clinical and research biological specimens.

The vision for the CHAMPS Network specimen archive is to create a standardized, reliable, quality management approach to the collection, storage, access, and use of CHAMPS Network specimens with equitable governance by the global public health community. Supporting high-quality specimen collection, maintaining long-term specimen integrity, preserving patient confidentiality and privacy, and establishing robust governance procedures are core objectives. Frozen tissues and non-tissue specimens would be stored at -80^{o}C at surveillance sites and under liquid nitrogen (-140^{o}C) at a central facility (initially at the CHAMPS CPL long-term storage facility). All tissue specimens processed will be stored as formalin-fixed paraffin blocks (FFPE) and slides. The location and key findings will be recorded in the CHAMPS database.

9. Sharing of Results with Participants

The CHAMPS site investigators will provide two opportunities for feedback to the family of the deceased: preliminary feedback within one month from the date of death, and final feedback following the DeCoDe determination of cause of death. CHAMPS will work with the local health authorities to determine which laboratory, clinical or other MITS findings may have ethical or public health implications (e.g., reportable diseases, preventable infections, intentional injuries), and apply similar policies as CHAMPS to undertake basic actions to improve the family's health status.

10. Study Timelines

Once families consent to the MITS procedure after all their questions have been answered, the procedure itself takes approximately 60 minutes to complete. Enrollment for MITS at two CHAMPS sites has already begun in August 2022 via protocols approved by local IRBs (Appendices D and E), with the goal of enrolling deaths during the peak malaria months in 2022 and continuing through the peak malaria months in 2023 (for a total of 14 months of enrollment). Additional CHAMPS sites with approved local protocols will aim for similar durations.

11. Inclusion and Exclusion Criteria

Inclusion criteria

1. Deceased adults, aged 18 years and above, and
2. Resident member of at least one of the CHAMPS catchment areas, and
3. Where the next of kin provides informed consent, and
4. Death occurred <24 hours before enrollment

Exclusion criteria

1. Mortality in individuals aged <18 years
2. Trauma-related deaths, including falls, drowning and road-traffic and other accidental accidents

3. Non-resident of the local CHAMPS catchment areas

12. Population

As death notifications are received by CHAMPS site study staff, all eligible adult deaths in the CHAMPS catchment areas will be recruited using consecutive convenience sampling.

This human subject research does not meet the definition of 'Clinical Research.' However, there are still important ethical considerations, including concerns of family members, to take into account, which are ethical and not regulatory human subjects concerns.

Deceased persons have been previously determined by institutional review boards not to be human subjects. In this study, those enrolled will all be 18 years of age and above.

13. Vulnerable Populations

This human subject research does not meet the definition of 'Clinical Research.' However, there are still important ethical considerations, including concerns of family members, to take into account, which are ethical and not regulatory human subjects concerns.

Deceased persons have been previously determined by institutional review boards not to be human subjects. In this study, those enrolled will all be 18 years of age and above.

14. Local Number of Participants

Each CHAMPS site will target 200-300 MITS cases. All eligible adult deaths in the CHAMPS catchment areas will be recruited using consecutive convenience sampling. MITS activities will be discontinued after the target number of deceased MITS cases is reached and enrollment covers at least two malaria seasons.

15. Recruitment Methods

Identification of cases will be performed through examination of mortuary and clinical records, and from community or hospital-based staff notifying the study personnel of deaths. Therefore, deaths will be identified through passive and active surveillance in the hospital and surrounding communities and will include deaths that occurred outside the hospital that are brought to the hospital. Deaths will be identified by study staff or informants at morgue admission through standard procedures for review of clinical summaries and death notification records.
Clinical consultants and their staff will identify mortalities and notify the study team for consenting and MITS. The next of kin of the deceased persons will be contacted by study staff. Supportive and grief counselling by trained staff will be offered before, during and after the consent process. Next of kin who are listed within the medical records will be contacted to consent on behalf of the dead persons. During this period, the study will be explained and informed consent for MITS will be sought. Spouses of deceased persons or close relations with power of attorney are eligible to offer informed consent.

16. Withdrawal of Participants

During the informed consent procedure, all potential participants will be informed that they can withdraw from the study at any time during or after consent, without any untoward consequences. All withdrawals and refusals will be appropriately recorded in the database.

17. Risk to Participants

The potential risks to the next of kin of the study subjects include stigma related to an infectious disease diagnosis established during postmortem testing, including HIV and COVID-19.

18. Potential Benefits to Participants

Although there are no direct benefits to the deceased, next of kin will be advised of the final cause of death determined and will benefit from a better understanding of what led to the death of their loved one. Families will also have information about possible exposure to important infectious pathogens. They will further be advised on prevention and treatment resources available in the area. Identification of death rates associated with malaria, infectious and non-infectious diseases will improve the MOH's prioritization of the control and clinical management of identified diseases among adults living in these high disease burden settings.

19. Compensation to Participants

Local site teams will provide specific assistance to the bereaved family participating in the study. This includes offers of transport to the family to take the body back to their home or burial site following the MITS procedure. Any medical expenses resulting from participation in this study will not be reimbursed by the investigators. Sites may contribute towards the cost of burial of the deceased and pay for the storage fees for the body for up to 5 days at one of the mortuaries where the sites conduct procedures from.

If the SBS formative research makes a finding that other forms of compensation are necessary, these will be assessed in the light of existing ethical and budgetary considerations.

20. Data Management and Confidentiality

The only document that will bear participant names will be the Informed Consent Forms (ICF). Emory staff will never receive ICFs or any names. Every deceased case participating in this study will be assigned a special unique study identification number which will not be linkable in any way to the names in the ICF but will be used in all the participants' documents throughout the study. Pictures used for publication will have the faces blinded and data sets that contain fields that may identify a specific study participant (e.g., photographs, date of death, service dates, date of birth) would not be published. Furthermore, the primary data with any identifier would be password protected and will only be accessible to authorized study staff and investigators.

If a participant declines to participate in all portions of the study, the participant will not be assigned a study ID number and the study coordinators/data collector will refrain from collecting any data on the participant. If the participant agrees to participate in some portions of the study but not others, the participant will be assigned a study ID number and the study

coordinators/data collectors will be instructed to collect data only on those aspects of the study to which the participant has agreed to participate. These procedures will help prevent unauthorized inclusion of the patient's data in the database

Data security will be ensured using secure servers, levels of authorization, password protection encryption and physical lock and key controls. Data quality and integrity will be reviewed weekly, with necessary checks and corrections made using standard protocols.

In all circumstances where data are shared, only de-identified data will be made available. If identifiable data are requested, the requesting researcher will need to complete a full IRB process prior to approval.

Confidentiality will be maintained at all study sites whenever possible. All specimens and data will be de-identified and coded. Reports will be submitted to the clinical management team for Determining Cause of Death (DeCoDe) meetings. De-identified data will be shared with surveillance teams of the MoH and respective hospitals for further analysis and for data to action. Summary de-identified feedback to individual physicians will be provided for the purpose of improvement of quality of clinical care. Coded confidential reports that lack identifying information will be issued to next of kin during debrief sessions. Loss of confidentiality may occur when notifiable diseases such as TB, HIV or SARS-COV-2 infection is confirmed and shared with MoH disease surveillance teams, who may perform contact tracing to require testing and isolation/treatment of contacts of the deceased. The principal investigators will liaise with relevant hospital and national surveillance teams to manage this process by adhering to national laws and relevant policies.

De-identified verbal autopsy data and COVID results will be shared with the World Health Organization's Verbal Autopsy Technical Advisory Group (TAG) for their internal analysis and use.

Publicly available data will be reported to relevant stakeholders regularly and may include aggregate data and analyses regarding causes of death in the community and de-identified case data for training and secondary analyses.

Results from the study may additionally be presented at scientific conferences and/or in peer-reviewed manuscripts to contribute to the body of knowledge of childhood morbidity and mortality. A publications committee will be constituted by the PO and sites to review proposed publications involving more than one site's data. Sites will have similar mechanisms for reviewing proposed uses of site-specific data.

21. Plans to Monitor the Data to Ensure Safety of Participants and Data Integrity

☒ **No more than minimal risk**

22. Provisions to Protect the Privacy Interest of Participants

The next of kin of the deceased persons will be contacted by study staff. Supportive and grief counselling by trained staff will be offered before, during and after the consent process.

23. Economic Burden to Participants

There is no economic burden to participants, except costs of phone calls for and transportation for consent and verbal autopsy. Any such costs will be covered by CHAMPS.

24. Informed Consent

The next of kin of the deceased persons will be contacted by site study staff. Supportive and grief counselling by trained site staff will be offered before, during and after the consent process. Next of kin who are listed within the medical records will be contacted to consent on behalf of the dead persons. During this period, the study will be explained and informed consent for MITS will be sought. Spouses of deceased persons or close relations with power of attorney are eligible to offer informed consent.

Informed consent procedures are specified in site-specific protocols (Appendices A and B); informed consent forms (Appendices F and G) have been approved by appropriate IRBs (Appendices D and E).

Emory staff will never receive ICFs and will not have access to names.

25. Setting

Site settings are described in local IRB protocols (Appendices A and B).

26. Resources Available

Resources are described in local IRB protocols (Appendices A and B).

27. Multi-Site Research When Emory is the Lead Site

The CHAMPS Network currently consists of 7 sites in Sub-Saharan Africa and South Asia. Plans for adding additional sites are in progress. Each site participating in this study will obtain local IRB approval prior to beginning the study. The target sample size is 200-300 MITS cases per site. Data will be stored locally as described in Data Management and Confidentiality.

The CHAMPS PO at Emory University will not be involved with the consent process and will not directly interact with study participants. The CHAMPS PO will receive data from site and support sites in the following activities:

1. Technical assistance in adaptation and implementation
2. Data management, including data quality assurance and quality control
3. Specimen reference testing and archive

4. Data analysis and dissemination of findings to key stakeholders

Sites will be closely linked to the PO through an established formal reporting structure.

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29. Protocol Checklist

Please note that protocol sections with an asterisk (*) should always be included in the protocol; if the section does not have an asterisk, and you have not included the section in the protocol, the IRB will consider it your attestation that the section does not apply to your study.

Protocol Section	Added to the protocol?

External Collaborators- if applicable, add each external collaborator information and indicate whether that institution's IRB will review (or has already reviewed) that individual's engagement in human participants research activities)	☐ **Yes**
Funding Source*: Include the information for the funding entity for this study. Please explain if this study is covered by a sub-award or other pertinent information. Say "department" if you do not have any other funding.	☐ **Yes**
Objectives*: Describe the purpose, specific aims, or objectives and state the hypotheses to be tested	☐ **Yes**
Background*: Describe the relevant prior experience and gaps in current knowledge. Describe any relevant preliminary data. Provide the scientific or scholarly background for, the rationale for, and significance of the research based on the existing literature and how will it add to existing knowledge	☐ **Yes**
Study Endpoints*: Describe the primary and secondary study endpoints. Describe any primary or secondary safety endpoints.	☐ **Yes**
Study Intervention/Investigational Agent*: Describe the study intervention and/or investigational agent (e.g., drug, device) that is being evaluated.	☐ **Yes**
Drug/Device Handling: If the research involves drugs or devices, describe your plans to store, handle, and administer those drugs or devices so that they will be used only on participants and be used only by authorized investigators. If using a drug, explain if the control of the drug is managed by IDS (or VA/Grady/CHOA research pharmacies). If not, provide IDS exemption document. If a device, explain how the device is being stored and managed.	☐ **Yes**
If the drug is under an FDA REMS, plan to complete the REMS checklist found here, on the IRB website.	☐ **Yes**
If the drug is considered a controlled substance, make sure you have filled out this form.	☐ **Yes**
If applicable, identify the holder of the IND/IDE/Abbreviated IDE. An Emory investigator who holds an IND or IDE is considered to be a Sponsor-Investigator (S-I). If the study is under an S-I, review this section of our website for additional requirements.	☐ **Yes**
Procedures involved*: Describe and explain the study design and include a study schema. Describe all research procedures being performed and when they are performed, including procedures being performed to monitor participants for safety or minimize risks	☐ **Yes**

Procedures-Minimizing risk*: describe the procedures performed to lessen the probability or magnitude of risks.	☐ **Yes**
Procedures- Drug/Device Use: describe all drugs and devices used in the research and the purpose of their use and their regulatory approval status	☐ **Yes**
Procedures-Source Records*: describe source records that will be used to collect data about participants. Attach all surveys, scripts, and data collection forms to the submission.	☐ **Yes**
Procedures-Data collection*: describe what data will be collected during the study and how that data will be obtained	☐ **Yes**
Procedures- Long Term Follow Up*: once all research-related procedures are complete, what data will be collected during this period. If no data is collected after procedures are completed, please state in the submission.	☐ **Yes**
Data and Specimen Banking: describe where the specimens will be stored, how long they will be stored, how the specimens will be accessed, and who will have access to the specimens. Depending on the volume and nature of the collection, this may require a separate repository-specific IRB submission. The VA Data Repository SOP is required if the study is creating a data repository at the Atlanta VA. List the data to be stored or associated with each specimen. Describe the procedures to release data or specimens, including the process to request a release, approvals required for release, who can obtain data or specimens, and the data to be provided with specimens.	☐ **Yes**
Sharing of Results with Participants*: Describe whether results (study results or individual subject results, such as results of investigational diagnostic tests, genetic tests, or incidental findings) will be shared with participants or others (e.g., the participant's primary care physicians) and if so, describe how the results will be shared If applicable (e.g. for studies involving scans and/or panels of exploratory testing on specimens) Plan for managing the types of findings that might arise. This should include any secondary findings that are being sought actively, findings that might be anticipatable, and findings that might be un-anticipatable. Plan for recognizing, analyzing, and handling incidental findings and how incidental findings will be communicated to participants during the consent process. If the plan is not to disclose any findings, then this should be included. This plan might include the option for participants to opt-out of receiving incidental findings. Description of the research team's responsibilities following disclosure of a finding. This should detail educational information about the nature of the finding, how to seek care	☐ **Yes**

from a clinician or specialist, obtaining health insurance to secure treatment, and/or referral to a clinical specialist, if one is required. Reminder to include language in the consent form to let the participants know your plans for this – see Modular Language for Informed Consent Forms on IRB website)	
Study timelines*: describe the duration of an individual participant's participation in the study; anticipated time to enroll all study participants and the estimated date for the investigators to complete this study (complete primary analyses)	☐ **Yes**
Inclusion and Exclusion Criteria*: describe how individuals will be screened for eligibility and the criteria that define who will be included or excluded in your final study sample	☐ **Yes**
Population*: describe the study popualation and indicate specifically whether you will include or exclude each of the following special populations: • Adults unable to consent • Individuals who are not yet adults (infants, children, teenagers) • Pregnant women • Prisoners Note: you cannot exclude people with limited English proficiency unless you can demonstrate the scientific need for such exclusion. Community Participation: For studies aimed at addressing issues that affect a certain community or group: How, if at all, will this study involve people from the target community in the design of the study? Conduct of the study? How will the results of the research be shared with the participants and/or the target community/ies? **If studying Race or Ethnicity, have you defined these terms, and explained their proposed mechanism of action if these characteristics will be used in an explanatory model?**	☐ **Yes**
Research with pregnant women, fetuses, or neonates: review this checklist to verify you have provided enough information to ensure the safety and well-being of this population.	☐ **Yes**
Research with neonates of uncertain viability: review this checklist to verify you have provided enough information to ensure the safety and well-being of this population.	☐ **Yes**
Research involving prisoners: review this checklist to verify you have provided enough information to ensure the safety and well-being of this population.	☐ **Yes**

Research involving children: review this checklist to verify you have provided enough information to ensure the safety and well-being of this population.	☐ **Yes**
Research involving cognitively impaired adults: review this checklist to verify you have provided enough information to ensure the safety and well-being of this population.	☐ **Yes**
Research involving economically or educationally disadvantaged persons: describe the additional safeguards that have been included in the study to protect the rights and welfare of these subjects	☐ **Yes**
Local Number of Participants*: Indicate the total number of participants to be accrued locally. If applicable, distinguish between the number of participants who are expected to be enrolled and screened, and the number of participants needed to complete the research procedures (i.e., numbers of participants excluding screen failures.) Provide your projected enrolling goals, including the percentage of participants according to sex and race.	☐ **Yes**
Recruitment Methods*: Describe when, where, and how potential participants will be recruited. Describe the source of participants. Describe the methods that will be used to identify potential participants. Describe materials that will be used to recruit participants. Attach copies of these documents with the application. If including advertisements, attach the final copy of them. When advertisements are taped for broadcast*, attach the final* audio/videotape. You may submit the wording of the advertisement before taping to preclude re-taping because of inappropriate wording, provided the IRB reviews the final audio/videotape. Describe the amount and timing of any payments to participants. Reimbursement for expenses/travel? If using contests or raffles as incentive, you must offer entry to all potential participants, not just those who enroll in the study/complete study-related procedures, per Georgia State Law. All research recruitment through social media needs to follow this guidance, which does not allow the use of personal social media accounts for some recruitment activities.	☐ **Yes**
Withdrawal of Participants*: Describe anticipated circumstances under which participants will be withdrawn from the research without their consent. Describe any procedures for orderly termination. Describe procedures that will be followed when participants withdraw from the research, including partial withdrawal from procedures with continued data collection.	☐ **Yes**
Risk to Participants*: List the reasonably foreseeable risks, discomforts, hazards, or inconveniences to the participants related to the participant's participation in the research.	☐ **Yes**

Include as may be useful for the IRB's consideration, a description of the probability, magnitude, duration, and reversibility of the risks. Consider physical, psychological, social, legal, and economic risks. If applicable, indicate which procedures may have risks to the participants that are currently unforeseeable. If applicable, indicate which procedures may have risks to an embryo or fetus should the subject be or become pregnant. If applicable, describe risks to others who are not participants.	
Potential Benefits to Participants*: Describe the potential benefits that individual participants may experience from taking part in the research. Include as may be useful for the IRB's consideration, the probability, magnitude, and duration of the potential benefits. Indicate if there is no direct benefit. Do not include benefits to society or others.	☐ **Yes**
Compensation to Participants*: Describe if/how subjects will be compensated for participation in this study. Indicate what method compensation will be delivered (e.g. cash, gift card, school credit). Describe the amount and timing of any payments to participants. How much? What kind? Is tax information required? (if so, must be reflected in the informed consent form). Will payments be pro-rated if a participant withdraws early?	☐ **Yes**
Data Management and Confidentiality*: Describe the data analysis plan, including any statistical procedures or power analysis. Describe the steps that will be taken to secure the data (e.g., training, authorization of access, password protection, encryption, physical controls, certificates of confidentiality, and separation of identifiers and data) during storage, use, and transmission. Describe any procedures that will be used for the quality control of collected data.	☐ **Yes**
Describe how data or specimens will be handled study-wide*: What information will be included in that data or associated with the specimens? • Where and how data or specimens will be stored? • How long the data or specimens will be stored? • Who will have access to the data or specimens? • Who is responsible for receipt or transmission of the data or specimens? • How data or specimens will be transported?	☐ **Yes**
Data Monitoring and Participants Safety (if this study is more than minimal risk, this section is required): Ensure that you review our Data and Safety Monitoring plan guidance for specific details about this section, and examples of what the IRB will be requiring according to the level of risk.	☐ **Yes**

If a DSMB is needed, please describe the composition of the board (if not already detailed in the protocol). Review this guidance for more information. If the sponsor protocol does not contain all required information, please in this section.

Describe the plan to periodically monitor the data at the site level according to risk level. Include the appropriate completed monitoring table, if applicable.

Description of the plan for notifying the IRB of reportable events, whether the sponsor requires reporting above and beyond the Emory IRB reporting requirements, and if so, a description of the requirements and plan for meeting them.

Please address the specific details below. If deemed not applicable, please provide rationale:

Subject safety:

- Specific subject safety parameters
- Frequency of subject safety observations
- Individual responsible for safety monitoring
- Subject stopping rules – under what conditions will a subject be removed from study participation and who will make the decision?
- Study stopping rules - under what conditions will the study be modified or stopped and who will make the decision?
- Reporting mechanisms (i.e. Deviations, adverse events, UPs)

Data Integrity:

- Specific data elements to be reviewed
- Frequency of monitoring data, points in time, or after a specific number of participants
- Individual responsible for data monitoring

Additional considerations for FDA regulated trials

Depending on the procedures affecting risks to participants, the site monitoring plan should specify:

- Categorization of activities done centrally and those on-site if applicable
- Monitoring methods (may include centralized/remote, on-site, and self-monitoring)
- Reference to any tools used (i.e. checklists)
- Identification of events that may trigger changes
- Identification of deviations or failures that would be critical to study integrity

Provisions to Protect the Privacy Interests of Participants*: • Describe the steps that will be taken to protect participants' privacy interests. "Privacy interest" refers to a person's desire to place limits on whom they interact with or whom they provide personal information. • Describe what steps you will take to make the participants feel at ease with the research situation in terms of the questions being asked and the procedures being performed. "At ease" does not refer to physical discomfort, but the sense of intrusiveness a participant might experience in response to questions, examinations, and procedures. • Indicate how the research team is permitted to access any sources of information about the participants.	☐ **Yes**
Economic Burden to Participants*: Describe any costs that participants may be responsible for because of participation in the research.	☐ **Yes**
Consent Process*: Describe where the consent process will take place, any waiting period available between informing the prospective subject and obtaining the consent; and the process to ensure ongoing consent. Describe the role of the individuals listed in the application as being involved in the consent process; the time that will be devoted to the consent discussion; steps that will be taken to minimize the possibility of coercion or undue influence; and steps that will be taken to ensure the participants' understanding. **Note**: If you are planning to obtain consent via electronic signature, please review this document. Additional guidance on consent documentation and process can be found on our website, under the consent toolkit.	☐ **Yes**
Consent Process-Non-English-Speaking Participants*: Indicate what language(s) other than English are understood by prospective participants or representatives. If participants who do not speak English will be enrolled, describe the process to ensure that the oral and written information provided to those participants will be in that language. Indicate the language that will be used by those obtaining consent. If you checked N/A, please provide reasoning of why subjects with limited English proficiency are excluded. **Note**: if you stated that subjects with LEP will be enrolled, you are approved for the use of the Emory IRB short forms. Please read the guidance about the use of short forms here.	☐ **Yes**

Consent Process-Children: After determining if the subject is a child per GA law (or if enrolled outside GA, per state/country law), please describe whether parental permission will be obtained from: • Both parents unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child. • One parent even if the other parent is alive, known, competent, reasonably available, and shares legal responsibility for the care and custody of the child. Describe whether permission will be obtained from individuals other than parents, and if so, who will be allowed to provide permission. Describe the process used to determine these individuals' authority to consent to each child's general medical care. When assent of children is obtained describe whether and how it will be documented per Emory Policies and Procedures	☐ **Yes**
Consent Process-Cognitively Impaired Adults: describe the process to determine whether an individual is capable of consent. The IRB allows the person obtaining assent to document assent on the consent document and does not routinely require assent documents and does not routinely require children to sign assent documents.	☐ **Yes**
Consent Process-Adults Unable to Consent: List the individuals from whom permission will be obtained in the order of priority. (E.g., durable power of attorney for health care, a court-appointed guardian for health care decisions, spouse, and adult child.) For research conducted in the state, review "46 LEGALLY AUTHORIZED REPRESENTATIVES AND SURROGATE CONSENT" to be aware of which individuals in the state meet the definition of "legally authorized representative." For research conducted outside of the state, provide information that describes which individuals are authorized under applicable law to consent on behalf of a prospective subject to their participation in the procedure(s) involved in this research. Describe the process for the assent of the participants. Indicate whether: • Assent will be required of all, some, or none of the participants. If some, indicated, which participants will be required to assent and which will not. • If assent will not be obtained from some or all participants, an explanation of why not. Describe whether the assent of the participants will be documented and the process to document assent. The IRB allows the person obtaining assent to document assent on the	☐ **Yes**

consent document and does not routinely require assent documents and does not routinely require participants to sign assent documents	
Waiver or Alteration of Consent Process (consent will not be obtained, required information will not be disclosed, or the research involves deception) Review the Emory IRB waiver document to ensure you have provided sufficient information for the IRB to make these determinations. If the research involves a waiver of the consent process for planned emergency research, please review the "CHECKLIST: Waiver of Consent for Emergency Research (HRP-419)" to ensure you have provided sufficient information for the IRB to make these determinations.	☐ **Yes**
Setting*: Describe the sites or locations where your research team will conduct the research including where the subject will be identified and recruited, where the research procedures will be performed, and if you will involve a community advisory board. For research conducted outside the organization and its affiliates describe the site-specific regulations or customs affecting the research outside the organization and the local scientific and ethical review structure outside the organization.	☐ **Yes**
Resources Available*: Describe the resources available to conduct the research such us the feasibility of recruiting the required number of suitable participants within the agreed recruitment period; describe the time that you will devote to conducting and completing the research; describe the availability of medical or psychological resources that participants might need as a result of an anticipated consequences of the human research; describe your process to ensure that all persons assisting with the research are adequately informed about the protocol, the research procedures, and their duties and functions.	☐ **Yes**
Multi-Site Research when Emory is the Lead Site: Study -Wide Number of Participants: indicate the total number of participants to be accrued across all sites. Study-Wide Recruitment Methods: If this is a multicenter study and participants will be recruited by methods not under the control of the local site (e.g., call centers, national advertisements) describe those methods. Describe when, where, and how potential participants will be recruited. Describe the methods that will be used to identify potential participants. Describe materials that will be used to recruit participants. Describe the processes to ensure communication among sites. See "WORKSHEET: Communication and Responsibilities (HRP-830)." All sites have the most current version of the protocol, consent document, and HIPAA authorization. All required approvals (initial, continuing review and modifications) have been obtained at each site (including approval by the site's IRB of record). All modifications have been communicated to sites and approved (including approval by the site's IRB of record) before the modification is implemented.	☐ **Yes**

All engaged participating sites will safeguard data, including secure transmission of data, as required by local information security policies. All local site investigators conduct the study in accordance with applicable federal regulations and local laws. All non-compliance with the study protocol or applicable requirements will reported in accordance with local policy Describe the method for communicating to engaged participating sites (see "WORKSHEET: Communication and Responsibilities (HRP-830)"):	
• Problems (inclusive of reportable events). • Interim results. • The closure of a study	
If this is a multicenter study where you are a participating site/investigator, describe the local procedures for maintenance of confidentiality. (See "WORKSHEET: Communication and Responsibilities (HRP-830).")	
• Where and how data or specimens will be stored locally? • How long the data or specimens will be stored locally? • Who will have access to the data or specimens locally? • Who is responsible for receipt or transmission of the data or specimens locally? • How data and specimens will be transported locally?	

30. Appendices

Appendix A. Kenya Protocol

Appendix B. Sierra Leone Protocol

Appendix C. Standard CHAMPS MITS Protocol

Appendix D. Kenya Ethical Approval

Appendix E. Sierra Leone Ethical Approval

Appendix F. Kenya Consent Form

Appendix G. Sierra Leone Consent Form