

# **A Case-Control Study to Evaluate Immune Responses to Malaria during Pregnancy**

## **Principal Investigator**

James Smith, Ph.D., United States University

## **Co-investigators**

Calinda Bockwirth, M.D., National Hospital

Pedro Rodriguez, M.D., National Ministry of Health

Margaret Trudeau, Ph.D., University of Canada

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TBA Post-doctoral fellow, Ph.D, United States University

## **Background**

Primigravidae women residing in malaria endemic areas are at increased risk for malaria infection when compared to multigravidae and non-pregnant peers. Maternal anemia, infant low birth weight and neonatal deaths are known complications of maternal malaria infection. The risk of symptomatic disease is highest in the 3<sup>rd</sup> trimester. Infection of the placenta with *Plasmodium falciparum* is common, but the factors that lead to high levels of parasitemia in the placenta during first pregnancies and reduced risk during subsequent pregnancies are poorly understood. It is generally agreed that local immunity to malaria develops during repeat pregnancies and leads to a decrease in the intensity of subsequent infections. We hypothesize that this effect is mediated by specific immune responses. Preliminary data indicate that these immune responses are perturbed in the presence of HIV and may partially explain the observations that pregnant women with HIV have more frequent and severe episodes of malaria when compared to women without HIV infection and that their children are at higher risk of death.

A better understanding of the factors that predispose primigravidae pregnant women to more frequent and severe episodes of malaria when compared to their non-pregnant and multigravidae counterparts will enhance our ability to develop effective prevention and treatment strategies. Understanding these factors in the setting of HIV co-infection is essential given the overlapping geographical distribution of these devastating infections.

## **Study Objectives**

1. To measure a 'panel of selected immunologic responses' to malaria of primigravidae and multigravidae women immediately after birth and compare them to those of previously pregnant women.
2. To identify variables from the 'panel of selected immunologic responses' associated with greater resistance or susceptibility to malaria infection.

3. To identify variables from the 'panel of selected immunologic responses' associated with greater susceptibility to malaria infection.
4. To compare the 'panel of selected immunologic responses' profile in HIV and non-HIV infected women

### **Study Design**

This study will be conducted in two regional hospitals (Regional Hospital A and Regional Hospital B) operated by the National Ministry of Health. Pregnant women presenting in labor will be eligible for enrollment. Most eligible women will be in active labor and it will not be possible to explain the study and seek consent from them until after delivery. Women will be approached by a health worker from 2-12 hours after delivery and have the study explained to them including the need for HIV testing. After they have had an opportunity to ask questions and provide consent, the health worker will obtain a 7 cc sample of peripheral blood, a fingerstick sample for thick and thin smears, and ask questions about their reproductive history and general health history. Data about the labor and delivery, including infant APGAR score, will be obtained from medical records. All enrolled subjects will receive HIV pre and post test counseling.

Timely collection and processing of the placenta samples is critical to the validity of the assay results and requires that the placenta be collected immediately after it is expelled. The routine in both of these hospitals is to discard placenta after the birth attendants have examined it. During the time this study is enrolling subjects, hospital routine will be altered so that the placenta from potentially eligible participants will be collected and stored. Cord blood and placental tissue will be collected and stored according to procedures detailed in the study operations manual. The peripheral blood, cord blood and placental tissue will be assessed for parasitemia, hemoglobin, CD4 counts, and the study specific immunology assays. The placenta of women who are not subsequently enrolled in the study will be discarded. A smear for parasitemia and the study specific immunologic assay panel will be repeated once 8 weeks after enrollment.

Two non-pregnant women will be recruited as controls for each primigravidae enrolled in the study. They will be recruited from mothers bringing children to the pediatric outpatient clinic. The study will be explained and consent obtained in the clinic at a time convenient to the mother. Those who agree and provide consent will have a serum sample obtained (for HIV testing, hemoglobin, CD4 count, and study specific immunologic assays). Smears will be prepared for parasitemia levels and they will be asked questions about their general and reproductive health history and recent use of antimalarial drugs. As with the recently delivered mothers, these women will receive standard HIV pre- and post-test counseling. There will be no 8 week follow up visit for this group of controls.

HIV testing for all subjects will be performed onsite using standard MOH criteria for interpretation of results. HIV tests results, identified only by study number to the lab staff, will be communicated in writing to the same counselor who performed pre-test counseling. Women with indeterminate results will be encouraged to return for repeat testing in 3 months.

Women testing positive for malaria in peripheral blood will be offered standard anti-malarial treatment according to MOH guidelines. Anemic women will also be treated according to MOH guidelines.

### **Selection of Subjects**

Inclusion criteria for all primigravidae women:

- a) age 15 to 40 years;
- b) no apparent infection (other than malaria or HIV) or underlying medical condition present as determined by history and physical examination;
- c) agreement to participate in the study.
- d) delivery in hospital

Inclusion criteria for multigravidae women:

- a) through e) above, plus prior history of at least one live birth at estimated gestational age > 35 weeks.

Inclusion criteria for non-pregnant women:

- a) through c) above, plus history of at least one previous live birth;

### **Sample size determination**

The total sample size for this study will be 150 women. It is estimated that 30 individuals in the primigravida group will be required to detect statistically significant differences (with confidence = 95% and power = 80%) and will be matched to two multigravidae controls and two non-pregnant controls. Enrollment of multigravidae women will be halted after 60 women have been enrolled in this group.

### **Laboratory and Data management**

Requirements for batch testing, materials and equipment, and other limitations require that study specific immunologic assays be performed offsite. Samples will be frozen and shipped for intermediate storage to the laboratory at the National University prior to shipment to the study labs in North America.

All demographic, clinical data and hospital laboratory data will be entered into an Access database. The results of clinical samples analyzed at the central University laboratory will be entered directly. The HIV test result files will be password protected and computer access will be restricted to key persons. The identifiers linking the HIV results to the participants will be kept locked at all times with access only by designated key persons.

### **Protocol time line**

The proposed studies are projected to begin July 2007 and to be completed by December 2010.

### **Human Subjects**

All women invited to participate in the proposed studies will receive a complete explanation of the study in their language of choice. All patients will be assured that participation is voluntary, that a participant may withdraw at any time during the study, and that access to health care is not dependent on participation. All risks and benefits to the individual participants will be explained verbally and included in the consent form.

Placentas collected from women who choose not to participate will be discarded as per hospital standard practice.

No study participant will be identified by name in any publication, meeting abstract or report derived from the study results or information collected. A unique study number will be assigned to each participant and used for all data analysis and laboratory reports. Essential records containing patient name and study number will be maintained in a separate password protected database and locked paper files. Individual laboratory results will be made available to clinical personnel involved in the care of patients and the patients themselves.

### **Potential risks for participants**

The amount of blood collected from an adult does not pose a health risk. Finger prick and venipuncture can cause minor pain and discomfort. There is no risk for either infants or their mothers from sampling blood and placental tissue after the placenta is expelled and the cord is cut. Appropriate steps will be taken to ensure that discomforts with venipuncture and fingerprick are minimized and the risks of transmission of bloodborne pathogens are reduced to the extent possible.

## INFORMED CONSENT FORM

### A Case-Control Study to Evaluate Immune Responses to Malaria during Pregnancy

Sponsor: **DMID**

Principal Investigator: **James Smith, Ph. D.**  
Address: **United States University**  
**POB 12345**  
**Researchtown, AB, 67890**  
**USA**

#### **Introduction**

This Consent Form contains information about the research named above. In order to be sure that you are informed about being in this research, we are asking you to read (or have read to you) this Consent Form. You will also be asked to sign it (or make your mark in front of a witness). We will give you a copy of this form. This consent form might contain some words that are unfamiliar to you. Please ask us to explain anything you may not understand.

#### **Reason for the Research**

You are being asked to take part in research because we want to understand why pregnant women are at higher risk for malaria. We also want to learn how pregnancy changes the way a woman's body fights malaria and how AIDS affects it. We hope to use what we learn to develop better ways to treat or prevent malaria.

#### **General Information**

We did not talk to you right before your baby was born, because we knew you would be busy. Now that you have more time, we are asking if you would like to take part in our study. We want to compare the body responses to disease of women who are pregnant for the first time with those of women who have already given birth previously. We are also comparing these women's bodies' reactions to those of women who have not been pregnant. Additionally, we are studying how the body reacts differently to disease in women who have AIDS.

#### **Your Part in the Research**

##### At this time:

If you agree to be in the research, you will have a small amount of blood drawn (about 1-2 teaspoons). We will take blood from your arm and your fingertip. We will check your blood for malaria and signs of anemia (low number of red blood cells). If you have malaria and/ or anemia, we will give you medicine. We will also test your blood for HIV infection. HIV is the virus that causes AIDS. One of our AIDS counselors will talk with you. Your test result will be available after about 30 minutes. The counselor will give you advice and facts about the HIV virus. The counselor will also describe the blood test that can tell whether or not a person is infected with HIV. You will learn how to prevent infection with HIV. Sometimes, the test does not show clearly if you have HIV or not. If this is true for your test result, you should come back in 3 months for another test.

We will ask you questions about your health. We will also collect information about the birth and the health of your baby.

In addition, we will study how your body fights infection. Our study requires special handling of your baby's placenta. This is why the hospital did not discard it right after it came out. If you do not agree to participate in this research, your baby's placenta will be discarded. The placenta consists of the tissues that provided food for your baby before birth. The placenta is no longer attached to the baby after it is delivered. We would like to examine the tissue and blood from the placenta to see whether it is infected with malaria. We also want to check for the cells and substances that protect the body from infection and foreign matter.

We will schedule you to return again in eight weeks for a short visit.

##### At the second visit in eight weeks:

When you return to the hospital, we will again draw a small amount of your blood (about 1-2 teaspoons). We will take the blood from your arm and your fingertip. We will check your blood for malaria and signs of anemia. If you have malaria and/ or anemia, we will give you medicine. We will also test your blood to see how your body fights infection.

We will ask you questions about your health and the health of your baby. This visit will take approximately 20 minutes.

Your part in the research will be over after you complete the second visit. About 150 women will take part in this research at this and one other hospital.

We cannot do all of the research tests in this hospital. Therefore, we will need to freeze and ship part of your blood and placenta for storage to the National University laboratory. Later on, these samples will be sent to the study labs in the United States and Canada. To protect your privacy, we will not put your name on the samples, only an identification number. If we decide to do additional tests that are not included in the current study using the stored samples, we will seek full approval from the NMOH IRB. You will not be informed of the results from these additional tests.

### **Possible Risks**

You may have some discomfort from the needle when we take blood from your arm. You may experience anger and distress if you are positive for HIV. We do not provide treatment for HIV. We will refer you for help if you are infected with HIV.

### **Possible Benefits**

All your tests in this study and the AIDS counseling will be free. If the tests show that you have malaria or anemia, you will receive medicine free of charge. The research results may lead to better ways of preventing malaria in the future.

### **If You Decide Not to Be in the Research**

You are free to decide if you want to be in this research. Your decision will not affect the health care you normally receive at this hospital.

### **Confidentiality**

You will not be named in any reports from this study. Any information that we collect about you in this study will remain confidential to the extent allowed by law. This includes the results of your HIV test. Whether your HIV test is negative or positive, we will only give the result to you. However, this choice is yours to make. We will only tell another person the HIV test result if you ask us to do so. However, the staff of DMID and/or other organizations authorized by DMID may sometimes look at your research records. Someone from DMID or their designees might want to ask you questions about being in the research, but you do not have to answer them. A court of law could order medical records shown to other people, but that is unlikely.

### **Compensation**

You will not be paid to take part in this research. We will provide you with X amount when you come back in eight weeks to help pay for your transportation.

### **Alternatives to Participation**

You do not have to participate in the research in order to receive medical care at this hospital.

### **Leaving the Research**

If you choose to take part, you can change your mind at any time and withdraw. You will still be able to use this hospital.

### **If You Have a Problem or Have Other Questions**

If you have a problem that you think might be related to taking part in this research or any questions about the research, please call Calinda Bockwirth, M.D., at the National Hospital, phone: (987) 654-3210. If you need more help, we may give you a referral where you may have to pay.

### **If You Get Sick or Have a Health Problem**

Please phone (987) 654-3210 or come back to the hospital right away, at any time during the research, if you:

- get sick, or
- have concerns about your health.

If you are sick or have a health problem due to your participation in this research, you will not have to pay for visits to see the research doctor/hospital staff. If you need more help, we will refer you to other clinics, where you may have to pay.

### **Your rights as a Participant**

This research has been reviewed and approved by the IRBs of United States University in the United States of America and the IRB of the National Ministry of Health. An IRB is a committee that reviews research studies in order to help protect participants. If you have any questions about your rights as a research participant you may contact [name, phone number and address of local Institutional Review Board (IRB) representative and/or Mr. Dogood, Institutional Review Board, United States University, USA, phone number: [International Access Code]-1-123-456-7890, e-mail: [dogood@usu.fiction](mailto:dogood@usu.fiction)].

## VOLUNTEER AGREEMENT

The above document describing the benefits, risks and procedures for the research titled “**A Case-Control Study to Evaluate Immune Responses to Malaria during Pregnancy**” has been read and explained to me. I have been given an opportunity to have any questions about the research answered to my satisfaction. I agree to participate as a volunteer.

\_\_\_\_\_  
Date

\_\_\_\_\_  
Signature or mark of volunteer

**If volunteers cannot read the form themselves, a witness must sign here:**

I was present while the benefits, risks and procedures were read to the volunteer. All questions were answered and the volunteer has agreed to take part in the research.

\_\_\_\_\_  
Date

\_\_\_\_\_  
Signature of Witness

I certify that the nature and purpose, the potential benefits, and possible risks associated with participating in this research have been explained to the above individual.

\_\_\_\_\_  
Date

\_\_\_\_\_  
Signature of Person Who Obtained Consent

## Protection of Human Subjects Committee Initial Review Form for Reviewers

FHI Project Leader: \_\_\_\_\_ Reviewer Name: \_\_\_\_\_  
 PHSC Number: \_\_\_\_\_ Review Date: \_\_\_\_\_  
 Protocol Title: \_\_\_\_\_

Type of Review:             Expedited       Full

### 1. BACKGROUND/RATIONALE/PURPOSE

<b>A. There is adequate justification for the study.</b>	
<input type="checkbox"/> YES  <input type="checkbox"/> NO	<p><b>Review Tips:</b></p> <ul style="list-style-type: none"> <li>Is the research problem/hypothesis adequately stated?</li> <li>Are the specific aims of the research and how these will contribute to scientific/medical knowledge adequately described?</li> </ul>
<b>Comments:</b>	

### 2. RISKS ARE MINIMIZED

<b>A. Risks to subjects are minimized by using procedures which are consistent with sound research design and which do not expose subjects to unnecessary risk.</b>	
<input type="checkbox"/> YES  <input type="checkbox"/> NO	<p><b>Review Tips:</b></p> <ul style="list-style-type: none"> <li>Consider physical, psychological, social, legal, and economic risks.</li> <li>Has the appropriate departmental scientific review occurred?</li> <li>Are the aims and objectives clearly defined?</li> <li>Are there adequate preliminary data and is there appropriate justification for the research?</li> <li>Would alternative procedures or subject populations reduce the likelihood or magnitude of harm, but still answer the question?</li> <li>Are there qualified staff and resources to conduct the research?</li> <li>Is there appropriate monitoring of the subject during and after the research?</li> <li>Are medical or psychological resources available that Subjects might require as a consequence of the research?</li> <li>Are adequate references provided?</li> </ul>
<b>Comments:</b>	
<b>B. Risks to subjects are minimized whenever appropriate, by using procedures already being performed on the Subjects for diagnostic or treatment purposes.</b>	

<input type="checkbox"/> YES  <input type="checkbox"/> NO	<p><b>Review Tips:</b></p> <ul style="list-style-type: none"> <li>• Consider physical, psychological, social, legal, and economic risks.</li> <li>• Are procedures that will answer the scientific question being performed anyway?</li> <li>• If so, can the data from these procedures be used to reduce the likelihood or magnitude of harm?</li> <li>• Is there a clear differentiation between research and standard of care procedures?</li> </ul>
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<p><b>Comments:</b></p>
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### 3. RISKS ARE REASONABLE

	<p><b>Risks to Subjects are reasonable in relation to anticipated benefits, if any, to Subjects, and the importance of the knowledge that may reasonably be expected to result.</b></p>
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<input type="checkbox"/> YES  <input type="checkbox"/> NO	<p><b>Review Tips:</b></p> <ul style="list-style-type: none"> <li>• In evaluating risk, consider physical, psychological, social, economic, and legal risks. Consider only those risks and benefits that may result from the research, not risks and benefits of therapies subjects would receive even if not participating in the research.</li> <li>• Consider physical, psychological, social, legal, and economic risks. Are the risks and benefits adequately described?</li> <li>• Does the investigator have access to a population that will allow recruitment of the necessary number of Subjects?</li> <li>• Does the investigator have sufficient time to conduct and complete the research?</li> <li>• Is the research and timeline for completion feasible?</li> <li>• Does the knowledge expected to result have importance?</li> <li>• Are there adequate plans to notify the subjects about the research results (clinical issues, suicidal, referrals)</li> </ul>
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<p><b>Comments:</b></p>
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### 4. SELECT RISK / BENEFIT ASSESSMENT

**Regulatory definition of minimal risk:** Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests (45 CFR 46.102(h)(i)).

**\*Choose Category 1 or 2 (and 2a or 2b):**

<input type="checkbox"/> Category 1: The research involves no more than minimal risk to subjects.
<input type="checkbox"/> Category 2: The research involves more than minimal risk to subjects.
<input type="checkbox"/> Sub-category 2a: The risk(s) represents a minor increase over minimal risk
<input type="checkbox"/> Sub-category 2b: The risk(s) represents more than a minor increase over minimal risk.

**Definition of Benefit:** The Belmont Report says that “the term ‘benefit’ is used in the research context to refer to something of positive value related to health or welfare. Unlike, ‘risk,’ ‘benefit’ is not a term that expresses probabilities.” Benefit can be realized at the individual and community/societal levels. Money or other compensation for participation in research is not considered to be a benefit, but rather compensation for research-related inconveniences.

**\*Choose Category 1, 2 or 3:**

<input type="checkbox"/> Category 1: No prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the
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subject's disorder or condition;
<input type="checkbox"/> Category 2: No prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge to further society's understanding of the disorder or condition under study;
<input type="checkbox"/> Category 3: The research involves the prospect of direct benefit to individual subjects.
<b>Comments:</b>

## 5. SUBJECT SELECTION

	<b>Additional safeguards have been included in the study to protect the rights and welfare of subjects likely to be vulnerable to coercion or undue influence. (Do not complete if these populations are not included, there is a separate section for children.)</b>
	<b>A. Is subject selection equitable?</b>
<input type="checkbox"/> YES  <input type="checkbox"/> NO	<b>Review Tips:</b> <ul style="list-style-type: none"> <li>• Consider the purpose of the research.</li> <li>• Are the inclusion and exclusion criteria adequately defined and equitable?</li> <li>• Are there subjects vulnerable to coercion and undue influence and has this been addressed?</li> <li>• Are there acceptable procedures for screening subjects prior to recruitment?</li> <li>• If there is inclusion of vulnerable populations are they justified?</li> </ul>
<b>Comments:</b>	
	<b>B. Are recruitment procedures acceptable?</b>
<input type="checkbox"/> YES  <input type="checkbox"/> NO	<b>Review Tips:</b> <ul style="list-style-type: none"> <li>• Is the setting, location and timing of recruitment appropriate for the research being conducted?</li> <li>• Are recruitment methods well defined and appropriate for the population?</li> <li>• Are all recruitment materials non coercive, and easily understood?</li> <li>• Are payments to subjects coercive?</li> </ul>
<b>Comments:</b>	

## 6. DATA MONITORING

	<b>The research plan makes adequate provisions for monitoring the data collected to ensure the safety of Subjects. (Not applicable if the research involves no more than minimal risk.)</b>
<input type="checkbox"/> YES  <input type="checkbox"/> NO  <input type="checkbox"/> NA	<b>Review Tips:</b> <ul style="list-style-type: none"> <li>• Does the protocol adequately specify:</li> <li>• Who will monitor the data? What data will be monitored? How frequently will data be monitored?</li> <li>• What analyses will be performed on the data? What decision rules (e.g., stopping rules) will be considered?</li> <li>• Is there a plan to promptly detect unexpected harms or an increase in frequency or severity of harms?</li> <li>• Is there an adequate plan to stop the protocol if benefits are proven to outweigh harms or harms are proven to outweigh benefits?</li> </ul>

Would use of a data & safety monitoring board or other research oversight process enhance subject safety?	<input type="checkbox"/> YES	<input type="checkbox"/> NO
<b>Comments:</b>		

7. PRIVACY AND CONFIDENTIALITY	
<input type="checkbox"/> YES  <input type="checkbox"/> NO	<b>A. There are adequate provisions to protect the privacy of Subjects.</b>
	<b>Review Tips:</b> <ul style="list-style-type: none"> <li>• Will Subjects have an expectation of privacy?</li> <li>• Will Subjects think that the information sought by the investigator is appropriate?</li> <li>• Will Subjects be comfortable in the research setting?</li> <li>• Are there adequate provisions to consider and assure the privacy of the subject?</li> </ul>
<b>Comments:</b>	
<input type="checkbox"/> YES  <input type="checkbox"/> NO	<b>B. There are adequate provisions to maintain the confidentiality of the data.</b>
	<b>Review Tips:</b> <ul style="list-style-type: none"> <li>• Will confidentiality be pledged?</li> <li>• Are there adequate provisions to protect the confidentiality of the data?</li> <li>• Are there legal/ethical requirements to breach confidentiality and is this well described and addressed?</li> <li>• Will data release cause risk of harm?</li> <li>• Are appropriate techniques being used to protect confidentiality (storage, coding, use of identifiers)</li> <li>• Does the protocol and consent specify where the data and consent form will be stored?</li> </ul>
<b>Comments:</b>	

8. INFORMED CONSENT PROCESS: Informed consent will be obtained from each prospective subject or subject's legally authorized representative Complete if informed consent will be obtained.	
<input type="checkbox"/> YES  <input type="checkbox"/> NO	<b>A. The investigator will obtain the legally effective informed consent of the participant or the participant's legally authorized representative.</b>
	<b>Review Tips:</b> <ul style="list-style-type: none"> <li>• Has the investigator indicated whether consent will be obtained from the participant, from a legally authorized representative, or both?</li> <li>• Are steps taken to help the Subjects or representatives understand the facts?</li> <li>• Are adequate steps taken to help the Subjects or representatives understand the research and the associated ramifications?</li> <li>• Does the investigator adequately address how he/she will determine that a subject understands the research prior to providing consent/assent?</li> </ul>

<b>Comments:</b>	
<input type="checkbox"/> YES <input type="checkbox"/> NO	<p><b>B. The circumstances of consent provide the prospective participant or the representative sufficient opportunity to consider whether or not to participate.</b></p> <p><b><u>Review Tips:</u></b></p> <ul style="list-style-type: none"> <li>• Is adequate time devoted to the consent discussion and decision making process?</li> <li>• Do the circumstances of consent minimize the possibility of coercion or undue influence?</li> <li>• Have all issues regarding the capacity to make a decision been addressed?</li> </ul>
<b>Comments:</b>	
<input type="checkbox"/> YES <input type="checkbox"/> NO	<p><b>C. The circumstances of consent minimize the possibility of coercion or undue influence.</b></p> <p><b><u>Review Tips:</u></b></p> <ul style="list-style-type: none"> <li>• Are consent procedures well defined?</li> <li>• Are the timing, location and setting of obtaining consent acceptable?</li> <li>• Are payment arrangements acceptable?</li> <li>• Will parents and children be compensated and if so is the amount fair and distributed appropriately between parent and child?</li> <li>• If study procedures are not complete or a subject withdraws is there any pro-rating of compensation?</li> <li>• Are there plans so families avoid out of pocket expenses in order to participate?</li> </ul>
<b>Comments:</b>	
<input type="checkbox"/> YES <input type="checkbox"/> NO	<p><b>D. The information that will be given to the participant or the representative will be in language understandable to the participant or the representative.</b></p> <p><b><u>Review Tips:</u></b></p> <ul style="list-style-type: none"> <li>• What language do the Subjects or representatives speak?</li> <li>• Can the research team communicate in understandable language to the Subjects or representatives?</li> <li>• Will written information be in the language understandable to the Subjects or representatives?</li> </ul>
<b>Comments:</b>	
<input type="checkbox"/> YES <input type="checkbox"/> NO	<p><b>No information will be provided to the participant or the representative that waives or appears to waive any of the participant's legal rights, or that releases or appears to release the investigator, the sponsor, the institution, or its agents from liability for negligence.</b></p>

Comments:

### 9. REVIEWER'S FINAL ASSESSMENT/OPINION

<b>Approval</b>	<input type="checkbox"/> No changes needed: there is an acceptable risk/benefit ratio and protocol is acceptable as submitted
<b>Approval with Stipulations and/or Suggestions</b>	<input type="checkbox"/> Minor changes needed in the informed consent document, protocol or other study materials
<b>Deferral</b>	<input type="checkbox"/> Clarifications or additional information is required regarding a specific aspect of study <input type="checkbox"/> There is an unacceptable risk/benefit ratio, because (check all that apply): <input type="checkbox"/> Protocol poorly written, lacking significant amounts of information regarding scientific justification, study procedures, risk reduction, etc. <input type="checkbox"/> It is possible that a response from the investigator could alter the risk/benefit ratio <input type="checkbox"/> There are ethical concerns that can be addressed by obtaining more information may require changes in study design and procedures.
<b>Disapproval</b>	<input type="checkbox"/> Risks significantly outweigh the benefit or value of the knowledge to be gained <input type="checkbox"/> There are significant ethical concerns or questions that deem the study unacceptable

### 10. APPROVAL PERIOD

Should review occur more frequently than once a year?	<input type="checkbox"/> YES	<input type="checkbox"/> NO	
↳ <b><i>IF YES</i></b> , please specify how often:			

Please complete this form and return it to the [PHSC Manager](#) before the scheduled PHSC meeting. Thank you for you cooperation and assistance.

\_\_\_\_\_  
Reviewer's Signature

\_\_\_\_\_  
Date

# INFORMED CONSENT REVIEWER'S CHECKLIST

## PHSC Study # \_\_\_\_\_

	<b>Applicable Regulation</b>	
<b>Introduction to the Research</b>	<b>21CFR50.25</b>	<b>45CFR46.116</b>
<input type="checkbox"/> Simple explanation of the informed consent process.	(a)(1)	(a)(1)
<input type="checkbox"/> Statement that the study involves research.	(a)(1)	(a)(1)
<b>General Information about the Research</b>		
<input type="checkbox"/> General purpose of the study.	(a)(1)	(a)(1)
<input type="checkbox"/> Description of the study methods, procedures, products or drugs.	(a)(1)	(a)(1)
<input type="checkbox"/> Approximate number of subjects involved in the study.	(b)(6)	(b)(6)
<b>Your Part in the Research</b>		
<input type="checkbox"/> Expected duration of the subject's participation, frequency of trips to the study site, etc.	(a)(1)	(a)(1)
<input type="checkbox"/> Procedures to be followed and identification of those that are experimental.	(a)(1)	(a)(1)
<b>Possible Risks and Benefits</b>		
<input type="checkbox"/> All reasonably foreseeable discomforts and risks to the subject. Whenever possible, likelihood, severity and duration of risks.	(a)(2)	(a)(2)
<input type="checkbox"/> When applicable: statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) that are currently unforeseeable.	(b)(1)	(b)(1)
<input type="checkbox"/> Benefits to subjects, or to others, which can reasonably be expected.	(a)(3)	(a)(3)
<b>If You Decide Not to Be in the Research</b>		
<input type="checkbox"/> Participation in voluntary.	(a)(8)	(a)(8)
<input type="checkbox"/> Subject is free to refuse to participate in the study at any time without penalty or loss of benefits to which you are otherwise entitled.	(a)(8)	(a)(8)
<b>Confidentiality</b>		
<input type="checkbox"/> Statement that confidentiality will be maintained and identification of organizations that may have access to the subjects' records (e.g. the IRB, sponsor, regulatory agencies).	(a)(5)	(a)(5)
<b>Payment</b>		
<input type="checkbox"/> When applicable: statement about any monetary or other inducements for participation and how these will be prorated for subjects who do not complete the study.	(a)(6)	(a)(6)

<b>Alternatives to Participation</b>	<b>21CFR50.25</b>	<b>45CFR46.116</b>
<input type="checkbox"/> Appropriate, alternative procedures or courses of treatment that may be advantageous to the subject.	(a)(4)	(a)(4)
<b>Leaving the Research</b>		
<input type="checkbox"/> Participation in voluntary.	(a)(8)	(a)(8)
<input type="checkbox"/> Subject is free to refuse to participate in the study at any time without penalty or loss of benefits to which you are otherwise entitled.	(a)(8)	(a)(8)
<input type="checkbox"/> Reasons why subjects may be asked to leave the study with or without the subject's consent.	(b)(2)	(b)(2)
<input type="checkbox"/> Significant new findings developed during research will be provided to the subject.	(b)(5)	(b)(5)
<input type="checkbox"/> When applicable: consequences of a subject's decision to withdraw from the study and procedures for orderly termination of participation by the subject.	(b)(4)	(b)(4)
<b>If You Have Questions About the Study</b>		
<input type="checkbox"/> Contact information for subjects who have questions about the study.	(a)(7)	(a)(7)
<b>If You Have a Health Problem</b>		
<input type="checkbox"/> Contact information for subjects who experience health problems while in the study.	(a)(7)	(a)(7)
<b>Research Related Injuries</b>		
<input type="checkbox"/> Explanation and description of any compensation and medical treatment available if injury occurs.	(a)(7)	(a)(7)
<input type="checkbox"/> If such a problem should occur and they need more help, what will happen and who is responsible for payment?	(a)(7)	(a)(7)
<b>Your Rights as a Participant</b>		
<input type="checkbox"/> Contact information for appropriate IRB for subjects who have questions about their rights while they are in the study.	(a)(7)	(a)(7)

Potential subjects **must** be given all information that might reasonably be expected to influence their willingness to participate. This information should be provided in language understandable to the subject or the representative preferably at a 6<sup>th</sup> grade level for developing countries and an 8<sup>th</sup> grade reading level for developed countries. The document must be free of any language through which the subject or the representative is made to waive or appear to waive any legal rights, or releases or appears to release the investigator, sponsor, the institution, or its agents from liability for negligence.

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Primary Reviewer's Signature

Date