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Introduction

The purpose of this manual is to document the policies of the PSI Research Ethics Board (REB) and the procedures by which the policies are implemented. The policies and procedures help the Research Ethics Program Manager and REB Chair act in a consistent fashion with each submission. In addition, as personnel change over time, this manual will help new REB staff transition into their roles more easily.

This manual is for a wider audience than just REB staff. Board members, for example, will find important information about their roles such as the logistics and requirements of board meetings. In addition, members might find it useful to review sections before board meetings including criteria for REB approval of study protocols, special considerations for vulnerable groups, and elements of informed consent. The section on board member conflict of interest is also of supreme importance in order for the PSI REB to function ethically.

Researchers themselves are perhaps the largest target group for this manual. By reading this manual, researchers will become familiar with the types of determinations the REB makes and the criteria for making them. Knowing this type of information in advance can save researchers valuable time in developing their submissions and assure a faster REB approval process for their studies. In essence, every section of this manual should be helpful to researchers through the various stages of their research. While researchers have many responsibilities when it comes to the ethical design and implementation of research, some of the most important responsibilities are highlighted in the chapter entitled “Responsibilities of Principal Investigators in Submissions and Continued Compliance”.

Because research cuts across all parts of PSI—not just the Research and Metrics Department—we hope many other PSI staff will find this manual useful as they deal with issues related to the ethical implementation of research. Staff in programs, technical departments and business development may all find useful information here.

This manual is a regulatory requirement of the Department of Health and Human Services’ Office of Human Research Protections (DHHS OHRP), which issues the regulations by which PSI has chosen to base its human subject protections for all research at PSI. As a result, in many cases regulations are either cited verbatim or are adapted to be more readable. We hope the content is understandable, but we know that the “legalese” of the regulatory language can be difficult. The REP Manager welcomes questions and clarifications at any time about the content of this manual.

This manual does not address donor requirements regarding the ethical review or conduct of research, since this is not the mandate of the PSI REB. It is up to researchers and program staff to be familiar with the award terms and conditions that fund their research in order to satisfy both the funder and REB requirements. Please contact the REP Manager if these two sets of requirements seem to contradict each other.

Finally, we anticipate there will be continual changes made to this manual as we improve the Research Ethics Program at PSI and as the nature of research at PSI changes. We welcome suggestions at any time to improve this manual.

Kelly O’Keefe, Research Ethics Program Manager
Jill L. Shumann, Research Ethics Board Chair
June 2012
Section 1: PSI Research Ethics Program and Board

1.1 Purpose
The purpose of the PSI Research Ethics Program is to protect the rights and welfare of human research subjects enrolled in research conducted by or under the direction of PSI. The PSI Research Ethics Board (hereafter referred to as the REB) functions as the review board for PSI human subject research, which includes research related to public health and other areas that involve research.

1.2 REB Authority
The PSI REB was established in 2009 by the PSI Board of Directors. It has the authority to approve, require modifications in (to ultimately secure approval), or disapprove research activities that fall within its jurisdiction as specified by both federal regulations and PSI policy.

1.3 Regulatory Requirements
The PSI REB complies with all federal regulations and state and local/country laws that are applicable to human subject research conducted at the institution by its employees or agents. All PSI REB policies pertaining to human subjects research are in accord with these laws and regulations, as amended. Some institutional policies may impose requirements that are more exacting than those mandated by law. The responsibility to follow the federal regulations, state and local/country laws, and institutional polices protecting human subjects lies with all investigators and research staff, REB members, and the organization in its work with funders.

PSI holds a Federalwide Assurance (FWA00009154) approved by the U.S. Department of Health and Human Services (DHHS) Office of Human Research Protection. Under this assurance, PSI complies with federal human research regulations under the DHHS (45 CFR 46) whenever it engages in research conducted or supported by any of the federal departments or agencies that have adopted the Common Rule (unless the research is otherwise exempt from the Common Rule). In addition, PSI has opted to use 45 CFR 46 as the basis for human subject protections for all research participants, regardless of donor.

Under the FWA, PSI designates the PSI Research Board (IRB# 00006961) as the board responsible for reviewing the majority of PSI’s human subject research and commits to keeping the roster of its members updated with the federal registry, including names of members, earned degrees, area of concentration, and employment status/relationship with organization. Its membership will remain compliant with regulatory requirements (45 CFR 46. 107)

1.4 Ethical Principles
In 1978, the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research issued The Belmont Report, a statement of the ethical principles that should guide the conduct of human subjects research.

The PSI REB is committed to upholding the ethical principles and guidelines for the protection of human research subjects as set forth in The Belmont Report. The conduct of research involving human participants at PSI is governed by the three principles espoused in the report – respect for persons, beneficence, and justice.
1.5 Ceding Review

1.5.1 PSI Research Ceded to an Alternate Ethical Committee

Principal Investigators may cede review of human subject research to an alternate ethical committee, provided the following criteria are met:

- The alternate ethical committee is active and registered with the Office for Human Research Protections at the Department of Health and Human Services, as confirmed by the REP Manager.
- The Principal Investigator determines that the alternate ethical committee will provide a quality review based on OHRP regulations as well as local context. See the document entitled “Guidelines for Deciding Whether to Cede Review”.
- An authorization agreement for ceding review is signed by both PSI and the alternate ethical committee. The agreement states that PSI will cede review to the alternate ethical committee and that the alternate ethical committee will follow DHHS OHRP regulations when conducting its review. Contact the REP Manager for a copy of the Authorization Agreement.
- The Authorization Agreement must be signed by both PSI and the alternate ethical committee prior to submitting the protocol for review by the alternate committee.
- Once signed by both parties, a copy of the Authorization Agreement should be sent to the REP Manager for the REB files.

Researchers should be aware of local laws regarding research review since some countries require that research be reviewed locally. In addition, funders who fund research may also have specific requirements regarding who should conduct the ethical review.

If research is required to be reviewed locally and the local IRB is registered with OHRP, the Principal Investigator can still request that the PSI REB review the protocol. However, either the local committee or the PSI REB must be identified as the “IRB of record”.

Researchers who cede review of their research to another committee should send copies of the following documents to the PSI REB:

- Fully executed Authorization Agreement
- Approval letter sent by the alternate ethical committee
- Reportable Events forms, as applicable, following the definition of “reportable event” used by the alternate ethical committee

Because this manual is based on OHRP regulations – the same regulations followed by any alternate ethical committee to which PSI will cede – the vast majority of this manual is still relevant for researchers preparing for an ethical review. The obvious exception is sections pertaining to the internal processes of the PSI REB. If researchers have questions regarding any aspect of ceding review, they should contact the REP Manager.

1.5.2 Non-PSI Research Ceded to the PSI REB

The PSI REB is willing to review research protocols from organizations or individuals who are not affiliated with PSI or its research. Examples include PSI staff providing technical assistance to an organization that does not have its own ethical committee, PSI collaborating with investigators where there is no registered ethical
committee operating locally, or research on a specific topic where PSI has expertise and the board is the most appropriate board to review the protocol.

If the research activity is funded by the US Government and the Principal Investigator is independent and not affiliated with an institution holding an FWA, the PSI REB can accept to review the protocol; however, an Individual Institutional Agreement must be put in place between the investigator and PSI prior to submitting materials for review. The purpose of the Individual Investigator Agreement is to extend PSI’s FWA to cover the individual. When the individual investigator signs the agreement, he/she is agreeing to abide by PSI’s FWA, US Regulations, and the policies in this manual.

If the research activity is funded by the US Government and the Principal Investigator has received funding through an institution, the institution must hold an FWA. An Authorization Agreement to cede review to the PSI REB must be executed prior to the PSI REB starting the review.

If the research activity is not funded by the US Government, the investigator must state that the PSI REB is the ethical committee of record on their submission form. There is no requirement for an Authorization Agreement or Individual Authorization Agreement.

1.6 REB Roles and Responsibilities

Institutional Official (IO): The IO, designated by the PSI Board of Directors, is legally authorized to act for the institution. He/She obligates PSI to the conditions listed in the Terms of Assurance. The IO represents the institution on the Federalwide Assurance and is the signatory on all Authorization Agreements to cede review. The IO assures that the Research Ethics Program functions effectively and has the necessary resources to comply with requirements related to human subject protections. Given these duties, it is important for the IO to have sufficient rank and oversight in PSI to meet these duties. This person should not be the REB Chair or the chair of any ethical committee listed under PSI’s FWA.

Chairperson: The Institutional Official nominates the REB Chair in writing. The REB Chair will be a highly respected individual, fully capable of leading the REB and the matters brought before it with fairness and impartiality. The PSI REB Chair may or may not be an employee of PSI. The Chair is responsible for the protection of human subjects by ensuring correct and adequate review or determination of exemption status. The Chair is a regular voting member of the REB. The Chair presides over the convened REB meetings and manages conflicts of interest.

Co-Chairperson: The Chair may designate a co-Chair, who will assume the responsibilities of the Chair in his/her absence, and may be given signing responsibilities by the Chair as appropriate.

Manager: The REP Manager is an employee of PSI and a voting member of the REB. He/She is responsible for supporting compliance with regulatory requirements for protocols involving human subject research submitted to the REB. The REP Manager is also responsible for maintaining PSI’s compliance with its FWA and ensuring that all information related to PSI’s IRB Registration is accurate and up to date. He/She also maintains all documentation related to ceding reviews to other ethical committees. He/She is the primary point of contact for all researchers submitting protocols. The Manager is responsible for initial reviews of all protocols to ensure their completeness and highlight potential questions or issues. The REP Manager is responsible for maintaining
thorough files for each submission and other required documents (see REB Record Keeping below). The Manager is responsible for training PSI staff on research ethics and keeping the Institutional Official informed of the activities of the REB.

1.7 REB Membership

Composition
- The REB will have at least five members but not more than fifteen regular members, who will represent a variety of backgrounds in order to conduct complete and adequate reviews of research activities commonly conducted by PSI.
- The REB will include at least one member whose primary concerns are in scientific areas (public health, social science, psychology, etc.) and at least one member whose primary concerns are in nonscientific areas. If PSI’s research expands into other technical or subject areas, membership will change to reflect these needs.
- Members must also include at least one member who is not otherwise affiliated with PSI, including never having worked for PSI as an employee or consultant and who is not part of the immediate family of a person who is affiliated with PSI. The nonaffiliated members of the REB should be drawn from the community at large, and may include individuals with special knowledge of the communities in which PSI research takes place. The nonaffiliated member(s) should be knowledgeable about developing countries and be willing and able to discuss issues and research from that perspective.
- Special safeguards are necessary to protect the rights and welfare of study participants who are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, persons with mental disabilities, or high risk groups with whom PSI regularly works such as commercial sex workers, HIV positive individuals, men who have sex with men, among others. Should the REB find that it regularly reviews research involving such vulnerable study participants, the REB members (or alternate members) will include persons who are knowledgeable about and experienced in working with these vulnerable study participants.
- The REB will make every effort to ensure that it does not consist entirely of men or entirely of women, though appointment to the REB should not be made solely on the basis of gender.
- The REB must also be sufficiently qualified through the experience and expertise of its members and the diversity of their backgrounds, including considerations of their racial and cultural heritage and their sensitivity to issues such as community attitudes, to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects.
- The REB may not consist entirely of members of one profession.

Appointment and Terms
The Chair and current members may offer nominations for new members, which will require the concurrence of Institutional Official. The Chair and members have a two year term, which may be renewed with the approval of the Institutional Official. All changes in IRB membership will be reported to OHRP.

Alternate Members
Alternate members may be sought for participation on the REB. Alternates will represent specific members in their absence or in the case of a specific member’s conflict of interest. Alternate members’ skill set will reflect the skill set of the member he/she replaces.

**Member Responsibilities**

Member responsibilities include:

- Remaining aware of REB meeting dates
- Responding promptly to e-mails checking for quorum
- Reading study documents prior to board meetings
- Conduct Primary Reviews, when asked by Chair
- Participating actively in board meetings
- Disclosing potential conflicts of interests prior to discussion of the related study

**Orientation and Training of New Members**

- Each new member of the REB will be provided orientation and training which includes the following:
  - Completion of two hour training with REP Manager to review basic precepts of human subject protections, the Common Rule (45 CFR 46) and roles and responsibilities of being an REB Member.
- Members will be provided a binder with the following documents: 45 CFR 46.111, The Belmont Report, OHRP Guidebook, (Chapter 3), PSI REB Forms, primary reviewer checklist, and the PSI REB Policy and Procedure Manual.

**1.8 Use of Expert Reviewers**

The REB may invite outside reviewers with expertise in specific areas, including local context, health area expertise, and research methodologies, to assist in the review of issues that require expertise or perspective beyond or in addition to that available on the REB. For minimal risk studies, the expert reviewer report will inform the REB Chair’s determination. The report will be included in the protocol’s file. For more than minimal risk studies and studies the Chair has determined should be discussed by a fully convened board, the expert reviewer’s report will be distributed to board members and presented by the Chair or the expert reviewer at the board meeting. The expert reviewer’s report will be added to the protocol’s file. It should be noted that expert reviewers may take part in the discussion of research protocols during board meetings, but they cannot vote.

**1.9 Meetings**

**Time, Place, Location**

REB meetings are scheduled monthly at a time and place that is determined by PSI.

**Deadlines for Submissions**

Deadlines for submissions to be considered by the full board are posted on the REB page of the PSI website. Researchers should plan for at least two weeks of revising protocol documents before these materials can be sent to board members. The REB chair will determine if materials are ready for full board review or whether further revisions are required – in which case the study will be reviewed at the subsequent board meeting.
Protocol documents being reviewed by the board are distributed to board members **seven** days prior to each REB meeting.

Research protocols that do not require full board review (either exempt or expedited research) are reviewed on a rolling basis.

**Meeting Materials**
A packet of information for each study submitted for full board review will be sent to all REB members. The materials for each study will include a copy of the completed Submission Form, Signature Page and Study Design (including annexes with consent form, screening questionnaire, questionnaire and/or interview guide). As applicable, the following documents may be required: recruitment scripts and materials, data use agreements and photo-narrative instructions.

Members may contact the REP Manager if additional information is needed. All members are expected to review materials for each of the studies on the agenda in advance of the meeting.

Relevant completed forms for continuing reviews and study modifications being considered by the full board will also be sent to REB members seven days prior to each meeting.

**Meeting Agendas**
In addition to the studies being reviewed at the meeting, the following elements will be included on each meeting’s agenda:

- Reminder of confidentiality of REB discussions and conflict of interest disclosure
- Vote to accept minutes of prior REB meeting (see below section on Meeting Minutes)
- A list of protocols approved by expedited review during the prior period
- A list of protocols determined to be exempt during the prior period
- Other updates, reminders, or information to board members as necessary

**Meeting Minutes**
Minutes of PSI REB meetings are the responsibility of the REP Manager. At a minimum, meeting minutes will include:

- Names of board members participating in the meeting - either physically present or by phone (see Attendance section below);
- Actions taken by the REB;
- Result of voting on actions, including the number of members voting for, against, and abstaining;
- The basis for requiring changes in or disapproving research;
- A written summary of the discussion of controversial issues and their resolution.

Draft minutes will be distributed to board members after the board meeting. Board members will have the opportunity to suggest changes to the minutes and the final draft will be re-circulated prior to the subsequent board meeting, where the minutes will be placed on the agenda for approval by voting.

**Attendance**
While it is preferred that members attend REB meetings in person, they may attend meetings by phone if the following two criteria are met:\footnote{Adapted from guidance issued at: \url{http://www.hhs.gov/ohrp/policy/irb1.pdf}}:

1. Members participating by phone have received all pertinent material prior to the meeting and
2. Members can actively and equally participate in the discussion of the protocols.

Minutes of the REB meetings must reflect that the above two criteria were met for any members participating by phone, in addition to the other requirements for board meetings (see Quorum section below).

A member who misses two consecutive meetings without contacting the REP Manager in advance or who misses half or more of the meetings in a year forfeits membership on the REB.

**Quorum**

An REB meeting can be called to order only when a quorum exists. A quorum is defined as a majority of members (half of the voting members plus one). The quorum must include one member whose primary concern or background is non-scientific. Should quorum not be reached during a meeting, no votes may be taken unless a quorum is restored. A member who is recused from the discussion and voting because he or she has a conflict of interest with a study may not be counted toward maintaining the quorum. However, a member who simply abstains from a vote is counted toward the quorum and is included in the total votes taken.

**Primary Reviewer System**

The PSI REB utilizes a Primary Reviewer System in which the Chair designates an individual member to conduct an in-depth analysis of each research study. This individual will lead the discussion of the study at the meeting, and will offer recommendations regarding risk determination, approval or disapproval, required changes, and the length of the approval period commensurate with risks to participants but not longer than one year. The Primary Reviewer should make every effort to contact the REP Manager before the meeting to request any clarifications from researchers or the REP Manager.

The Primary Reviewer will use the New Study Reviewer Checklist to guide his/her review and subsequent discussion. He/she will sign the checklist and give it to the REP Manager after the meeting for inclusion in the study file.

**1.10 REB Record Keeping**

**Protocol Files**

Upon initial submission of a protocol to the PSI REB, the REP Manager assigns the next available consecutive protocol number and creates a protocol file electronically. The file will be maintained for the entire period the protocol is active, and all subsequent related documents are to be filed in the order in which they are received.

REB protocol files will include the following documents:
All records should be accessible for inspection and copying whenever necessary.

**Other Required REB Records**
The PSI REB will also maintain the following records:

- Minutes of REB meetings as described in the section on Meeting Minutes above
- A list of IRB members identified by name, earned degrees, representative capacity, past experience sufficient to describe each member’s principle anticipated contributions to REB discussions, and any employment or other relationship between the member and PSI
- Written procedures for the REB consistent with federal regulations

**Record Retention and Access**
All records relating to research reviewed by the REB shall be retained for at least 3 years after completion of the research. This policy refers to records kept by the REP Manager as well as records kept by researchers in PSI countries. Records should be stored and managed by PSI and not by research agencies.

An exception to the above policy can be made for documents with identifying or sensitive information. In these cases, the REB may determine that research participants are better protected by destroying these documents rather than storing them. Study protocols should clearly identify documents that will be destroyed as well as those that will be stored.

All other records shall be maintained for three years. All records shall be accessible for inspection and copying by authorized representatives of federal agencies.

Funder award documents may also have requirements about record retention. If so, researchers should choose whichever time period is longer – the REB’s or the funder’s.

**Section 2: REB Review Process**
2.1 Definition of Human Subjects Research
The PSI REB reviews studies that meet the federal definitions of “human subject” and “research” according to the following definitions:

- Human Subject: “a living individual about whom an investigator conducting research obtains data through intervention or interaction with the individual or identifiable private information.”
- Research: “a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge”

The PSI REB reviews three types of submissions: initial (the first time a protocol is submitted to the REB); modifications (for changes to approved protocols, more details are provided below) and continuing reviews (mostly for studies lasting more than one year, more details are provided below). For each type of submission, the REB Chair decides which category of review is appropriate as explained below.

2.2 Categories of Review

2.2.1 Exempt Research
Research determined to be exempt will have no further oversight by the REB after any contingencies raised by the REB review are addressed by the PI. Modification requests and continuing reviews are not required to be submitted to the REB unless the study changes its protocol so that it is no longer can be considered exempt.

A research protocol may be determined exempt if it falls into one of the six categories described below. The most common categories used by PSI are in italics2.

- Research conducted in established or commonly accepted educational settings to evaluate educational strategies, instructional techniques or classroom management methods
- Research involving survey procedures, interview procedures or observation that does not directly or indirectly identify the subjects and where any disclosure of human subject responses outside the research context would not put the subject at risk
- The use of existing data sources that are publicly available or if the data does not contain direct or indirect identifiers
- Demonstration Projects conducted by the U.S. Federal Government
- Research on public benefit programs
- Taste and food quality evaluation and consumer acceptance studies

Reviews to determine exemption may be made by the REB Chair and/or designated REB members. Reviewers will complete the Exempt Checklist to guide their decision and document their determination.

2.2.2 Expedited Research
Expedited research protocols do not require discussion by the full convened board. These protocols are reviewed by the REP Manager, the REB Chair and experienced board members/expert reviewers as necessary. Expedited protocols will be held to the same regulatory standards and receive the same rigorous review as those reviewed by the full board.

2 Adapted from 45 CFR 46.101b
According to federal regulations, a study may be expedited if the research involves minimal risk\(^3\) and meets the criteria for one of nine categories. The nine categories are described in general terms below and the most common categories used by PSI are in italics\(^4\).

- Clinical studies of drugs and medical devices when research on drugs does not require an investigational new drug application/investigational device exemption application or the medical device is cleared for marketing and it is being used within its cleared/approved labeling
- Blood samples collected by finger stick, heel stick, ear stick or venipuncture (with specific restrictions, see regulations)
- Prospective collection of biological specimens for research purposes by noninvasive means.
- Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves.
- Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for non-research purposes (such as medical treatment or diagnosis).
- Collection of data from voice, video, digital, or image recordings made for research purposes.
- Research on individual or group characteristics or behavior or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies.
- Continuing review of research previously approved by the convened IRB when the protocol is nearing closure and subjects have finished all activities or only data analysis remains or only active subjects are those for long-term follow-up.
- Continuing review of research, not conducted under an investigational new drug application or investigational device exemption where the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified.

The REB Chair and/or designated REB members may conduct reviews to determine whether study protocols, modifications or continuing reviews can be expedited. Reviewers will use the Expedited Checklist to guide their decision and document their determination.

### 2.2.3 Full-board reviewed research

Research that is reviewed by the full board presents more than minimal risk, as determined by the REB Chair. This determination may be made because of the presence of vulnerable groups, sensitive information, identifying information, or any other issue that causes the REB chair to believe the study warrants discussion by the full board.

### 2.3 Criteria for REB Approval

In order to approve initial submissions, modifications and continuing reviews, the PSI REB will determine that all of the following requirements are satisfied:

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\(^3\) **Minimal risk** is defined as risks no greater than those ordinarily encountered in daily life or during the performance of routine physical or psychological exams or tests.

\(^4\) Adapted from 45 CFR 46.110 and guidance published at [http://www.hhs.gov/ohrp/policy/expedited98.html](http://www.hhs.gov/ohrp/policy/expedited98.html)
• Risks to subjects are minimized by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.

• 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. In evaluating risks and benefits, the REB should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research). The REB should not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.

• Selection of subjects is equitable. In making this assessment, the REB should take into account the purposes of the research and the setting in which the research will be conducted and should be particularly cognizant of the special problems of research involving vulnerable populations, such as children, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons.

• Informed consent will be sought from each prospective subject or the subject’s legally authorized representative, in accordance with, and to the extent required by 45 CFR 46.116.

• Informed consent will be appropriately documented, in accordance with, and to the extent required by 45 CFR 46.117.

• When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.

• When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data. When making this assessment, the REB must differentiate between privacy and confidentiality. Privacy refers to persons and their interest in controlling the access of others to themselves. Confidentiality refers to the agreement between the investigator and participant in how data will be managed and used.

• When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, additional safeguards will be included in the study to protect the rights and welfare of these subjects.

• For research conducted outside of the United States, knowledge of the local research context is critical to an effective review by the PSI REB. Researchers should demonstrate in their protocols a thorough knowledge of their research context, which includes but is not limited to: relevant epidemiologic background, gaps in current research, legal context of target group, social/stigma/psychological context of target group, legal requirements for research including age at which a respondent may consent for him/herself and requirements for local review.

• Researchers must not routinely or arbitrarily exclude women and ethnic minorities from PSI research unless there is an appropriate justification for exclusion. The inclusion of women and ethnic minorities in research is important, both to ensure that they receive an appropriate share of the benefits of research and that they do not bear a disproportionate burden.

• Women of childbearing potential should also not be routinely or arbitrarily excluded from participation even though there are ethical/risk issues to consider for inclusion and exclusion. Pregnancy status may need to be determined prior to enrollment for some studies and, if necessary, during an intervention to safeguard the participants' health.
2.4 REB Actions/Decisions

Study Approved as Submitted, No Revisions: The approval letter will include the date of approval, and the date of expiration of approval.

Study Approved with Modifications: If a study requires specific modifications, the PI must make changes to the study design prior to receiving final approval. The REP Manager will send the PI a memo outlining the specific issues/contingencies to be addressed. The revised submission will be reviewed by the Chair, REP Manager and other reviewers as appropriate, for completeness. Once reviewed and approved, the REP Manager will issue a final approval letter.

Study Tabled: A protocol is tabled when the convened board does not have enough information to conduct a complete review and make a reasonable risk/benefit determination. A letter describing the issues raised will be sent to the Principal Investigator following the meeting. Once the PI responds and the response is reviewed by the PSI Chair or designee, the revised protocol will be placed on the agenda for the next convened meeting.

Study Disapproved: When the REB determines that it is unable to approve a study, a letter will be sent to the Principal Investigator informing him/her of the Board’s decision and the reasons. The letter should include the procedures for appeal of the decision. Only the full board can disapprove a study (i.e. the REP Manager and/or REB Chair cannot disapprove the study without a full board meeting).

2.5 Appeal Procedure for Disapproval

An Investigator may appeal any aspect of the REB review and decision and may request an opportunity to address concerns at a convened meeting of the REB. The REB may reconsider a study in light of new information or changes in the protocol, but the REB retains authority for the final decision.

2.6 Study Modifications

The Principal Investigator is responsible for submitting a request for modification when the investigator is interested in making changes to an approved protocol. The request for modification, using the Application for Review of a Study Modification Form, must be submitted and approved by the REB prior to implementation of the proposed changes. Only in the rare circumstance when it is necessary to eliminate apparent immediate hazards to the research participants is a researcher permitted to modify an approved study without the prior review and approval of the REB. In this case, the REB must be informed within 5 days of the change following its implementation. The change will be reviewed to determine that it is consistent with protection of human participants.

Administrative changes are changes that do not require review by the REB since they do not impact risk and are largely related to successful implementation. Examples of administrative changes include re-formatting the questionnaire, changing the order of questions, correcting spelling of questions or other study materials, revising wording of questions and adding questions to questionnaires related to exposure to PSI messages or programs. Researchers are encouraged to consult the REP Manager if they have questions regarding administrative changes versus minor changes.

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5 As noted in 45 CFR 46.103(b)(4)(iii)
Minor changes are those that do not increase risks to participants. Minor changes may be approved by the Chair under the expedited process. These may involve changes to principal investigator or other key personnel, to the number of participants, catchment/recruitment areas, changes in questionnaires or surveys so long as they do not fall outside the topics of inquiry originally planned or alter the risk level of the study.

Major changes are those that increase risk to participants. These changes must be reviewed by the convened REB. The following materials must be submitted to the REB by the submission deadline in order to be put on the agenda for the next board meeting: Modification Form; most recently approved protocol, and revised protocol and applicable materials consistent with the modification.

The modification request will be reviewed with the same rigor and concern for human participants as used in the review of a new protocol, emphasizing risks to the participants.

2.7 Continuing Reviews

The interval for continuing reviews of research protocols will be decided as part of the initial review, but cannot be longer than one year. In most cases, the continuing review will take place one year from the approval date. However, in cases of more than minimal risk to participants, the REB may decide that more frequent continuing reviews are necessary.

Continuing reviews must be substantive and meaningful, and must be conducted by the convened REB, unless the research is appropriate for expedited review. Continuing reviews will include determinations by the REB regarding risks, potential benefits, informed consent, and safeguards for human subjects.

Ordinarily, if research did not qualify for expedited review at the time of initial review, it will not qualify for expedited review at the time of continuing review. Studies with minimal risk that have minor or no changes, and no new risks have been identified, may qualify for expedited continuing review. Studies that involve a completed intervention, but remain open only for data analysis may also qualify for expedited review.

The PI will submit a request for continuing review using the Application for Continuing Review form. It is the responsibility of the investigator to submit the required documentation in a timely fashion; however, the REP Manager will send reminder emails to investigators 6 weeks prior to expiration to remind investigators of the need to submit a request for a continuing review. The REB will conduct an administrative review to identify issues/contingencies to be addressed prior to expedited approval or the board meeting.

2.8 Language of Submissions and Communication

Initial submissions, continuing review applications and modification requests can be sent to the REB in English, French, Spanish and Portuguese. However, any documents requiring full board review must be translated into English. It is the responsibility of the PI to see that the submission form and study design are translated into English at least one week in advance of the board meeting. The questionnaire does not need to be translated into English; however the board must have at least one member present who can translate the questionnaire if needed.

All communications from the REP Manager to researchers will be in English.
Section 3: Conflicts of Interest

For the purposes of this manual, a conflict of interest is defined as “a set of conditions in which a person’s judgment concerning a primary interest (e.g. subject’s welfare, integrity of research) may be biased by a secondary interest (e.g. personal gain).” Both REB members and researchers may have conflicts of interest.

3.1 REB Member Conflicts of Interest
The PSI REB will ensure the objectivity of human-subjects research at PSI by avoiding actual or perceived conflicts of interests in the review of research by REB members or consultants. Conflicts of interest may be due to:

Financial interests related to the research: A monetary interest of the REB member/consultant or his/her family members in the study’s donor, product, or service being tested, or in the competitor of the donor or product or service being tested.

Non-financial interests related to the research: Other types of relationships which may reasonably appear to influence the judgment of the REB member/consultant reviewing the project. Examples include, but are not limited to:
- Serving as an investigator, co-investigator, or consultant to the study being reviewed by the REB.
- Participation in the project such that the member/consultant is listed on the protocol, or will be included as a co-author on a publication of the research results.

REB members will disclose all financial and non-financial interests with respect to the protocols they are asked to review to the REB Chair or his or her designee. Any individual member for whom the REB Chair determines an actual conflict of interest exists may neither be assigned as a primary or secondary reviewer nor be involved in the final discussion and vote on a protocol. This policy also applies to consultants who are not REB members but are sometimes asked to conduct ad hoc reviews of research projects because of their expertise.

3.2 Investigator Conflicts of Interest
The PSI REB will ensure the objectivity of human-subjects research at PSI by avoiding actual or perceived conflicts of interest in the conduct of such research by Principal Investigators or members of the research team, including consultants, research agency staff, and staff of partner organizations conducting research. Conflicts of interest for researchers may be due to:

Financial interests related to the research: A monetary interest of a researcher or his/her family members in the study’s donor, product, or service being tested, or in the competitor of the donor or product or service being tested.

Non-financial interests related to the research: Other types of relationships which may reasonably appear to influence the judgment of the researcher conducting the study. Examples include, but are not limited to:
- Performing dual roles such as being a health care provider participating in the study and also leading or conducting the research.

Principal Investigators will disclose all financial and non-financial interests of their research teams with respect to the study submitted for REB review. This disclosure must be submitted with the initial protocol documents or as soon as the PI becomes aware of the actual or potential conflict of interest.

The REB Chair will determine whether an actual or perceived conflict of interest exists and will decide whether to convene an REB meeting to discuss the conflict of interest or whether it can be addressed by the Chair, REP Manager and other PSI staff or consultants as appropriate. Generally, the decision to convene a board meeting will be based on the risks posed to human subjects as a result of the conflict of interest. The Principal Investigator of the study will be asked to submit a conflict of interest management plan with the objective of identifying mechanisms to eliminate or minimize the conflict of interest. The REB will assess whether subjects will be protected as a result of the plan or whether changes to the plan are required. Some or all of the following actions may be taken:

- Disclosure to subjects through the consent process.
- Modification of the research protocol or safety monitoring plan.
- Monitoring of research by independent reviewers.
- Disqualification of the conflicted party from participation in all or a portion of the research.
- Appointment of a non-conflicted Principal Investigator.
- Divestiture of significant financial interests.
- Severance of relationships that create actual or potential conflicts.
- Prohibition of the conduct of the research

The REP Manager will communicate all decisions related to management of conflicts of interest to the PSI Institutional Official.

Section 4: Responsibilities of Principal Investigators in Submissions and Continued Compliance

Researchers, and particularly the Principal Investigator, are responsible for the accuracy and completeness of their submissions to the PSI REB, which must include specific information about the context in which the study will take place. Lack of such specificities will slow the approval process. In addition, researchers continue to be responsible for the implementation of the study after REB approval to ensure that the study is conducted as described in the study design documents.

Prior to submission, Principal Investigators are responsible for the following:

- Documentation of human subject training for all key personnel. Refer to the REB’s training policy for further information.
• Review and explanation of all relevant local laws regarding the conduct of research in a country as well as laws related to the target groups being studied. In addition, information should be included about enforcement of relevant laws.
• Explanation of the social situation (stigma or other effects) experienced by the target group.
• Disclosure of any possible conflicts of interest on the part of any researcher involved in implementing the study.
• Understand and comply with requirements of the donor(s) funding the research. Donor requirements may relate to who should conduct the review, record retention and reportable events, among other topics. Both donor and REB policies must be followed. In case of conflict between the two, researchers should discuss the conflict with the REP Manager.

After approval, Principal Investigators continue to be responsible for the ethical implementation of their study. This includes:

• Ensuring that the study is implemented as it is described in the study design.
• Requesting study modifications, if necessary, according to the modification policy stated in this manual. See section 2.
• Reporting any events that qualify as “reportable events” as explained in section 6 of this manual.
• Ensuring that research agencies implement the study as described in the study design including the implementation of the informed consent process.
• Ensure that the Informed Consent Document is translated in such a way that the meaning is the same as the REB-approved informed consent document and the document is understandable to the target group.
• Disclosure of any possible conflicts of interest that arise during implementation on the part of any researcher involved in the study.

Section 5: Research with Vulnerable Populations

Research with vulnerable populations must include additional safeguards to protect them from coercion, undue influence, or increased risks from participating in research. Vulnerable populations are defined by DHHS as pregnant women, children, prisoners and persons with mental disabilities. However, PSI also works with other populations that require additional protections given their behaviors, economic and/or educational status, or disease status. These groups include intravenous drug users, commercial sex workers and men who have sex with men, among others.

Note that some funders have requirements related to research with specific groups. Principal Investigators should check the donor contracts for this information.

5.1 Research Involving Prisoners

The PSI REB reviews all research that involves prisoners based on the DHHS regulations that provide additional protections for this population group. These regulations are found in 45 CFR 46 subpart C.

Research that involves prisoners may not be exempt from REB review.
A prisoner is defined as any individual involuntarily confined or detained in a penal institution. The term is intended to encompass individuals sentenced to such an institution under a criminal or civil statute, individuals detained in other facilities by virtue of statutes or commitment procedures that provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing. Adolescents who are detained in juvenile facilities meet this definition and are considered prisoners.

REB membership requirements for research involving prisoners:
- A majority of the REB shall have no association with the prison(s) involved, apart from their membership on the REB.
- At least one member of the REB shall be a prisoner representative with appropriate background and experience to serve in that capacity. Where a particular research project is reviewed by more than one REB (IRB) only one REB need satisfy this requirement.

Requirements for approval of research involving prisoners:
- The research under review must fall into one of the following categories:
  i. Study of the possible causes, effects, and processes of incarceration, and of criminal behavior, provided that the study presents no more than minimal risk and no more than inconvenience to the participants.
  ii. Study of prisons as institutional structures or of prisoners as incarcerated persons, provided that the study presents no more than minimal risk and no more than inconvenience to the participants.
  iii. Research on conditions particularly affecting prisoners as a class (for example, vaccine trials and other research on hepatitis which is much more prevalent in prisons than elsewhere; and research on social and psychological problems such as alcoholism, drug addiction and sexual assaults).
  iv. Research on practices, both innovative and accepted, which have the intent and reasonable probability of improving the health or well-being of the participant.
- Any possible advantages accruing to the prisoner through his or her participation in the research, when compared to the general living conditions, medical care, quality of food, amenities and opportunity for earnings in the prison, are not of such a magnitude that his or her ability to weigh the risks of the research against the value of such advantages in the limited choice environment of the prison is impaired.
- The risks involved in the research are commensurate with risks that would be accepted by non-prisoner volunteers.
- Procedures for the selection of participants within the prison are fair to all prisoners and immune from arbitrary intervention by prison authorities or prisoners. Unless the principal investigator provides to the REB justification in writing for following some other procedures, control participants must be selected randomly from the group of available prisoners who meet the characteristics needed for that particular research project.
- The information is presented in language which is understandable to the participant population.
Adequate assurance exists that parole boards will not take into account a prisoner’s participation in the research in making decisions regarding parole, and that each prisoner is clearly informed in advance that participation in the research will have no effect on his or her parole.

Where the REB finds that there may be a need for follow-up examination or care of participants after the end of their participation, adequate provision has been made for such examination or care, taking into account the varying lengths of individual prisoners’ sentences, and for informing participants of this fact.

Additional requirements for research involving prisoners:
- For studies funded by a US Federal agency, upon approval of the study by the REB, the REB Chair will notify OHRP about the research, the category under which it is permitted and that the regulatory duties of the REB have been fulfilled.
- All PSI research protocols involving prisoners as research participants must meet all applicable local laws.

### 5.2 Research Involving Pregnant Women, Fetuses and Neonates

The PSI REB reviews all research that involves pregnant women, fetuses and neonates based on the DHHS regulations that provide additional protections for this population group (45 CFR 46 subpart B). Researchers planning to conduct studies involving pregnant women, fetuses, or neonates are encouraged to contact the REP Manager early on in the design process.

Studies with pregnant women, fetuses or neonates can be exempted under the conditions listed under “Exempt Review” in Section 2 of this manual.

Requirements for research with pregnant women or fetuses (all of the following conditions must be met):
- For biomedical studies, where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies, including studies on non-pregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses;
- The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus; or, if there is no such prospect of benefit, the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge which cannot be obtained by any other means.
- Any risk is the least possible for achieving the objectives of the research;
- If the research holds out the prospect of direct benefit to the pregnant woman, the prospect of a direct benefit both to the pregnant woman and the fetus, or no prospect of benefit for the woman nor the fetus when risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means, her consent is obtained in accord with the informed consent regulations (see section 6 of this manual).
If the research holds out the prospect of direct benefit solely to the fetus then the consent of the pregnant woman and the father is obtained in accord with the informed consent regulations (see section 6), except that the father’s consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity or the pregnancy resulted from rape or incest.

Each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate;

For children who are pregnant, assent and parental consent are obtained in accord with the regulations related to children as research subjects (see section 6);

No inducements, monetary or otherwise, will be offered to terminate a pregnancy;

Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy; and

Individuals engaged in the research will have no part in determining the viability of a neonate.

Researchers planning to conduct studies involving fetuses or neonates should contact the REP Manager for further information about the regulations pertaining to these two groups.

5.3 Research Involving Children

Definition:

Children are persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research is conducted.

The PSI REB reviews all research that involves children based on the DHHS regulations that provide additional protections for this population group. These regulations are found in 45 CFR 46 subpart D.

Survey or interview research with minors cannot be exempt from REB review. Other types of research with children may be exempt following the appropriate regulations7. Contact the REP Manager for further information.

REB membership requirements for research involving children:

The REB shall require the inclusion of a child advocate as a member of the REB. The advocate shall be an individual who has the background and experience to act in, and agrees to act in, the best interests of child participants and who is not associated in any way with the research, the investigator(s), or any local entity that oversees wards of the state.

7 See 45 CFR 46.401b
The REB must consider the benefits, risks, and discomforts of the research and assess their justification for children's participation in light of the benefits to the child-participant(s) or to society as a whole. In calculating the risks and benefits, the REB should consider the circumstances of the participants under study, the magnitude of risks or discomforts that may accrue from research participation and the potential benefits the research may provide to the participant or class of participants.

Categories for Research Involving Children: The REB must classify research with children into one of the following four categories and must document in the minutes the category or research under discussion:

- Research that does not involve greater than minimal risk to children: The REB may approve research in this category if adequate provisions are made for obtaining assent of the children and the consent of their parents or guardian. The REB may decide that the consent of one parent is sufficient for the research to be conducted.

- Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual (child) participant: To approve research in this category, the REB must determine that the risk is justified by the anticipated benefit to the participants, the relation of the anticipated benefits to the risk is at least as favorable to the participants as that presented by available alternative approaches, and adequate provision is made for obtaining assent of the children and consent of their parents or guardian. The REB may decide that the consent of one parent is sufficient for the research to be conducted.

- Research involving greater than minimal risk and no prospect of benefit to the individual (child) participant, but likely to yield generalizable knowledge about the participant’s disorder or condition: To approve this category of research, the REB must first determine that the risk of the research represents no more than a minor increase over minimal risk; that the intervention or procedure presents experiences to the child-participants that are reasonably commensurate with those inherent in their actual, or expected medical, dental, psychological, social, or educational situations; the intervention or procedure is likely to yield generalizable knowledge about the participant’s disorder or condition which is of vital importance for understanding or amelioration of the disorder or condition; and adequate provisions are made for obtaining assent of the children and consent of their parents or guardian. The consent of both parents must be obtained 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.

- Research not otherwise approvable under one of the other three categories but the REB determines that the study presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children: If this research is funded by a US Federal agency, upon approval by the REB, the REB Chair will seek approval from OHRP who will provide final approval for the research.

Any study involving children as research participants must meet all applicable local laws.
5.4 Research Involving Other Vulnerable Groups

As stated above, PSI works with other groups who by nature of their behaviors, economic status, or disease status may make them vulnerable to coercion and/or increased risks from participating in research. These groups include intravenous drug users, commercial sex workers and men who have sex with men, transgender individuals and people living with HIV, among others.

Research protocols involving these groups must include the following:
- Justification for studying the group, including a review of research with the group and why a research gap still exists.
- The social, economic and legal context for the group being studied. Legal context should involve the laws relating to these groups as well as how police and authorities interact with them.
- A thorough presentation of the risks of participating in research including social, psychological, physical, economic and legal and any others.
- A thorough presentation of how these risks will be mitigated.

5.5 Research Involving HIV Antibody Testing

Given the severity and sensitivity of an HIV diagnosis, extreme care must be taken when designing research that involves HIV testing. The following components should be included in PSI research protocols that include HIV testing. In cases where some components cannot be included, researchers should fully explain the situation in their research protocol and show that their absence does not present increased risks to the participants:
- The study design must include a justification as to why HIV testing is being performed.
- The study design must include the process of how HIV testing will be performed.
- The study design should include pre- and post-test counseling of the participants by qualified personnel and participants must be informed of their test results. The study design should also discuss current practices in country for testing, counseling, results disclosure and how the current study design does or does not follow local practices.
- The study design should discuss what treatment options are available for individuals who are HIV positive and how participants will access this treatment.
- The study design must state how HIV test results will be stored, managed and kept confidentially.
- The study design must state if the test results will be shared with local health authorities for surveillance and if there will be any identifiers attached to these data.
- The study design must discuss the social and legal context of people living with HIV in the country where the research is conducted.
- The informed consent form must state that HIV testing is being performed for purposes of the study and include the risks associated with HIV testing as well as the risks associated with being HIV positive.
- The informed consent form must state the options for treatment if the participant is HIV positive and how treatment can be accessed.
- The informed consent form must state that the HIV test results are confidential.
Section 6: Reportable Events During Research Implementation

Definitions:

Reportable Event: An unexpected occurrence during the implementation of a research study that may or may not have an unfavorable impact on human subjects.

Unexpected means that the occurrence was not discussed in the study design or in the informed consent documents especially when describing risks to subjects.

Unfavorable: Any event that affects the scientific integrity of the study design or the rights, safety or welfare of the participants. “Safety and welfare” encompasses a wide range of harms including physical, psychological, emotional, social, economic or legal consequences associated with participation in a research project.

6.1 Reporting a Reportable Event to the REB

All reportable events must be reported to the PSI REB by the PI immediately but no later than 5 days of learning of the occurrence using the “Reportable Events” form.

Note that if a study has been reviewed by an alternate ethical committee, researchers must follow that committee’s definitions and procedures for reportable events, which are often called “unanticipated problems”, “adverse events” or “serious adverse events”. Copies of the information/forms sent to the alternate ethical committee should also be sent to the PSI REP Manager.

6.2 Investigation and Determination of Reportable Events

Once a Reportable Event form is received by the REP Manager, the following actions will occur:

- The form will be screened by the REP Manager to make an initial determination of whether the reportable event presents no greater than minimal risk to subjects or greater than minimal risks to subjects. The form will then be forwarded to the REB Chair.
- If the Chair agrees that the reportable event presents no more than minimal risk to subjects, then the event will be handled on an expedited basis. The PI will be asked to develop a plan to address the event within the ongoing study. The PI will be notified upon REB approval of the plan.
- If the Chair agrees that the event presents greater than minimal risk to subjects, the event will be placed on the agenda of the next scheduled meeting of the full REB. The REP Manager will obtain from the PI a copy of the approved informed consent document(s) and any other pertinent documents for committee review. The PI will be asked to develop a plan that includes corrective actions to ensure that the reportable event does not re-occur and protects subjects – both those who have already participated and those who have yet to enroll.
- If the event presents more than minimal risk and there is an immediate concern that subjects already enrolled or subjects to be enrolled may be subject to immediate increased harm to their health, safety, or
welfare, the Chair will require that the protocol be suspended or terminated. In most situations this will not be necessary.

- All REB members participating in the review of the reportable event will receive copies of the Reportable Event form and the original submission materials, including the informed consent document(s).
- The REB will deliberate on the event during the convened meeting and either approve the corrective plan submitted by the PI or require additional actions to protect human subjects.
- The PI must comply with REB requirements and modifications in order to continue implementation of the study.

6.3 Possible REB Actions Regarding Reportable Events

In reviewing and addressing reportable events, the PSI REB may impose any remedy, or take any action, including but not limited to:

- Initiate immediate corrective action, if necessary;
- Delegate a subcommittee or individual to perform further investigation;
- Require that individuals who have already consented to participation be notified;
- Require modification of any other aspect of the conduct of the research including recruitment, informed consent, research and clinical procedures, monitoring and safety assurance, and continuing review;
- Alter the frequency of continuing review;
- Require that enrolled subjects be provided with an amended informed consent form, and that the process of informed consent be repeated with revised information. This will be required whenever the information may relate to the participants willingness to continue participating;
- Determine the incident involves serious or continuing noncompliance (see Section 8 of this manual on Noncompliance)
- Determine that the protocol should be terminated or suspended
- Require the investigator to inform other research participants or individuals who may be affected by the event or problem;
- Require the investigator to notify investigators at other sites;
- Observe the consent process;
- Refer concerns or findings to other parts of PSI that manage contracts, programs, donor relations and/or institutional risks.
- Require a change in key personnel, (PI)
- Any other action deemed appropriate to minimize risks to subjects

6.4 Notifications

The investigator will receive an initial response from the REB within five days of receipt of the Reportable Event form. This response will include next steps on the part of the PI and the REB. Once final determinations have been made, the Country Representative, Regional Researcher, the PI's direct supervisor and the Institutional Official will be notified.

All reportable events that meet the US regulatory definition of “unanticipated problem” and were at least partly funded by a US Agency will be reported to the US Government (DHHS, Office of Human Research Protections).
6.5 Appeal Procedure

An Investigator may appeal any aspect of the REB review and decision and may request an opportunity to address concerns at a convened meeting of the REB. The REB may reconsider a reportable event in light of new information or changes in the protocol, but the REB retains authority for the final decision.

Section 7: Informed Consent

7.1 General Requirements for Informed Consent

Except as provided below, no researcher may involve a human being as a subject in research conducted by or under the auspices of PSI unless the researcher has obtained the legally effective informed consent of the subject or the subject’s legally authorized representative.

Researchers shall seek such consent under circumstances that provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence.

The information that is given to the subject or the representative shall be in language understandable to the subject or the representative.

No informed consent, whether oral or written, may include any language that waives or appears to waive the subject’s legal rights, or releases or appears to release the researcher, PSI or PSI’s funders from liability for negligence.

In cases where research agencies are contracted to conduct the informed consent process, the PI for the study remains responsible for ensuring that the PSI policies and procedures for informed consent are followed. Researchers must develop oversight and management mechanisms with research agencies to ensure that proper consent is obtained. PIs are also responsible for the documentation of the consent procedure and the storage of consent documents.

7.2 Elements of Informed Consent

The following information shall be provided to each subject as part of the informed consent process:

- A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject’s participation, a description of the procedures to be followed, and identification of any procedures which are experimental;
- A description of any reasonably foreseeable risks or discomforts to the subject;
- A description of any benefits to the subject or to others which may reasonably be expected from the research;
- A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject;
When applicable, the following elements should also be added to the informed consent document:

- A 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) which are currently unforeseeable;
- Anticipated circumstances under which the subject’s participation may be terminated by the investigator without regard to the subject’s consent;
- Any additional costs to the subject that may result from participation in the research;
- The consequences of a subject’s decision to withdraw from the research and procedures for orderly termination of participation by the subject;
- A statement that significant new findings developed during the course of the research which may relate to the subject’s willingness to continue participation will be provided to the subject;
- The approximate number of subjects involved in the study.

7.2.1 Alterations or Waivers of Informed Consent

In order to alter or waive the consent process, the PSI REB must find and document that:

- The research involves no more than minimal risk to the subjects;
- The waiver or alteration will not adversely affect the rights and welfare of the subjects;
- The research could not practicably be carried out without the waiver or alteration; and
- Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

Researchers should request a waiver or alteration of informed consent in the study submission and justify the request by referring to the above requirements.

7.3 Documentation of Informed Consent

Except as provided below, informed consent shall be documented by the use of a written consent form approved by the REB and signed by the subject or the subject’s legally authorized representative. A copy shall be given to the person signing the form, unless the participant does not want a copy for fear of exposing him/herself as a member of a vulnerable group. The consent form shall include the basic elements described above and may be read to the subject or the subject’s legally authorized representative. The researcher shall give the subject or the representative adequate opportunity to read it before it is signed.
7.3.1 Waivers of Documentation of Informed Consent
In order to use oral consent forms, the PSI REB must find that either of the following two conditions apply to the research study:

- The only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern; or

- The research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.

7.4 Requirements for Consent by Parents/Guardians and Assent by Children

When children are involved in research, the researchers must make provisions for parental or guardian consent as well as assent (permission) by children, as explained below.

7.4.1 Parental/Guardian Consent
Definitions:

- **Parent** means a child's biological or adoptive parent.

- **Guardian** means an individual who is authorized under applicable state or local law to consent on behalf of a child to general medical care.

- **Parental/Guardian Consent** means the agreement of parent(s) or guardian to the participation of their child or ward in research.

Adequate provisions must be made for soliciting the consent of each child’s parents or guardians. Consent of one parent is sufficient in research that does not involve greater than minimal risk or involves greater than minimal risk but presents the prospect of direct benefit to the subject. Consent of both parents is required in all other cases 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.

Consent by parents or guardians shall be documented in accordance with the above section on Documentation of Informed Consent.

**Waivers of Parental/Guardian Consent**: If researchers decide that their research protocol is designed for conditions or for a participant population for which parental or guardian consent is not a reasonable requirement to protect the participants (for example, orphans, neglected or abused children, girls who are married at a young age, or children in countries where the legal age of consent is lower than 18), they may request a waiver of parental/guardian consent, provided an appropriate mechanism for protecting the children who will participate in the research is substituted, and provided further that the waiver is consistent with federal, state, and local laws. The choice of an appropriate mechanism depends upon the nature and purpose
of the activities described in the study, the risk and anticipated benefit to the research participants, and their age, maturity, status, and condition.

Waivers of parental or guardian consent may also be granted by the PSI REB if all of the following conditions are met:

- The research involves no more than minimal risk to the subjects;
- The waiver or alteration will not adversely affect the rights and welfare of the subjects;
- The research could not practicably be carried out without the waiver or alteration; and
- Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

Researchers requesting a waiver of parental/guardian consent should provide a thorough explanation and justification in their submission documents referring to the above criteria.

7.4.2 Assent by Children

Definition:

**Children** are persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted.

**Assent** means a child’s affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent.

Children should be asked whether they wish to participate in research. This is particularly true if children can comprehend and appreciate what it means to be a volunteer for the benefit of others and the research is not likely to benefit them directly. Taking into account such factors as the nature of the research and the age and maturity, psychological status and medical condition of potential participants, researchers must determine whether children participating in a study are capable of assenting to participation. This determination can be made for all children in a study or for each child separately, as deemed appropriate by the researcher and justified to the REB in the submission documents. There is no requirement that assent be sought at a specific age, but that it be sought when children are capable of providing assent. Generally, the REB will require that assent be obtained from children 7 years and older.

Assent documents should be written in language understandable to the participating children and contain at a minimum the following elements:

- A description of the research study
- What the child is being asked to do
- The risks and benefits of the study
- The voluntariness of the study (i.e. the child can skip questions they do not want to answer and can end their participation in the study at any time).

Researchers should thoroughly describe how assent will be obtained and whether the assent form will be signed by the participant.
**Waivers of assent:** Waivers of assent may be granted by the REB if either of the following two criteria are met:
- The capability of the participating children is so limited that they cannot reasonably be consulted;
- The intervention or procedure involved in the research has a prospect of direct benefit that is important to the health or well-being of the children and is available only in the context of the research;

Waivers of assent may also be granted by the REB if all of the following criteria are met:
- The research involves no more than minimal risk to the subjects;
- The waiver or alteration will not adversely affect the rights and welfare of the subjects;
- The research could not practicably be carried out without the waiver or alteration; and
- Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

Researchers requesting a waiver of assent should provide a thorough explanation and justification in their submission documents referring to the above criteria where appropriate.

### 7.4.3 Wards of a State/Country

**Definition:**
**Ward:** A child who is placed in the legal custody of a state, or other agency, institution or entity consistent with applicable federal, state or local law.

Researchers proposing to involve wards in their research should thoroughly explore the legal aspects of wards in their country as part of their study design. Specifically, researchers should give the legal definition of “ward” for the country in which the research will take place as well as identify the person or agency who can consent to the ward’s participation in research. Note that the person or agency who has physical custody of a child is not always the same person or agency who can give consent for the ward’s participation in research.

Wards can be included in research only if such research is:
- related to their status as wards; or
- conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as participants are not wards.

The REB will require appointment of an advocate for each child who is a ward, in addition to any other individual acting on behalf of the child as guardian or in loco parentis. One individual may serve as advocate for more than one child. The advocate shall be an individual who has the background and experience to act in, and agrees to act in, the best interests of the child for the duration of the child’s participation in the research and who is not associated in any way (except in the role as advocate or member of the REB) with the research, the investigator(s), or the guardian organization.

Research including Wards cannot be determined exempt, but may be expedited or reviewed by the full board.

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Section 8: Noncompliance and Scientific Misconduct

Researchers in all PSI research must avoid research misconduct and non-compliance, which includes fabrication, falsification, plagiarism, or other practices that seriously deviate from those that are commonly accepted for proposing, conducting, or reporting research. Non-compliance with REB Policies and Procedures and research misconduct have serious consequences for the investigator and the organization. Researchers who knowingly violate PSI’s policies may face serious consequences including dismissal.

Scientific Misconduct and Noncompliance are considered to include:

- Fabrication, falsification, plagiarism or other unaccepted practices in proposing, carrying out or reporting results from research;
- Material failure to comply with US Federal requirements for the protection of human subjects, researchers and/or the public;
- Failure to meet other material legal requirements governing research;
- Failure to follow the study design protocol as approved by the REB.

Reports of non-compliance may come to the REB from a variety of sources, including subjects and their family members, researchers, researcher supervisors, program staff and others. Note that PSI’s Whistleblower Policy and the Whistleblower Hotline (found on KIX) are also applicable to ethical misconduct in research. The PSI REB will take each report of non-compliance seriously and investigate each report thoroughly.

In general, the following procedures will take place when investigating a report of non-compliance:

- The REB will determine whether a study under investigation should have its REB approval terminated, which would require that enrollment in the study be halted. This authority is based on the federal regulations which give the REB the authority to suspend or terminate approval of research that is not being conducted in accordance with the REB’s requirements or that has been associated with unexpected serious harm to subjects. This decision will be made by the REB Chair in consultation with the REP Manager and others as appropriate.
- If suspension or termination of REB approval is not necessary, the issue will be resolved by any combination of the following individuals: REB Chair, REP Manager, PI, Research and Metrics Director, or others. All communications will be documented.
- If suspension is necessary, a notice of suspension will be sent immediately to the PI, the PI’s supervisor, the Research and Metrics Director, and others as necessary. As soon as possible, a meeting will be called with the relevant individuals to discuss the nature of the situation and if it qualifies as serious and continuing non-compliance. Review of study materials may be necessary to make this determination.
  - If the incident appears to be isolated and therefore does not qualify as serious and continuing, the REB will write a letter of findings to the PI and the PI must reply with suggested corrective actions. When the corrective actions are approved by the REB, suspension of enrollment of new participants will be lifted.
  - If the incident is considered to be serious and continuing, the DHHS OHRP will be notified as soon as possible via a letter that describes incident, the preliminary steps taken so far, and time frame for a full audit and full report to follow, including corrective actions so that similar
incidents do not occur again at PSI.
- An audit will be performed of all research conducted by the PI.
- Continued communications with OHRP and the PI will occur.
- The Institutional Official will be informed.
- Suspension of subject enrollment will be lifted once the audit process and communication process are completed to the satisfaction of the REB.*