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REPLY TO ATTENTION OF
FCMR-UWS-HP

23 June 2023

MEMORANDUM FOR RECORD

SUBJECT: WRAIR Institutional Review Board (IRB) Guidance for Management of Principal Investigator (PI) Changes (Version 1, dated 05 June 2023)

References:

- US Food and Drug Administration Guidance Document: Investigator Responsibilities – Protecting the Rights, Safety, and Welfare of Study Subjects, October 2009
- US Department of Health & Human Services, Investigator Responsibilities FAQs
- WRAIR Policy 29, Assignment of Principal Investigators to Human Subjects Research Conducted under the WRAIR Human Research Protection Program
- 21 CFR 56, US FDA, Institutional Review Boards
- 32 CFR 219, DoD, Protection of Human Subjects
- 45 CFR 46, Protection of Human Subjects

Purpose: This guidance document serves to clarify standards for changes of PIs of human subjects research studies. This guidance is intended to inform investigators and study staff regarding substantive requirements, submission processes, and review procedures for PI changes while maintaining subject/participant safety, scientific integrity, and regulatory compliance.

This guidance is in effect immediately, unless rescinded or further extended.

Background: The role of PI is critical in human subjects research studies for maintaining the integrity of the study, compliance with study procedures and regulatory standards, protection of human subjects, reporting of adverse events and unanticipated problems, and communication with sponsor and regulatory bodies. Therefore, ensuring that all PIs are appropriately qualified for their role and that there is continuity of PI responsibility on each study is essential to the protection of human subjects and the integrity of the research.

At WRAIR, there may be frequent changes of PI on research studies due to military permanent change of station (PCS), turnover of personnel, retirement, or unanticipated issues such as illness or deployment. Due to the need to address PI changes frequently, this guidance is intended to clarify PI change processes, streamline where appropriate, and ensure that research responsibility and continuity are maintained.

The IRB must prospectively approve permanent changes to PI. In the event of an urgent situation in which the current PI is unavailable and another investigator needs to assume PI responsibilities, changes can be made without IRB approval when the changes reduce apparent immediate hazards to subjects. This is permitted by both the Common Rule (32 CFR 219.108(a)(3)(iii)), 45 CFR 46.108(a)(3)(iii), and US FDA regulations (21 CFR 56.108(a)(4)). In

any case in which a change is made to eliminate immediate hazards to subjects, the IRB must be notified as soon as possible.

As a best practice when submitting a new protocol for review, each research team should consider a contingency plan in the event that the PI departs unexpectedly, either temporarily or permanently. Study teams may choose to formally designate within the protocol one or more Associate Investigator(s) (AI) as qualified to take over in the event the PI must go on leave or depart the study. In these cases, the IRB would evaluate the qualifications of the AI for that role and this would streamline the approval process for a temporary or permanent PI change.

Procedures:

1. Permanent Change of PI

a) All permanent changes of PI (i.e., changes planned or reasonably expected to last longer than 4 months) must be accomplished with a protocol amendment which undergoes IRB review and receives WRAIR Commander Authorization. If a PI is leaving WRAIR (which includes its Directorates), changes in the PI should be reported to the IRB prior to the current PI leaving the research study. An amendment should be fully processed prior to the departure of the existing PI.

b) Amendments will follow routine amendment submission and review procedures, to include a revised protocol with updated version/date. For protocols still undergoing subject interactions, informed consent documents, assents, contact cards and other communications with research participants that include PI name and contact information must be updated.

c) In order for the IRB to ensure the incoming PI has the appropriate qualifications and experience, amendments with changes of PI must include the incoming PI's C.V. (dated and signed within 2 years) and a copy of their institutional human subjects protection training.

d) *For clinical trials:* If the incoming PI has not previously served as a PI on a WRAIR clinical trial, then the submission must also include the PI Qualification Summary (Appendix A). For FDA-regulated studies, the submission must contain an updated US FDA Form 1572.

e) Sponsors must be notified of permanent changes of PI, and in most cases, must review and approve/concur changes of PI prior to submission for IRB review.

f) Other oversight bodies, such as in-country ethics committee review boards at OCONUS sites, must also be notified and receive amendments for review and approval prior to assumption of the role of PI, as applicable.

2. Temporary Delegation of PI Duties:

Temporary delegation of PI duties may be needed if the currently approved PI cannot provide oversight of a research study for a planned period of time (e.g., parental leave, sabbatical) or in the event of unplanned leave or departure (e.g., injury, illness, incapacitation, removal, or deployment). Unplanned temporary delegation of PI duties should be processed expeditiously to ensure coverage of the PI responsibilities on the protocol. *Please note*: *Routine leave or medical leave (for common, short-term illnesses) lasting less than 30 days do not require submission of the temporary change in PI to the WRAIR IRB.* In most cases during the conduct of a study, AIs will have responsibilities to assist PIs with study related procedures such as eligibility screening, informed consent procedures, study visits, adverse event reporting, regulatory documentation, etc. It is recommended as a best practice that at least one AI be fully briefed on and familiar with study procedures in case the PI is unavailable.

a) It is the responsibility of the currently approved PI to inform the IRB(s), funding agencies, and sponsor of any temporary or unplanned changes in PI oversight of an ongoing study lasting more than 30 days. If the current PI is unable to do so (for example, due to illness or incapacitation), the PI's Branch/Center/Directorate Director must promptly ensure the applicable entities above receive the appropriate communications.

b) A temporary delegation of PI duties may be processed using Appendix B: Temporary Change of PI. *Please note that this form is not intended to substitute for a protocol amendment for a **permanent** PI change, or a delegation that is planned or reasonably expected to last longer than 4 months. However, if a full amendment is in process and not yet approved, the temporary PI form may be needed in the interim.*

c) For studies with ongoing subject interactions, as well as, for all FDA regulated studies, the PI-delegate must currently be serving as an AI on the study and have access to all current and previous regulatory and participant file documentation, as applicable. For non-FDA regulated studies with no further subject interactions and no further recruitment (e.g., protocol is in data/specimen analysis only), the PI-delegate does not have to be a current AI on the study.

d) Temporary delegation of PI duty submissions should include PI-delegate C.V., (current and signed/dated within 2 years), and a copy of their institutional human subjects protection training.

e) *For clinical trials:* If the PI-delegate has not previously served as a PI on a WRAIR clinical trial, then the submission must also include the PI Qualification Summary (Appendix A). For FDA-regulated studies, the submission must contain an updated US FDA Form 1572.

f) Temporary delegation of PI duties may not extend beyond 4 months, for either unplanned or planned absences of the currently approved PI. An amendment to

permanently change the PI must be submitted to the WRAIR HSPB prior to 4 months of the currently approved PI's inability to provide oversight of the research, please refer to Section 1: Permanent Change of PI, above.

IRB Review Procedures

1. All permanent changes of PI are reviewed by the IRB and authorized by the WRAIR Commander. For temporary changes of PI, the WRAIR Commander is notified only.

2. In most cases, changes of PI may be reviewed via expedited review procedures. However, the IRB Chair or IRB Chair designee may choose to review a PI change via full board review procedures if deemed necessary.

3. Considerations for full Board review might include PI qualifications and experience, study risks, phase of study, stage of study, location and study population, study history/track record, and core protocol versus SSA change.

4. If no approved PI is available for a study, the study may need to be placed on hold or permanently discontinued. Plans should be in place for notifying participants and making sure that any necessary medical follow-up is put in place, as applicable. All holds and discontinuations must be reported immediately (within 24 hours) to the IRB and to the sponsor.

Research at OCONUS Locations

This guidance applies to studies taking place at CONUS and OCONUS locations. Local IRB/ethics committee guidance at OCONUS sites must be followed. This guidance does not supersede or substitute for host nation requirements.

External (non-WRAIR) IRB of Record

1. If the WRAIR IRB is not the IRB of Record for a study, the research team must follow the appropriate guidance/policy supplied by the IRB of Record for all PI changes. In these cases, WRAIR Commander authorization is required for permanent PI changes and Commander notification for temporary PI changes.

2. Changes of PI must be reported to the sponsor, and the US FDA Form 1572 updated as applicable.

3. Changes of PI should be reported to WRAIR HSPB at the same time they are reported/submitted to the IRB of Record for purposes of institutional record-keeping, triaging, and oversight.

All notifications pertaining to PI changes should be sent to the USARMY Ft Detrick MEDCOM WRAIR Mailbox HSPB at usarmy.detrick.medcom-wrair.mbx.hspb@health.mil.

The points of contact for IRB-related guidance are:

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