

FOR Distribution

SUBJECT: Guidance on Reporting Protocol Deviations to the WRAIR Division of Human Subjects Protection

The role of the Principal Investigator (PI) is complete responsibility of all aspects of the research activity. The research must be appropriately conducted in accordance with federal and Army regulations and ethical principles, as well as, WRAIR policies and procedures. The role of the Division of Human Subjects Protection (DHSP) is to collaborate with researchers to ensure the rights and welfare of participants are protected. Although the PI is ultimately responsible, this collaborative effort is an important function of research conducted at the WRAIR.

Pursuant to federal regulations and guidance from the Office for Human Research Protection (OHRP) and Army Regulations, the DHSP provides the following procedures related to the reporting of protocol deviations applicable to all Investigators and study staff.

1) **Major Deviations**

A major deviation is non-adherence to the Institutional Review Board (IRB) approved protocol **that has the potential to affect the rights and welfare of the research participant, to increase the risk to the research participant, to change the willingness of the volunteer to continue participation, or to compromise the integrity of the study data in such a way that the study objectives may not be achieved. Major deviations must be promptly reported (within 48 hours upon becoming aware of the event) to the DHSP, and recorded in the study deviation log.** The PI is responsible for making the initial determination; however, guidance may be obtained from the DHSP office.

Major deviations may include, but are not limited to:

- a) Written consent not obtained or consent form missing;
- b) Therapy or protocol interventions initiated prior to consent;
- c) Inclusion or exclusion criteria deviation without IRB approval;
- d) Delayed reporting of Serious Adverse Events (SAEs), unexpected adverse events, or unanticipated problems;
- e) Incorrect dosing of any study product; OR
- f) Pregnancy in studies for which pregnancy is strictly to be avoided.

2) **Timeliness of Major Protocol Deviation Reporting and Responses to Request for More Information**

The WRAIR IRB requires reporting of protocol deviations that pose immediate hazards to study subjects be reported by telephone or Email immediately upon

becoming aware of the event. These timelines are further explained in WRAIR SOP, Prompt Reporting to the Human Use Review Committee (UWZ-C-611). A written report must be submitted within 10 working days of a major deviation to the DHSP.

Responses to additional requests for information made by the DHSP or IRB must be submitted within 5 business days from the receipt of the request. Failure to respond to requests for additional information will result in a directed monitoring visit, study suspension or study termination, as appropriate.

3) Reporting Major Protocol Deviations to the WRAIR IRB

Major deviations should be reported in writing to the DHSP using the Deviation Report Form or a memorandum with similar content. The description of the event, summary of any harm to study participant(s), and steps to prevent further deviations should be described. These reports should be filed in person and via email to wrairdhsp@amedd.army.mil.

The event will be reviewed at DHSP, additional information may be requested, and it will then be passed on to the Chair, WRAIR IRB or designee for review.

4) Eligibility Deviation Exception

Individuals who do not meet Institutional Review Board (IRB) approved eligibility criteria may not be enrolled into a research study. A researcher may request an individual exception to the approved criteria in order to enroll a participant, but **prior IRB approval** is required. In this case, the WRAIR IRB must receive a submission via the DHSP.

Procedure to request an exception: A request for a volunteer eligibility deviation must be emailed to the Director, Division of Human Subject Protection and the Chair, WRAIR IRB. The email should contain: WRAIR protocol #, PI name, Reason for eligibility deviation request. The eligibility deviation will be reviewed as soon as possible and notice of IRB approval will be returned via email. Enrollment of a subject or subjects based on the exception request cannot occur until a return email acknowledging approval is received. If recurrent eligibility deviation requests are made, consideration of revising the approved eligibility criteria will be suggested.

If an eligibility deviation has occurred without prior IRB approval, this is considered a major deviation and must be reported to the IRB. The Protocol Deviation Report Form is found at: www.wrairdhsp.com.

5) All Other Protocol Deviations:

Protocol deviations that do not affect or potentially affect the health and welfare of study participants, and do not compromise the integrity of the results in such a way that the study objectives may not be achieved, may nonetheless affect the study results. All other protocol deviations, not to be

considered major deviations, should be reported in the deviation log and reported to the IRB as part of the protocol continuing review (see DHSP Continuing Review SOP).

Other protocol deviations include, but are not limited to:

- a) Study procedure conducted out of sequence;
- b) Consent form not given to the person signing the form;
- c) Subject's visit was outside of study window (less than 2 days)
- d) Over-enrollment (depending on the nature of the study and the number enrolled)
- e) Failure to perform a required lab test and this lab test is not known to be adversely affected by the study intervention
- f) Failure of subject to return unused study drug

To note, any of the above listed deviations can be assessed as a major deviation depending on the study, severity and frequency.

6) If you have any questions regarding the above guidance, please contact the Division of Human Subjects Protection, Walter Reed Army Institute of Research, at (301) 319-9940.

Division of Human Subjects Protection
Walter Reed Army Institute of Research