



DEPARTMENT OF THE ARMY
WALTER REED ARMY INSTITUTE OF RESEARCH
503 ROBERT GRANT AVENUE
SILVER SPRING, MD 20910-7500

REPLY TO
ATTENTION OF

MCMR-UWZ-C

12 September 2012

MEMORANDUM FOR SEE DISTRIBUTION

SUBJECT: WRAIR Policy Letter 12-29, Assignment of Principal Investigators to Human Subjects Research Conducted under the WRAIR Human Research Protection Program (HRPP)

1. References:

- a. Department of Defense (DOD) Instruction 3216.02, Protection of Human Subjects and Adherence to Ethical Standards in DOD-Supported Research, November 2011
- b. 32 Code of Federal Regulation (CFR) 219, Protection of Human Subjects, 1 July 2007
- c. 21 CFR 50, Protection of Human Subjects, 1 April 2011
- d. 21 CFR 56, Institutional Review Boards, 1 April 2011
- e. Army Regulation (AR) 70-25, Use of Volunteers as Subjects of Research, 25 January 1990
- f. ALARACT 031/2008, Army Human Subjects Protection Requirements, DTG 141557Z
- g. Belmont Report, Ethical Principles and Guidelines for the Protection of Human Subjects of Research, 1979
- h. HRPP, Walter Reed Army Institute of Research (WRAIR), July 2008
- i. WRAIR Policy 12-09, Determination that an Activity is Research Involving Human Subjects
- j. WRAIR Policy 12-05, Submission of Protocols Involving Human Subjects, Human Specimens, and/or Human Data for Scientific and Ethical Review
- k. Guidance for Industry E6 Good Clinical Practice: Consolidated Guidance. ICH. April 1996

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I. Guidance for Industry. Investigator Responsibilities: Protecting the Rights, Safety and Welfare of Human Subjects. October 2009

2. History: While this is the first version of this official policy and is effective upon signature, this has been a long-standing best practice established by the WRAIR Institutional Review Board (IRB). This version of the policy will remain in effect until amended or rescinded.

3. Purpose: The purpose of this policy is to ensure proper oversight of human subjects research protocols by stipulating that only one (1) qualified individual be designated as the responsible party, i.e. Principal Investigator (PI) for the overall conduct for any given study.

4. Definitions:

a. *Engaged in Human Subjects Research*. An institution is engaged in research if its employees (i) intervene or interact with living individuals for research purposes; or (ii) obtain individually identifiable private information for research purposes. This means any research that involves human subjects, identifiable human data, or identifiable human anatomical substances/specimens.

b. *Human Research Protection Program (HRPP)*. An integrated institution-wide program coordinated by the Human Subjects Protection Branch. The main purpose of a WRAIR-specific HRPP is to ensure that all of WRAIR's activities related to human subjects research are conducted in accordance with regulatory requirements and ethical principles as set forth in the Belmont Report. Major components of the HRPP include the IRB, several additional groups that provide research review, such as, the Office of Research Technology Applications (ORTA), Institutional Biosafety Committee (IBC), WRAIR Safety Office, MRMC Human Research Protections Office (HRPO), and Translational Medicine Branch. Additional components include: assurances, regulations, policies, SOPs, investigators, sponsors, overseas commanders, MRMC headquarters, etc.

c. *Institutional Official (IO)*. Individual ultimately responsible for implementation of the U.S. Health and Human Services (HHS) Federal Wide Assurance and DOD Assurance of Compliance for the Protection of Human Research Subjects and the associated HRPP at an institution engaged in research involving human subjects.

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Within the U.S. Army Medical Research and Materiel Command (USAMRMC), the Commander of the institution/organization engaged in research is the IO.

d. *Multi-Site Study*: A study involving more than one performance site engaged in research within the WRAIR or its detachments. Typically, each site will have its own site PI.

e. *Principal Investigator (PI)*: The individual who is responsible and accountable for conducting a human research study; this individual will have the appropriate scientific training and experience, as well as the ethical training and experience, to assume full responsibility and accountability for the scientific integrity of the research data and results. The PI is the individual responsible and accountable for designing, conducting, and monitoring a clinical study, and has access to the data. The PI, as the leader of the research team, assumes full responsibility for the treatment and evaluation of subjects, either directly or indirectly (designee of a healthcare provider). The PI may formally delegate roles and responsibilities to other members of the study team, as appropriate, but retains full responsibility for the conduct of all study activities. The PI also is responsible for protecting the rights and welfare of human subjects and is responsible for carrying out sound ethical research consistent with research plans in a protocol approved by a properly-constituted IRB.

(1) ICH E6 Definition: Investigator means a person responsible for the conduct of the clinical trial at a trial site. If a trial is conducted by a team of individuals at a trial site, the investigator is the responsible leader of the team and may be called the principal investigator. See also Subinvestigator.

(2) FDA definition: *Investigator* means an individual who actually conducts a clinical investigation, i.e., under whose immediate direction the test article is administered or dispensed to, or used involving, a subject, or, in the event of an investigation conducted by a team of individuals, is the responsible leader of that team. *Please note: This is not necessarily the same as a PI listed on a grant or research award, which may include other responsibilities not involving human subjects research.*

f. *Protocol*: A document that describes the objective(s), design, methodology, statistical considerations, and organization of a research study. The protocol usually also describes the background and rationale for the study and roles/responsibilities of the investigators. (ICH E6)

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g. *Research*: A systematic investigation, including research development, and testing and evaluation, designed to develop or contribute to generalizable knowledge (32 CFR 219.102d).

h. *Sponsor*: An individual, company, institution or organization that takes responsibility for the initiation, management, and/or financing of clinical research. (ICH E6). For DoD intramural research without a formal "Sponsor", this is typically the laboratory commander accepting the funding.

i. *Sub or Associate Investigator, Co-Investigator*: An individual member of the research team designated and supervised by the principal investigator at a study site to perform critical study-related procedures and/or to make important study-related decisions.

j. *WRAIR Point of Contact (POC)*: An individual, affiliated with WRAIR or its detachments, who is responsible for submission of protocol documents to the Human Subjects Protection Branch (HSPB) over the lifecycle of the study as new protocol actions are processed, remains in continual communication regarding the study to regulatory authorities, and directs study execution wherein WRAIR is participating; is generally the lead WRAIR investigator on the protocol, but is not the overall study PI. The POC can be the PI, a clinical coordinator, program manager, associate investigator, or other individual involved in the study in a scientific or administrative capacity.

5. Background:

a. The PI is ultimately responsible for the ethical conduct of human subjects research and for compliance with federal regulations, DoD/U.S. Army requirements, applicable state and local laws, and WRAIR policies.

b. One individual must take responsibility for the overall conduct of a protocol. Defining and delegating roles and responsibilities is a critical aspect of protocol execution to ensure risks are minimized to the study subjects and to ensure consistent evaluable data are captured. Furthermore, the PI must ensure that all individuals are adequately trained to complete the roles and responsibilities of which they have been delegated.

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c. While it is recognized that human subjects research is truly a team effort, more than one PI has led to deferral of responsibility when non-compliance, unanticipated problems, deviations, etc. events have occurred. Additionally, disagreement has occurred between Co-PIs as to specific study aspects.

6. Applicability and Scope:

a. This policy applies to all WRAIR personnel engaged in research, including contractors conducting research under the WRAIR HRPP.

b. This policy applies to all studies conducted under the WRAIR HRPP. Of note, research conducted at WRAIR's overseas detachments, or at non-WRAIR sites, are also subject to the national requirements of the host-country, and/or local institutional policies.

7. Policy: Only one (1) individual may serve as the PI of a human subjects research protocol. The principal investigator will be held responsible for all aspects in the conduct of human subjects research.

8. Implementation:

a. An individual PI will be identified on the protocol, as determined through the standard qualifications process of the Sponsor or submitting Branch.

b. The specific roles and responsibilities of the PI will be defined in the protocol.

(1) The roles and responsibilities of all other individuals identified on the protocol will be defined in the protocol. Specific details to be included are the individuals involvement in:

(2) Obtaining information about subjects by intervening or interacting with them for research purposes;

(3) Obtaining identifiable private information about the subjects for research purposes;

(4) Obtaining the subjects voluntary informed consent; and

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(5) Studying, interpreting, or analyzing identifiable private information or data for research purposes

c. *Responsibility:* The PI (and/or WRAIR POC) and Branch Directors/Detachment Commanders are responsible for ensuring the above is complete.

d. Failure to comply with this policy will lead to designation as an incomplete protocol submission and delay in processing. Additionally, if failure to do so is repeated, involvement of the Deputy Commander will occur, who could intervene via multiple avenues including, but not limited to, poor performance review and/or disciplinary action.

9. Exceptions:

a. Described below are the only exceptions to this policy:

(1) When the appointment of a co-principal investigator (Co-PI) is required by the sponsor;

(2) When the appointment of a Co-PI is a requirement under the national law of the host-country; and/or

(3) When the appointment of a Co-PI is a requirement under the local institutional policy (i.e., studies being conducted at a non-WRAIR location). Note: This does not preclude the establishment of site-specific PIs for multi-site projects with an overarching "study director" or parent protocol PI.

b. If an exception to this policy, the appointment of a Co-PI, is necessary, the responsibilities between the co-principal investigators will be clearly delineated in the protocol, as each principal investigator will be held solely responsible for their specific assigned responsibilities. Exceptions not listed in the above, must be approved by the Deputy Commander, WRAIR, and the Chair, WRAIR IRB, in writing. The submission memorandum should provide a justification for this request.

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10. Points of Contact: The points of contact for this policy are the Chair, WRAIR IRB, and the Director, Human Subjects Protection Branch, at (301) 319-9940.

Signature on File

RALPH L. ERICKSON
COL, MC
Commanding

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