



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

5 Feb 2021

FCMR-UWZ (100)

MEMORANDUM FOR All Personnel, Walter Reed Army Institute of Research (WRAIR)

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

1. References.

a. Department of Defense Instruction (DODI) 3216.02 (Protection of Human Subjects and Adherence to Ethical Standards in DOD-Conducted and -Supported Research), 15 April 2020.

b. National Defense, 32 Code of Federal Regulations (C.F.R.) §§ 219.101-219.124, (2018).

c. Food and Drugs, 21 C.F.R. §§ 50.1-50.56 and §§ 56.101-56.124 (2018).

d. Army Regulation (AR) 70-25 (Use of Volunteers as Subjects of Research).

e. Message, ALARACT 031/2008 (Army Human Subjects Protection Requirements), 14 February 2008.

f. National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Biomedical and Behavioral Research), 1979.

g. WRAIR Policy #25 (Determination that an Activity is Research Involving Human Subjects).

h. WRAIR Policy #24 (Submission of Protocols Involving Human Subjects, Human Information or Biospecimens, for Scientific and Ethical Review).

i. U.S. Department of Health and Human Services Food and Drug Administration, Center for Drug Evaluation and Research (CDER), Center for Biologics Evaluation and Research (CBER) (E6(R2) Good Clinical Practice: Integrated Addendum to ICH E6(R1) Guidance for Industry), dtd March 2018, exp. 30 September 2020.

*This supersedes WRAIR Policy Letter 12-29, dtd 12 September 2012.

FCMR-UWZ (100)

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

j. U.S. Department of Health and Human Services Food and Drug Administration, Center for Drug Evaluation and Research (CDER), Center for Devices and Radiological Health (CDRH), Center for Biologics Evaluation and Research (CBER), FDA-2013-S-0610 (Guidance for Industry, Investigator Responsibilities - Protecting the Rights, Safety and Welfare of Human Subjects), October 2009.

2. History. This policy is being issued in accordance with WRAIR and U.S. Army Medical Research and Development Command (USAMRDC) requirements and is effective upon signature by the WRAIR Commander. This version of the policy includes updated definitions aligned with current federal and Army regulations and guidance, and minor editorial changes. This version of the policy will remain in effect until amended or rescinded.

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

4. Definitions.

a. Engaged in Human Subjects Research: An institution is engaged in research involving human subjects if its employee(s) (i) obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens for research purposes; or (ii) obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens for research purposes.

b. Human Research Protection Program (HRPP): An integrated institution-wide program coordinated by the Human Subjects Protection Branch (HSPB) with the main purpose of ensuring 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 Institutional Review Board (IRB), research review groups (the Office of Research Technology and Applications (ORTA), Scientific Review Committee (SRC), Institutional Biosafety Committee (IBC), WRAIR Safety Office, USAMRDC Human Research Protections Office (HRPO), and Translational Medicine Branch), assurances, regulations, policies, standard operating procedures (SOPs), investigators, sponsors, overseas Directors, USAMRDC headquarters, etc.

c. Institutional Official (IO): Individual ultimately responsible for the implementation of the U.S. Department of Health and Human Services (DHHS) Federal wide Assurance and the DOD Assurance of Compliance for the Protection of Human Research Subjects

FCMR-UWZ (100)

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

and the associated HRPP at an institution engaged in research involving human subjects. Within the USAMRDC, 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 research study. This individual will have the appropriate scientific and ethics 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 the research study, and has access to the data. For studies involving human research subjects, the PI, as the leader of the research study team, assumes full responsibility for the medical care and evaluation of subjects, either directly or indirectly (designee of a healthcare provider). 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. The PI may formally delegate roles and responsibilities to other members of the research study team, as appropriate, but retains full responsibility for the conduct of all study activities.

(1) 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.

(2) 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.

Note: The above definition is not necessarily the same as that of 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).

FCMR-UWZ (100)

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

g. Research: A systematic investigation, including research development, and testing and evaluation, designed to develop or contribute to generalizable knowledge.

h. Research Involving Human Subjects: Activities that include both a systematic investigation designed to develop or contribute to generalizable knowledge AND involve a living individual about whom an investigator conducting research (i) obtains information or biospecimens through intervention or interaction with the individual and uses, studies, or analyzes the information or biospecimens, or (ii) obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens.

i. Site-specific PI: For research studies conducted at multiple study sites, the individual who is responsible and accountable for conducting the research study at a specific study site.

j. Sponsor: An individual, company, institution or organization that takes responsibility for the initiation, management, and/or financing of clinical research (ICH E6). The sponsor does not actually conduct the investigation unless the sponsor is a sponsor-investigator. A person other than an individual that uses one or more of its own employees to conduct an investigation that it has initiated is a sponsor, not a sponsor-investigator, and the employees are investigators. The USAMRDC Principal Assistant for Acquisition (PAA) serves as the Sponsor's Representative when programs within USAMRDC initiate the development of a new experimental product and conduct clinical investigations with the new experimental product. There are no sponsor-investigators in the USAMRDC.

k. Study Director, Protocol Chair or parent protocol PI: An individual who is designated as responsible for the oversight of multiple site clinical trial studies, including study design, providing support the site PIs with clinical trial guidance, protocol preparation, protocol review and regulatory approvals, serving as a liaison between the study sites, and contributing support to overall project management and the analysis and reporting of study data.

Note: A determination on whether these activities would engage the individual in human subjects research will be made by the HSPB on a case-by-case basis.

l. Subinvestigator or Associate Investigator, Co-Investigator: An individual member of the research team delegated and supervised by the PI at a study site to perform critical study-related procedures and/or to make important study-related decisions.

m. WRAIR Point of Contact (POC): An individual, affiliated with WRAIR or its detachments, who is responsible for submission of protocol documents to the HSPB over the lifecycle of the study as new protocol actions are processed, remains in

FCMR-UWZ (100)

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

continual communication regarding the study to regulatory authorities, and directs study execution wherein WRAIR is participating. This individual is generally the lead WRAIR investigator on the protocol, but is not the overall study PI. The POC can be the site PI, a clinical coordinator, program manager, associate investigator, or other individual involved in the study in a scientific or administrative capacity.

5. Background.

a. While it is recognized that human subjects research is truly a team effort, having more than one PI has in the past led to deferral of responsibility and disagreements when events of non-compliance, unanticipated problems, deviations, etc., have occurred.

b. 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.

c. The PI must take responsibility for the overall conduct of a research protocol. Defining and delegating roles and responsibilities is a critical aspect of protocol execution to ensure risks to the study subjects are minimized and consistent, evaluable data are captured.

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 directorates, 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 PI will be held responsible for all aspects of the conduct of human subjects research.

8. Execution.

a. An individual PI will be identified by name and institution on the protocol, as determined through the standard qualifications process of the Sponsor or submitting Branch/Directorate. The IRB is also responsible for reviewing and confirming the PI's qualifications to conduct and supervise the study.

FCMR-UWZ (100)

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

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

c. The roles and responsibilities of all other individuals identified in the protocol will be defined in the protocol. Specific details to be included are the individuals' involvement in:

(1) obtaining information about subjects by intervening or interacting with them for research purposes

(2) obtaining identifiable private information about the subjects for research purposes

(3) obtaining the subjects voluntary informed consent

(4) studying, interpreting, or analyzing identifiable private information, specimens or data for research purposes

d. The PI (and/or WRAIR POC) and Directorate/Center/Branch Directors are responsible for ensuring the information required above is included in the protocol and is complete.

e. Failure to comply with this policy will lead to the designation "incomplete protocol submission" and will result in delays in processing. Additionally, if failure to comply with the requirements of this policy is repeated, involvement of the Commander or 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-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", "Protocol Chair" or parent protocol PI.

FCMR-UWZ (100)

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

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

10. Point of contact for this memorandum is

[REDACTED]

Signature on file