HRP-001 | 2/2/2024 | Author: T. Bechert | Approver: I. Irizarry

SOP: Definitions

1 PURPOSE

1.1 This policy establishes the definitions followed by the human research protection program. This is a non-exhaustive list and regulatory agencies should be referenced for complete definitions where applicable.

2 REVISIONS FROM PREVIOUS VERSION

2.1 None

3 POLICY

3.1 Allegation of Non-Compliance: An unproved assertion of Non-Compliance.

3.2 Assurance of Compliance (Human Subjects) or Federalwide Assurance: An assurance is a written commitment to protect human research subjects and comply with the requirements of the Common Rule.

3.3 Authorization Agreement: Also called a Reliance Agreement, is the agreement that documents respective authorities, roles, responsibilities, and communication between an institution/organization providing the ethical review and a participating institution relying on the ethical review.

3.4 Certificate of Confidentiality: A Certificate of Confidentiality is a document issued by a component of HHS pursuant to The Public Health Service Act Section 301(d), 42 U.S.C. 241(d) amended by Section 2012 of the 21st Century Cures Act, Public Law 114-255, to protect the privacy of individuals who are subjects of certain specified research activities by authorizing investigators to withhold from all persons not connected with the conduct of such research the names or other identifying characteristics of such subjects. Persons so authorized to protect the privacy of such individuals may not disclose information in any Federal, State, or local civil, criminal, administrative, legislative, or other proceedings to identify such individuals.

3.5 Certification: The official notification by the institution to the supporting Federal department or agency component that a research project or activity involving human subjects has been reviewed and approved by an IRB in accordance with an approved assurance.

3.6 Clinical Trial: A research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of the interventions on biomedical or behavioral health-related outcomes.

3.7 Collaborating Individual Investigator: The Office for Human Research Protections notes that some human subjects research conducted by an assured institution may involve the following two types of collaborating individual investigators:

3.7.1 Collaborating independent investigator: not otherwise an employee or agent of the assured institution; conducting collaborative research activities outside the facilities of the assured institution; and not acting as an employee of any institution with respect to his or her involvement in the research being conducted by the assured institution.

3.7.2 Collaborating institutional investigator: not otherwise an employee or agent of the assured institution; conducting collaborative research activities outside the facilities of the assured institution; acting as an employee or agent of a non-assured institution with respect to his or her

involvement in the research being conducted by the assured institution; and employed by, or acting as an agent of, a non-assured institution that does not routinely conduct human subjects research.

3.8 Collaborative Study: A study in which two or more institutions coordinate, with each institution completing a portion of the research activities outlined in a specific protocol.

3.9 Conflicting Interest: An individual involved in research review is automatically considered to have a conflicting interest when the individual or the individual's spouse, domestic partner, children, and/or dependents have any of the following interests in the sponsor, product or service being tested, or competitor of the sponsor held by the individual or the individual's immediate family:

3.9.1 Involvement in the design, conduct, or reporting of the research.

3.9.2 Ownership interest, stock options, or other ownership interest of any value exclusive of interests in publicly-traded, diversified mutual funds.

3.9.3 Compensation of any amount in the past year or of any amount expected in the next year, excluding compensation for costs directly related to conducting research.

3.9.4 Proprietary interest including, but not limited to, a patent, trademark, copyright or licensing agreement.

3.9.5 Board or executive relationship, regardless of compensation.

3.9.6 Reimbursed or sponsored travel by an entity other than a federal, state, or local government agency, higher education institution or affiliated research institute, academic teaching hospital, or medical center.

3.9.7 Any other reason for which the individual believes that he or she cannot be independent.

3.10 Continuing Non-Compliance: A pattern of Non-Compliance that suggests the likelihood that, without intervention, instances of Non-Compliance will recur, a repeated unwillingness to comply, or a persistent lack of knowledge of how to comply.

3.11 Designated Reviewer: The IRB chair or an Experienced IRB Member designated by the IRB chair to conduct Non-Committee Reviews.

3.12 Experienced IRB Member: An IRB member is considered experienced if the IRB chair considers the IRB member to have sufficient experience in and knowledge of conducting IRB reviews.

3.13 Experimental Subject: For Department of Defense (DOD) research, research involving an "experimental subject" is an activity, for research purposes, where there is an intervention or interaction with a living individual for the primary purpose of obtaining data regarding the effect of the intervention or interaction. Research involving "experimental subjects" is a subset of research involving human participants.

3.14 Expiration Date: The first date that the protocol is no longer approved. The date after the end date of the approval period.

3.15 Finding of Non-Compliance: Non-Compliance in fact.

3.16 Human Research: Any activity that either:[1]

3.16.1 Is Research as Defined by DHHS and involves Human Subjects as Defined by DHHS;

3.16.2 or

3.16.3 Is Research as Defined by FDA and involves Human Subjects as Defined by FDA.

3.17 Human Subject as Defined by DHHS: A living individual about whom an investigator (whether professional or student) conducting research (1) obtains information or biospecimens through Intervention or Interaction with the individual, and uses, studies, or analyzes the information or

[1] The terms "Human Subject Research," "Research Involving Human Subjects," "Clinical Research," "Clinical Investigation," "Clinical Study" and similar phrases are considered to be synonyms for the term Human Research.

biospecimens; or (2) obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens. For the purpose of this definition:

3.17.1 Intervention: Physical procedures by which information or biospecimens are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.

3.17.2 Interaction: Communication or interpersonal contact between investigator and subject.

3.17.3 Private Information: Information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and that the individual can reasonably expect will not be made public (for example, a medical record).

3.17.4 Identifiable Private Information[2]: Private Information for which the identity of the subject is or may readily be ascertained by the investigator or associated with the information.

3.17.5 Identifiable Biospecimen[3]: A biospecimen for which the identity or the subject is or may be readily ascertained by the investigator or associated with the biospecimen.

3.18 Human Subject as Defined by FDA: An individual who is or becomes a subject in research, either as a recipient of the test article or as a control. A subject may be either a healthy human or a patient. A human subject includes an individual on whose specimen a medical device is used.

3.19 Immediate Family: Spouse, domestic partner; and dependent children.

3.20 Individual Investigator Agreement: a permissible mechanism under which an institution holding an Office for Human Research Protections (OHRP)-approved Federalwide Assurance (FWA) may extend – for one or more research protocols – the applicability of its FWA to cover two types of collaborating individual investigators: collaborating independent investigators and collaborating institutional investigators employed by a non-assured institution.

3.21 Institutional Official/ Organizational Official (IO/OO):

3.21.1 Institutional Official (IO): Term utilized by DHHS. The Institutional Official (IO) is the individual who is legally authorized to act for the institution and, on behalf of the institution, obligates the institution to the Terms of the Assurance. The IO is responsible for ensuring that the Human Research Protection Program (HRPP) functions effectively and that the institution provides the resources and support necessary to comply with all requirements applicable to research involving human subjects. The IO represents the institution named in the Federalwide Assurance (FWA)[4]. The IO is Associate Director, HRPP

3.21.2 Organizational Official (OO): Term utilized by AAHRPP.

3.21.2.1 An identified, knowledgeable leader of the HRPP who is responsible for the program and has the authority to implement the program. This individual may rely on others for the interpretation of laws, regulations, codes, and guidance and the day-to-day operations of the HRPP, and should have a basic understanding of the relevant laws, codes, regulations and guidance that govern research involving human participants, the responsibilities of an organizational official, and the responsibilities of the IRB or EC and researchers and research staff in protecting research participants. This individual should be directly involved in the allocation of resources to the HRPP. In some circumstances, more than one individual serves in this capacity[5].

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[2] Definitions of "identifiable private information" and "identifiable biospecimen" are included in FDA's proposed rule to amend part 50, Protection of Human Subjects, and part 56, Institutional Review Boards (87 FR 58733, September 28, 2022). In that rule, the proposed definitions of "identifiable private information" and "identifiable biospecimen" harmonize with the revised Common Rule's definitions of these terms (45 CFR 46.102(e)(5) and (6)).

[3] ibid.

[4] https://www.hhs.gov/ohrp/sachrp-committee/recommendations/2008-september-18-letter-attachment/index.html

[5] AAHRPP Evaluation Instrument (2018-10-15); http://www.aahrpp.org/apply/web-document-library/domain-i-organization

3.22 Institutional Profile: A record of information an institution keeps about another collaborating institution/organization for one or more Collaborative Studies or Multi-Site Studies.

3.23 Investigation: A searching inquiry for facts; detailed or careful examination.

3.24 Legally Authorized Representative (LAR): An individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedures(s) involved in the research.

3.24.1 If there is no applicable law addressing this issue, then this individual is recognized by institutional policy as acceptable for providing consent in the non-research context on behalf of the prospective subject to the subject's participation in the procedure(s) involved in the research.

3.24.2 See HRP-013 - SOP - LARs, Children, and Guardians for who may serve as a Legally Authorized Representative at this institution.

3.25 Minimal Risk: The probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.[6]

3.25.1 For research involving prisoners Minimal Risk is the probability and magnitude of physical or psychological harm that is normally encountered in the daily lives, or in the routine medical, dental, or psychological examination of healthy persons.

3.25.2 When following Department of Defense regulations, the definition of minimal risk in 32 CFR 219 does not include the inherent occupational risks that certain participants face in their everyday life, such as those:

3.25.2.1 Encountered by Service members, law enforcement, or first responders while on duty.

3.25.2.2 Resulting from or associated with high-risk behaviors or pursuits.

3.25.2.3 Experienced by individuals whose medical conditions involve frequent tests or constant pain.

3.26 Multi-Site Study: A study in which two or more institutions coordinate, with each institution completing all research activities outlined in a specific protocol.

3.27 Non-Committee Review: Any of the following:

3.27.1 Determination of whether an activity is Human Research.

3.27.2 Determination of whether Human Research is exempt from regulation.

3.27.3 Reviews of non-exempt research using the expedited procedure.

3.27.4 Determinations of which subjects can continue in expired research.

3.27.5 Concurrence of IRB Chair or designee for non-emergency individual patient/small group expanded access for an unapproved medical device (commonly known as Compassionate Use) or non-emergency individual patient expanded access IND with request for authorization to use alternative IRB review procedures.

3.28 Non-Compliance: Failure to follow the regulations, or the requirements or determinations of the IRB.

3.28.1 In the case of research funded or conducted by the Department of Defense (DOD), Non-Compliance includes failure of a person, group, or institution to act in accordance with Department of Defense (DOD) instruction 3216.02, its references, or applicable requirements

3.29 Participating Site (pSite): An institution that participates in a Single IRB (sIRB) Study.

3.30 Prisoner: 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 which provide alternatives to

[6] The phrase "ordinarily encountered in daily life or during the performance of routine physical or physiological examinations or tests" should not be interpreted to include the inherent risks certain categories of subjects face in their everyday life. For example, the risks imposed in research involving human subjects focused on a special population should not be evaluated against the inherent risks encountered in their environment (e.g., emergency responder, pilot, soldier in a combat zone) or having a medical condition (e.g., frequent medical tests or constant pain).

criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing.

3.30.1 For Department of Defense (DOD) research the term includes military personnel in either civilian or military custody.

3.31 Protocol Exception: a one-time, intentional action or process that departs from the approved protocol. Protocol Exceptions are generally for a single subject (e.g., the subject does not meet eligibility criteria or is allergic to one of the medications provided as supportive care). IRB approval of the Protocol Exception is required prior to implementation by the study team.

3.32 Related to the Research: A financial interest is Related to the Research when the interest is in:

3.32.1 A sponsor of the research;

3.32.2 A competitor of the sponsor of the research;

3.32.3 A product or service being tested; or

3.32.4 A competitor of the product or service being tested.

3.33 Research as Defined by DHHS: A systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.

3.33.1 The following activities are not considered Research as Defined by DHHS:

3.33.1.1 Scholarly and journalistic activities (e.g., oral history, journalism, biography, literary criticism, legal research, and historical scholarship), including the collection and use of information, that focus directly on the specific individuals about whom the information is collected.

3.33.1.2 Public health surveillance activities conducted by a public health authority, limited to those necessary to allow a public health authority to identify, monitor, assess, or investigate potential public health signals, onsets of disease outbreaks, or conditions of public health importance.

3.33.1.2.1 Including the collection and testing of information or biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health authority.

3.33.1.2.2 Including trends, signals, risk factors, patterns in diseases, or increases in injuries from using consumer products.

3.33.1.2.3 Including those associated with providing timely situational awareness and priority setting during the course of an event or crisis that threatens public health (including natural or man-made disasters).

3.33.1.3 Collection and analysis of information, biospecimens, or records by or for a criminal justice agency for activities authorized by law or court order solely for criminal justice or criminal investigative purposes.

3.33.1.4 Authorized operational activities (as determined by the relevant federal agency) in support of intelligence, homeland security, defense, or other national security missions.

3.33.1.5 Secondary research involving non-identifiable newborn screening blood spots.

3.34 Research as Defined by FDA: Any experiment that involves a test article and one or more Human Subjects, and that meets any one of the following:

3.34.1 Must meet the requirements for prior submission to the Food and Drug Administration under section 505(i) of the Federal Food, Drug, and Cosmetic Act meaning any use of a drug other than the use of an approved drug in the course of medical practice;

3.34.2 Must meet the requirements for prior submission to the Food and Drug Administration under section 520(g) of the Federal Food, Drug, and Cosmetic Act meaning any activity that evaluates the safety or effectiveness of a device; OR

3.34.3 Any activity the results of which are intended to be later submitted to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit.

3.35 Restricted: Applies to investigators who are delinquent in meeting IRB requirements.

3.36 Serious Non-Compliance: Non-Compliance such that the failure to comply could adversely affect the rights, safety, or welfare of a human subject; place a human subject at increased risk of harm; cause harm to a human subject; affect a human subject's willingness to participate in research; or damage or compromise the scientific integrity of research data.

3.37 Single IRB (sIRB) Study: A study in which two or more institutions (participating sites, or pSites) coordinate to complete the research activities, but all institutions rely on a single institution's/organization's IRB for ethical review. The reviewing IRB may or may not be affiliated with any of the pSites.

3.38 Suspension of IRB Approval: An action of the IRB, IRB designee, Institutional Official/Organizational Official, or designee of the Institutional Official/Organizational Official to temporarily or permanently withdraw IRB approval of some or all research procedures short of a Termination of IRB Approval. Suspended studies remain open and are subject to continuing review.

3.39 Systematic: Having or involving a system, method, or plan.

3.40 Termination of IRB Approval: An action of the IRB, IRB designee, Institutional Official/Organizational Official, or designee of the Institutional Official/Organizational Official to permanently withdraw IRB approval of all research procedures. Terminated studies are permanently closed and no longer require continuing review.

3.41 Unanticipated Problem Involving Risks to Subjects or Others: Any information that is (1) unanticipated, (2) related to the research, and (3) indicates that subjects or others are at increased risk of harm.[7]

3.41.1 For Department of Defense (DOD) research the term Unanticipated Problem Involving Risks to Subjects or Others includes any incident, experience, or outcome that meets ALL three of the following conditions:

3.41.1.1 Is unexpected (in terms of nature, severity, or frequency) given the procedures described in the research protocol documents (e.g., the IRB-approved research protocol and informed consent document) and the characteristics of the human subject population being studied.

3.41.1.2 Is related or possibly related to participation in the research (in this Instruction, possibly related means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research).

3.41.1.3 Suggests that the research places human subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized, even if no harm has actually occurred.

4 RESPONSIBILITIES

4.1 Individuals writing policies and procedures are to indicate terms defined in this policy with a double underline.

4.2 Individuals using policies and procedures are to consult this policy for the definitions of double underlined terms.

5 PROCEDURE

[7] See OHRP guidance "Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events: OHRP Guidance (2007)" at https://www.hhs.gov/ohrp/regulations-and-policy/guidance/reviewing-unanticipated-problems/index.html

5.1 None

6 MATERIALS

6.1 HRP-013 - SOP - LARs, Children, and Guardians

7 REFERENCES

7.1 45 CFR §46.102

7.2 21 CFR §50.3, 21 CFR §56.102, 21 CFR §312.3, 21 CFR §812.2(a), 21 CFR §812.3(p)

7.3 AAHRPP elements I.1.A, I.1.E, I.5.D, I.6.B, I.7.C, I-9, II.1.D, II.2.A, II.2.B, II.2.G, II.2.H, II.2.E-II.2.E.2, II.2.F-II.2.F.3, II.2.I, II.3.A, II.4.A, III.1.B, III.2.D