

SOP: Definitions				
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## 1 PURPOSE

- 1.1 This policy establishes the definitions followed by the human research protection program.

## 2 REVISIONS FROM PREVIOUS VERSION

- 2.1 None

## 3 POLICY

- 3.1 Adverse Event (AE): An AE in research can be any unfavorable or unintended event, including abnormal laboratory findings, symptom or disease, or death associated with the research or the use of a medical investigational test article. An AE in research may occur even in the absence of any error or protocol deviation and does not necessarily have to be caused by any identifiable aspect of the research.
- 3.2 Allegation of Non-Compliance: An unproved assertion of Non-Compliance.
- 3.3 Assurance of Compliance (Human Subjects) or Federalwide Assurance: A legally binding written document that commits an institution to complying with the Federal Policy (Common Rule) and other applicable Federal standards for the protection of human subjects.
- 3.4 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.
- 3.5 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 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.
- 3.8 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 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:
- 3.8.1 Involvement in the design, conduct, or reporting of the research.
  - 3.8.2 Ownership interest, stock options, or other ownership interest of any value exclusive of interests in publicly-traded, diversified mutual funds.
  - 3.8.3 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.
  - 3.8.4 Proprietary interest including, but not limited to, a patent, trademark, copyright or licensing agreement.
  - 3.8.5 Board or executive relationship, regardless of compensation.
  - 3.8.6 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.
  - 3.8.7 Any other reason for which the individual believes that he or she cannot be independent.
- 3.9 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.

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- 3.10 Designated Reviewer: The IRB chair or an Experienced IRB Member designated by the IRB chair to conduct Non-Committee Reviews.
- 3.11 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.
- 3.12 Expiration Date: The first date that the protocol is no longer approved. The date after the end date of the approval period.
- 3.13 Finding of Non-Compliance: Non-Compliance in fact.
- 3.14 Human Research: Any activity that either:<sup>1</sup>
  - 3.14.1 Is Research as Defined by DHHS and involves Human Subjects as Defined by DHHS; or
  - 3.14.2 Is Research as Defined by FDA and involves Human Subjects as Defined by FDA.
- 3.15 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 biospecimens; or (2) obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens. For the purpose of this definition:
  - 3.15.1 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.
  - 3.15.2 Interaction: Communication or interpersonal contact between investigator and subject.
  - 3.15.3 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).
  - 3.15.4 Identifiable Private Information: Private Information for which the identity of the subject is or may readily be ascertained by the investigator or associated with the information.
  - 3.15.5 Identifiable Biospecimen: A biospecimen for which the identity or the subject is or may be readily ascertained by the investigator or associated with the biospecimen.
- 3.16 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.
- 3.17 Immediate Family: Spouse, domestic partner; and dependent children.
- 3.18 Institutional Official/ Organizational Official (IO/OO):
  - 3.18.1 Institutional Official (IO): Term utilized by DHHS.
    - 3.18.1.1 : 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

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<sup>1</sup> 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.

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human subjects. The IO represents the institution named in the Federalwide Assurance (FWA)<sup>2</sup>. The IO is the Chief Medical Officer.

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

3.18.2.1 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<sup>3</sup>.

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

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

3.21 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.

3.21.1 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.

3.21.2 See "SOP: LARs, Children, and Guardians (HRP-013)" for who may serve as a Legally Authorized Representative at this institution.

3.22 Minimal Risk: The probability and magnitude of harm or discomfort anticipated in the research that 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.<sup>4</sup>

3.22.1 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.

3.22.2 When following Department of Defense regulations, the definition of minimal risk based on the phrase "ordinarily encountered in daily life or during the performance of routine physical or physiological examination or tests" shall not be interpreted to

<sup>2</sup> <https://www.hhs.gov/ohrp/sachrp-committee/recommendations/2008-september-18-letter-attachment/index.html>

<sup>3</sup> AAHRPP Evaluation Instrument (2018-10-15); <http://www.aahrpp.org/apply/web-document-library/domain-i-organization>

<sup>4</sup> 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).

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include the inherent risks certain categories of human participants face in their everyday life. For example, the risks imposed in research involving human participants focused on a special population should not be evaluated against the inherent risks encountered in their work environment (e.g., emergency responder, pilot, soldier in a combat zone) or having a medical condition (e.g., frequent medical tests or constant pain).

- 3.23 Multi-Site Study: A study in which two or more institutions coordinate, with each institution completing all research activities outlined in a specific protocol.
- 3.24 Non-Committee Review: Any of the following:
  - 3.24.1 Determination of whether an activity is Human Research.
  - 3.24.2 Determination of whether Human Research is exempt from regulation.
  - 3.24.3 Reviews of non-exempt research using the expedited procedure.
  - 3.24.4 Determinations of which subjects can continue in expired research.
  - 3.24.5 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.
- 3.25 Non-Compliance: Failure to follow the regulations, or the requirements or determinations of the IRB.
  - 3.25.1 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
- 3.26 Participating Site (pSite): An institution that participates in a Single IRB (sIRB) Study.
- 3.27 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 criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing.
  - 3.27.1 For Department of Defense (DOD) research the term includes military personnel in either civilian or military custody.
- 3.28 Related to the Research: A financial interest is Related to the Research when the interest is in:
  - 3.28.1 A sponsor of the research;
  - 3.28.2 A competitor of the sponsor of the research;
  - 3.28.3 A product or service being tested; or
  - 3.28.4 A competitor of the product or service being tested.
- 3.29 Research as Defined by DHHS: A systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.
- 3.30 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:
  - 3.30.1 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;
  - 3.30.2 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
  - 3.30.3 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.

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- 3.31 Restricted: Applies to investigators who are delinquent in meeting IRB requirements.
- 3.32 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.
  - 3.32.1 For Department of Defense (DOD) research Serious Non-Compliance includes failure of a person, group, or institution to act in accordance with Department of Defense (DOD) Instruction 3216.02 and its references such that the failure 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.
- 3.33 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.
- 3.34 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.
- 3.35 Systematic: Having or involving a system, method, or plan
- 3.36 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.
- 3.37 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.
  - 3.37.1 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:
    - 3.37.1.1 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.
    - 3.37.1.2 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).
    - 3.37.1.3 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.
    - 3.37.1.4 The term "serious adverse event" refers to an untoward occurrence in human research that results in death, a life-threatening experience, inpatient hospitalization, persistent or significant disability or incapacity, congenital abnormality, or birth defect, or that requires medical, surgical, behavioral, social, or other intervention to prevent such outcome.

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- 3.37.1.5 The terms “unanticipated” and “unexpected” refer to an event or problem in human research that is new or greater than previously known in terms of nature, severity, or frequency, given the procedures described in protocol documents and the characteristics of the study population.
- 3.37.1.6 The term “related” means the problem may reasonably be regarded as caused by, or probably caused by, the research.

#### **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**

- 5.1 None

#### **6 MATERIALS**

- 6.1 SOP: LARs, Children, and Guardians (HRP-013)

#### **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)