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.

2. REVISIONS FROM PREVIOUS VERSION

2.1. 6/9/21.

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 regulations 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. Certificate of Confidentiality: A Certificate of Confidentiality is a document issued by a component of U.S. Department of Health and Human Services (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.

3.6. 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.

3.7 Clinical Investigation (FDA definition): any experiment that involves a test article and one or more human subjects, and that either must meet the requirements or not meet the requirements for prior submission to the Food and Drug Administration (FDA) but the results of which are intended to be later submitted to, or held for inspection by, the FDA as part of an application for a research or marketing permit. The terms *research, clinical research, clinical study, study,* and *clinical investigation*s are synonymous.
Test article refers to a drug, device, biologic, or diagnostic test, whether the item is investigational or FDA-approved.

3.8. Clinical Trial (HHS, Common Rule definition): 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.

3.9. 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.

3.10. Compassionate Use: The administration of investigational (i.e., as yet unapproved) drugs to a patient in a special circumstance in which it is felt that the drug may lifesaving or effective when no other therapy would be. The procedure requires the treating physician to contact either the Food and Drug Administration (FDA) or the drug manufacturer to obtain permission. Compassionate Use is an older term that is still often used by clinicians. The regulatory processes for "Compassionate Use" have been replaced with the "Expanded Access" process.

3.11. Conflicting Interest (IRB member, Consultant, Ex Officio or IRB Staff: An individual involved in research pre-review or review is automatically considered to have a conflicting interest when:

3.11.1. The individual is involved in the design, conduct, and reporting of the research, or plans to enroll as a subject in the research.

3.11.2. An immediate family member (spouse, partner, child, parent or sibling) is involved in the design, conduct, and reporting of the research or plans to enroll as a subject in the research.

3.11.3. The individual or an immediate family member (spouse, partner, child, parent or sibling) has a significant financial or other personal interest that reasonably appears to be related to the individual's institutional responsibilities:

3.11.3.1. Service as an officer, director or in any other fiduciary role for a financially interested company, whether or not remuneration is received for such service.

3.11.3.2. Intellectual property rights (e.g., pending patent applications, patents, licenses, material transfer agreements, copyrights and royalties of any amount from such rights, including those royalties distributed by the University.

3.11.3.3. With regard to any remuneration received from the entity in the twelve months preceding the disclosure and the value of any equity interest in the entity as of the date of disclosure, when aggregated, exceeds $5,000. (See Rutgers Policy 90.2.5, Section 5 Definitions for more information if these applies.)

3.11.3.4. Greater than 1% of the ownership of stock assets or profits of a company which has, or seeks to have an agreement with the University, where the agreement is for the development of scientific or technological discoveries or innovations in which the University has or will have a property right.

3.11.3.5. Equity interests, including stock options, of any amount in a non-publicly traded financially interested company (or entitlement of same).

3.11.3.6. Equity interests (or other entitlement to the same) that in aggregate exceed $5,000 in a publicly-traded financially interested company.

3.11.4. Any other situation where the individual believes that another interest conflicts with his or her ability to pre-review or review objectively a submitted research project.

3.12. Conflict of Interest (Investigator): An investigator is automatically considered to have a significant conflict of interest if a financial or other personal interest of the investigator, his or

her spouse, domestic partner, children, parent or siblings that reasonably appears to be related to the Investigator's institutional responsibilities:

3.12.1. Service as an officer, director or in any other fiduciary role for a financially interested company, whether or not remuneration is received for such service;

3.12.2. Intellectual property rights (e.g., pending patent applications, patents, licenses, material transfer agreements, copyrights and royalties of any amount from such rights, including those royalties distributed by the University.

3.12.3. With regard to any publicly traded entity, a significant financial interest exists if the value of any remuneration received from the entity in the twelve months preceding the disclosure and the value of any equity interest in the entity as of the date of disclosure, when aggregated, exceeds $5000. For purposes of this definition, remuneration includes compensation, royalties, consulting fees, honoraria, gifts or other emoluments, bonuses, enrollment incentives or milestone payments, and "in kind" compensation or entitlement to same made directly or indirectly to the investigator by a financially interested company (or entitlement to the same), whether for consulting, lecturing travel (including reimbursed travel or sponsored travel), service on an advisory board, or for any purpose not directly related to the reasonable costs of conducting the research (as specified in the research agreement between the sponsor and the University), as determined through reference to public prices or other reasonable measures of fair market value, either in the year prior to the grant application or initiation of unsponsored research and submission of the accompanying Disclosure in the Rutgers eCOI System, or in the twelve months following the grant application or initiation of unsponsored research.

3.12.4. Greater than 1% of the ownership of stock, assets or profits of a company which has, or seeks to have an agreement with the University, where the agreement is for the development of scientific or technological discoveries or innovations in which the University has or will have a property right.

3.12.5. With regard to any non-publicly traded entity, a significant financial interest exists if the value of any remuneration received from the entity in the twelve months preceding the disclosure, when aggregated, exceeds $5,000, or when the investigator (or the investigator's spouse or dependent children) holds any equity interest (e.g., stock, stock option, or other ownership interest).

3.12.6. Equity interests (or entitlement to the same) that in aggregate exceed $5,000 in a publicly-traded financially interested company.

3.13. Continuing Non-Compliance: Any noncompliance that has been previously identified during an audit or investigation, confirmed by the IRB or an external authority (e.g., OHRP, FDA, sponsor, etc.), and the findings of noncompliance have been communicated in writing to the investigator or research team and those incidents of noncompliance occur again. Continuing Non-Compliance also includes failure to respond to a request to resolve an episode of Non-Compliance.

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

3.15. Emergency Use: When FDA applies, the use of an investigational drug or biological product with a human subject in a life-threatening situation in which no standard acceptable

treatment is available and in which there is not sufficient time to obtain IRB approval 21 CFR 56.102(d). See 1.002 (HRP-103) Investigator Manual, Section 29 (page 18) for further information.

3.16. Engaged in Research: An institution is engaged in non-exempt human subject research when its employees or agents for the purposes of the research project obtain: (1) data about the subjects of the research through intervention or interaction with them; (2) identifiable biospecimens or private information about the subjects of the research; or (3) the informed consent of human subjects for the research.

3.17. Expanded Access: a potential pathway for a patient with an immediately life-threatening condition or serious disease or condition to gain access to an investigational medical product (drug, biologic, or medical device) for treatment outside of clinical trials when no comparable or satisfactory alternative therapy options are available. The pathway is sometimes still referred by its former term, "Compassionate Use". The FDA regulations governing Expanded Access are codified in 21 CFR 312 Subpart I.

3.18. 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.

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

3.20. Federalwide Assurance (FWA): A written commitment by an institution, filed with the Office for Human Research Protections ("OHRP"), to comply with the HHS' regulations for the protection of Human Subjects.

3.21. Generalizable Knowledge: Information expressed in theories, principles and statements of relationships that can be applied more widely than the specific site and individuals participating the research project.

3.22. Human Research: Any activity that either:[1]

3.22.1. Is Research as defined by HHS and involves Human Subjects as defined by HHS; or

3.22.2. Is Research as defined by FDA and involves Human Subjects as defined by FDA.

3.23. Human Subject as Defined by HHS: 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:

3.23.1. 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.

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

3.23.3. 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

[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.

the individual can reasonably expect will not be made public (for example, a medical record).

3.23.4. 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.

3.23.5. 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.

3.24. 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.

3.25. Humanitarian Use Device: A device intended to benefit patients by treating or diagnosing a disease or condition that affects or is manifested in fewer than 8,000 individuals in the United States per year.

3.26. Institutional Official (IO): Term utilized by OHRP.

3.26.1. 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 human subjects. The IO represents the institution named in the Federal-wide Assurance (FWA)[2]. The IO is often the Vice President for Research.

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

3.26.2.1. 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[3].

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

3.28. Institutional Review Board (IRB): Any board, committee, or other group formally designated by an institution and established in accordance with federal regulations to review, to approve the initiation of, and to conduct periodic review of, human subjects research in accordance

[2] September 18, 2008 SACHRP letter to HHS Secretary Recommendations | HHS.gov

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

with federal regulations for the protection of human subjects in research and with these policies and procedures.

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

3.30. Investigational New Drug (IND): A drug not yet approved for marketing by the FDA and available only for use in experiments to determine its safety and effectiveness. An IND# allows the investigational drug to be used in a clinical study in order to collect safety and effectiveness data.

3.31. Investigational Device Exemption (IDE): A device not yet approved for marketing by the FDA and available only for use in experiments to determine its safety and effectiveness. An IDE# allows the investigational device to be used in a clinical study in order to collect safety and effectiveness data. Clinical studies are most often conducted to support a Premarketing Approval (PMA).

3.32. IRB Approval: The determination of the IRB that the research has been reviewed and may be conducted at an institution within the constraints set forth by the IRB and by other institutional and federal requirements.

3.33. Key Personnel: The National Institutes of Health (NIH) replaced the term "key personnel" with "senior/key personnel" in September 2010. In addition to the Program Director/Principal Investigator (PD/PI), senior/key personnel are defined as individuals who contribute to the scientific development or execution of the project in a substantive, measurable way, whether or not salaries or compensation are requested. In addition, an NIH Funding Opportunity Announcement (e.g., RFA, PA) may instruct certain types of personnel to be identified as senior/key.

3.34. 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.

3.34.1. NJ State Statute 26:14.1 - 26:14.5 outlines how and from whom to obtain informed consent to medical research on behalf of adults who lack decisional capacity. If conducted outside of New Jersey, the research must comply with the applicable surrogacy laws in the jurisdictions where the research is taking place. If there is no applicable law addressing this issue, then the Legally Authorized Representative 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.

3.34.2. See 7.001 (HRP-013) - SOP: LARs, Children, and Guardians for who may serve as a Legally Authorized Representative at this institution.

3.35. 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[4].

[4] 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

3.35.1. 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.

3.35.2. 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 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).

3.36. Minor Non-Compliance: Non-substantive or technical violations which result from inadvertent errors, inattention to detail, or failure to follow operational procedures which do not pose immediate or potential risks to subjects, the environment, or researchers and/or violate research subject's rights and/or welfare.

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

3.38. Non-Committee Review: Any of the following:

3.38.1. Determination of whether an activity is Human Research.

3.38.2. Determination of whether Human Research is exempt from regulation.

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

3.38.4. Determinations of which subjects can continue in expired research.

3.38.5. 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.

3.39. Non-Compliance: Failure to follow the laws or regulations that govern human research, the organization's policies or procedures, or the requirements or determinations of the IRB.

3.39.1. 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.

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

3.41. Principal Investigator: An individual who actually conducts human subjects research or clinical investigation (e.g., under whose immediate direction whatever procedures described in the protocol are conducted, whether or not a test article is administered or dispensed to, or used involving subjects) or, in the event of an investigation conducted by a team of individuals, is the responsible leader of that team.

3.42. 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

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responder, pilot, soldier in a combat zone) or having a medical condition (e.g., frequent medical tests or constant pain).

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.

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

3.43. Protocol Deviation: A non-compliance incident caused by change to a research protocol without approval by the IRB prior to its initiation or implementation.

3.43.1. Major Deviation: One that: a) has increased the risk and/or decreased the benefit to individual participants or resulted in detrimental change to a participant's clinical or emotional status or compromised the integrity or validity of the study; b) has occurred without appropriate IRB review and approval; c) is egregious or intentional; and/or d) has been determined by the IRB to be a major deviation.

3.43.2. Minor Deviation: An unintentional deviation or omission from a protocol that does not impact research participant safety or does not substantially alter risks to research participants or the integrity to the study.

3.44. Related to the Research: A financial interest is Related to the Research when the interest is in:

3.44.1. A sponsor of the research;

3.44.2. A competitor of the sponsor of the research;

3.44.3. A product or service being tested; or

3.44.4. A competitor of the product or service being tested.

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

3.43.1 The following activities are not considered Research as Defined by HHS:

3.43.2 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.

3.43.3 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.

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

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

3.43.6 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).

3.43.7 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.

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

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

3.46. 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:

3.46.1. 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;

3.46.2. 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

3.46.3. 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.

3.47. Research Misconduct: Any fabrication, falsification, or plagiarism of research or research results.

3.48. Restricted/On Probation: Applies to investigators who are delinquent in meeting IRB requirements.

3.49. 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; decreases potential benefits; affect a human subject's willingness to participate in research; or damage or compromise the scientific integrity of research data or the integrity of the human research protection program.

3.49.1. 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.

3.50. 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.

3.51. Suspension of IRB Approval: An action of the IRB, IRB Chair or 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.

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

3.53. Termination of IRB Approval: An action of the IRB, IRB Chair or 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.

3.54. 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.

3.54.1. 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:

3.54.1.1. 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.

3.54.1.2. 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).

3.54.1.3. 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.

3.54.1.4. The term “related” means the problem may reasonably be regarded as caused by, or probably caused by, the research.

4. RESPONSIBILITIES

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

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

5. PROCEDURE

5.8. None.

6. MATERIALS

6.8. 1.002 (HRP-103) Investigator Manual.

6.9. 7.001 (HRP-013) SOP: LARs, Children, and Guardians .

7. REFERENCES

7.8. 45 CFR §46.102.

7.9. 21 CFR §50.3, 21 CFR §56.102, 21 CFR §312.3, 21 CFR §812.2(a), 21 CFR §812.3(p).

7.10. DoD Instruction 3216.002