TITLE: **Definitions**

PURPOSE: Definitions followed by the Human Research Protection Program

RESPONSIBILTIES: HSSP Staff

DEFINITIONS:

Affiliation as Defined by DHHS: An employee or agent of the organization registering the IRB/IEC (or a member of that person's Immediate Family) is considered affiliated. Affiliated members include, but are not limited to individuals who are: part-time employees; current students; members of any governing panel or board of the institution; paid or unpaid consultants; healthcare providers holding credentials to practice at the institution; and volunteers working at the institution on business unrelated to the IRB/IEC. An individual that has no affiliation with the organization registering the IRB/IEC, other than as an IRB/IEC member, is considered unaffiliated with the entity operating the IRB/IEC. Unaffiliated members may include people whose only association with the institution is that of a patient, subject, or former student at that institution. Paying an unaffiliated member a reasonable market value for their services would not make the member "otherwise affiliated" as stated in the regulations or cause the member to have a conflicting interest.

Agent: An agent is an individual who: (1) acts on behalf of the institution; (2) exercises institutional authority or responsibility; or (3) performs institutionally designated activities. "Employees and agents" can include staff, students, contractors, and volunteers, among others, regardless of whether the individual is receiving compensation.

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

Alternate Members as Defined by DHHS: HHS regulations at 45 CFR 46 do not address the designation of alternate IRB/IEC members. However, for many years, the Office for Human Research Protections (OHRP) has permitted organizations submitting IRB registrations to OHRP to identify alternate members for primary members. When reviewing rosters that include alternate members OHRP assumes that, in general, with respect to the capacity in which the primary IRB member was intended to serve, each alternate IRB member has experience, expertise, background, professional competence, and knowledge comparable to that of the primary IRB member whom the alternate would replace. The minutes of an IRB meeting should document the attendance of all primary and alternate IRB members who attended any part of the IRB meeting. If both a primary IRB member and his or her alternate(s) attend the same IRB meeting, OHRP assumes that the primary member is acting as the official voting member of the IRB for review of research protocols, unless the minutes clearly indicate otherwise. A designated alternate IRB member for a primary IRB member may substitute for the primary IRB member for an entire meeting or at any time during a meeting. Substitution during a meeting commonly occurs when the primary member is (a) absent from the room for part of the meeting, or (b) recused from review of certain research protocols because the primary IRB member has a conflicting interest with respect to a specific research protocol. Whenever this occurs, the minutes of the IRB meeting should indicate clearly that the alternate IRB

member has replaced the designated primary IRB member. OHRP recommends that the reason for the substitution of the alternate IRB member also be documented in the minutes.

Clinical Investigation as defined by the Food and Drug Administration (FDA) (21CFR 56.102(C)): Any experiment that involves a test article and one or more human subjects, and that either must meet the requirements for prior submission to the Food and Drug Administration under section 505(i) or 520(g) of the act or need not meet the requirements for prior submission to the Food and Drug Administration under these sections of the act but 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. The term does not include experiments that must meet the provisions of part 58, regarding nonclinical laboratory studies. The terms *research, clinical research, clinical study, study,* and *clinical investigation* are deemed to be synonymous for purposes of this part.

Clinical Trial as defined by the National Institutes of Health (NIH): A biomedical or behavioral research study of human subjects designed to answer specific questions about biomedical or behavioral interventions (drugs, treatments, devices, or new ways of using known drugs, treatments, or devices). Clinical trials are used to determine whether new biomedical or behavioral interventions are safe, efficacious, and effective. Clinical trials of an experimental drug, treatment, device, or intervention may proceed through four phases:

Phase I. Study in a small group of people (e.g., 20-80) to determine efficacy and evaluate safety (e.g., determine a safe dosage range and identify side effects).

Phase II. Study in a larger group of people (e.g., several hundred) to determine efficacy and further evaluate safety.

Phase III. Study to determine efficacy in large groups of people (e.g., from several hundred to several thousand) by comparing the intervention to other standard or experimental interventions, to monitor adverse effects, and to collect information to allow safe use.

Phase IV. Studies done after the intervention has been marketed. These studies are designed to monitor the effectiveness of the approved intervention in the general population and to collect information about any adverse effects associated with widespread use.

Confidentiality (The American Heritage Medical Dictionary): The ethical principle or legal right that a physician or other health professional will hold secret all information relating to a patient, unless the patient gives consent permitting disclosure.

Conflicting Interest: An individual involved in the design, conduct or reporting of the research is automatically considered to have a conflicting interest when the individual or the individual's Immediate Family have any of the following:

- Ownership interest, stock options, or other ownership interest Related to the Research of any value exclusive of interests in publicly-traded, diversified mutual funds.
- Compensation Related to the Research of $5,000 or more in the past year.
- Proprietary interest Related to the Research including, but not limited to, a patent, trademark, copyright or licensing agreement.
- Any other reason for which the Institution determines that the individual cannot be independent or in circumstances in which the individual believes that he or she cannot be independent.

Continuing Non-Compliance: A pattern of behavior of noncompliance by the Investigator that indicates a lack of understanding about the regulations or ethical requirements that may affect the rights and welfare of participants. The pattern of noncompliance is assessed by repeated incidents occurring during the course of a protocol(s), and whether the same noncompliant action was repeated or many different noncompliant events occurred. If allowed to continue the noncompliance is likely to increase risk to subjects, adversely affects the rights, welfare, and safety of research subjects, or adversely affect the scientific integrity of the study and/or institution.

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

Engaged in Human Research: In general, an institution is considered *engaged* in a particular non-exempt human subjects research project 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 private information about the subjects of the research; or (3) the informed consent of human subjects for the research.

The University of Arizona follows the Office of Human Research Protections (OHRP) guidance on "Engagement of Institutions in Research" to apply this definition.

Enrolled Participants: Individuals who are eligible for participation (i.e., meet the inclusion criteria for the study), have given informed consent and participated in some or all study procedures (excluding screening procedures where applicable)

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

Expiration Date: The last day of the approval period.

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

Human Research: Any activity that either:[1]

- Is Research as Defined by DHHS and involves Human Subjects as Defined by DHHS; or
- Is Research as Defined by FDA and involves Human Subjects as Defined by FDA.

Human Subject as Defined by DHHS: A living individual about whom an investigator (whether professional or student) conducting research obtains (1) data through Intervention or Interaction with the individual, or (2) information that is both Private Information and Identifiable Information. The following terms are defined for the purpose of this definition:[2]

- Intervention: Physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.
- Interaction: Communication or interpersonal contact between investigator and subject.
- 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 which the individual can reasonably expect will not be made public (for example, a medical record).
- Identifiable Information: Information that is individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information).

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.

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

Investigator: The investigator is the person responsible for the conduct of the Human Research at one or more sites. If the Human Research 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.

Minimal Risk (45 CFR §46.102(i)): 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.

Non-Committee Review: Any of the following:

- Determination of whether an activity is Human Research;

[1] The terms "Human Subject Research," "Research Involving Human Subjects," "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.

[2] **For research conducted or funded by the Department of Defense (DOD)**: When 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, the data are considered to be about the living individual.

- Determination of whether Human Research is exempt from regulation;
- Reviews of non-exempt research using the expedited procedure;
- Verification that modifications required to secure approval have been made; or
- Determinations of which subjects can continue in expired research.

Non-Compliance: Failure to comply with the regulations; policies and process of the Human Subjects Protection Program; or the determinations of the IRB.

- In the case of research funded or conducted by the Department of Defense (DOD), Non-Compliance includes failure to comply with Department of Defense directives regarding protection of Human Subjects.
- In the case of research funded or conducted by the Department of the Navy (DON), Non-Compliance includes failure to comply with Department of the Navy instructions regarding protection of Human Subjects.

Organizational Official: Institutional Official: The Senior Vice President for Research.

Privacy: The study's participant's ability to control how other people see, touch, or obtain information about them. Violations of privacy can involve circumstances such as being seen without clothing or partially clothed, being photographed without consent, being asked personal questions in a public setting, etc.

Related to the Research: A financial interests is considered Related to the Research when the interest :

- the sponsor of the research and the financial interest are the same entity or organization;
- the research is similar to activities, services or products of the entity or organization.

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

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:

- 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;
- 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
- 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.

Restricted: Applies to investigators or research staff members who are delinquent in meeting IRB requirements.

Scientist/Nonscientist as Defined by DHHS: Members whose training, background, and occupation would incline them to view scientific activities from the standpoint of someone within a behavioral or biomedical research discipline should be considered a Scientist, while members whose training, background, and occupation would incline them to view research activities from a standpoint outside of any biomedical or behavioral scientific discipline should be considered a Nonscientist. In addition, the IRB/IEC must have members with sufficient knowledge of the specific scientific discipline(s) relevant to the research that it reviews.

Serious Non-Compliance: Non-Compliance that affects the rights or welfare of subjects.

Suspension of IRB Approval: An action of the IRB, IRB designee, or 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.

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

Unanticipated Problem Involving Risks to Subjects or Others: Any information that meets all three of the following criteria:

- Unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent; and (b) the characteristics of the subject population being studied. Harms are "unexpected" when their specificity and severity are not accurately reflected in the consent document;
- Related or possibly related to participation in the research (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); and
- Suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized. A harm is "at least probably related to the Human Research procedures" if in the opinion of the investigator, the research procedures more likely than not caused the harm.

ABBREVIATIONS:

AAHRPP: Association for the Accreditation of Human Research Protection Programs

ABOR: Arizona Board of Regents

ASU: Arizona State University

CBRP: Community-Based Research Principles

CFR: Code of Federal Regulations

CIRB: Central IRB

CITI: Collaborative Institutional Training Initiative

CoC: Certificate of Confidentiality

COI: Conflict of Interest
Co-PI: Co-Principal Investigator
DHHS: Department of Health and Human Services
DOD: Department of Defense
DOE: Department of Energy
DOJ: Department of Justice
DON: Department of Navy
ED: Department of Education
EPA: Environmental Protection Agency
ERC: Executive Review Committee
FERPA: Family Educational Rights and Privacy Act
FDA: Food and Drug Administration
GINA: Genetic Information Nondiscrimination Act
HIPAA: Health Insurance Portability and Accountability Act
HSPP: Human Subjects Protection Program
HUD: Humanitarian Use Device
IBC: Institutional Biosafety Committee
ICH: International Council on Harmonisation
IEC: Institutional Ethics Committee
IDE: Investigational Device Exemption
IND: Investigational New Drug application
IRB: Institutional Review Board
IRC: Institutional Review Committee
MOU: Memorandum of Understanding
NAU: Northern Arizona University
NIH: National Institutes of Health
OGC: Office of General Counsel
ORCR: Office for the Responsible Conduct of Research
OHRP: Office of Human Research Protections
ORCA: Office of Research and Contract Analysis
OHA: Oral History Association
ORD: Office for Research & Discovery
PHI: Protected Health Information
PI: Principal Investigator
PII: Personally Identifiable Information (Department of Energy specific term)
PPRA: Protection of Pupil Rights Amendment
PTSD: Post-traumatic stress disorder

SAVAHCS: Southern Arizona VA Healthcare System
SOW: Statement of Work (Department of Energy specific term)
SPS: Sponsored Projects Services
SSN: Social Security Number
UA or University: University of Arizona
UAHN: University of Arizona Health Network
UAR: UAccess Research
UMC: University Medical Center
University Administrator: [as defined in the Institutional COI policy]
UPH: University Physician's Healthcare
VOTF: Verification of Human Subjects Training Form
VA: Veteran's Administration
VPR: Vice President for Research
WIRB: Western IRB

MATERIALS:
None

REFERENCES:
- 45 CFR §46.102
- 21 CFR §50.3, 21 CFR §56.102, 21 CFR §312.3, 21 CFR §812.2(a), 21 CFR §812.3(p)
- UA Policy: Investigator Conflict of Interest in Research
- UA Policy: Managing Institutional Conflicts of Interest

REVIEW/REVISIONS: From 10/01/01 version: Added Enrolled participants; Added Unanticipated Problems; Added Privacy; Changed 'UAMC' to 'UAHN'; Changed Organization Official from 'Vice President for Research' to 'Senior Vice President for Research'; Updated Conflicting Interest and Related to the Research to be consistent with new COI policies; Updated Abbreviations list.

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