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:** For Veterans Administration (VA) research any untoward physical or psychological occurrence in a human subject participating in research. It can be any unfavorable and unintended event, including an abnormal laboratory finding, symptom, or disease associated with the research or the use of a medical investigational test article. It does not necessarily have to have a causal relationship with the research.

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

3.3 **Clinical Trial:** A biomedical or behavioral research study of human subjects designed to answer specific questions about diagnostic procedures or therapeutic interventions (drugs, treatments, devices, or new ways of using known drugs, treatments, or devices). Clinical trials are used to determine whether new diagnostic procedures or therapeutic interventions are safe, efficacious, and effective.

3.4 **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:
3.4.1 Involvement in the design, conduct, or reporting of the research.
3.4.2 Ownership interest, stock options, or other ownership interest of any value exclusive of interests in publicly-traded, diversified mutual funds.
3.4.3 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.
3.4.4 Proprietary interest including, but not limited to, a patent, trademark, copyright or licensing agreement.
3.4.5 Board or executive relationship, regardless of compensation.
3.4.6 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.
3.4.7 Any other reason for which the individual believes that he or she cannot be independent.

3.5 **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.
3.5.1 For Veterans Administration (VA) research Continuing Non-Compliance includes a persistent failure to adhere to the laws, regulations, or policies governing Human Research.

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

3.7 **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.

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

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

3.10 **Human Research:** Any activity that either:
3.10.1 Is Research as Defined by DHHS and involves Human Subjects as Defined by DHHS; or

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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.
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3.10.2 Is Research as Defined by USFDA and involves Human Subjects as Defined by USFDA.

3.11 **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**. For the purpose of this definition:

3.11.1 **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.

3.11.2 **Interaction:** Communication or interpersonal contact between investigator and subject.

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

3.11.4 **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).

3.12 **Human Subject as Defined by USFDA:** 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.

3.13 **Immediate Family:** The immediate family of a Faculty member or Staff member includes his or her spouse, dependent children, domestic or civil union partner, and others as defined in the Faculty Handbook and Staff Handbook. Also included are parents, siblings, aunts, uncles, nephews, nieces, grandparents, and grandchildren (whether related by blood, marriage or adoption).

3.14 **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.²

3.14.1 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.

3.14.2 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).

3.15 **Non-Committee Review:** Any of the following:

3.15.1 Determination of whether an activity is Human Research.

3.15.2 Determination of whether Human Research is exempt from regulation.

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

3.15.4 Determinations of which subjects can continue in expired research.

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

3.16.1 In the case of research funded or conducted by the US Department of Defense Defense (USDOD), Non-Compliance includes failure of a person, group, or institution to act in

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² 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).
accordance with Department of Defense (USDOD) instruction 3216.02, its references, or applicable requirements

3.16.2 In the case of Veterans Administration (VA) research, Non-Compliance includes failure to following the requirements of VHA Handbook.

3.17 Institutional Official: The Northwestern University Vice President for Research.

3.18 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.

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

3.19 Protected Health Information: Individually identifiable health information that is (1) transmitted by electronic media; (2) maintained in electronic media; and, (3) transmitted or maintained in any other form or medium. For purposes of this definition, protected health information excludes individually identifiable health information in: (a) educational records covered by the Family Educational Rights and Privacy Act; (b) records maintained by an educational agency or institution, or by a person acting for such agency or institution, on a student who is eighteen years of age or older, or is attending an institution of postsecondary education, which are made or maintained by a physician, psychiatrist, psychologist, or other recognized professional or paraprofessional acting in his professional or paraprofessional capacity, or assisting in that capacity, and which are made, maintained, or used only in connection with the provision of treatment to the student, and are not available to anyone other than persons providing such treatment, except that such records can be personally reviewed by a physician or other appropriate professional of the student’s choice; and (c) employment records held by a covered entity in its role as an employer.

3.19.1 Individually Identifiable Health Information: Information that is a subset of health information, including demographic information collected from an individual, and

3.19.1.1 Is created or received by a health care provider, health plan, employer, or health care clearinghouse and;

3.19.1.2 Relates to the past, present, or future physical or mental health or condition of an individual; the provision of health care to an individual; or the past, present, or future payment for the provision of health care to an individual; and

3.19.1.2.1 That identifies the individual; or

3.19.1.2.2 With respect to which there is a reasonable basis to believe the information can be used to identify the individual.

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

3.20.1 A sponsor of the research;

3.20.2 A competitor of the sponsor of the research;

3.20.3 A product or service being tested; or

3.20.4 A competitor of the product or service being tested.

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

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

3.22.1 Must meet the requirements for prior submission to the US 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;

3.22.2 Must meet the requirements for prior submission to the US 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
3.22.3 Any activity the results of which are intended to be later submitted to, or held for inspection by, the US Food and Drug Administration as part of an application for a research or marketing permit.

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

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

3.24.1 For Department of Defense (USDOD) research Serious Non-Compliance includes failure of a person, group, or institution to act in accordance with Department of Defense (USDOD) 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.

3.24.2 For Veterans Administration (VA) research Serious Non-Compliance includes a failure to adhere to the laws, regulations, or policies governing Human Research that might reasonably be regarded as:

3.24.2.1 Involving substantive harm, or a genuine risk of substantive harm, to the safety, rights, or welfare of human research subjects, research staff, or others; or

3.24.2.2 Substantively compromising the effectiveness of a Veterans Administration (VA) facility’s human research protection or human research oversight programs.

3.24.3 For Veterans Administration (VA) research the unfounded classification of a serious adverse event as “anticipated” constitutes Serious Non-Compliance.

3.25 Suspension of IRB Approval: An action of the IRB, IRB Director, Institutional Official, or designee of the Institutional 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.

3.25.1 For Veterans Administration (VA) Research Suspension of IRB Approval:

3.25.1.1 Refers to a temporary interruption in the enrollment of new subjects, activities involving previously enrolled subjects, or other research activities.

3.25.1.2 Applies to interruptions related to concerns regarding the safety, rights, or welfare of human subjects, research investigators, research staff, or others.

3.25.1.3 Do not include interruptions in research resulting solely from the expiration of a project approval period, and voluntary interruption of research enrollments, and ongoing research activities by an appropriate VA facility official, research investigator, or sponsor (including the Office of Research and Development (ORD) when ORD is the sponsor).

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

3.26.1 For Veterans Administration (VA) Research Termination of IRB Approval:

3.26.1.1 Refers to a permanent halt in the enrollment of new subjects, activities involving previously enrolled human subjects, or other research activities.

3.26.1.2 Applies to interruptions related to concerns regarding the safety, rights, or welfare of human subjects, research investigators, research staff, or others.

3.26.1.3 Do not include interruptions in research resulting solely from the expiration of a project approval period, and voluntary interruption of research enrollments, and ongoing research activities by an appropriate VA facility official, research investigator, or sponsor (including the Office of Research and Development (ORD) when ORD is the sponsor).

3.27 Unanticipated Problem Involving Risks to Subjects or Others: Any information, including any incident, experience, or outcome that meets ALL three of the following conditions: (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; (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); and (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.

3.27.1 For Veterans Administration (VA) research:

3.27.1.1 The terms "unanticipated" and "unexpected" refer to an event or problem that is new or greater than previously known in terms of nature, severity, or frequency, given the procedures described in protocol-related documents and the characteristics of the study population.

3.27.1.2 The term Unanticipated Problem Involving Risks to Subjects or Others includes any event or problem that is serious, unexpected, and related to the research, where "related" means the event or problem might reasonably be regarded as caused by, or probably caused by, the research.

3.27.1.3 Serious Unanticipated Problems Involving Risks to Subjects or Others includes:

3.27.1.3.1 Interruptions of subject enrollments or other research activities due to concerns about the safety, rights, or welfare of human research subjects, research staff, or others.

3.27.1.3.2 Any work-related injury to personnel involved in human research, or any research-related injury to any other person, that requires more than minor medical intervention (i.e., basic first aid), requires extended surveillance of the affected individual, or leads to serious complications or death.

3.27.1.3.3 Any VA National Pharmacy Benefits Management (PBM) Bulletins or Communications (sometimes referred to as PBM Safety Alerts) relevant to one or more of the VA facility's research projects.

3.27.1.3.4 Any data monitoring committee, data and safety monitoring board, or data and safety monitoring committee report describing a safety problem.

3.27.1.3.5 Any sponsor analysis describing a safety problem for which action at the VA facility level might be warranted.

3.27.1.3.6 Any unanticipated problem involving substantive harm, or a genuine risk of substantive harm, to the safety, rights, or welfare of human research subjects, research staff, or others;

3.27.1.3.7 Any problem reflecting a deficiency that substantively compromises the effectiveness of a VA facility's human research protection or human research oversight programs.

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 None

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 45 CFR §160.103.