



## Policy: Definitions

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### 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 PREVIOUS VERSION

- 2.1 Revised from previous version dated 08/01/2023

### 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 Participants<sup>1</sup>) or Federalwide Assurance (FWA): 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 participants.
- 3.4 Certification: The official notification by the institution to the supporting Federal department or agency component that a research project or activity involving human participants has been reviewed and approved by an IRB in accordance with an approved assurance.
- 3.5 Clinical Trial: A research study in which one or more human participants 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.
- 3.6 Collaborative Study: Human Research involving more than one institution and/or site participating in the same research protocol, where each site completes a portion or portions of the study.
- 3.7 Conflicting Interest: Refer to the following University Policies:
  - 3.7.1 Policy on Conflict of Interest and Conflict of Commitment
  - 3.7.2 Policy on Conflict of Interest in Research
- 3.8 Continuing Non-Compliance: A pattern of non-compliance through failure to adhere to the regulations or institutional requirements that protect the rights and welfare of participants and others and suggests a likelihood that non-compliance will continue without intervention, or involves frequent instances of minor non-compliance.

Continuing non-compliance may also include failure to respond to a request from the IRB to resolve an episode of non-compliance or a pattern of minor non-compliance.
- 3.9 Cooperative Research: Human Research covered by a signatory agency of the revised Common Rule involving more than one institution and/or site. When conducting cooperative research, each institution and/or site is responsible for safeguarding the rights and welfare of human participants and for complying with this provision. Any institution and/or site located in the United States that is engaged in cooperative research must rely upon approval by a Single IRB for that portion of the research that is conducted in the United States.
- 3.10 Cooperative Research Requirement: Cooperative Research studies sponsored by signatories of the revised Common Rule involving multiple research sites conducting human research with IRB approval dates on or after January 20, 2020, must use a Single IRB. This requirement expands upon the NIH Single IRB Policy.

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<sup>1</sup> The terms "Subject" and "Participant" are synonymous. Northwestern uses "Participant" over "Subject."



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- 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 Expiration Date (Lapsed Date): The first date that the study is no longer IRB approved. The date after the end date of the approval period.
- 3.14 External IRB: An IRB from an external institution or organization that the Northwestern University IRB may rely on for the ethical review of Human Research.
- 3.15 Finding of Non-Compliance: Non-Compliance in fact.
- 3.16 Human Research: Any activity that either<sup>2</sup>:
- 3.16.1 Is Research as Defined by DHHS and involves Human Participants as Defined by DHHS; or
  - 3.16.2 Is Research as Defined by USFDA and involves Human Participants as Defined by USFDA.
- 3.17 Human Participant 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:
- 3.17.1 Intervention: Physical procedures by which information or biospecimens are gathered (for example, venipuncture) and manipulations of the participant or the participant's environment that are performed for research purposes.
  - 3.17.2 Interaction: Communication or interpersonal contact between investigator and participant.
  - 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 that 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<sup>3</sup>: Private Information for which the identity of the participant is or may readily be ascertained by the investigator or associated with the information.
  - 3.17.5 Identifiable Biospecimen<sup>4</sup>: A biospecimen for which the identity of the participant is or may readily be ascertained by the investigator or associated with the biospecimen.
- 3.18 Human Participant as Defined by USFDA: An individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A participant may be either a healthy human or a patient. A human participant includes an individual on whose specimen an investigational medical device is used. When medical device research involves in vitro diagnostics and unidentified tissue specimens, the FDA defines the unidentified tissue specimens as human participants.
- 3.19 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

<sup>2</sup> The terms "Human Participant Research," "Research Involving Human Participants," "Human Participant Research," "Research Involving Human Participants," "Clinical Research," "Clinical Investigation," "Clinical Study" and similar phrases are considered to be synonyms for the term Human Research.

<sup>3,4</sup> 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)).



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- 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.
- 3.20 Immediate Family: The immediate family of a Faculty member or Staff member includes a spouse, domestic partner, parents, children, siblings, aunts, uncles, nephews, nieces, grandparents, and grandchildren.
- 3.21 Institutional Official/Organizational Official (IO/OO): The Institutional Official/Organizational Official (IO/OO) has the authority to take the following actions or delegate these authorities to a designee:
- 3.21.1 Ensure that the HRPP has sufficient resources, including IRBs appropriate for the volume and types of Human Research to be reviewed, so that reviews are accomplished in a thorough and timely manner.
- 3.21.2 Determine what IRBs the institution will rely on.
- 3.21.3 Ensure that the research review process is independent and free of undue influence.
- 3.21.4 Create policies and procedures related to the HRPP that are binding on the Institution.
- 3.22 Institutional Profile: A record of information an institution keeps about another collaborating institution/organization.
- 3.23 Institutional Review Board (IRB): The IRB is established in accordance with and for the purposes expressed in (45 CFR 46).
- 3.24 IRB of Record: The IRB that is responsible for the ethical review of Human Research on behalf of an institution, site, or individual investigator.
- 3.24.1 Also known as the Reviewing IRB, this can be the IRB designated through a reliance agreement to review research for an external institution, external site, or external investigator.
- 3.25 Lead Site: The primary institution or site that develops a research protocol.
- 3.25.1 In the case of federally funded research, this role is identified as the primary awardee of federal funds responsible for selecting the sIRB for Cooperative Research.
- 3.26 Legally Authorized Representative (LAR): An individual or judicial or other body authorized under applicable law to consent on behalf of a prospective participant to the participant’s participation in the procedures(s) involved in the research.
- 3.26.1 If there is no applicable law addressing this issue, then this individual is recognized by institutional policy as acceptable for providing consent in the nonresearch context on behalf of the prospective participant to the participant’s participation in the procedure(s) involved in the research.
- 3.26.2 See “SOP: Legally Authorized Representatives, Children, and Guardians (HRP-013)” for who may serve as a Legally Authorized Representative at this institution.
- 3.27 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.
- 3.27.1 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.
- 3.27.2 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:
- 3.26.2.1 Encountered by Service members, law enforcement, or first responders while on duty.
- 3.26.2.2 Resulting from or associated with high-risk behaviors or pursuits.
- 3.26.2.3 Experienced by individuals whose medical conditions involve frequent tests or constant pain.
- 3.28 Multi-Site Study: Human Research involving more than one institution or site participating in the same research protocol where each site completes the entire study.
- 3.28.1 In the case of federally funded research, a multi-site study involves more than one institution or site conducting non-exempt Human Research, with each site completing all research activities outlined in the protocol. It may be subject to the NIH Single IRB Policy and/or Cooperative Research Requirement.



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- 3.29 NIH Policy on the Use of a Single IRB for Multi-Site Research: This policy establishes the expectation that a single IRB (sIRB) of record will be used in the ethical review of non-exempt human participants research protocols funded by the NIH that are carried out at more than one site in the United States. This policy applies to all competing grant applications for multi-site studies with NIH receipt dates on or after January 25, 2018.
- 3.30 Non-Committee Review: Any of the following:
- 3.30.1 Determination of whether an activity is Human Research.
  - 3.30.2 Determination of whether Human Research is exempt from regulation.
  - 3.30.3 Reviews of non-exempt research using the expedited procedure.
  - 3.30.4 Determinations of which participants can continue in expired research.
  - 3.30.5 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 the request for authorization to use alternative IRB review procedures.
- 3.31 Non-Compliance: Failure to follow the federal regulations governing human research, requirements and/or determinations of the IRB.
- 3.31.1 In the case of research funded or conducted by the US Department of Defense (USDOD), Non-Compliance includes failure of a person, group, or institution to act in accordance with Department of Defense (USDOD) instruction 3216.02, its references, or applicable requirements.
- 3.32 Participating Site: An institution or site engaged in a Multi-Site or Collaborative Study, where a local investigator is responsible for the conduct of Human Research at their institution or site.
- 3.33 Possibly Related to the Research: There is a reasonable possibility that the adverse event, incident, experience, or outcome may have been caused by the procedures involved in the research (modified from the definition of *associated with the use of the drug* in FDA regulations at 21 CFR 312.32(a)).
- 3.34 Prisoner: Any individual involuntarily confined or detained. The term is intended to encompass individuals sentenced under a criminal or civil statute, individuals detained in other facilities by virtue of statutes or commitment procedures that provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing.
- 3.34.1 For Department of Defense (USDOD) research, the term includes military personnel in either civilian or military custody.
- 3.35 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.
- 3.35.1 Individually Identifiable Health Information: Information that is a subset of health information, including demographic information collected from an individual, and
    - 3.35.1.1 Is created or received by a health care provider, health plan, employer, or health care clearinghouse and; 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
      - 3.35.1.1.1 That identifies the individual; or
      - 3.35.1.1.2 With respect to where there is a reasonable basis to believe the information can be used to identify the individual.



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- 3.36 Related to the Research: A financial interest is Related to the Research when the interest is in:
- 3.36.1 A sponsor of the research;
  - 3.36.2 A competitor of the sponsor of the research;
  - 3.36.3 A product or service being tested; or
  - 3.36.4 A competitor of the product or service being tested.
- 3.37 Reliance Agreement: Also called an Authorization Agreement, it is the agreement that documents respective authorities, roles, responsibilities, and communication between one institution/organization providing the ethical review of human research and another institution or an investigator that is relying on that ethical review.
- 3.38 Relying IRB: An IRB designated through a reliance agreement to cede review to an External IRB for a particular study.
- 3.39 Reportable New Information: Information that becomes known during the course of a research study that will need to be reported to the IRB in a timely, meaningful way so that research participants can be protected from avoidable harm. This information may be Unanticipated Problems Involving Risk to Subjects or Others (UPIRSOs) and/or Non-compliance.
- 3.40 Research as Defined by DHHS: A Systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge.
- 3.40.1 The following activities are not considered Research as Defined by DHHS:
    - 3.40.1.1 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.
    - 3.40.1.2 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.
      - 3.40.1.2.1 Including the collection and testing of information or biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health authority.
      - 3.40.1.2.2 Including trends, signals, risk factors, patterns in diseases, or increases in injuries from using consumer products.
      - 3.40.1.2.3 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).
    - 3.40.1.3 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.
    - 3.40.1.4 Authorized operational activities (as determined by the relevant federal agency) in support of intelligence, homeland security, defense, or other national security missions.
    - 3.40.1.5 Secondary research involving non-identifiable newborn screening blood spots.
- 3.41 Research as Defined by USFDA: Any experiment that involves a test article and one or more Human Participants, and that meets any one of the following:
- 3.41.1 Must meet the requirements for prior submission to the US Food and Drug Administration under section 505(j) 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;
  - 3.41.2 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
  - 3.41.3 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.
- 3.42 Restricted: Applies to investigators who are delinquent in meeting IRB requirements.



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- 3.43  Serious Adverse Event (SAE): An adverse event that results in ANY of the following:
- 3.43.1 death,
  - 3.43.2 a life-threatening experience (the term “life-threatening” in the definition of “serious” refers to an event in which the patient was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe [Explanatory text from ICH E2A]),
  - 3.43.3 inpatient hospitalization or prolongation of existing hospitalization,
  - 3.43.4 a persistent or significant disability/incapacity,
  - 3.43.5 a congenital anomaly/birth defect, or
  - 3.43.6 any other adverse event that, based upon appropriate medical judgment, may jeopardize the participant’s health and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition (examples of such medical events include allergic bronchospasm requiring intensive treatment in an emergency room or at home, blood dyscrasias, or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse).
- 3.44  Serious Non-Compliance:  Non-compliance with the federal regulations governing human research or with the requirements or determinations of the IRB that causes harm, increases the risk of harm, adversely affects the rights or welfare of participants or undermines the scientific integrity of the data.
- 3.44.1 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 participant; place a human participant at increased risk of harm; cause harm to a human participant; affect a human participant’s willingness to participate in research; or damage or compromise the scientific integrity of research data.
- 3.45  Single IRB (sIRB): A sIRB is the selected  IRB of Record that conducts the ethical review for each site participating in a  Multi-Site or  Collaborative Study.
- 3.46  Suspension of IRB Approval: An action of the IRB, IRB Executive Director,  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.
- 3.47  Systematic: Having or involving a method or plan.
- 3.48  Termination of IRB Approval: An action of the IRB, IRB Executive Director,  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.
- 3.49  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 participant 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 participants 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.
- 3.49.1 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:
    - 3.49.1.1 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 participant population being studied.



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3.49.1.2 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).

3.49.1.3 Suggests that the research places human participants 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.

3.50 Vice President for Research: The Vice President for Research has the authority to take the following actions:

3.50.1 Place limitations or conditions on an investigator's or research staff's privilege to conduct Human Research.

3.50.2 Ensure that officials of the Institution cannot approve research that has not been approved by one of the IRBs designated by the Institution.

3.50.3 Impose corrective actions up to and including barring individuals from conducting Human Research at the Institution if the Institutional Official concludes such actions are required to maintain compliance.

3.50.4 Disallow research approved by the Institution's IRB or an external IRB

## 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 GENERAL DOCUMENTS: Human Research Protection Program Plan (HRP-101)

6.2 GENERAL DOCUMENTS: Investigator Manual and Appendices (HRP-103)

6.3 WORKSHEET: Human Research Determination (HRP-310).

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

## 7 REFERENCES

7.1 21 CFR §50.3, 21 CFR §56.102, 21 CFR §312.3, 21 CFR §312.32, 21 CFR §812.2(a), 21 CFR §812.3(p)

7.2 NOT-OD-16-094: Final NIH Policy on the Use of a Single Institutional Review Board for Multi- Site Research

7.3 45 CFR §46.102

7.4 45 CFR §160.103

7.5 DoD Instruction 3216.02, Glossary, Part II. Definitions

7.6 International Conference on Harmonization (ICH) E2A: Guideline for Industry on Clinical Safety Data Management