AdventHealth

POLICY

Policy #	Policy Name
CW AHC 107	Definitions in Human Research
Policy Location	**Responsible Department**
*Company-Wide Policies	Research Services
Executive Owner	**Original Creation Date**
Executive Director of Research Services	01/18/2022
Policy Effective Date	**Policy Review Date**
04/04/2022	04/04/2022

I. **SCOPE:** This policy applies to all employees and agents of AdventHealth conducting human subjects research.

II. **PURPOSE:** This policy establishes definitions for the corporate-wide Human Research Protection Program (HRPP).

III. **POLICY:** Not Applicable

IV. **PROCEDURE/GUIDELINES:** Not Applicable

V. **DEFINITION(S):**

2018 Requirements or Revised Rule: The Federal Policy for the Protection of Human Subjects requirements contained in 45 CFR §46 Subparts A as revised January 18, 2017, as well as Subpart B, C, and D, exclusive of requirements for reporting to, certification by, or review by a federal department of agency head.

AdventHealth: Adventist Health System Sunbelt Healthcare Corporation and its wholly owned subsidiaries and affiliates.

Allegation of Noncompliance: An unproven assertion of Noncompliance.

Children: Persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted.

Classified Research: Research involving any information or material, regardless of its physical form or characteristics, that is owned by the United States Government, and determined pursuant to Executive Order 12356, April 2, 1982, or prior orders to require protection against unauthorized disclosure, and is so designated.

Clinical Investigation: A synonym for Research as Defined by FDA.

Committee Review: All review processes that require a convened IRB.

Compassionate Use: The use of an unapproved device on an individual who has a life-threatening or serious disease or condition and, no generally acceptable alternative treatment for the condition exists.

Conflicting Interest: An IRB member or consultant has a conflicting interest if any of the following are true for the member/consultant or an individual in the member's Immediate Family:

- Involvement in the design, conduct, or reporting of the research.
- Equity interest Related to the Research, exclusive of interests through mutual funds.
- Compensation Related to the Research in the preceding 12 months.
- Proprietary interest Related to the Research, including copyrights, or patents, trademarks.
- Any other reason for which the IRB member believes that he or she cannot be objective.

Continuing Noncompliance: A pattern of Noncompliance that is likely to continue without intervention or failure to work with the IRB to resolve Noncompliance.

Designated Reviewer(s): An Experienced IRB Member designated by the IRB Executive Chair to conduct Non-Committee Review.

Emergency Use: The use of an unapproved drug, biologic, or device on an individual 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.

End Approval Date: The last date that a study is IRB approved and the last date that a study can be conducted without undergoing continuing review.

Experienced IRB Member: An IRB member who based on professional competence in the opinion of the IRB Executive Chair has gained over a period of time sufficient knowledge and skill in conducting IRB reviews to serve as Designated Reviewer.

Experimental Subject as Defined by DOD: An activity, for research purposes, where 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.

Fetus: The product of conception from implantation until delivery.

Guardian: An individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care.

HRPP Personnel: Individuals involved in the oversight of human subjects research.

Human Research: Any activity that is Human Research as Defined by HHS or Human Research as Defined by FDA.

Human Research as Defined by FDA: Any activity that is Research as Defined by FDA and involves Human Subjects as Defined by FDA.

Human Research as Defined by HHS: Any activity that is Research as Defined by HHS and involves Human Subjects as Defined by HHS.

Human Research Protection Program (HRPP): A comprehensive system to ensure the protection of human subjects taking part in research.

Human Subject as Defined by FDA: An individual who is or becomes a participant in Research as Defined by FDA, either as a recipient of the test article or as a control, or an individual on whose specimen an investigational device is used.

Human Subject as Defined by HHS:

- For Research as Defined by HHS subject to Pre-2018 Requirements: A living individual about whom an investigator conducting Research as Defined by HHS obtains (1) data through Intervention or Interaction with the individual, or (2) information that is both Identifiable Information and Private Information.
- For Research as Defined by HHS subject to 2018 Requirements or Hybrid Requirements: A living individual about whom an investigator conducting Research as Defined by HHS:
    - Obtains information or biospecimens through Intervention or Interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or
    - Obtains, uses, studies, analyzes, or generates Identifiable Private Information or Identifiable Biospecimens.

Humanitarian Device Exemption (HDE): Defined at 21 CFR 814.3(m) and is a marketing application that is similar to a premarket approval (PMA) application in that the applicant must demonstrate a reasonable assurance of safety, but in a HDE application, the applicant seeks an exemption from the PMA requirement of demonstrating a reasonable assurance of effectiveness. A device that has received HUD designation is eligible for HDE approval if, among other criteria, the device will not expose patients to an unreasonable or significant risk of injury or illness from its use, taking into account the probable risks and benefits of currently available devices and alternative forms of treatment.

Humanitarian Use Device (HUD): A medical device intended to benefit patients in the treatment or diagnosis of a disease or condition that affects or is manifested in not more than 8,000 individuals in the United States per year (FDA 21 CFR 814.3(n)).

Hybrid Requirements: 2018 Requirements exclusive of 45 CFR §46.103(e), §46.109(e), §46.116(a)(5), §46.116(b)(9), §46.116(d)(7)-(9), §46.116(e)(1)-(2), §46.116(f)(1)-(2), §46.116(f)(3)(ii).[1]

ICH-GCP Definition of Clinical Trial: Any investigation in human subjects intended to discover or verify the clinical, pharmacological, and/or other pharmacodynamic effects of an investigational product(s), and/or to identify any adverse reactions to an investigational product(s), and/or to study absorption, distribution, metabolism, and excretion of an investigational product(s) with the object of ascertaining its safety and/or efficacy. The terms clinical trial and clinical study are synonymous.

Identifiable Biospecimen: A biospecimen for which the identity of the Human Subject as Defined by HHS is or may readily be ascertained by the investigator or associated with the biospecimen.

Identifiable Information:

- For Research as Defined by HHS subject to Pre-2018 Requirements: Information for which the identity of the subject is or may readily be ascertained by the investigator or readily be associated with the information.
- For Research as Defined by HHS subject to 2018 Requirements or Hybrid Requirements: Information or a biospecimen for which the identity of the subject is or may readily be ascertained by the investigator or readily be associated with the information

Identifiable Private Information: Private Information for which the identity of the Human Subject as Defined by HHS is or may readily be ascertained by the investigator or associated with the information.

Immediate Family: Spouse and dependent children.

Impartial Witness: A person, who is independent of the trial, who cannot be unfairly influenced by people involved with the trial, who attends the entire consent process and reads the consent document and any other written information supplied to the subject as part of the consent process. This specifically excludes Research Personnel on the study.

Institutional Clearance: Action required and provided by the Office of Sponsored Programs (OSP) in order to initiate a research project.

Institutional Review Board (IRB): The committee that prospectively reviews and makes decisions concerning Human Research, Emergency Use, and HUDs.

Interaction(s): Communication or interpersonal contact between Investigator and subject.

Intervention(s): Physical procedures by which information or biospecimens are gathered and manipulations of the environment, of a Human Subject as Defined by HHS or Human Subject as Defined by FDA, that are performed for research purposes.

Investigator(s): Any individual, regardless of title or position, who is responsible for the design, conduct, or reporting of research, which may include, collaborators or consultants.

IRB Authorization Agreement (IAA): A written agreement between two or more institutions used to document the delegation of IRB review responsibilities (i.e., the institution serving as the IRB of record and the institution relying on that IRB). It describes the reliance of an institution or an IRB for the oversight of research and the responsibilities that each entity will undertake to ensure compliance with regulatory requirements, which can be embodied in a written agreement between the institution, and institution-wide policy directive, or a research protocol. This agreement may also be referred to as a reliance agreement or cede review agreement.

Legally Authorized Representative (LAR): An individual, judicial, or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research.

- At AdventHealth, this is the Legally Authorized Person (LAP)
- For Research as Defined by HHS NOT subject to FDA regulations and subject to 2018 Requirements or Hybrid Rule: Where there is no applicable law addressing this issue, legally authorized representative means an individual recognized by institutional policy as acceptable for providing consent in the non-research context on behalf of the prospective Human Subject as Defined by HHS to the Human Subject's participation in the procedure(s) involved in the research.

Meeting Chair: The IRB member running a convened IRB meeting. The Meeting Chair may be an IRB Executive Chair, an IRB vice-chair, or an IRB member temporarily designated by the IRB Executive Chair.

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.

- The IRB interprets the phrase "Ordinarily encountered in daily life or during the performance of routine physical or physiological examination or tests" to refer to normal healthy individuals in general and exclude the risks that certain subcategories of individuals face in their everyday life. For example, the IRB does not evaluate the risks imposed in research focused on a special population 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).
- For Human Research as Defined by HHS that involves Prisoners as Human Subjects Defined by HHS: 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.

Neonate of Uncertain Viability: A neonate after delivery that, although living, is uncertain to survive (given the benefit of available medical therapy) to the point of independently maintaining heartbeat and respiration.

Non-Committee Review: All review processes that do not require a convened IRB including non-human research determinations, non-engagement determinations, exemption determinations, and expedited review.

Non-significant Risk Device: An investigational device that is not a Significant Risk Device.

Noncompliance: Failure to follow the regulations or the requirements or determinations of the IRB.

Nonviable Neonate: A neonate after delivery that, although living, is unable to survive (given the benefit of available medical therapy) to the point of independently maintaining heartbeat and respiration.

Pre-2018 Requirements or Original Rule: The Federal Policy for the Protection of Human Subjects requirements contained in 45 CFR 46 §46 Subparts A as published in the 2016 edition of the Code of Federal Regulations, as well as Subpart B, C, and D, exclusive of requirements for reporting to, certification by, or review by a federal department of agency head.

Pregnant Woman: A woman during the period of time from implantation until delivery.

Principal Investigator (PI): The primary Investigator responsible and accountable for the preparation, conduct, and management of a clinical trial, research grant, cooperative agreement, training or public service project, contract, other sponsored projects (internal or external funding), treatment INDs, or Emergency Uses, in compliance with applicable laws and regulations and AdventHealth policy governing the conduct of research.

Prisoner(s): 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 that provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing.

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.

Regulatory Review: Review of administrative and regulatory issues unrelated to the regulatory criteria for approval that under the regulations must be determined by a convened IRB or reviewer using the expedited procedure.

Regulatory Reviewer: Individual who conducts Regulatory Review.

Related to the Research: A financial interest is Related to the Research when the financial interest is in the sponsor or in an entity that could be affected by the research outcomes, or is in the product or service being evaluated.

Research as Defined by FDA: Any experiment that involves a test article and one or more Human Subjects as Defined by FDA, 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, where:

- Act: The Federal Food, Drug, and Cosmetic Act, as amended (§§201-902, 52 Stat 1040 et. seq., as amended (21 USC 321-392).
- Test article: Any drug for human use, biological product for human use, medical device for human use, human food additive, color additive, electronic product, or any other article subject to regulation under the act or under sections 351 or 354-360F of the Public Health Service Act.

Research as Defined by HHS: A systematic investigation designed to develop or contribute to generalizable knowledge. [2]

Research Personnel: Investigators and other individuals involved in the design, conduct, or reporting of research.

Research Services Personnel: Individuals involved in the oversight and management of research.

Restricted: A status for Investigators indicating that new submissions will not be accepted for review.

Serious Injury: An injury or illness that (1) is life-threatening, (2) results in permanent impairment of a bodily function or permanent damage to a body structure, or (3) necessitates medical or surgical intervention to preclude permanent impairment of a bodily function or permanent damage to a body structure.

Serious Noncompliance: Noncompliance that may adversely affect the rights and welfare of subjects. For Human Research conducted or funded by DOD, Serious Noncompliance is failure of a person, group, or institution to act in accordance with this Instruction 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.

Significant Risk Device: An investigational device that:

- Is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject;
- Is purported or represented to be for a use in supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a subject;
- Is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety, or welfare of a subject; or
- Otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.

Single Patient Expanded Access: Treatment with an investigational drug under an IND where the FDA granted an IND pursuant to 21 CFR §312.310.

Suspension of IRB Approval: Temporary or permanent withdrawal of IRB approval for some or all research procedures short of Termination of IRB Approval.

Termination of IRB Approval: Withdrawal of IRB approval for all research procedures where the IRB does not anticipate re-opening the study.

Unanticipated Adverse Device Effect: Unanticipated adverse device effect is any serious adverse effect on health or safety, any life-threatening problem or death caused by, or

associated with a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the application; or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

Unanticipated Problems Involving Risks to Subjects or Others: Information that:

- Is unexpected (inconsistent with information previously reviewed by the IRB); and
- Indicates that subjects or others are at increased risk of harm because of the research study.

Wards: Children who are cared for and the responsibility of the state or any other agency, institution, or entity.

VI. EXCEPTION(S):

For abbreviations not defined in this policy, refer to CW AHC 102 Abbreviations in Research

For capitalized designations not defined in this policy, refer to CW AHC 103 Designations in Research.

If there is a conflicting definition in an individual HRPP policy, the definition listed in the specific policy takes precedence.

See CW AHC 101 Research Oversight

VII. REFERENCE(S):

[1] 45 CFR §46.103(e), §46.109(e), §46.116(b)(9) and §46.116(d)(7)-(9) are requirements of the Federal Policy for the Protection of Human Subjects as revised January 18, 2017 that are not requirements of the Federal Policy for the Protection of Human Subjects requirements published in the 2016 edition of the Code of Federal Regulations. 45 CFR §46.103(e) is the requirements for reliance agreements. §46.109(e) is the criteria when continuing review is not required. §46.116(a)(5) is the criteria for the concise summary. §46.116(b)(9) is required consent disclosures. §46.116(d)(7)-(9) is required additional disclosures. §46.116(e)(1)-(2), §46.116(f)(1)-(2), §46.116(f)(3)(ii) are the limitations on wavier and alteration of consent.

[2] The following activities are deemed not to be Research as Defined by HHS: (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. (2) Public health surveillance activities, including the collection and testing of information or biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health authority. Such activities are 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 (including trends, signals, risk factors, patterns in diseases, or increases in injuries from using consumer products). Such activities include 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) 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. (4) Authorized operational activities

(as determined by each agency) in support of intelligence, homeland security, defense, or other national security missions. Public health authority means an agency or authority of the United States, a state, a territory, a political subdivision of a state or territory, an Indian tribe, or a foreign government, or a person or entity acting under a grant of authority from or contract with such public agency, including the employees or agents of such public agency or its contractors or persons or entities to whom it has granted authority, that is responsible for public health matters as part of its official mandate.

Electronic Code of Federal Regulation (*e-CFR™*). (June 17, 2015). 45 CFR §46.102: Protection of Human Subjects. Retrieved from: Click here.

Electronic Code of Federal Regulation (*e-CFR™*). (June 17, 2015). 45 CFR §46.202: Protection of Human Subjects. Retrieved from: Click here.

Electronic Code of Federal Regulation (*e-CFR™*). (June 17, 2015). 45 CFR §46.303: Protection of Human Subjects. Retrieved from: Click here.

Electronic Code of Federal Regulation (*e-CFR™*). (June 17, 2015). 45 CFR §46.402: Protection of Human Subjects. Retrieved from: Click here.

Electronic Code of Federal Regulation (*e-CFR™*). (June 17, 2015). 21 CFR §50: Protection of Human Subjects. Retrieved from: Click here.

Electronic Code of Federal Regulation (*e-CFR™*). (June 17, 2015). 21 CFR §56.102: Institutional Review Boards. Retrieved from: Click here.

Electronic Code of Federal Regulation (*e-CFR™*). (June 17, 2015). 21 CFR §312.3: Investigational New Drug Application. Retrieved from: Click here.

Electronic Code of Federal Regulation (*e-CFR™*). (June 17, 2015). 21 CFR §812.3: Investigational Device Exemptions. Retrieved from: Click here.

VIII. RELATED DOCUMENT(S) / ATTACHMENT(S):

- CW AHC 101 Research Oversight
- CW AHC 103 Designations in Research
- CW AHC 108 Human Research Protection Program
- CW AHC 111 Prompt Reporting Requirements in Research
- CW AHC 112 Investigator Obligations in Research
- CW AHC 110 Legally Authorized Representatives, Children and Guardians in Research
- CW AHC 109 IRB Member Review Expectations