Appendix: DEFINITIONS

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45 CFR 46: Title 45, Part 46 of the Code of Federal Regulations**,** Protection of Human Subjects. These regulations govern human subjects research conducted by all federal agencies. This body of regulations governs the conduct of human subject research. https://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/index.html

510(K) Device: A medical device that is considered substantially equivalent to a device that was or is being legally marketed. https://www.fda.gov/medical-devices/device-approvals-denials-and-clearances/510k-clearances

A

Adjuvant Therapy: Therapy provided to enhance the effect of a primary therapy.

Adverse Effect: An undesirable and unintended, although not necessarily unexpected, result of therapy or other intervention.

Adverse Event (AE): Any experience or abnormal finding that has taken place during the course of a research project and was harmful to the subject participating in the research, or increased risks of harm from the research, or had an unfavorable impact on the risk/benefit ratio; any untoward or unfavorable medical occurrence in a clinical research study participant, including any abnormal sign, symptom, or disease, temporarily associated with the participant's involvement in the research, whether or not considered related to participation in the research.

Assent: An agreement by an individual not competent to give legally-valid informed consent (e.g., a child aged 7+ or a cognitively impaired person) to participate in research.

Assent of a Child: Assent means a child's affirmative agreement (verbal or written) to participate in a clinical investigation. Failure to object (absent affirmative agreements) may not be construed as assent.

B

Baseline: The initial time point in a clinical trial that provides a basis for assessing changes in subsequent assessments or observations. At this reference point, measurable values such as physical exam, laboratory tests, and outcome assessments are recorded.

***Belmont Report*:** A statement of basic ethical principles governing research involving human subjects issued by the National Commission for the protection of Human Subjects in 1978. https://www.hhs.gov/ohrp/regulations-and-policy/belmont-report/index.html

Beneficence: The ethical principle of beneficence can be expressed in two general rules: (1) do not harm; (2) protect from harm by maximizing possible benefits and minimizing possible risks of harm.

Bias: A point of view or preference which prevents impartial judgement in the way in which a measurement, assessment, procedure, or analysis is carried out or reported.

Biologic: Any therapeutic serum, toxin, antitoxin, or analogous microbial product application to the prevention, treatment, or cure of diseases or injuries.

C

Case-Control Study: A study comparing persons with a given condition or disease (the treatment) and persons without the condition or disease (the control) with respect to the antecedent factors.

Case Report Form (CRF): A printed, optical or electronic (eCFR) document designed to capture all protocol required for a study.

Case Report or Case Study: A case report is one in which three or fewer records are accessed. Case reports do not meet the definition for human subjects research and do not require submission to the IRB if the project meets the following criteria:

- Nothing was done to the patient(s) with prior research intent.
- The case report does not contain elements of a systematic investigation (e.g., statistical methods).
- The case report describes an interesting treatment, presentation, or outcome.
- The published article will not contain any identifiable information or authorization has been obtained.

CAT Scan (CT Scan): Abbreviation for Computerized Axial Tomography, and X-ray technique for producing image of internal bodily structure through the assistance of a computer.

Centers for Disease Control and Prevention (CDC): The CDC is an agency with the Public Health Service, DHHS. https://www.cdc.gov/

Cell Lines: A cell-line refers to a collection of a participant's white blood cells that are kept alive, usually stored for repeated studies of these cells in future years.

Central Institutional Review Board (CIRB): The CIRB initiative is designed to help reduce the administrative burden of local IRBs and investigators while continuing a high level of protection for research participants.

Certificate of Confidentiality: A document that provides additional protection of data from legal subpoena. The certification provides protection against compelled disclosure of identifying information or other identifying characteristics of a research participant enrolled in biomedical, and other forms of sensitive research.

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

Class I, II, III Devices: Classification by the Food and Drug Administration of medical devices according to potential risks or hazards.

Clinical Investigation: As defined by the FDA, any experiment that involves a test article and one or more human subjects and is subject to requirements for submission to the FDA. Clinical investigations must not be initiated unless that investigation has been reviewed and approved by an IRB. https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm?fr=50.3

Clinical Research: The NIH defines clinical research as:

- Patient-oriented research. Research conducted with human subjects (or on material of human origin such as tissues, specimens, and cognitive phenomena) for which an investigator directly interacts with human subjects. Excluded from this definition are in vitro studies that utilize human tissues that cannot be linked to a living individual. Patient-oriented research includes: (a) mechanisms of human disease, (b) therapeutic interventions, (c) clinical trials, or (d) development of new technologies.
- Epidemiologic and behavioral studies.
- Outcomes research and health.
- https://www.nih.gov/health-information/nih-clinical-research-trials-you/what-is-clinical-research

Clinical Research or Study Coordinator (CRC): An individual that manages the administrative and day-to-day responsibilities of a clinical trial and acts as a liaison for clinical site. An individual in this role may manage both administrative and study procedures.

Clinical Trial: The definition of a clinical trial according to the revised Common rule and NIH is 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 outcomes.

The FDA definition of a clinical investigation does not encompass some studies, such as behavioral interventions or surgical procedures. The FDA regulates safety/efficacy for only some kinds of therapeutics and diagnostics that are related to pharmaceuticals, devices, and biologics. Therefore, there are some studies that will not meet the definition of a clinical investigation according to the FDA but are still considered a clinical trial according to the revised Common Rule and the NIH.

> ***Phase 1 Trial:*** Includes the initial introduction of an investigational new drug into humans. These studies are typically conducted with healthy volunteers, typically a very small numbers of individuals (e.g., 20-80 people). Phase 1 trials are designed to determine the metabolic and pharmacological actions of the drug in humans, the side effects associated with increasing dose range (to establish a safe dose range), and, if the possible, to gain early evidence of effectiveness. The goal of Phase 1 trials is to obtain sufficient information about the drug's pharmacokinetics and pharmacological effects to permit the design of well controlled, valid Phase 2 studies.
>
> ***Phase 2 Trial****:* Includes controlled clinical studies conducted to evaluate the drug's effectiveness for a particular indication in patients with the disease or condition under

study, and to determine the common short term side effects and risks associated with the drug. These studies are well controlled, closely monitored, and conducted with a relatively small number of patients, usually involving no more than several hundred subjects.

Phase 3 Trial: Involves the administration of a new drug to a larger number of patients (e.g., several hundred to several thousand) in different clinical settings to determine its safety, efficacy, and appropriate dosage. In Phase 3 studies, the drug is used the way it would be administered when marketed. When these studies are completed and the sponsor has evidence that the drug is safe and effective under specific conditions, the sponsor will apply to the FDA for approval to market the drug.

Phase 4 Trial*:* Studies conducted after a drug has been approved by the FDA, to delineate additional information about the drug's risks, benefits, and optimal use. These studies could include, but would not be limited to, studying different doses or schedules of administration that were used in Phase 2 studies, use of the drug in other patient populations or other stages of the disease, or use of the drug over a longer period of time. These studies are designed to monitor effectiveness of the approved intervention in the general population and to collect information about any adverse effects associated with widespread use.

Code of Federal Regulations (CFR): The CFR is a codification of the general and permanent rules published in the Federal Register by the executive departments and agencies of the Federal Government. The CFR is divided into 50 Titles representing board areas subject to Federal Regulations. Each Title is divided into parts and each part is then divided into sections - the basic unit of the CFR. The purpose of the CFR is to present the official and complete text of agency regulations in one organized publication and to provide a comprehensive and convenient reference.

Cognitively Impaired: The inability to make sound decisions in their best interest by having either a psychiatric disorder (e.g., psychosis, neurosis, personality or behavior disorders, or dementia) or a developmental disorder, that affects cognitive or emotional functions to the extent that capacity for judgement and reasoning is significantly diminished. Others, including persons under the influence of or dependent of drugs or alcohol, those suffering from degenerative diseases affecting the brain, terminally ill patients, and persons with severely disabling physical handicaps, may also be compromised in their ability to make decisions in their best interests.

Cohort: A group of subjects initially identified as having one or more characteristics in common, who are followed over time. In social science research, this term may refer to any group of persons who are born at about the same time and share common historical or cultural experiences.

Collaborative IRB Training Initiative (CITI): An internet-based set of educational modules on the protection of human participants in research. It is sponsored by a consortium of IRB professionals and researchers from universities and medical schools across the country and is administered by the University of Miami. https://about.citiprogram.org/

Common Rule: The Common Rule which governs research with human subjects conducted or supported by 15 Federal departments and agencies, establishes a comprehensive

framework for the review and conduct of proposed human subjects research. The central requirements of the Common Rule are:

- Individuals who participate in covered research are selected equitably, fully informed, and fully voluntarily consent; and
- The proposed research is reviewed by an independent oversight group, an IRB, and is approved only if risks to subjects have been minimized and are reasonable in relation to the anticipated benefits, if any, to the subjects and the importance/relevance of the knowledge that may reasonably be expected to result.

https://www.hhs.gov/ohrp/regulations-and-policy/regulations/common-rule/index.html

Compassionate Use of an Investigational Product: The FDA defines "compassionate use" as the use of a investigational product or non-FDA approved product on human subjects with a serious disease or condition for which there is no acceptable treatment available. The FDA and IRB approval for compassionate use is required. The IRB cannot approve an application for requested compassionate use until it has been approved by the FDA.

Concomitant Medication: Prescription and over-the-counter drugs and supplements a study participant has taken along with the study intervention.

Conflicts of Interest: Investigators and Research Staff

A conflict/potential conflict of interest exists if activities or relationships with other persons or organizations render an individual unable or potentially unable to remain impartial, may potentially impair that individual's objectivity, or unfairly advantages the individual by the information that may be acquired.

Information that is relevant to a conflict-of-interest determination includes:

- Stock holdings
- Investments of the individual and/or the individual's family members or significant other
- Current positions held or under negotiations
- Other sources of income
- Involvement in the design, conduct, or reporting of relevant information that may have a bearing on the individual's proposed participation in such activity.

Considerations for members of the Prisma Health employed medical staff, also includes:

- Contractual, employment or financial interest with a non-affiliated hospital or other health care organization that competes with Prisma Health or any affiliate.
- Service in a position of strategic or medical leadership in any non-affiliated hospital or health care organization, membership on another provider's medical staff, or a membership of a group practice, shall not be considered as a conflict of interest.

Significant Financial Interest:

- Remuneration including, but not limited to salary, consulting fees, honoraria, and paid authorship received from a publicly traded company during the twelve-month period preceding the date on which an investigator is making a disclosure, and/or equity interest held in such a publicly traded company, if the aggregate value of

such remuneration, plus the value of the equity interest as the date of disclosure, exceeds $5,000;
- Any equity interest in a non-publicly traded company or business regardless of value;
- Intellectual property rights and interest upon receipt of income related to such rights and interest; or,
- Any reimbursed travel or travel expenses paid on an investigator's behalf related to Prisma Health employed medical staff or team member responsibilities.

Conflict of Interest: Institution

A Significant Organizational Conflict of Interest may exist when Prisma Health employed medical staff, team members, including Prisma Health Management Team, have a Financial Interest that could cause a conflict with clinical care or research.

Organizational conflicts of interest may include Prisma Health employed medical staff or team member interest in the following:

- Licensing, technology transfer, and patents, when Prisma Health employed medical staff, team member owns the intellectual property.
- Investments of Prisma Health employed medical staff or team members, in excess of $500,000 or gifts, when the donor has an interest in the research in excess of $500,000.
- Financial Interests of Prisma Health Management in excess of $250,000.

Organizational conflicts of interest in research may include Prisma Health interest in the following:

- Licensing, technology transfer, and patents, when Prisma Health owns the intellectual property.
- Investments of Prisma Health in excess of $500,000 .
- Gifts, when the donor has an interest in the research in excess of $500,000 .
- Financial Interests of Prisma Health Management in excess of $250,000 .
- Other Financial Interests that are determined to be a conflict of interest.

Consent: See ***Informed Consent***

Control Group: A group of individuals in a clinical trial assigned to a comparison intervention.

Controlled Trial: A type of clinical trial in which observations during the trials are compared to a standard (the control).

Covered Entity: Health care providers who conduct certain financial and administrative transactions electronically such as billing and fund transfers, these criteria also include health plans and health care clearinghouses. Covered Entities must comply with HIPAA.

D

Data and Safety Monitoring Board (DSMB): A committee of scientists, physicians, statisticians, and other participants as relevant to a particular research study that collects and analyzes data during the course of a clinical trial for the purpose of monitoring trends and adverse effects that would warrant modification of the protocol and study procedures, safety monitoring of inclusion/exclusion criteria or other elements of the protocol, and/or notification of participants of new information that may impact their willingness to continue in the trial.

Data Management: The process of handing data collected during a clinical trial from development of the forms for data collection, database management and security, and transmission to any external source for analysis.

Data Management Plan: A plan that documents the processes for handling the flow of data from collection through analysis. Software and hardware systems along with quality control and validation of these systems as relevant are described.

Data Safety Monitoring Plan (DSMP): Data and Safety Monitoring is a process implemented to ensure and maintain the scientific integrity of human subjects research and to protect the safety of the human subjects. This plan defines the oversight and monitoring of data to ensure the safety of participants and the validity of the data. A DSMP describes the timing, tools, and/or method(s) for monitoring and evaluating and defines the circumstances that would result in halting and terminating the research. The plan also includes the timing of these evaluations and reporting to relevant oversight bodies.

Data Use Agreements (DUA): A DUA is a contractual document used to define the terms/processes for transfer of data outside of the organization. Often this data is a necessary component of a research project, and it may or may not be human subjects data from a clinical trial or a limited data set as defined by HIPAA regulations.

Declaration of Helsinki: A code of ethics for clinical research approved by the World Medical Association in 1964 and widely adopted by medical associations in various countries. It has been revised several times, most recently in October 2020.

https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects

Device Determination, Non-Significant Risk Device: An investigational device that does not present significant risks to the patient and does not meet the FDA Significant Risk Device indications.

Device Determination, Significant Risk Device: Under 21 CFR 812.3(m), an SR device means 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 use 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.

https://www.ecfr.gov/current/title-21/chapter-I/subchapter-H/part-812/subpart-A/section-812.3

E

Efficacy: Indication that the clinical trial intervention produces a desired therapeutic effect on the disease or condition under investigation.

Eligibility Criteria: List of criteria guiding enrollment of participants into a study. The criteria will describe both inclusionary and exclusionary factors.

Emergency Use: The FDA defines "emergency use" as the use of a test article on a human subject in a life-threatening situation in which no standard, acceptable treatment is available, and time is not sufficient to obtain IRB approval. [21CFR56.102(d)]

https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm?fr=56.102

Exempt Review: A review of proposed research activity that can be categorized as "less than minimal risk" and meets one of the exempt review criteria as defined in 45 CFR 46.104(D). https://www.govinfo.gov/app/details/CFR-2019-title45-vol1/CFR-2019-title45-vol1-sec46-104

Expanded Access: A process regulated by the FDA that allows the manufacturers to provide investigational new drugs to patients with serious conditions who do not meet criteria to participate in a clinical trial. Expanded use may be applied to a single patient or a group of patients.

Expedited Review: A review of proposed research by a designated member of the IRB rather than a convened IRB committee, is determined to be minimal risk, and meets the expedited review criteria as defined in in the [Common Rule 45 CFR 46.110] and FDA regulations. [21 CFR 56.110]

F

Federal-Wide Assurance: A standing agreement on file with the OHRP that describes in detail that commitment to protect the rights and welfare of human subjects in research.

https://www.hhs.gov/ohrp/register-irbs-and-obtain-fwas/fwas/fwa-protection-of-human-subjecct/index.html

Food and Drug Administration (FDA): An agency within the U.S. Department of Health and Human Services (DHHS) responsible for protecting the public health by assuring the safety, efficacy, and security of human and veterinary drugs, biological products, medical devices, food supply, cosmetics, and products that emit radiation. https://www.fda.gov/

G

Good Clinical Practice (GCP): A standard for the design, conduct, performance, monitoring, auditing, recording, analysis, and reporting of clinical trials. These standards provide guidance and structure to assure that the data and reported results of clinical trials are credible and accurate and that the rights, integrity, and confidentiality of clinical trial participants are protected. [See ICH definition]

Guardian: An individual who is authorized under applicable State or local law to consent on behalf of a child or a cognitively impaired adult to receive medical care and participate in research when research is part of the delivery of medical care.

H

Health Insurance Portability and Accountability Act (HIPAA):

https://www.hhs.gov/hipaa/for-professionals/security/laws-regulations/index.html

Privacy Rule: Rule that establishes national standards for the protection of certain health information. The DHHS issued the Privacy Rule to implement the requirements of the Health Insurance Portability and Accountability Act of 1996 (HIPAA). The Privacy Rule standards address the use and disclosure of individuals' health information called protected health information (PHI) by organizations subject to the Privacy Rule, as well as standard for individuals' privacy rights to understand and control how their health information is used. The Office for Civil Rights has the responsibility for implementing and enforcing the Privacy rule with respect to compliance activities and civil monetary penalties.

Security Rule: *The Security Standards for the Protection of Electronic Protected Health Information* establishes a national set of security standards for protecting certain health information that is held or transferred in electronic form. The Security Rule operationalizes the protections contained in the Privacy Rule by addressing the technical and non-technical safeguards that organizations called "covered entities" must put in place to secure individuals' electronic PHI.

HIPAA and Research: 45 CFR 164.501, 164.508, 164.512(i) (See also 45CFR164.514(e), 164.528, 164.532)

The HIPAA Privacy Rule establishes the conditions under which PHI may be used or disclosed by covered entities for research purposes. Research is defined in the Privacy Rule as, "a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge".

The Privacy Rule also defines the means by which individuals will be informed of uses and disclosures of their medical information for research purposes and their rights to access information about them held by covered entities.

Disclosure: The release, transfer, provision of access to, or divulging in any other manner of information outside the covered entity holding the information.

Protected Health Information (PHI): Information about the past, present, or future physical or mental health of an individual that identifies or could be used to

identify the individual and is created or received by a covered entity. Information about the provision of healthcare and payment for health care is included.

Waiver of HIPAA Authorization: A waiver is a request to forgo the authorization requirement based on the fact that the disclosure of PHI involves minimal risk to the participant and the research cannot practically be done without access to/use of PHI.

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. [Section 3052 of the 21st Century Cures Act (Pub. L. No. 114-255]

Humanitarian Device Exemption (HDE): A marketing application for an HUD. [Section 520(m) of the Federal Food, Drug, and Cosmetic Act (FD&C Act)] An HDE is exempt from the effectiveness requirements of Sections 514 and 515 of the FD&C Act and is subject to certain profit and use restrictions.

Human Subjects Research: As defined by the FDA, activities are considered human subjects research subject to FDA regulations when the activity meets the FDA definition of "clinical investigation" and research "subject".

FDA Clinical Investigation:

- Use of a drug other than the use of an approved drug in the course of medical practice.
- Use of a medical device other than the use of an approved medical device in the course of medical practice.
- Gathered data that will be submitted to or held for inspection by FDA in support of an FDA marketing permit for a food, including a dietary supplement that bears a nutrient content claim, or a health claim, in infant formula, a food or color additive, a drug for human use, a medical device for human use, a biological product for human use, or an electronic product utilized in patient care, diagnosis and/or treatment.

Human Subject: Individuals are considered "subjects" when they become a participant in research either as recipient of the test article (drug or device) or as a control subject in the research.

DHHS Regulations: Activities are considered human subjects research, subject to DHHS regulations when the activity meets the DHHS definition of research AND human subject as defined in DHHS regulation (Common Rule).

- **DHHS Definition-Research** is a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge.
- **DHHS Definition-Human Subjects** is a living individual about whom an investigator (whether professional or student) is conducting research:
    - obtains information through intervention, or interaction with the individual and uses, studies, or analyzes the information or bio-specimen.
    - Obtains, uses, studies or generates identifiable private information or bio-specimens.

I

International Conference on Harmonization of Technical Requirements for Registration of Pharmaceutical for Human Use (ICH) **https://www.ich.org/page/ich-guidelines**

The International Conference on Harmonization (ICH) guidance provides a unified standard for the European Union, Japan, and the United States to facilitate the mutual acceptance of clinical data by the regulatory authorities in those jurisdictions.

ICH aims to achieve greater harmonization worldwide for the development and approval of safe, effective, and high-quality medicines in the most resource-efficient manner.

Good Clinical Practice (GCP)E6(R2) is an international ethical and scientific quality standard for designing, conducting, recording, and reporting trials that involve the participation of human subjects. Compliance with this standard provides public assurance that the rights, safety, and well-being of trial subjects are protected, consistent with the principles that have their origin in the Declaration of Helsinki, and that the clinical trial data are credible.

The objective of this ICH GCP Guideline is to provide a unified standard for the European Union (EU), Japan and the United States to facilitate the mutual acceptance of clinical data by the regulatory authorities in these jurisdictions. The guideline was developed with consideration of the current good clinical practices of the European Union, Japan, and the United States, as well as those of Australia, Canada, the Nordic Countries, and the World Health Organizations.

IND Safety Report: A formal written report of an adverse experience that is associated with the drug that is serious and unexpected. The study sponsor must send this report to the FDA and all investigators working with the drug.

Informed Consent: A process by which a potential research participant or legally authorized representative confirms a willingness to participate in a particular research project after having been informed of all aspects of the research that are relevant to the potential subject's willingness to participate. Informed consent is documented by means of a written, signed, and dated informed consent form approved by an Institutional Review Board (IRB), a waiver of consent is determined to be applicable based on the criteria set forth in 45 CFR 46.116(c).

https://www.hhs.gov/ohrp/regulations-and-policy/guidance/faq/informed-consent/index.html

Waiver of Documented Informed Consent:

When an Institutional Review Board (IRB) has not waived the requirement for seeking prospective informed consent of the subjects or the parental permission of children who are subjects, under the HHS regulations at 45 CFR 46.117(c), it may waive the requirement for the investigator to obtain a signed consent form for some or all subjects if it finds either:

- That the only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants

documentation linking the subject with the research and the subject's wishes will govern; or

- That the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context (e.g., drawing a blood sample, or asking shoppers in a mall about the ambient lighting or temperature).

Waiver of Consent:

Research in general: an IRB may waive or alter the requirement of informed consent under 45 CFR 46.116(d), provided that the IRB finds and documents that all of the following four conditions are met:

- the research involves no more than minimal risk to the subjects;
- the waiver or alteration will not adversely affect the rights and welfare of the subjects;
- the research could not practicably be carried out without the waiver or alteration; and
- whenever appropriate, the subjects will be provided with additional pertinent information after participation.

Institutional Review Board (IRB): IRBs were initially codified in the 1974 National Research Act. An IRB is an appropriately constituted group that has been formally designated to review and monitor biomedical research involving human subjects. In accordance with FDA regulations, an IRB has the authority to approve, require modifications in (to secure approval), or disapprove research. This group review serves an important role in the protection of the rights and welfare of human research subjects.

The purpose of IRB review is to assure, both in advance and by periodic review, that appropriate steps are taken to protect the rights and welfare of humans participating as subjects in the research. To accomplish this purpose, IRBs use a group process to review research protocols and related materials (e.g., informed consent documents and investigator brochures) to ensure protection of the rights and welfare of human subjects of research. Detailed description of the functions of the IRB are codified in 45 CFR 46.108(a)(3)(4).

https://www.ecfr.gov/current/title-45/subtitle-A/subchapter-A/part-46/subpart-A/section-46.108 (Common Rule) and 21 CFR 56.108(a)(b)
https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm?fr=56.108

Investigator Brochure (IB): A compilation of the clinical and nonclinical data on the investigational product(s) that is relevant to the study of the investigational product(s) in human subjects. The IB will provide relevant information to provide the investigator with a clear understanding of the possible risks and adverse effects, safety monitoring requirements, as well as observations and precautions required for the safe conduct of a clinical trial. Information based on the available physical, chemical, pharmaceutical, pharmacological, toxicological, and clinical information on the investigational product is included. The study sponsor will maintain up to date information in the IB and provide amended versions as new

or updated information becomes available. The IRB will review the IB on initial review and when amended.

Investigational Device: A device, including a transitional device, that is the object of a clinical investigation involving one or more subjects to determine the safety and/or effectiveness of the device. [21 CFR 812.3] Investigational use also includes clinical evaluation of modification or new intended uses of legally marketed devices. The use of an investigational device in human subjects requires approval by the IRB and may also require approval by the FDA.

> **Investigational Device Exemption (IDE):** An IDE allows the investigational device to be used in a clinical study to collect safety and effectiveness data. Investigational use also includes clinical evaluation of certain modifications or new intended uses of legally marketed devices. All clinical evaluations of investigational devices, unless exempt, must have an approved IDE before the study is initiated. https://www.fda.gov/medical-devices/premarket-submissions-selecting-and-preparing-correct-submission/investigational-device-exemption-ide

Investigational Drug: Defined by the FDA, an investigational drug is a drug or biologic that used in a clinical investigation. [21 CFR 312] https://www.ecfr.gov/current/title-21/chapter-I/subchapter-D/part-312. The use of an investigational drug in human subjects requires approval by the FDA and the IRB.

> **Investigational New Drug Application (IND):** A request for authorization from the FDA to administer an investigational drug or biological product to humans.
>
> https://www.fda.gov/drugs/investigational-new-drug-ind-application/ind-applications-clinical-investigations-regulatory-and-administrative-components

In Vitro: A term used to refer to processes that are conducted outside the human body, usually in a laboratory.

In Vivo: A term used to refer to processes that occur in the human body, not in a laboratory setting.

J

Justice: This principle advocates 1) fair treatment for all and 2) a fair distribution of the risks and benefits of the research. It forbids exploitation of vulnerable people (for instance, economically disadvantaged or those with limited cognitive capacity) or those who are easily manipulated as a result of their situation.

K

L

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 procedure(s) involved in the research. [45 CFR 46.102(c)]

The South Carolina Adult Health Care Consent Act: Act which provides specifics related to obtaining consent and the hierarchy of who may act as an LAR for an individual unable to consent. https://www.scstatehouse.gov/code/t44c066.php

Limited Data Set: A limited data set under HIPAA is a set of identifiable healthcare information that the HIPAA Privacy Rule permits covered entities to share with certain entities for research purposes, public health activities, and healthcare operations without obtaining prior authorization from patients, if certain conditions are met.

A HIPAA limited data set can only be shared with entities that have signed a data use agreement with the covered entity. The data use agreement allows the covered entity to obtain satisfactory assurances that the PHI will only be used for specific purposes, that the PHI will not be disclosed by the entity with which it is shared, and that the requirements of the HIPAA Privacy Rule will be followed.

M

Medical Device: FDA determines a medical device is an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component part, or accessory which is:

- Recognized in the official National Formulary, or United States Pharmacopoeia, or any supplement to them,
- Intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or animals, or
- Intended to affect the structure or any function of the body of man or other animals, and which does not achieve any of its primary intended purposes through chemical action on the body of man or other animals and which is not dependent upon being metabolized for the achievement of any of its intended purposes.

  https://www.fda.gov/medical-devices/classify-your-medical-device/how-determine-if-your-product-medical-device

Minimal Risk: 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. [45CFR46.102(i)]

N

National Institute of Health (NIH): A federal agency within the Public Health service, DHHS, comprising 21 institutes and centers. It is responsible for carrying out and supporting biomedical and behavioral research.

National Research Act: Act created at the National Commission for Protection of Human Subjects of Biomedical and Behavioral research in 1974 and mandated review of studies by institutional review boards and subject protection by informed consent.

New Drug Application (NDA): An application submitted by the manufacturer of a drug to the FDA, after the clinical trial has been completed, for a license to market for a specified indication.

Nuremberg Code: *The Nuremberg Code* (German: Nürnberger Kodex) is a set of ethical research principles for human experimentation created by the court in U.S. v Brandt, one of the Subsequent Nuremberg trials that were held after the Second World War.

Though it was articulated as part of the court's verdict in the trial, the Code would later become significant beyond its original context; in a review written on the 50th anniversary of the Brandt verdict, Jay Katz writes that "a careful reading of the judgment suggests that [the authors] wrote the Code for the practice of human experimentation whenever it is being conducted".

O

Observational Study: A clinical study in which participants identified as belonging to study groups are assessed for biomedical or health outcomes. Participants may receive diagnostic, therapeutic, or other types of interventions, but which does not assign participants to specific interventions.

Office for Human Research Protection (OHRP): A federal government agency within The Department of Health and Human Services (DHHS) charged with the protection of human subjects participating in government funded research. It issues assurances and oversees compliance with regulatory guidelines.

Open-Label Trial: Describes a clinical trial in which masking/blinding is not used. All parties involved in conduct of and participation in the trial are aware of treatment and interventions of the trial.

P

Parental Permission: The agreement of parent(s) or guardian to the participation of their child or ward in research. [45 CFR46.402c.]

Placebo: An inactive pill, liquid, powder, or other intervention that has no treatment value, utilized in clinical research to provide control comparisons to assess the effectiveness of other treatments.

Principal Investigator (PI): The individual who assumes full responsibility for a research study, including but not limited to, the oversight and training of research assistants, administration of informed consent and protecting participant confidentiality.

Prisoner: is defined by HHS regulations at 45 CFR part 46.303(c) as "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.

Protocol: A research protocol is a document that describes the background, rationale, objectives, design, methodology, statistical considerations, and organization of a research project.

Protocol Amendment: Any modification to a protocol which may impact the conduct of the study, potential benefit of the participant or possible effect to participant safety, including changes of study objectives, study design, participant population, sample size, study procedures, or significant administrative aspects.

Protocol Deviation: Any departure from the study procedures or treatment plans as specified in the IRB approved protocol, protocol deviations occur when some aspect of a research study as approved by the reviewing IRB is not implemented or followed as required.

Protected Health Information: Also referred to personal health information, PHI is the demographic information, medical histories, test and laboratory results, mental health conditions, insurance information and other data that a healthcare professional collects to identify an individual and determine appropriate care.

Q

R

Randomization: The process of assigning research trial participants to different study "arms" or "cohorts" (treatment or control) using an element of chance to determine assignments to reduce bias.

Remuneration: Something of value provided to research participants as compensation for added time/effort required to participate in a research study.

Reseach Misconduct: Fabrication, falsification, plagiarism, or other practices that seriously deviate from those accepted within the scientific community for conducting and reporting research.

Respect for Persons: Codified in the ***Belmont Report*** respect for persons incorporates at least two ethical convictions: first, that individuals should be treated as autonomous agents, and second, that persons with diminished autonomy are entitled to protection.

Retrospective Study: A study performed a posteriori, using information on events that have taken place in the past. In most cases some or most of the data has already been gathered and stored in a registry, existing databases or medical records. Unlike the prospective studies, a retrospective study usually does not need to follow patients into the future and often requires less time to conduct than a prospective study. In a retrospective study, different patient populations can be compared for one or several outcomes.

Risk Determination/Assessment: An assessment of the probability of harm or injury to include physical, psychological, social, or economic, that may occur as the result of participation in a research study. Both the probability and magnitude of harm are considered in relationship to the potential for benefit to both the individual and the broader societal benefit. Strategies and procedures must be included in the research protocol for mitigating and managing risks.

S

Secondary Data: Research data that has previously been gathered and can be accessed by researchers for future or ongoing research.

Serious Adverse Event: A serious adverse event is defined as any adverse event occurring, which results in any of the following outcomes: death, a life-threatening experience, inpatient hospitalization, or prolongation of existing hospitalization, a persistent or significant disability, incapacity, a congenital anomaly, or birth defect. [21 CFR 312.32(a) and 21 CFE 812.3(s)]

Short Form Consent: Short form consent is an alternative to using a translated consent form, for use when few limited English proficiency speakers are expected or when few subjects who speak a particular language are expected (if at all). The short form consent form is a document, translated into the subject's preferred language, that contains a description of the required elements of informed consent and notes that these elements, as they pertain to the study, will be presented orally to the subject or legally authorized representative.

T

U

Unanticipated Problem (UP): An unexpected event that occurs in the context of research that might cause harm or represents a risk of harm, which may be unexpected in terms of nature, frequency, or severity; it may be related or possibly related and suggests that the research places subjects or others at a greater risk of harm than was previously known or recognized. [DHHS2007]

V

Vulnerable Populations: Research subjects that are likely to be vulnerable to coercion or undue influence, such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons. When some or all of these subjects are determined to be vulnerable, additional safeguards must be included in the study to protect the rights and welfare of these subjects.

W

Waiver of Consent: See Informed Consent

Waiver of Documentation of Consent: See Informed Consent

Waiver of HIPAA Authorization: See Health Insurance Portability and Accountability Act (HIPAA)

Ward of the State: A person placed in the legal custody of the State or other agency, institution, or entity consistent with applicable Federal, State, or local laws. Additional consideration and protections are required if a "ward" is to be considered for a research study.

X

Y

Z

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