UC San Diego Health

Department of Neurosciences

Research Glossary: Unlocking Research Terminology

A

ACTRI: Altman Clinical & Translational Research Institute: The ACTRI at UCSD serves as a dynamic hub for accelerating scientific discoveries from bench to bedside. ACTRI supports a wide array of adult and pediatric research studies spanning neurology, cardiac disease, obesity, diabetes, infectious disease, dermatology, and more. Its overarching goal is to facilitate translational research by providing robust infrastructure, essential resources, specialized expertise, and cutting-edge technologies. Its services extend beyond specific patient populations or research categories, and welcomes investigators from all disciplines to leverage its resources fully.

Adverse Effect: An undesirable and unintended, although not necessarily unexpected, result of therapy or other intervention (e.g., headache following spinal tap or intestinal bleeding associated with aspirin therapy).

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 the 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 (e.g. abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the participants' involvement in the research, whether or not considered related to participation in the research.

Arm: A group or subgroup of participants in a clinical trial that receives specific interventions, or no intervention, according to the study protocol. This is decided before the trial begins.

Assent : An agreement by an individual not competent to give legally-valid informed consent (e.g., a child aged 7+ or 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. Mere failure to object may not, absent affirmative agreement, be construed as assent.

Audit: A systematic review, inspection, or verification, typically conducted by an independent individual or group of a research clinical investigation.

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.

Basic Research: Systematic study directed toward greater knowledge or understanding of the fundamental aspects of phenomena and of observable facts without specific applications towards processes or products in mind. (32 CFR 272.3)

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

Beneficence: An ethical principle discussed in the Belmont Report that entails an obligation to protect persons from harm. The principle of beneficence can be expressed in two general rules: (1) do not harm; and (2) protect from harm by maximizing possible benefits and minimizing possible risks of harm.

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

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

Blinding: The process by which investigators and/or participants do not know to which study group the participants are assigned. There are single blind studies (in which the participant is blind) and double-blind studies (in which both the participant and the investigator are blind).

C

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

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

Case Report or Case Study: A case report is one in which three or fewer records are accessed to develop a publication for the purpose of reporting on some novel aspect of the case. Case reports do not meet the definition for human subjects research and do not require submissions 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.
- A worksheet is available on our website that can help an investigator determine if their project qualifies as a case report.

Cede Review: The act of transferring IRB review and oversight to another IRB committee.

CT Scan: Abbreviation for Computerized Axial Tomography, an X-ray technique for producing images of internal bodily structures through the assistance of a computer.

CDC: Centers for Disease Control and Prevention; an agency within the Public Health Service, Department of Health and Human Services.

Central Institutional Review Board (CIRB): The Central IRB (CIRB) Initiative is designed to help reduce the administrative burden on local IRBs and investigators while continuing a high level of protection for human research participants. A local IRB's use of the CIRB facilitated review mechanism is intended to enable an investigator to enroll patients into adult and pediatric clinical trials significantly faster than when employing traditional method of IRB review.

Certificate of Confidentiality: A Certificate of Confidentiality (CoC) helps researchers protect the confidentiality of participants enrolled in sensitive human subjects research studies. Certificates protect against compulsory legal demands, such as U.S. court orders and subpoenas, for identifying information or identifying characteristics of a research participant.

Any researcher can apply for a CoC to protect their participants, however a CoC is issued automatically for applicable NIH awards as part of the award terms and conditions.

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 (FDA Definition): Any experiment that involves a test article and one or more human subjects and is subject to requirements for submission to the Food and Drug Administration under section 505(i) or 520(g) of the Food, Drug, and Cosmetic Act (FDCA) or is not subject to requirements for prior submission to the FDA but the results of which are intended to be submitted later to, or held for inspection by, the FDA as part of an application for a research or marketing permit. Clinical investigations must not be initiated unless that investigation has been reviewed and approved by an IRB.

Clinical Research (NIH Definition): 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 services research.

Clinical Research or Study Coordinator (CRC): An individual that handles the administrative and day-to-day responsibilities of a clinical trial and acts as a liaison for the clinical site. This person may collect the data or review it before it is entered into a study database.

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-related outcomes.

The FDA definition of a clinical investigation does not encompass some studies, such as behavioral interventions and surgical procedures. The FDA regulates safety/efficacy for only some kinds of therapies 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 in a very small number 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 doses (to establish a safe dose range), and, if possible, to gain early evidence of effectiveness. The ultimate 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, sufficiently valid Phase 2 studies. Other examples of Phase 1 studies include studies of drug metabolism, structure-activity relationships, and mechanisms of actions in humans, as well as studies in which investigational drugs are used as research tools to explore biological phenomena or disease processes.
- 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 typically 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 - several thousand) in different clinical settings to determine its safety, efficacy, and appropriate dosage. They are performed after preliminary evidence of effectiveness has been obtained, and are intended to gather necessary additional information about effectiveness and safety for evaluating the overall benefit-risk relationship of the drug, and to provide an adequate basis for physician labeling. An NIH-defined Phase III clinical trial is a broadly-based prospective Phase III clinical investigation, usually involving several hundred or more human subjects, for the purpose of evaluating an experimental intervention in comparison with a standard or controlled intervention or comparing two or more existing treatments. Often the aim of such investigation is to provide evidence leading to a scientific basis for consideration of a change in health policy or standard of care. The definition includes pharmacologic, non-pharmacologic, and behavioral interventions given for disease prevention, prophylaxis, diagnosis, or therapy. Community trials and other population-based intervention trials are also included. In Phase 3 studies, the drug is used the way it would be administered when marketed. When these studies are completed and the sponsor believes that the drug is safe and effective under specific conditions, the sponsor applies to the FDA for approval to market the drug.
- Phase 4 Trial: Studies conducted after a drug has been approved by 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 than 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.

Coded Information/Biospecimens: Identifying information (such as name or social security number) or biospecimens that would enable the investigator to readily ascertain the identity of the individual to whom the private information or biospecimens pertain that has been replaced with a number, letter, symbol, or combination thereof (i.e. the code); and for which a key to decipher the code exists that enables linkage of the identifying information or biospecimens to the private information or biospecimens.

Code of Federal Regulations (CFR): The Code of Federal Regulations is an annual 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 broad areas subject to Federal regulation. Each Title is divided into chapters that are assigned to agencies issuing regulations pertaining to that broad subject area. Each

chapter 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 for all those who may need to know the text of general and permanent Federal regulations (National Archives).

Conflict of Interest: A conflict of interest arises for an IRB member or consultant engaged in research review when the member or consultant, as well as their spouse, domestic partner, children, or dependents, possess any of the following interests in the sponsor or the product or service being tested. (e.g. investigational drug)

- Involvement in the design, conduct, or reporting of the research.
- Ownership interest, stock options, or other ownership interest of any value exclusive of interests in publicly-traded, diversified mutual funds.
- Compensation of any amount in the past year or of any amount expected in the next year, excluding compensation for costs directly related to conducting research.
- Proprietary interest including, but not limited to, a patent, trademark, copyright or licensing agreement.
- Board or executive relationship, regardless of compensation.
- Reimbursed or sponsored travel by an entity other than a federal, state, or local government agency, higher education institution or affiliated research institute, academic teaching hospital, or medical center.
- Any other reason for which the member/consultant believes that he or she cannot be independent.

Cognitively Impaired: Having either a psychiatric disorder (e.g., psychosis, neurosis, personality or behavior disorders, or dementia) or a developmental disorder (e.g., mental retardation) that affects cognitive or emotional functions to the extent that capacity for judgment and reasoning is significantly diminished. Others, including persons under the influence of or dependent on 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 (see: www.citiprogram.org).

Common Rule: The Common Rule, which governs research with human subjects conducted or supported by 15 federal departments and agencies including EPA, establishes a comprehensive framework for the review and conduct of proposed human research to ensure that it will be performed ethically. EPA's codification of the Common Rule. The central requirements of the Common Rule are:

- That people who participate as subjects in covered research are selected equitably and give their fully informed, fully voluntary written consent; and
- That proposed research be reviewed by an independent oversight group referred to as an Institutional Review Board (IRB), and approved only if risks to subjects have been minimized and are reasonable in relation to anticipated benefits, if any, to the subjects, and the importance of the knowledge that may reasonably be expected to result.

Compassionate Use of Investigational Devices: The FDA defines "compassionate use or expanded access" as the use of a test article on a human subject with a serious disease or condition for which there is no acceptable treatment available. FDA and IRB approval for compassionate use is required. This use is based on a compassionate use protocol approved by the FDA or other regulatory authorities, allowing patients access to the investigational drug when no satisfactory alternative treatments are available.

Compensation: Payment, merchandise, class credit, or other gifts or services provided to research participants or their legally authorized representatives for their time and effort associated with research participation. Compensation should be appropriate to the population, the cultural norms of the research location, and research activities.

Competence: Used to denote capacity to act on one's own behalf; the ability to understand information presented, to appreciate the consequences of acting (or not acting) on that information, and to make a choice.

Concomitant Medication: Prescription and over-the-counter drugs and supplements a study participant has taken along with the study intervention. This information may be collected as a history item as well as during the study. Some studies may collect only those medications that may interact with the study or intervention or that may exclude an individual from participating in a study.

Confidentiality: How a researcher has agreed to handle, manage, and disseminate the information disclosed by or data regarding a participant. There is a relationship of trust between these parties, and the expectation that confidential information or data will not be divulged to others by the researcher without the participant’s permission in ways that are inconsistent with the agreement regarding disclosure of the information or data.

Conflict of Interest (COI): The real or apparent interference of one person's interests with the interests of another person, where potential bias may occur due to prior or existing personal or professional relationships. A conflict of interest occurs when individuals involved with the conduct, reporting, oversight, or review of research also have financial or other interests, from which they can benefit, depending on the results of the research.

Consent Document(s): Commonly referred to as the "ICF" or "Informed Consent Form." These are the documents presented to a subject or parent guardian prior to beginning a study. Most studies will have this document submitted with the proposal, unless requesting a Waiver (see below). The IRB has provided a template on the web site for investigators to prepare their documents.

- **Adult Informed Consent:** This is required when subjects are 18 years and older. This should be written to the subject using appropriate language ("you").
- **Parental Permission Document:** This is required when subjects are 17 years and younger. This should be written to the parent/guardian using appropriate language ("your child").
- **Assent Document:** Assent is an agreement by an individual not competent to give legally valid informed consent (e.g., a child aged 7+ or cognitively-impaired person) to participate in research. This is required for children enrolled in studies that are 7-17 years of age. If the board deems appropriate, this can be requested for younger children.

Continuing Review: Category of review of human subjects' research, and subject to IRB review and approval to assure the continued protection of the rights and welfare of the participants in that research. In order to re-approve the research, the IRB must assess the study based on the federal requirements for approval: minimized risks to participants, equitable selection of participants, informed consent process, appropriate data management and security, appropriate participant privacy and confidentiality of data, and safeguards for vulnerable populations. The continuing review process is defined by federal regulations.

Contraindicated: Disadvantageous, perhaps dangerous; a treatment that should not be used in certain individuals or conditions due to risks (e.g., a drug may be contraindicated for pregnant women and persons with high blood pressure).

Convene IRB: A meeting of the IRB at which a majority of IRB members are present.

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

Controlled Trial: A type of clinical trial in which observations made during the trial are compared to a standard (called the control). The control may be observations from a group of participants in the same trial or observations from outside the trial (for example, from an earlier trial, called a historical control).

Controls, Historical: Control subjects (followed at some time in the past or for whom data are available through records) who are used for comparison with subjects being treated concurrently. The study is considered historically controlled when the present condition of subjects is compared with their own condition on a prior regimen or treatment.

Coordinating Center: A group organized to coordinate the planning and operational aspects of a multi-center clinical trial. CCs may also be referred to as Data Coordinating Centers (DCCs) or Data Management Centers (DMCs).

Cooperative Research: Those projects which are determined to be human subjects research and that involve more than one institution. Cooperative research involves researchers, institutions, or organizations collaborating to address research questions that are beyond the capacity of a single entity. T In cooperative research projects, experts from different institutions join forces to design, execute, and analyze studies, often combining resources, skills, and data to achieve common research objectives.

Coverage Analysis: Coverage analysis involves a comprehensive evaluation of the clinical trial protocol, budget, and contractual agreements to determine the extent of financial coverage and responsibilities for patient care costs incurred during the trial. This analysis ensures compliance with federal regulations, institutional policies, and sponsor requirements regarding billing practices and reimbursement for clinical trial-related services.

Covered Entity: Health care providers who conduct certain financial and administrative transactions electronically, such as billing and fund transfers; also, all health plans and health care clearinghouses (45 CFR 160.103). Covered Entities must comply with HIPAA regulations. The University of California, San Diego Health Sciences is a Covered Entity Contact the HIPAA Regulatory Office (587 9241) or go to Covered Entity for information on the University offices that are inside or outside the Covered Entity.

Crossover Design: Describes a clinical trial in which groups of participants receive two or more interventions in a particular order. For example, a two-by-two crossover design involves two groups of participants. One group receives drug A during the initial phase of the trial, followed by drug B during a later phase. The other group receives drug B during the initial phase, followed by drug A during a later phase. So, during the study, participants "cross-over" to the other drug. All participants receive drug A and drug B at some point during the study, but in a different order, depending on the group to which they are assigned.

D

Data and Safety Monitoring (DSM): The process for reviewing data collected as research progresses to ensure the continued safety of current and future participants as well as the scientific validity and integrity of the research.

Data and Safety Monitoring Board (DSMB): A committee of scientists, physicians, statisticians, and others that collects and analyzes data during the course of a clinical trial to monitor for adverse effects and other trends (such as an indication that one treatment is significantly better than another, particularly when one arm of the trial involves a placebo control) that would warrant modification or termination of the trial or notification of subjects about new information that might affect their willingness to continue in the trial.

Data Management: The processes of handling the data collected during a clinical trial from development of the study forms/CRFs through the database locking process and transmission to statistician for final analysis.

Data Management Plan (DMP): 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: Data and Safety Monitoring means the process to ensure and maintain the scientific integrity of human subject research and to protect the safety of human subjects, a system for appropriate oversight and monitoring to ensure the safety of participants and the validity of the data. The section of a protocol that describes the steps to identify physical, social, or psychological occurrences that may result from participation in the research study and explains in detail how such occurrences will be handled and reported. A DSMP describes the timing, tools and/or method(s) for monitoring and evaluation, procedures for treatment or resolution (including circumstances which would result in halting or terminating research), procedures for and timing of reports to oversight bodies, and description of oversight bodies involved with the study (e.g. FDA, IRB, or Data and Safety Monitoring Board). A study does not need to have a Data and Safety Monitoring Board to have a DSMP.

Data Repository: A place that holds research data and makes that data available for future use by the broader research community. Data repositories may have specific requirements concerning the research topic, data re-use and access, file format and data structure, and the types of metadata that can be used. Many data repositories have restrictions on who can deposit and access data.

Data Use Agreement: A written agreement between two (or more) parties to ensure that research data will only be used for specific uses and disclosures. DUAs can be incoming (data coming to UCSD) or outgoing (data being sent outside of UCSD) or involve sharing across multiple parties. Investigators are not permitted to sign DUAs on behalf of the University. Use Agreement (DUA) is a contractual document used for the transfer of data that has been developed , where the data is nonpublic or is otherwise subject to some restrictions on its use. Often this data is a necessary component of a research project and it may or may not be human subject data from a clinical trial, or limited data set information as defined in HIPAA.

Deception in Research: Deception is the intentional misleading of subjects or the withholding of full information about the nature of a research experiment or procedure. Misleading or omitted information might include the purpose of the research, the role of the researcher, or what procedures in the study are actually experimental. If participants are given false information or are otherwise misled during a study, then the participants are not provided with all of the required elements of informed consent: in these instances, approval for a waiver or alteration of informed consent is required.

Decisional Capacity: A prospective participant's ability to make a meaningful and conscious decision about whether or not to participate in a research study. The four elements of decisional capacity are a participant's ability to (i) understand the information presented to the participant, (ii) appreciate the risks and benefits involved, (iii) reason and engage with research personnel about the information presented to the participant, and (iv) express a choice about whether or not to participate.

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, 2000.

Deferred: An IRB action taken when the convened IRB cannot fully evaluate the research under review and make the determinations required for IRB approval without (i) modifications to the Application and/or informed consent document(s), or (ii) submission of clarifications or additional materials prior to reconsideration of the research.

De-Identified: All direct personal identifiers are permanently removed (e.g., from data or specimens), no code or key exists to link the information or materials to their original source(s), and the remaining information cannot reasonably be used by anyone to identify the source(s).

Deviations: A protocol deviation is not defined by DHHS or the FDA. Broadly, a protocol deviation is an unapproved departure from the procedures described in the IRB-approved materials. Deviations may occur for a variety of reasons, maybe anticipated and/or intentional, may be known or identified before they occur or discovered after the fact.

Device Determination, Non-significant Risk Device: An investigational medical device that does not present significant risk to the patient.

Device Determination, Significant Risk Device: An investigational medical device that presents a potential for serious risk to the health, safety, or welfare of the subject.

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

Double Blind Masking: A type of masking in which two or more parties involved with the clinical trial do not know which participants have been assigned which interventions. Typically, this includes the investigator and participant.

E

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

Electronic Data Capture (EDC): A digital system used to collect, manage, and store data for clinical research. EDC systems replace traditional paper-based data collection, enhancing data accuracy, security, and accessibility. These systems allow researchers to enter data directly into electronic forms, streamline data management processes, facilitate real-time data monitoring, and ensure compliance with regulatory standards.

Eligibility Criteria: List of criteria guiding enrollment of participants into a study. The criteria describe both inclusionary and exclusionary factors, (e.g. inclusion criterion - participants must be between 55 and 85 years old; exclusion criterion – must not take drug X three month prior to the study).

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 in which there is not sufficient time to obtain IRB approval [21CFR 56.102 (d)]. This use occurs in emergency settings where there is an urgent need to address the immediate health condition of the participant. It may be authorized under emergency use provisions or compassionate use protocols, depending on the specific circumstances and regulatory requirements

Enrolled: Individuals who have given informed consent or assent to participate in the screening or study procedures. Individuals can enroll in a study and not complete any or all procedures, including being deemed ineligible through screening procedures.

Exculpatory: Pertaining to that which relieves of a responsibility, obligation, or hardship; clearing from accusation or blame.

Exempt Review: This is a streamlined review process reserved for research projects with very minimal risk or for projects such as registries that do not have a set expiration date. Studies undergoing exempt review have been determined by the IRB to pose minimal risk to participants and do not require ongoing continued review. However, amendments may still be necessary during the course of the project, and the study will need to undergo a close-out process upon completion.

Expanded Access: A process regulated by the Food and Drug Administration (FDA) that allows manufacturers to provide investigational new drugs to patients with serious diseases or conditions who cannot participate in a clinical trial.

Expedited Review: Review of proposed research by the IRB Chairperson or a designated voting member or group of voting members rather than by the entire IRB. Federal rules permit expedited review for certain kinds of research involving no more than minimal risk, minor changes in approved research, continuing reviews, and some federal exemption categories.

Expired Study: When a continuing review of the research does not occur prior to the end of the approval period specified by the IRB, IRB approval expires automatically. The study expires on the date specified on the approval letter and the informed consent document. No activities can occur on the expiration date or after.

F

Financial Conflict of Interest: An interest of an IRB member or Immediate Family member of monetary value (a) that is, could be, or could be perceived to be impacted by the research under review, including an IRB member or Immediate Family member's interest in or relationship to an entity that the research impacts, may impact, or could be perceived to impact; or (b) that influences, could influence, or could be perceived to influence the IRB member's professional judgment in exercising his/her role as an IRB member. Financial interests may include, but are not limited to, salary or other payments for services (e.g., consulting fees or honoraria); equity interests (e.g., stocks, stock options, or other ownership interests); and intellectual property rights (e.g., patents, copyrights, and royalties from such rights).

Federal-Wide Assurance (FWA): A standing agreement on file with the Office for Human Research Protections that describes in detail the procedures it will use to protect the rights and welfare of the human subjects.

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, nation's food supply, cosmetics, and products that emit radiation.

G

Genetic Information Nondiscrimination (GINA): Genetic Information Nondiscrimination Act (GINA) is a Federal law that prohibits discrimination in health coverage and employment based on genetic information. Along with the nondiscrimination provisions of HIPAA, GINA generally prohibits health insurers or health plan administrators from requesting or requiring genetic

information of an individual or an individual's family members, or using such information for decisions regarding coverage, rates, or preexisting conditions. GINA also prohibits employers from using genetic information for hiring, firing, or promotion decisions, and for any decisions regarding terms of employment.

Gene Therapy: The treatment of genetic disease accomplished by altering the genetic structure of either somatic (non-reproductive) or germline (reproductive) cells.

Good Clinical Practice (GCP): A standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial participants are protected.

Grandfathered: To exempt an existing or in progress study from new regulations

Guardian: An individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care when general medical care includes participation in research. It also means an individual who is authorized to consent on behalf of a child to participate in research.

H

Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule: The first comprehensive Federal protection for the privacy of personal health information. The Privacy Rule regulates the way certain health care groups, organizations, or businesses, called covered entities under the Rule, handle the individually identifiable health information known as protected health information (PHI).

HIPAA Terminology:

- Authorization: Permission from individuals to use or disclose their Protected Health Information; generally required for research involving PHI. Certain statements are required; similar to but in addition to the Common Rule's informed consent; can be added to a consent form. (45 CFR 164.508)
- Covered Entity: Defined as health care providers who conduct certain financial and administrative transactions electronically, such as billing and fund transfers; also, all health plans and health care clearinghouses. (45 CFR 160.103) Covered Entities must comply with HIPAA. (45 CFR 160.103 [PDF]).
- The University of California, San Diego Health Sciences is a Covered Entity.
- Disclosure: The release, transfer, provision of access to, or divulging in any other manner of information outside the Covered Entity holding the information (45 CFR 164.501 [PDF]).

- 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. (45 CFR 160.301, 164.501; information about the provision of health care and payment for health care is included; some educational and employment records are excluded.)
- Humanitarian Device Exemption: An HDE is a pre-market approval application submitted to the FDA (
- Humanitarian Use Device (HUD): A Humanitarian Use Device (HUD) is a device that is intended to benefit patients by treating or diagnosing a disease that affects fewer than 4,000 individuals in the United States per year. To be considered for HUD status, a device sponsor must complete a humanitarian device exemption (HDE) application with the FDA. An approved HDE application authorizes the applicant to market the HUD. The labeling for the HUD must state that the device is a HUD and that the effectiveness of the device has not been demonstrated.
- Human Participants: Individuals whose physiologic or behavioral characteristics and responses are the object of study in a research project. Under the federal regulations, human participants are defined as: living individual(s) about whom an Investigator conducting research obtains: (1) data through intervention or interaction with the individual; or (2) identifiable private information. NOTE: FDA's regulations define human subject as an individual and do not use the adjective "living."
- Human Participants Research: This term applies to federally regulated research in which human participants (see definition above), their data, tissue, genetic material or other is investigated in a systematic fashion. It includes clinical trials, retrospective studies (subject to IRB oversight or exempt from continuing IRB oversight), outcome studies, surveys, etc.

Human Subject: Under DHHS regulations "subjects" means a living individual about whom an investigator (whether professional or student) conducting research obtains:

- data through intervention or interaction with the individual
- identifiable private information.

Intervention includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes. Interaction may include communication or interpersonal contact between investigator and subject.

Private information includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record).

Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects.

Human Subjects Research: According to IRB policy, research involving human subjects (participants) is defined as any one of the following:

Human subjects research subject to FDA regulation: Activities are human research subject to FDA regulations when they meet the FDA definition of "clinical investigations" and involve a "subject" as defined in FDA regulation.

Under FDA regulation activities are "clinical investigations" when they involve:

- 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
- Gather 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, an 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.

In the above criteria "approved" means "approved by the FDA for marketing."

Under FDA regulations, individuals are considered "subjects" when they become a participant in research, either as a recipient of the test article or as a control. If the research involves a medical device, individuals are considered "subjects" when they participate in an investigation, either as an individual on whom or on whose specimen an investigational device is used or as a control.

Human subjects research subject to DHHS regulation: Activities are human subject research subject to DHHS regulations when they meet the DHHS definition of "research and involve a "subject" as defined in DHHS regulations.

Under DHHS regulations activities are "research" when they are a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.

Research that does not meet the definition of research involving human subjects must be determined by the IRB staff, not an individual investigator. Investigators must complete and submit an IRB new study application with any applicable documents.

Healthy Volunteer: A healthy volunteer is a person with no known significant health problems who participates in clinical research to test a new drug, device, or intervention.

Human Subject: A patient or healthy individual who is or becomes a participant in research, either as a recipient of the intervention or as a control.

I

IDS-Pharmacy: Clinical research within The University of California, San Diego Health System is supported by Investigational Drug Service (IDS) staff at Thornton Medical Center and at the Altman Clinical and Translational Research Center. These locations provide comprehensive pharmacy services to support clinical trials, such as:

- Pharmacist review of all drug orders and monitoring parameters, if applicable.
- Drug preparation and dispensing, pursuant to a valid order or prescription (OPRX)
- Drug management, accountability support for clinical trials.

When the IDS pharmacy controls the investigational drug for a study, all necessary control and recordkeeping functions are conducted for the investigator by the IDS pharmacy.

Incentive: Financial payments and/or other inducements to investigators, research staff, or referring physicians to promote enrollment of subjects in research study. These do not include payments to subjects themselves. Examples include:

- the sponsor provides financial reimbursement to the research and/or study staff that exceeds the fair market value of the services provided.
- the sponsor provides payment or services outside the scope of the research study requirement, such as, unrestricted educational grants.

Independent Investigator: An investigator whose home institution does not have an IRB or who is not affiliated with an institution.

Institutional Biosafety Committee (IBC): Committee that evaluates and provides oversight of the use of biohazardous agents to ensure compliance with appropriate regulations and guidelines and to safeguard the health and safety of UCSD personnel, the community, and the environment. IBC oversight also includes human source material, including blood, body fluids, tissues and/or cell lines, infected clinical specimens or biologically contaminated specimens.

Institutional Official (IO): The senior associate vice chancellor for health sciences to whom the Chancellor delegates authority to sign assurances of, and to oversee the university's responsibility for, the protection of human subjects.

International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH): ICH guidance was published in the Federal Register on May 9, 1997 (62 FR 25692).

Informed Consent: A process by which a participant or legal guardian voluntarily confirms his or her willingness to participate in a particular research project, after having been informed of all aspects of the research that are relevant to the subject's decision to participate. Informed consent is documented by means of a written, signed, and dated informed consent form approved by an IRB, unless such documentation is waived by the IRB (45 CFR 46).

A person's voluntary agreement, based upon adequate knowledge and understanding of relevant information, to participate in research or to undergo a diagnostic, therapeutic, or preventive procedure. In giving informed consent, subjects may not waive or appear to waive any of their legal rights, or release or appear to release the investigator, the sponsor, the institution or agents thereof from liability for negligence [Federal Policy §116; 21 CFR 50.20 and 50.25] (OHRP).

Informed Consent Form: A document that describes the rights of a study participant and provides details about the study, such as its purpose, duration, required procedures, and key contacts. Risks and potential benefits are explained in the informed consent document.

Institutional Review Board (IRB)/Independent Ethics Committee (IEC): An independent body constituted of medical, scientific, and nonscientific members whose responsibility it is to ensure the protection of the rights, safety, and well-being of human subjects involved in a trial by, among other things, reviewing, approving, and providing continuing review of trials, protocols and amendments, and of the methods and material to be used to obtaining and documenting informed consent of the trial participant.

Intervention: A procedure or treatment such as a drug, nutritional supplement, gene transfer, vaccine, behavior or device modification that is performed for clinical research purposes (45 CFR 46.102(f)). Interventions can also include noninvasive approaches such as surveys, education, and interviews.

Investigational Brochure (IB): In drug development, the Investigator's Brochure is a comprehensive document summarizing the body of information about an investigational product or "study drug" obtained during a drug trial. The IB is a document of critical importance throughout the drug development process and is updated with new information as it becomes available. The purpose of the IB is to compile data relevant to studies of the study drug in human subjects gathered during preclinical and other clinical trials.

An IB is intended to provide the investigator with insights necessary for management of study conduct and study subjects throughout a clinical trial. An IB may introduce key aspects and safety measures of a clinical trial protocol, such as: dose (of the study drug), frequency of dosing interval, methods of administration, and safety monitoring procedures.

An IB contains a "Summary of Data and Guidance for the Investigator" section, of which the overall aim is to "provide the investigator with a clear understanding of the possible risks and adverse reactions, and of the specific tests, observations, and precautions that may be needed for

a clinical trial. This understanding should be based on the available physical, chemical, pharmaceutical, pharmacological, toxicological, and clinical information on the investigational product(s). Guidance should also be provided to the clinical investigator on the recognition and treatment of possible overdose and adverse drug reactions that is based on previous human experience and on the pharmacology of the investigational product".

The sponsor is responsible for keeping the information in the IB up-to-date. The IB should be reviewed annually and must be updated when any new and important information becomes available, such as when a drug has received marketing approval and can be prescribed for use commercially.

Investigational Device: According to the Food and Drug Administration (FDA), an investigational device is a device, including a transitional device, that is the object of a [clinical] investigation involving one or more subjects to determine the safety or effectiveness of the device (21 CFR 812.3). Investigational use also includes clinical evaluation of certain modifications 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 from the FDA.

Investigational Device Exemption (IDE): Exemptions from certain regulations found in the Medical Device Amendments that allow shipment of unapproved devices for use in clinical investigations [21 CFR 812.20].

Investigational Product: According to the Food and Drug Administration (FDA), investigational new drug means a new drug or biological drug that is used in a clinical investigation. The term also includes a biological product that is used in vitro for diagnostic purposes. The terms "investigational drug" and "investigational new drug" are deemed to be synonymous. (21 CFR 312.3)

The use of an investigational drug (IND) in human subjects requires approval by the FDA and the IRB.

An IND number is generally required for a drug (including a drug with marketing authorization) if it is intended to:

- Support a new indication for use, establish safety or efficacy of the drug, support a change in the approved route of administration (including method of assembly) or dosage level;
- Support a change in the approved patient population (e.g. pediatric vs. adults) or a population at greater/increased risk (e.g. immunocompromised, elderly, etc.);
- Support a change in the promotion/ advertising/ labeling/ packaging of an approved drug.

An IND number may also be required for investigations that attempt to gain further information about an approved use. The study sponsor and/or investigator cannot represent (in a promotional setting) that the drug is safe and effective for the purposes in which it is under investigation.

Investigational New Drug Application (IND): An IND is a request for authorization from the Food and Drug Administration (FDA) to administer an investigational drug or biological product to humans. Such authorization must be secured prior to interstate shipment and administration of any new drug or biological product that is not the subject of an approved New Drug Application or Biologics/Product License Application (21 CFR 312).

Investigational New Drug (IND) or Device (IDE): A drug or device permitted by FDA to be tested in humans but not yet determined to be safe and effective for a particular use in the general population and not yet licensed for marketing (Also, see Investigational Device Exemption (IDE)).

Investigator's Brochure: A compilation of the clinical and non-clinical data on the investigational product(s) that is relevant to the study of the investigational product(s) in human subjects.

In Vitro: Literally, "in glass" or "test tube;" used to refer to processes that are carried out outside the living body, usually in the laboratory, as distinguished from in vivo.

In Vivo: Literally, "in the living body;" processes, such as the absorption of a drug by the human body, carried out in the living body rather than in a laboratory (in vitro).

IRB of Record: The IRB that has been designated through an IRB Authorization Agreement (IAA) to provide ethical oversight of a study in which more than one organization is engaged in the research.

J

Justice: An ethical principle discussed in the Belmont Report requiring fairness in distribution of burdens and benefits; often expressed in terms of treating persons of similar circumstances or characteristics similarly.

K

Key Personnel: Study team members that interact or intervene with the human subjects or their identifiable data.

Kuali Institutional Review Board (IRB) Portal: Is the University's electronic and comprehensive platform designed to streamline the management and oversight of the IRB review process. It provides tools for researchers, administrators, and IRB members to efficiently manage

the entire lifecycle of a research project, from protocol submission and review to approval and ongoing monitoring.

Kuali Research Platform: Is a comprehensive system designed to facilitate the management of research administration tasks within academic institutions and other research organizations. The platform streamlines various aspects of the research administration process, including the submission and management of agreements, proposals, awards, compliance documents, and other related activities.

Key features of Kuali Research include: proposal development, award management, agreements management, and compliance tracking.

L

Legally Authorized Representative (LAR): A person authorized either by statute or by court appointment to make decisions on behalf of another person. In human subject research, 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. There are several considerations that must be addressed when the inclusion of a LAR is proposed, such as, whether periodic re-consenting is warranted, and whether the probability of benefit is greater than the probability of harm.

Licensed Medical Provider: A person conducting clinical assessments in a clinical trial or making a clinical judgment who has the independent authority to treat patients. The licensed medical provider should have appropriate expertise in the area of research inquiry.

Limited Data Set: A limited data set could include the following (potentially identifying) information:

- Admission, discharge, and service dates;
- Dates of birth and, if applicable, death;
- Age (including age 90 or over); and
- Five-digit zip code or any other geographic subdivision, such as state, county, city, precinct and their equivalent geocodes (except street addresses).

Covered entities must condition the disclosure of the limited data set on execution of a "data use agreement," which

- establishes the permitted uses and disclosures of such information by the recipient, consistent with the purposes of research, public health, or health care operations;
- limits who can use or receive the data; and
- requires the recipient to agree not to re-identify the data or contact the individuals.

In addition, the data use agreement must contain adequate assurances that the recipient will use appropriate physical, technical and administrative safeguards to prevent use or disclosure of the limited data set other than as permitted by HIPAA and the data use agreement, or as required by law.

Longitudinal Study: A study designed to follow subjects forward through time.

M

Manual of Procedures (MOP): A set of procedures describing study conduct. A MOP is developed to facilitate consistency in protocol implementation and data collection across study participants and clinical sites.

Masking/Blinding: A procedure in which the investigator administering the assessments and intervention as well as the participants in a clinical trial are kept unaware of the treatment assignment(s). Single blinding usually refers to the study participant(s) being unaware, and double blinding usually refers to the study participant(s) and any of the following being unaware of the treatment assignment(s): investigator(s), monitor, and data analyst(s).

Material Transfer Agreement: A Material Transfer Agreement (MTA) is a document that is used by scientists and their institutions to transfer materials to other scientists and institutions. MTAs provided by outside organizations may contain clauses that are not consistent with the University of California, San Diego policies and procedures and/or federal law. Signing one of these agreements could severely impede a scientist's ability to carry out his or her research or to publish in a timely fashion. It is important that all MTAs are evaluated and signed by an authorized TVC representative. The Technology Venture Commercialization Office handles and processes these agreements.

Medical Device: According to the FDA, a 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 the 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 other 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 within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of any of its primary intended purposes.

Metabolism (of a drug): The manner in which a drug is acted upon (taken up, converted to other substances, and excreted) by various organs of the body.

Minimal Risk: Minimal risk means that 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 (45 CFR 46.102(i)). For example, the risk of drawing a small amount of blood from a healthy individual for research purposes is no greater than the risk of doing so as part of routine physical examination. This is not interpreted to include the inherent risks certain categories of human subjects face in their everyday lives. For example, the risks imposed in research focused on a special population should not be evaluated against the inherent risks encountered in their work environment (e.g., emergency responder, pilot, soldier in a combat zone).

In addition, the IRB generally subscribes to the recommendations related to 45 CFR 46.404 from Secretary's Advisory Committee on Human Research Protections (SACHRP) regarding research involving children.

Monitor: An individual designated by a sponsor or contract research organization to oversee the progress of a clinical investigation. The monitor may be an employee of a sponsor, or a consultant to the sponsor, or an employee of or consultant to a contract research organization.

N

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 the drug for a specified indication.

NIH: National Institutes of Health: 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.

Non-Affiliated Member: Member of an Institutional Review Board who has no ties to the parent institution, its staff, or faculty. This individual is usually from the local community (e.g., minister, business person, attorney, teacher, homemaker).

Non-Inferiority Design: A non-inferiority trial compares a test treatment to a control treatment of established effectiveness and seeks to show that the test treatment is not materially worse than or inferior to the control treatment. A non-inferiority trial seeks to show that any difference between the two treatments is small enough to allow a conclusion that the test treatment has at least some effect or, in many cases, an effect that is not significantly less than the active control. A non-inferiority trial may proceed under 21 CFR 50.24 if it meets the requirements of the regulation.

For a non-inferiority trial to be informative, there would need to be clear data about the effectiveness of the control treatment (to make the non-inferiority study interpretable) and about known safety or other problems associated with the control treatment. Non-inferiority trials are generally used in situations where a placebo-controlled trial would be unethical and where there are no data to suggest the new treatment would be more effective than the standard treatment.

Non-Therapeutic Research: Research that has no likelihood or intent of producing a diagnostic, preventive, or therapeutic benefit to the current subjects, although it may benefit subjects with a similar condition in the future.

Null Hypothesis: The proposition, to be tested statistically, that the experimental intervention has "no effect," meaning that the treatment and control groups will not differ as a result of the intervention. Investigators usually hope that the data will demonstrate some effect from the intervention, thereby allowing the investigator to reject the null hypothesis.

Nuremberg Code: A code of research ethics developed during the trials of Nazi war criminals following World War II and widely adopted as a standard during the 1950s and 1960s for protecting human subjects.

O

Observational Study: A clinical study in which participants identified as belonging to study groups are assessed for biomedical or health outcomes. The investigator simply records observations and analyzes data, without administration of an intervention or alteration of the care participants receive. These studies may focus on risk factors, natural history, variations in disease progression or disease treatment without delivering an intervention. They often assess specific health characteristics of the enrolled human subjects by collecting medical/dental history, exposure, or clinical data; obtaining biospecimens (e.g., for biomarker or genomic analyses); or obtaining photographic, radiographic or other images from research participants

Office of Clinical Trials Administration (OCTA): The Office of Clinical Trials Administration (OCTA) at UC San Diego supports and manages the administration of clinical trials, ensuring compliance with federal, state, and institutional regulations. OCTA handles contract negotiation, financial oversight, and regulatory adherence, providing training and educational resources for investigators and research staff.

Office of Grants Administration (OCGA): Office of Grants Administration (OGA), UC San Diego: The Office of Grants Administration at UC San Diego oversees the management and administration of research grants from pre-award to post-award stages. This office provides comprehensive support in grant proposal preparation, submission, and compliance with funding agency guidelines. It ensures financial and regulatory compliance, manages grant budgets, and assists with financial reporting. The OGA serves as a liaison between researchers, funding

agencies, and university administration, facilitating effective grant management and supporting the university's research mission.

Office for Human Research Protections (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 of regulatory guidelines by research institutions.

Office of IRB Administration (OIA): Formerly known as HRPP. OIA's mission is to protect the rights and welfare of human participants in research and to oversee compliance with human research protection regulations and policies.

Office of Sponsored Projects (OSP): The Office of Sponsored Projects is responsible for preparing, interpreting, negotiating, and executing agreements on behalf of the University of California, San Diego for projects funded by federal and state agencies, foundations, and other public and private sources. They also draft, negotiate, and execute awards and sub-awards for collaborative research.

Open-Label (Open-Label Trial): Describes a clinical trial in which masking is not used. This means that all parties involved with the trial know which participants have been assigned which interventions.

P

Parallel Design: Describes a clinical trial in which two or more groups of participants receive different interventions. For example, a two-arm parallel design involves two groups of participants. One group receives drug A, and the other group receives drug B. So, during the trial, participants in one group receive drug A "in parallel" to participants in the other group who receive drug B.

Parental Permission: The agreement of parent(s) or guardian to the participation of their child or ward in research [45 CFR 46.402(c)].

Pass-Through Funding: Funds issued by a federal agency that are then transferred to other eligible groups per the award eligibility terms. The "prime awardee" issues the subawards as competitive or noncompetitive as dictated by the prime award terms and authorizing legislation. Prime awardee institutions on a pass-through funding grant are considered engaged by the Department of Health and Human Service's (DHHS) Office for Human Research Protections (OHRP) and must ensure ethical oversight for their role in the research.

Pharmacodynamics (PD): Pharmacodynamics is the process that studies the biochemical and physiological effects of drugs on the body, as well as the mechanisms of drug action and the relationship between drug concentration and its effects.

Pharmacokinetics (PK): The process (in a living organism) that studies how the body processes drugs. It focuses on understanding the absorption, distribution, metabolism, and excretion of a drug or vaccine over time.

Pharmacology: The scientific discipline that studies the action of drugs on living systems (animals or human beings).

Phase 1, Phase 2, Phase 3, Phase 4 Clinical Trial: See "Clinical Trial".

Phenotype: The physical manifestation of a gene function.

Placebo: A placebo is an inactive pill, liquid, powder, or other intervention that has no treatment value. In clinical trials, experimental treatments are often compared with placebos to assess the treatment's effectiveness.

A method of investigation in which an inactive substance/treatment (the placebo) is given to one group of participants, while the test article (e.g. investigational drug)is given to another group. The results obtained in the two groups are then compared to see if the investigational treatment is more effective in treating the condition.

Principal Investigator (PI): The person who is responsible for the scientific and technical direction of the entire clinical study (for example, for all sites of a multisite study).

Prisoners: An individual involuntarily confined in a penal institution, including persons: (1) sentenced under a criminal or civil statue; (2) detained pending arraignment, trial, or sentencing; and (3) detained in other facilities (e.g., for drug detoxification or treatment of alcoholism) under statutes or commitment procedures providing such alternatives to criminal prosecution or incarceration in a penal institution. The definition of "minimal risk" for research involving prisoners differs somewhat from that given for non-institutionalized adults.

Privacy: Control over the extent, timing, and circumstances of sharing oneself (physically, behaviorally, or intellectually) with others.

Proband: The person whose case serves as the stimulus for the study of other members of the family to identify the possible genetic factors involved in a given disease, condition, or characteristic.

Prophylactic: Preventive or protective; a drug, vaccine, regimen, or device designed to prevent, or provide protection against, a given disease or disorder.

Prospective Studies: Studies designed to observe outcomes or events that occur subsequent to the identification of the group of subjects to be studied. Prospective studies need not involve manipulation or intervention but may be purely observational or involve only the collection of data.

Protocol: A document that describes the objective(s), design, methodology, statistical consideration, and organization of a trial. Protocols may be developed by industry, non-governmental entities, Principal Investigators and others. This term also includes amendments made to the original document.

Protocol Amendments: A written description of a change(s) to or formal clarification of a protocol.

Protocol Deviations: Failure to conduct a study as described in the protocol. The failure may be accidental or due to negligence and in either case, the protocol deviation should be documented. This also includes failure to comply with federal laws and regulations, the institution's commitments and policies, and standards of professional conduct and practice. Examples of noncompliance include:

- failure to obtain/maintain approval for research,
- failure to obtain informed consent when required,
- failure to file adverse event reports,
- performance of an unapproved study procedure,
- performance of research at an unapproved site,
- failure to file protocol modifications and
- failure to adhere to an approved protocol.

Protocol Deviation Report: Internal document created as part of the ongoing quality control process of a research study summarizing compliance with the protocol and listing protocol deviations and/or violations.

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. (45 CFR 160.301, 164.501; information about the provision of health care and payment for health care is included; some educational and employment records are excluded.)

Q

Quality Assurance/Quality Improvement (QA/QI): An activity conducted to assess, analyze, critique, and improve current practice or process in an institutional setting or ensure it conforms to expected norms, involving data-guided, systematic activities designed to bring about prompt improvements regardless of any professional benefit to the investigator.

R

Radiation Safety Committee (RSC): An institutional committee responsible for the use of all uses of radioactive material or radiation-producing equipment that results in exposure to human subjects.

Research involving human subjects that proposes to use of radioactive drugs or equipment that produces radiation must meet various FDA requirements, including limitations on the pharmacological dose and the radiation dose. Furthermore, the exposure to radiation must be justified by the quality of the study and the importance of the information it seeks to obtain. The committee is also responsible for continuing review of the drug use to ensure that the research continues to comply with FDA requirements, including reporting obligations. The committee must include experts in nuclear medicine and the use of radioactive drugs, as well as other medical and scientific members [21 CFR 36.1].

The University of California's radiation safety program is designed to prevent unnecessary radiation exposures, and to control those that are necessary. RSC is an ancillary committee to the University of California, San Diego Institutional Review Board, which is responsible for the review and approval of research protocols involving human participants and radiation exposure, and the administration or use of radioactive drugs. Clinical investigations that include exposing human participants to radiation (x-rays, PET Scans, etc.) require RSC approval before IRB approval may be granted.

Radiopharmaceutical or Radiotracer Agents: In nuclear medicine, a radiopharmaceutical or radiotracer is a radioactive compound that is administered to research participants as part of a research investigation. These compounds typically consist of a radioactive isotope (the tracer) attached to a biologically active molecule that targets specific tissues, organs, or physiological processes within the body. Radiopharmaceuticals are used as tracers to visualize physiological functions or detect abnormalities within the body using imaging techniques such as positron emission tomography (PET), single-photon emission computed tomography (SPECT), or gamma camera imaging.

Randomization: The process of assigning clinical trial participants to treatment or control groups using an element of chance (e.g. like flipping a coin) to determine the assignments in order to reduce bias.

Recombinant DNA Technology: "The ability to chop up DNA, the stuff of which genes are made, and move the pieces, [which] permits the direct examination of the human genome," and the identification of the genetic components of a wide variety of disorders [Holtzman (1989), p. 1]. Recombinant DNA technology is also used to develop diagnostic screens and tests, as well as drugs and biologics for treating diseases with genetic components.

Recruitment: The process of identifying and reaching potential participants to enroll in a research study. It is considered the beginning of the participant selection and informed consent/assent processes.

Recruitment Materials: May include (but are not limited to) printed materials, newsletters, recruitment lists, phone scripts, e-mails, electronic advertisements, and video/audio scripts. Recruitment materials must contain enough information to provide potential participants a sense of the study and the ability to decide if they may be eligible to participate.

Recruitment Plan: The plan that outlines how individuals will be recruited for the study and how the study will reach the recruitment goal.

Reimbursement: Payment provided to research participants or their legally authorized representatives that reflects their out of pocket expenses associated with participating in a research study. These expenses could be parking, transportation, childcare costs, lost wages, accommodations, food, etc. and are usually approved by the sponsor and described in the informed consent form.

Reliance Agreement: Reliance Agreement, also known as an IRB Authorization Agreement (IAA) or Individual Investigator Agreement (IIA), is a formal written arrangement. Under this agreement:

- An external institution agrees to defer to the determinations made by the UCSD IRB.
- UCSD agrees to defer to the determinations made by an IRB external (Central IRB) to UCSD.
- The UCSD IRB may agree to act as the overseeing IRB for an investigator who is not affiliated with UCSD.

This agreement streamlines the review process by avoiding redundant reviews for multi-site research projects and ensures consistency in ethical oversight. It's an essential component of institutional review board policies, facilitating collaboration and adherence to ethical standards in research involving multiple institutions or investigators.

Reportable Event: A type of unanticipated event or occurrence related to a human subjects research study that requires review by the IRB as defined in the IRB Reportable Events Policy.

Repository or Specimen Bank: Collection of data and/or specimens obtained and stored for future research uses and/or distribution, including a collection not originally or primarily obtained for research purposes.

Research: A systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalized knowledge. Key terms: systematic and generalizable

Research Involving a Human Being as an Experimental Subject: According to the Department of Defense Directive 3216.02 section E2.1.3., this means an activity, for research purposes, where there is an intervention or interaction with a human being for the primary purpose of obtaining data regarding the effect of the intervention or interaction. Examples of

interventions or interactions include, but are not limited to, a physical procedure, a drug, a manipulation of the subject or subject's environment, the withholding of an intervention that would have been undertaken if not for the research purpose.

Respect for Persons: An ethical principle discussed in the Belmont Report requiring that individual autonomy be respected and persons with diminished autonomy be protected.

Retention Plan: The plan that details the methods in which the study will use in order to retain study participation in the clinical trial.

Retrospective Study: Research conducted by reviewing records from the past (e.g., imaging, death certificates, medical records, etc.) or by obtaining information about past events elicited through interviews or surveys. Case control studies are an example of this type of research.

Reviewing IRB: The IRB of record performing review on behalf of one or more institutions, also referred to as the single IRB, central IRB, and/or IRB of record.

Risk Determinations: The probability of harm or injury (physical, psychological, social, or economic) occurring as a result of participation in a research study. Both the probability and magnitude of possible harm may vary from minimal to significant. Federal regulations define only "minimal risk." (See also: Minimal Risk.) These can include:

- Greater than minimal risk: The subject will undergo procedures that will increase their risks above those normally encountered in daily life. Equivalent term is "more than minimal risk." These can include, but are not limited to: clinical drug trials, device trials, genetic studies, and risks that include insurability and employability.
- Minimal Risk: The subject will undergo procedures that do not appear to increase the risks above those normally encountered in daily life. These can include but are not limited to studies that involve survey, questionnaire, interview, medical records review, observation of behaviors, drawing a small amount of blood from a healthy individual, etc.

Exempt: These studies are not usually reviewed by board members, but are reviewed by the chairman. These have been determined to fit certain federal regulations as exempt from IRB review.

S

Safe Harbor De-Identification: Potential identifiers include obvious ones like name and social security number, and also:

All geographic subdivisions smaller than a state, including street address, city, county, precinct, zip code, and their equivalent geocodes, except for the initial three digits of a zip code if, according to the current publicly available data from the Bureau of the Census: the geographic

unit formed by combining all zip codes with the same three initial digits contains more than 20,000 people; and [t]he initial three digits of a zip code for all such geographic units containing 20,000 or fewer people is changed to 000.

All elements of dates (except year) for dates directly related to an individual, including birth date, admission date, discharge date, date of death; and all ages over 89 and all elements of dates (including year) indicative of such age, except that such ages and elements may be aggregated into a single category of age 90 or older; Voice and fax telephone numbers; Electronic mail addresses; Medical record numbers, health plan beneficiary numbers, or other health plan account numbers; Certificate/license numbers; Vehicle identifiers and serial numbers, including license plate numbers; Device identifiers and serial numbers, Internet Protocol (IP) address numbers and Universal Resource Locators (URLs); Biometric identifiers, including finger and voice prints; Full face photographic images and any comparable images; and any other unique identifying number, characteristic, or code.

Under HIPAA's "safe harbor" standard, information is considered de-identified if all of the above have been removed, and there is no reasonable basis to believe that the remaining information could be used to identify a person.

Screening Log: An essential document that records all individuals who entered the screening process. The screening log demonstrates the investigator's attempt to enroll a representative sample of participants.

Screening Process: A process designed to determine individual's eligibility for participation in a clinical research study.

Secondary Data: Secondary data is data collected by someone other than the user. Common sources of secondary data for social science include censuses, surveys, organizational records and data collected through qualitative methodologies or qualitative research. Primary data, by contrast, are collected by the investigator conducting the research.

Secondary Research: Study of existing information or materials (e.g., data or specimens) that have been previously collected for a purpose (including non-research purposes) other than the currently proposed activity.

Serious Adverse Event (SAE): Any adverse event occurring in a patient or human subject enrolled in a research study is serious if it results in any of the following outcomes:

- Results in death
- Is life threatening, or places the participant at immediate risk of death from the event as it occurred
- Requires or prolongs hospitalization
- Causes persistent or significant disability or incapacity

- Results in congenital anomalies or birth defects
- Is another condition which investigators judge to represent significant hazards
- Important medical events that may not result in death, or require hospitalization, may be considered an SAE when, based upon appropriate medical judgment, the event may jeopardize the patient or human subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition

Serious Non-Compliance: Any incident of noncompliance that involves a willful disregard or knowing violation of the federal, state, or local regulations that governs human subjects research, or the institutional policies and procedures that apply to human subjects research, which may have included or led to a (i) significant harm, or a risk of significant harm, to the rights, welfare, or safety of participants; or (ii) significant compromise of the quality or scientific integrity of a human subjects research study.

Sham Comparator Arm: A group of participants that receives a procedure or device that is made to be indistinguishable from the actual procedure or device being studied but does not contain active processes or components.

Short Form Consent Document: The Short Form was created in an effort to increase the University's compliance with regard to non-English speaking participants. The regulations state that informed consent information should be presented "in a language understandable to the subject", and in most situations, that informed consent be documented in writing. This means that participants who do not speak English should be presented with a consent document written in a language understandable to them. Any time a study proposes to use the Short Form as an alternative consent process, the form and the process must be approved by the convened board. The Board should determine whether or not the process is adequate and appropriate for the study, or if a fully-translated consent document should be required.

Single IRB (sIRB) Review: A review performed by one institution (commonly referred to as the "IRB of record") for multi-site research to establish the expectation that an sIRB of record will be used in the ethical/scientific review of non-exempt human subjects research protocols.

SMART IRB: SMART IRB is part of an integrated, comprehensive platform aimed at addressing common challenges in initiating multisite research projects. Its purpose is to facilitate the implementation of the NIH Single IRB Review policy, which became effective on January 25, 2018. The SMART IRB is not an IRB group/committee itself, but rather a framework and set of guidelines designed to streamline and harmonize the IRB review process across multiple institutions participating in collaborative research studies.

Source Data: Data or other information necessary to perform the research received from a party external to UCSD n via a properly executed agreement. Source Data does not include original data generated by UCSD researchers or the results of analyses conducted using Source Data.

Source Documents: Original forms, documents, data, and records (e.g., hospital records, clinical and office charts, laboratory notes, memoranda, participant diaries, recorded data from automated instruments, x-rays, etc.) that are used in a clinical trial.

Sponsor: A person or other entity who initiates a clinical investigation, but does not actually conduct the investigation (e.g., the test article is administered, dispensed to, or used involving a subject under the immediate direction of another individual).

Note: This is defined by the FDA federal regulations. A person other than an individual (e.g., corporation or agency) that uses one or more of its own employees to conduct a clinical investigation it has initiated is considered to be a sponsor (not a sponsor-investigator), and the employees are considered to be investigators.

Sponsor-Investigator: An individual who both initiates and actually conducts - alone or with others - a clinical investigation (e.g. under whose immediate direction the test article is administered, dispensed, or used involving subject.). Corporations, agencies, or other institutions do not qualify as Sponsor-Investigators.

Sponsor Protocol: A document used to define and manage the trial usually sent by the Industry Sponsor or the lead site if it is a multi-center study. Not all studies will include a protocol, but studies that involve investigational drugs; investigational devices will always have this document. The protocol describes the scientific rationale, objective(s), design, methodology, statistical considerations and organization of the planned trial. The protocol contains a precise study plan to assure safety and health of the trail subjects and to provide an exact template for trial conduct by investigators. This allows data to be combined across all investigators/sites. The format and content of clinical trial protocols sponsored by pharmaceutical, biotechnology, or medical device companies in the United States, European Union, or Japan have been standardized to follow Good Clinical Practice guidance.

Standard Operating Procedures (SOPs): Detailed written instructions to achieve uniformity of the performance of a specific function across studies and patients at an individual site.

Standard Operating Guidance (SOGs): Detailed written instructions to achieve uniformity of the performance of a specific function across studies and patients at an individual site but are not mandatory.

Stopping Rules: Established safety criteria that would either pause or halt a study due to reasons including but not limited to futility or risk(s) to the participants.

Stratification: Separation of a study cohort into subgroups or strata according to specific characteristics such as age, gender, etc., so that factors which might affect the outcome of the study, can be considered.

Suspension of IRB Approval: An action of the IRB, IRB designee, institutional official, or designee of the institutional official to temporarily or permanently withdraw IRB approval of some or all research procedures short of a termination of IRB approval. Suspended studies remain open and are subject to continuing review. For the purposes of this definition, an enrollment hold shall not be considered a suspension of IRB approval if no other research procedures have had their IRB approval withdrawn.

T

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 by FDA or the Public Health Service Act.

Tissue/Specimen Banking: Specimen collection banks, whether they are described as "banks" or not, are many and varied. They cover the spectrum from individual clinicians' research specimen collections, (often gathered with no specific project in mind) to institutional "Tissue Banks" (such as neurological center shared resource banks) to multi-center, industry-sponsored drug trials which usually collect at least some blood or tissue for unspecified future research.

Tracked Changes: In word processing, track changes is an editing command that is commonly used when you create an original document and make changes and want to keep track of the changes that are made to that original document. It is also a useful tool for collaborating on a document, as it allows multiple users to make revisions without losing the context of the original document. Changes to text and formatting are noted in a number of different ways, depending on the word processing software you use. Tracking changes allows the IRB staff and board members to clearly see what changes, modifications, updates, and additions have been made to study documents.

Translation Certification Letter: This letter certifies the authenticity of the translation of a translated Consent Document. Sponsors typically provide this certification for study-related materials, primarily Informed Consent Forms (ICFs) that have been translated into other languages.

U

Unanticipated Adverse Device Effect: 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 FDA

Investigational Device Exemption application; or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

Unanticipated Problem (UP) Involving Risks to Subjects or Others/Unanticipated Problem Report (UPR): Unanticipated problems are defined as any incident, experience or outcome that occurs during the course of a study that meets all of the following criteria:

- Unexpected (not expected by the researcher or the research participant) given the research procedures as described in the protocol and other study-related documents such as the Informed Consent and Investigational Brochure, and the characteristics of the subject population being studied.
- Related or probably related (greater than or equal to 50% probability) that the incident, experience, or outcome may have been caused by participation in the research or if the event or problem probably or definitely affects the safety, rights and welfare of current participants; and
- Suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic or social harm) than was previously known or recognized, even if no harm actually occurred.

Undue Influence: Excessive or inappropriate reward or other overture in order to persuade a person to act against that person's own interests or without adequate consideration of the consequences in order to obtain compliance.

Unmasking/Unblinding: A procedure in which one or more parties to the trial are made aware of the treatment assignment(s).

Unexpected Adverse Event (UAE): Any adverse event (AE) occurring in one or more participants in a research study, the nature, severity, or frequency of which (i) is not considered consistent with either the known or foreseeable risk of AEs associated with the procedures involved in the research that are described in the protocol-related documents, investigator brochure, informed consent document, or other relevant sources of information regarding the research, such as product or device labeling and package inserts; or (ii) is not considered consistent with the expected natural progression of any underlying disease, disorder, or condition of the participant(s) experiencing the AE and the participant’s predisposing risk factor profile for the AE.

Unrelated: Unassociated or without a timely relationship; evidence exists that an outcome is definitely related to a cause other than the event in question. This definition should be considered in the context of determining whether an adverse event is related or possibly related to participation in research for purposes of determining whether it qualifies as a Reportable Event.

V

Velos Account: A Velos account at UCSD is an electronic research management system utilized for overseeing and monitoring clinical research studies and their associated data. This web-based platform serves as a centralized hub for various aspects of clinical research. A key feature of Velos is its integration with the Epic electronic health record (EHR) system. This integration enables the smooth transfer of study-related charges from clinical care settings to the correct study project number within Velos. This ensures that subjects are not billed for any study-related charges. The information in the Velos account originates directly from the study Coverage Analysis.

Vulnerable Populations: Individuals whose willingness to volunteer in a clinical trial may be unduly influenced by the expectation, whether justified or not, of benefits associated with participation, or of a retaliatory response from senior members of a hierarchy in case of refusal to participate. A population's vulnerability may change depending on the nature of the research and may fluctuate over time. Investigators must take special care and consideration when recruiting, consenting, and conducting research activities with these populations. Examples are members of a group with a hierarchical structure, such as medical, pharmacy, dental and nursing students, subordinate hospital and laboratory personnel, employees of the pharmaceutical industry, members of the armed forces, and persons kept in detention (prisoners). Other vulnerable subjects include patients with incurable diseases, persons in nursing homes, unemployed or impoverished persons, and patients in emergency situations, ethnic minority groups, homeless persons, refugees, minors, pregnant women, and those incapable of giving consent.

W

Waiver of Authorization: In some situations, the IRB can waive the requirement that research subjects sign an Authorization Form. To qualify for a Waiver of Authorization, the research use of the health information should not represent more than a minimal risk to privacy, and the researcher should indicate that the research could not be done without the requested health information, that it would not be practical to obtain signed authorizations from the research subjects, and that the specific elements of health information that are requested are not more than the minimum necessary to accomplish the goals of the study.

Waiver of Documentation of Informed Consent: An IRB 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.

Waiver of Informed Consent: Occasionally there are reasons to waive written consent or to alter the requirements of consent. Only the IRB can make the determination to waive some (written) or all (written and verbal) consent requirements. In order to qualify for a Waiver of Consent, the following conditions should be met:

- That the research poses no more than minimal risk to subjects
- No adverse effects as a result of the waiver or alteration
- Without the waiver or alteration, the research in question could not be carried out
- Information will be provided after participation is completed, if appropriate.

Washout Period: The action or process of progressively reducing the concentration of a substance (i.e. drug) in a subject. Washout periods are used in some drug trials to prevent medications the subject is already taking from interacting with the tested drug. Under the Placebo Guidelines, board reviewers must ensure that the proposed placebo exposure (and any corresponding washout periods) is of a specified duration such that evidence supports the exposure as no more than minimal risk. These are reviewed by the IRB on a case-by-case basis.

Withdrawn Participants: Individuals who have given informed consent or assent to participate in study procedures, but who choose to no longer participate or who are removed by the PI from the study.

X

Y

Z