1 PURPOSE

1.1 This guidance establishes the definitions followed by the human research protection program.

2 REVISION FROM PREVIOUS VERSION

2.1 If applicable, previous versions available in Human Research Protection Program Change Log.

3 POLICY STATEMENT

3.1 Advance Directive: Documents written in advance of a serious illness in which a person states their choices for healthcare or names someone to make those choices. When a person is selected to make the medical decisions, the document is called a Durable Power of Attorney and the designated person is called an agent. The agent can serve as a legally authorized representative to provide surrogate consent. See *GUIDANCE: Legally Authorized Representatives (Surrogate Consent) (HRP-013)*.

3.2 Adverse Event (AE): Any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding e.g., ANC of 450), symptom, a diagnosis (e.g., HTN) or disease temporally associated with the use of a medicinal (investigational) product, whether related to the medicinal (investigational) product.

3.3 Agent: A Sharp HealthCare (SHC) employee in the course of their on-duty time or a non-SHC person who is engaged by SHC for the purposes of review of human research. Legal counsel has the ultimate authority to determine whether someone is acting as an agent of SHC. See *POLICY: Human Research Protection Program (16500.99)* for more information.

3.4 Allegation of Non-Compliance: An unproved assertion of Non-Compliance. See *GUIDANCE: Institutional Review Board (IRB) Review of Promptly Reportable Information Items (HRP-024)* and *GUIDANCE: Prompt Reporting Requirements (HRP-027)*.

3.5 Amendment: Changes to an IRB approved research protocol or associated documents that are to be submitted to, and approved by, the IRB before implementation (e.g., revised protocol, updated investigator's brochure or instructions for use, revised consent document, research team changes, identification of additional risks, etc.). Amendments involving more than minor changes or changes that pose more than minimal risk will be reviewed by the full committee.

3.6 Assent: A child's affirmative agreement to participate in research or an affirmative agreement to participate in research given by a person with impaired decision-making capacity. Mere failure to object is not the same as assent.

3.7 Biologic: Any therapeutic serum, toxin, anti-toxin, or analogous microbial drug applicable to the prevention, treatment, or cure of disease or injury. See *POLICY: Investigational Drugs (43019.01)* and *GUIDANCE: Investigational Drugs and Biologics (HRP-096)*.

3.8 Broad Consent: Under the Revised (2018) Common Rule, "Broad Consent" is an alternative consent process for use only for the storage, maintenance, and secondary research use of private information or identifiable biospecimens for future, yet-to-be-specified research. Sharp HealthCare will not adopt the use of Broad Consent on an institutional level as the tracking requirements are burdensome. Therefore, Exemption Categories 7 and 8, which are specific to Broad Consent, will not be utilized or allowed at Sharp HealthCare.

3.9 California Experimental Subject's Bill of Rights (CA BOR): A list of rights of a subject in a medical experiment as set forth under Health & Safety Code § 24172. It is the policy of Sharp HealthCare that all research subjects or their legally authorized representatives sign and date this document, in addition to providing their signature on the informed consent.

3.10 Capacity to Consent (to research): The ability of the individual to understand the choices presented, to appreciate the implications of choosing one alternative or another, and to make and communicate a decision (e.g., whether or not to participate in a study). See *GUIDANCE: Legally Authorized Representatives (Surrogate Consent) (HRP-013)*.

3.11 Case Report (also see "Limited Case Series"): A description (i.e., publication or presentation) of the clinical characteristics or treatment(s) provided to three or fewer patients that share a

common condition, which did not involve activities defined as research (i.e., without intent to form a research hypothesis, draw conclusions or generalize findings). See *GUIDANCE: Case Report or Limited Case Series (HRP-094)*.

3.12 Case Report Form (CRF): A printed, optical, or electronic document designed to record all of the protocol-required information to be reported to the clinical trials sponsor or entered into the research database for each clinical trial participant.

3.13 Case Study: An intensive, prospective, systematic investigation of a single individual, group, community, or some other unit in which the researcher examines in-depth data relating to several variables and involves the use of data that would not ordinarily be collected during treatment. This activity constitutes "research" and requires IRB approval prior to initiation. The intent is to publish or present the case study results.

3.14 Central Tendency: The single most representative value or typical value of a set of data and it is computed using a variety of measures that are each calculated differently.

3.15 Certificate of Confidentiality: Certificates of Confidentiality (Certificate or CoC) protect the privacy of research participants by prohibiting disclosure of identifiable, sensitive research information to anyone not connected to the research except when the participant consents or in a few other specific situations.

3.16 Certified Copy: A copy (irrespective of the type of media used) of the original record that has been verified (i.e., by a dated signature or by generation through a validated process) to have the same information, including data that describe the context, and structure, as the original.

3.17 Children: Children means under the following:

- Department of Health and Human Services (DHHS) and Food and Drug Administration (FDA): Persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in that the research will be conducted.
- California Law: The legal age for consent is generally 18, but there are important exceptions (see "Minors Who May Consent as Adults").

3.18 Clinical Research Coordinator (CRC): The CRC works under the supervision of the Principal Investigator (PI) and can serve as a designee across the continuum of the study.

3.19 Clinical Trial: 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.

3.20 Code of Federal Regulations (CFR): The United States code, which codifies the general and permanent rules and regulations published by the executive departments and agencies of the federal government of the U.S.

3.21 Coded Data: Replacing identifiable data/private information (e.g., name or social security number) with a 'code' (e.g., letters, symbols, or numbers) with the goal of protecting the subject.

3.22 Coded Samples: Biospecimens that are identified by a code or link to the subjects' identities rather than by a direct identifier such as a name or medical record number. These samples may also be called "linked." See *GUIDANCE: IRB Review of Research using Human Biological Materials (HRP-087)*.

3.23 Common Rule: The federal rules and regulations that outlines the basic provisions for IRBs, informed consent, and Assurances of Compliance. These regulations were codified in 1991 in the Department of Health and Human Services (DHHS) Policy for the Protection of Human Subjects (45 CFR 46). This policy is frequently called the "The Common Rule" because it has been adopted by all federal agencies and departments conducting or supporting human subjects' research.

- Pre-2018 Requirements (hereafter, "Pre-2018"): The Common Rule requirements through January 20, 2019.

- 2018 Requirements (hereafter, "2018"): The Common Rule was revised substantially in 2017, and institutions are expected to comply with the Revised Common Rule effective January 21, 2019. Also known as the "2018 Requirements" and the "2018 Rule."

3.24 Community: Individuals with a common issue or problem, individuals with a common interest, or individuals in a geographical area.

3.25 Community Based Participatory Research (CBPR): A partnership approach to research that equitably involves, for example, community members, organizational representatives, and researchers in all aspects of the research process and in which all partners contribute expertise and share decision making and ownership. The aim of CBPR is to increase knowledge and understanding of a given phenomenon and integrate the knowledge gained with interventions and policy and social change to improve the health and quality of life of community members.

3.26 Community Based Research (CBR): Research that is conducted in partnership with researchers and members of the community.

3.27 Compliance: Adherence to protocol specifications, good clinical practice (GCP), regulatory requirements, and IRB determinations. See *GUIDANCE: IRB Review of Promptly Reportable Information Items (HRP-024)* and *GUIDANCE: Prompt Reporting Requirements (HRP-027)*.

3.28 Concomitant Medications: Any prescribed or over-the-counter medications, folk and herbal treatments, vitamin supplements, and drugs or agents used on the street to alter body or mind function.

3.29 Confidentiality: Describes the protections taken to safeguard data/information obtained from subject.

3.30 Conflicting Interest: An individual involved in research review is automatically considered to have a conflicting interest when the individual or the individual's immediate family have any of the following:

- Involvement in the design, conduct, or reporting of the research.
- Ownership interest, stock options, or other ownership interest related to the research of any value exclusive of interests in publicly traded, diversified mutual funds.
- Compensation related to the research of any amount in the past year or of any amount expected in the next year, including compensation for costs directly related to conducting research.
- Proprietary interest related to the research including, but not limited to, a patent, trademark, copyright or licensing agreement.
- Any other reason for which the individual believes that he or she cannot be independent (including non-financial conflicts of interest).
- See *GUIDANCE: Financial Conflicts of Interests (HRP-055).*

3.31 Continuing Non-Compliance: A pattern of noncompliance that is likely to continue without intervention or failure to work with the IRB to resolve noncompliance. See *GUIDANCE: IRB Review of Promptly Reportable Information Items (HRP-024) and GUIDANCE: Prompt Reporting Requirements (HRP-027)*.

3.32 Continuing Review: Periodic re-review of a research study by the IRB to evaluate if risks to participants remain reasonable in relation to potential benefits, to evaluate if the study continues to meet regulatory criteria for approval of research, and institutional requirements. Continuing review shall be conducted at intervals appropriate to the degree of risk but not less than once per year. See *MANUAL: Investigator Guidance (HRP-101)* and *MANUAL: IRB Committee Member Guidance (HRP-102)*.

3.33 Controlled Substances Act (CSA): The CSA is the federal United States drug policy under which the manufacture, importation, possession, use and distribution of certain substances is regulated. See *POLICY: Investigational Drugs (43019.01)* and *GUIDANCE: Investigational Drugs and Biologics (HRP-096)*.

3.34 Corrective Action: An action usually required of the Principal Investigator, which is necessary to reduce the risk to the subjects and/or prevent a recurrence of the reported protocol deviation/violation. Examples of corrective actions include revision of the protocol and/or

consent form, re-consent of subjects, further training of study staff, or formal notification to the appropriate government oversight agencies. See *GUIDANCE: IRB Review of Reportable Information Items (HRP-024) and GUIDANCE: Prompt Reporting Requirements (HRP-027)*.

3.35 Coverage Analysis: Process to ensure compliant clinical research billing. A Coverage Analysis identifies all clinical items or services associated with a particular clinical trial, including identification of the financially accountable party, such as the trial sponsor, other funding source, patient, or a third-party payor. See *CHECKLIST: Coverage Analysis Required Documents (HRP-449)*

3.36 Covered Entity: An organization that has to comply with HIPAA. A Covered Entity is one of the following *(See 45 CFR 160.103 for further information)*:

- A Health Care Provider that includes doctors, clinics, psychologists, dentists, chiropractors, nursing homes, pharmacies; but only if they transmit any information in an electronic form in connection with a transaction for which HHS has adopted a standard.
- A Health Plan that includes Health Insurance Companies, HMOs, Company Health Plans, Government programs that pay for health care, such as Medicare, Medicaid, and the Military and Veterans healthcare programs.
- A Health Care Clearinghouse that includes entities that process non-standard health information they receive from another entity into a standard (i.e., standard electronic format or data content), or vice-versa.

3.37 Data and Safety Monitoring Board (DSMB) or Committee (DSMC): A committee (generally independent of the trial sponsor) of scientists, physicians, statisticians, and others that collect and analyze data during a clinical trial. The DSMB monitors adverse events and data to identify trends (such as an indication that one treatment is significantly better than another) that warrant study modification, termination, or notification to the subjects when information is obtained that might affect their willingness to continue. The National Institute of Health (NIH) requires that DSMBs oversee all Phase III clinical trials. The SHC IRB may require DSMB monitoring when the degree of risk is significant.

3.38 Data Manager: An individual who handles the data gathered during a study. Responsibilities may also involve managing data entry, database generation and/or maintenance. Compliance with regulations and protection and integrity of private information and study data.

3.39 Data Use Agreement: A written agreement meeting the requirements of 45 CFR 164.514(e)(4), pursuant to which a Health Insurance Portability and Accountability (HIPAA) Covered Entity may use or disclose a Limited Data Set for research purposes.

3.40 Deception: Deception is the intentional misleading of subjects or intentional withholding of information about the nature of a study. Deception limits the ability of subjects to provide truly 'informed consent'; however, it is sometimes necessary for certain types of behavioral research. Deception is often justified because humans act differently depending on circumstances, and full disclosure of study information may bias the results.

3.41 De-identified Data: Data is considered de-identified when unique identifiable information (e.g., name, address, social security number, telephone number, etc.) is removed from the data so that the subject/source cannot be re-identified.

3.42 Descriptive Statistics: Ways of summarizing and describing sets of data by using tables, graphs, measures of central tendency and measures of variability.

3.43 Designated Reviewer: The Institutional Review Board (IRB) member (chair or an experienced IRB member designated by the IRB chair) who conducts expedited (non-committee) reviews. See *GUIDANCE: Expedited Review Preparation (HRP-031)* and *GUIDANCE:* Expedited *Review Conduct (HRP-032)*.

3.44 Deviation: The term "protocol deviation" is not defined by either the U.S. Department of Health and Human Services (HHS) (45 CFR 46) or the FDA (21 CFR 50) human subjects regulations. For SHC IRB purposes, a protocol deviation is a departure from the IRB approved protocol made by the PI or research team. See *MANUAL: Investigator Guidance (HRP-101).*

3.45 Direct Access: Permission to examine, analyze, verify, and reproduce any records and reports that are important to evaluation of a clinical trial. Any party (e.g., domestic and foreign regulatory authorities, sponsor's monitors and auditors) with direct access should take all reasonable precautions within the constraints of the applicable regulatory requirement(s) to maintain the confidentiality of subjects' identities and sponsor's proprietary information.

3.46 Dispense: To prepare, label and provide drugs or biologics (including investigational drugs and biologics) to those who are to use them. See *POLICY: Investigational Drugs (43019.01)* and *GUIDANCE: Investigational Drugs and Biologics (HRP-096).*

3.47 Distribution: The receipt, storage and dispensing of drugs (including investigational drugs or biologics). See *POLICY: Investigational Drugs (43019.01*) and *GUIDANCE: Investigational Drugs and Biologics (HRP-096)*.

3.48 Distribution in Statistics: A set of numbers and their frequency of occurrence collected from measurements of a population/data. A distribution is a summary of the data by the number of observations in each category, value or interval.

3.49 Documentation: All records, in any form (including but not limited to written, electronic, magnetic and optical records; and scans, x-rays, and electrocardiograms) that describe or record the methods, conduct and/or results of a clinical trial, and the factors affecting a clinical trial and the actions taken.

3.50 Drug: Any chemical compound that may be used on or administered to humans as an aid in the diagnosis, treatment, cure, mitigation or prevention of disease or other abnormal condition. See *POLICY: Investigational Drugs (43019.01)* and *GUIDANCE: Investigational Drugs and Biologics (HRP-096).*

3.51 Drug Administration: The direct application of a drug to the body of a patient or research subject by injection, inhalation, ingestion or other means. See *POLICY: Investigational Drugs (43019.01)* and *GUIDANCE: Investigational Drugs and Biologics (HRP-096)*.

3.52 Drug Enforcement Agency (DEA): The United States Drug Enforcement Agency, a federal law enforcement agency charged with the responsibility of combating drug abuse and enforcing laws and regulations for drugs or medical devices. See *POLICY: Investigational Drugs (43019.01)* and *GUIDANCE: Investigational Drugs and Biologics (HRP-096)*.

3.53 Elective: Human Research Protection Program (HRPP) content that is for informational purposes and the document does not need to be completed or retained.

3.54 Electronic Investigator Site File (eISF): The computer system used to house Essential Documents required for the conduct of clinical research by the investigator.

3.55 Emergency Deviation: A deviation from the SHC IRB approved protocol that occurred in an emergency situation, such as when a departure from the protocol is required to protect the life or physical well-being of a participant. The sponsor and SHC IRB are to be notified as soon as possible, but not later than five days after the emergency situation occurred. See *FORM: Promptly Reportable Information (HRP-214)*.

3.56 Emergency Use: The use of an investigational drug or device on a human subject in accordance with a treatment/procedure in a life-threatening situation in which no comparable or standard acceptable treatment is available and the patient requires treatment before a written submission to the IRB can be made. See *GUIDANCE: Emergency Use Review (HRP-023)*.

3.57 Essential Documents: Those documents which individually and collectively permit evaluation of the conduct of a trial and the quality of the data produced. These documents serve to demonstrate the compliance of the investigator, sponsor and monitor with the standards of Good Clinical Practice and with all applicable regulatory requirements. Often referred to as regulatory documents.

3.58 Estimated Number of Subjects: The number of subjects the investigator wishes to enroll in a particular study. This number can change, depending on the stage and goal of the study. For example, a pilot study may have 5 subjects and a Phase III clinical trial may have 500 subjects.

3.59 Exempt Research: Certain kinds of research involving minimal or less than minimal risk may be "exempt" from IRB oversight when the activities fall into one or more of the exempt categories at 45 CFR 46.104. Investigators are not permitted to determine if their research is exempt. Investigators must submit proposed exempt research to the IRB for review and exempt determination.

3.60 Expanded Access: The use of an investigational drug, biologic, or medical device to treat a patient with a serious disease or condition when there is no comparable or satisfactory alternative treatment available.

3.61 Expedited Review (also known as Non-Committee Review): Federal regulations allow for an expedited review (one or more designated reviewers, outside of the convened meeting) for certain kinds of research involving no more than minimal risk, and minor changes to ongoing research. IRB Chairs and IRB Specialists are designated to conduct expedited reviews at SHC. See *GUIDANCE: Expedited Review Conduct (HRP-032)*.

3.62 Experienced IRB Member: An IRB member is considered experienced if the IRB chair considers the IRB member to have sufficient experience in and knowledge of conducting IRB reviews.

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

3.64 External Users: Users of the eISF who are not employees of Sharp HealthCare but are granted direct access to the eISF to fulfill their responsibilities as outlined by regulatory authorities, contract, and the HIPAA waivers in the capacity of sponsor or inspector.

3.65 Financial Conflict of Interest (FCOI): see Conflicting Interest above.

3.66 Finding of Non-Compliance: Non-compliance in fact. See *GUIDANCE: IRB Review of Reportable Information Items (HRP-024) and GUIDANCE: Prompt Reporting Requirements (HRP-027)*.

3.67 Food and Drug Administration (FDA): The United States Food and Drug Administration, a federal agency responsible for monitoring trading and safety standards in the food and drug industries.

3.68 Full Board Review: Research involving greater than minimal risk must be reviewed at a fully convened meeting, where a majority of the committee members is present.

3.69 Generalizable Knowledge: Refers to an activity that is designed to draw general conclusions, inform policy, or generalize findings beyond a single individual, an internal program, or an individual unit / hospital / institution.

3.70 Good Clinical Practice (GCP): An international quality standard that is provided by the International Conference on Harmonisation (ICH), an international body that defines 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 subjects are protected.

3.71 Guardian: An individual who is authorized under applicable State or local law (including tribal law passed by the official governing body of an American Indian or Alaska Native tribe) to consent on behalf of a child to general medical care.

- In California, a guardian may be either parent, if both parents have legal custody, the parent or person having legal custody, a court appointed guardian, or others as consistent with an order of a court having jurisdiction over the minor.
- A guardian has the authority to consent on behalf of a child to general medical care. This authority, however, is subject to restrictions.

3.72 Health Insurance Portability and Accountability Act (HIPAA): This act went into effect April 14, 2003. The law generally prohibits health care providers such as health care practitioners, hospitals, nursing facilities and clinics from using or disclosing protected health information without written authorization from the individual (HIPAA Authorization). It is often called the "Privacy Rule."

3.73 Human Research as Defined by DHHS:

- Pre-2018: A systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge, and involves Human Subjects as Defined by DHHS. Activities which meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program that is considered research for other purposes. For example, some demonstration and service programs may include research activities.
  - A systematic investigation is an activity that involves a prospective plan that incorporates data collection, either quantitative or qualitative, and data analysis to answer a question.
- 2018 to present: A systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. Activities that meet this definition constitute research for purposes of 45 CFR 46, whether or not they are conducted or supported under a program that is considered research for other purposes. For example, some demonstration and service programs may include research activities. See the definition of "Not Human Subjects Research (NHSR)" for activities that are not considered research.

3.74 Human Research as Defined by FDA: Any experiment that involves a test article or one or more human subjects, and that meets any one of the following:

- Must meet the requirements for prior submission to the FDA under section 505(i) of the Federal Food, Drug and Cosmetic Act meaning any use of a drug other than the use of an approved drug in the course of medical practice;
- Must meet the requirements for prior submission to the FDA under section 520(g) of the Federal Food, Drug and Cosmetic Act meaning any activity that evaluates the safety or effectiveness of a device; OR
- Any activity, the results of which are intended to be later submitted to, or held for inspection by, the FDA as part of an application for a research or marketing permit.

3.75 Human Subject as Defined by DHHS:

- Pre 2018: A living individual about whom an investigator (whether professional or student) conducting research obtains
  - Data through intervention or interaction with the individual, or
  - Information that is both Private Information and Identifiable Information.
- 2018: A living individual about whom an investigator (whether professional or student) conducting research:
  - Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or
  - Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens.

3.76 Human Subject as Defined by FDA: An individual who is or becomes a subject in research, either as a recipient of the test article or as a control. A subject may be either a healthy human or a patient. A human subject includes an individual on whose specimen a medical device is used.

3.77 Human Subjects Training: Human subjects training is required for research approval at many institutions, including SHC. Many funding agencies require key research personnel to complete educational modules relevant to their research as a condition of funding. The SHC Protecting Human Research Participants (PHRP) training is available via: https://sharp.cloud-cme.com/default.aspx?EID=10524&P=3000&CaseID=314%23.

3.78 Hybrid Rule Requirements: The "Hybrid Rule: follows the Revised Rule (2018), unless the Pre-2018 Rule is substantially less restrictive, in which case the Pre-2018 Rule is followed.

3.79 Identifiable Biospecimens: A biological sample for which the identity of the Human Subject is or may be readily be ascertained by the investigator or associated with the biospecimen. For example, a personal identifier (such as a name or medical record number) that allows

researchers to link the biological information derived from the research directly to the individual from whom the material was obtained. See *GUIDANCE: IRB Review of Research using Human Biological Materials (HRP-087)*.

3.80 Identifiable Private Information: Private Information for which the identity of the subject is or may readily be ascertained by the investigator or associated with the information.

3.81 Identifiable Sensitive Information: The National Institutes of Health (NIH) Certificate of Confidentiality (CoC) policy and 42 CFR 241(d) define identifiable, sensitive information as information that is about an individual and that is gathered or used during the course of research where the following may occur:

- Through which an individual is identified; or
- For which there is at least a very small risk, that some combination of the information, a request for the information, and other available data sources could be used to deduce the identify of an individual.

3.82 Immediate Family: Spouse, domestic partner; and dependent children.

3.83 Inferential Statistics: Statistical methods that are used to generalize from a sample of data to make inferences about a larger population.

3.84 Informed Consent: A person's voluntary agreement to participate in research, once they have understood the possible risks and benefits of participation. Consent may be written or oral in defined circumstances.

3.85 Informed Consent Form (ICF): A document delineating the purpose of the research with a description of the experimental procedures involved and the foreseeable risks and benefits to the subject. See *TEMPLATE: Informed Consent Document with California Bill of Rights (HRP-502), TEMPLATE: Consent – Emergency Use (HRP-506), TEMPLATE: Consent – Short Form (HRP- 507),* and *TEMPLATE: Consent Form for Case Report or Case Series (HRP-508)*.

3.86 Institutional Official (IO): At SHC, the Institutional Official (IO) is the Executive Vice President. The SHC IO is legally authorized to act for the institution, is responsible for ensuring that the HRPP functions effectively, and that the institution provides the resources and support necessary to comply with all requirements applicable to research involving human subjects.

3.87 Institutional Review Board (IRB): An independent committee comprised of at least five members from diverse disciplines and backgrounds relevant to the research being reviewed. At least one member must be unaffiliated with SHC. Members may include staff, nurses, physicians, pharmacists from SHC, and persons from the local San Diego community.

3.88 Institutional Review Board (IRB) of Record (also known as Central IRB): The IRB of Record assumes IRB responsibilities for oversight of research conducted at another organization, per 45 CFR 46 and/or 21 CFR 56. When the research is conducted or supported by any Federal department or agency, the Relying Organizations designate the IRB of Record on its Federalwide Assurance (FWA) with the Federal Office of Human Research Protection (OHRP). See *GUI - IRB of Record and Reliance Agreements (HRP-009)*, and definition for "Single IRB Process (sIRB)."

3.89 Interaction:

- Pre 2018: Communication or interpersonal contact between an investigator, designee and research participant.
- 2018: Communication or interpersonal contact between investigator and subject.

3.90 Intervention:

- Pre 2018: Physical procedures by which data are gathered (for example venipuncture) and manipulations of the participant or the participant's environment that are performed for research purposes.
- 2018: Both physical procedures by which information or biospecimens are gathered (e.g., venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.

3.91 International Conference on Harmonisation (ICH): The complete name of ICH is the "International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use." The objective of ICH is to increase international harmonisation of technical requirements to ensure that safe, effective, and high-quality medicines are developed and registered in the most efficient and cost-effective manner.

3.92 Investigational Device: A new, non-FDA approved medical device or procedure which is regulated as part of a research or clinical trial protocol, or an FDA-approved medical device which is being used for a new purpose. See *POLICY: Investigational Devices (16509)* and *GUIDANCE: Investigational Devices (HRP-095)*.

3.93 Investigational Device Exemption (IDE): An exemption issued by the FDA to allow the use of investigational devices in human subjects. The IDE permits use of the device in a clinical investigation to evaluate the safety and/or efficacy of the investigational device. See *POLICY: Investigational Devices (16509)* and *GUIDANCE: Investigational Devices (HRP-095)*.

3.94 Investigational Drug: A pharmaceutical form of an active ingredient being tested or used as a reference in a clinical trial. This includes drugs with a marketing authorization when used or assembled (formulated or packaged) in a way different from the approved form, or drugs used to gain further information about an approved use. See *POLICY: Investigational Drugs (43019.01)* and *GUIDANCE: Investigational Drugs and Biologics (HRP-096)*.

3.95 Investigational New Drug (IND) Application: Means by which permission may be obtained to 1) ship an investigational drug, biologic or agent across state lines and 2) use in humans prior to an FDA review of clinical data has determined a new drug, agent, or biologic is safe and effective for a specific use. Testing of an investigational drug may proceed once a valid IND is in effect or an IND exemption has been granted by the FDA. See *POLICY: Investigational Drugs (43019.01) and GUIDANCE: Investigational Drugs and Biologics (HRP-096)*.

3.96 Investigational Product (IP) (also known as "Test Article"): Any drug, biological product or medical device for human use in a clinical trial. See *POLICY: Investigational Drugs (43019.01)*; *GUIDANCE: Investigational Drugs and Biologics (HRP-096); POLICY: Investigational Devices (16509);* and *GUIDANCE: Investigational Devices (HRP-095)*.

3.97 Investigator (also known as "Researcher" or "Research Team Member"): The Investigator is the person responsible for the conduct of the research. If the research is conducted by a team of individuals, the Principal Investigator (PI) is the responsible leader of the team.

3.98 Investigator-Initiated: A research activity or project initiated and conducted by a Sponsor-Investigator.

3.99 Investigator Site File (ISF): The investigator site file includes all Essential Documents which individually and collectively permit evaluation of the conduct of a trial and the quality of the data produced by the investigator. These documents serve to demonstrate the compliance of the investigator with the standards of Good Clinical Practice and with all applicable regulatory requirements. The ISF does not include the full scope of Trial Master File documents which apply to the sponsor role in research.

3.100 Key Personnel: These are individuals involved with a research project who include but are not limited to: Principal Investigators (PIs), Sub-Investigators, study coordinators, regulatory specialists, recruiters, and anyone else performing study procedures and interventions.

3.101 Legally Authorized Representative (LAR):

- Pre 2018: An individual or judicial, or other body authorized under applicable law to grant permission on behalf of a prospective subject for their participation in research activities.
- 2018: 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. If there is no applicable law addressing this issue, legally authorized representative means an individual recognized by institutional policy as acceptable for providing consent in the non-research context on behalf of the prospective subject to the subject's participation in the procedure(s) involved in the research. See *GUIDANCE: Legally Authorized Representatives (Surrogate Consent) (HRP-013).*

3.102 Limited Case Series: A description (i.e., publication or presentation) of the clinical characteristics or treatment(s) provided to four or more patients that share a common condition. This activity constitutes "research". See *GUIDANCE: Case Report or Limited Case Series (HRP-094)*.

3.103 Limited Data Set (LDS): As defined in 45 CFR 164.514(e)(2), Protected Health Information that excludes the following direct identifiers of the individual or relatives, employers, or household members of the individual: name; postal address information, other than town or city, state and zip code; telephone numbers; fax numbers; electronic mail addresses; social security numbers; medical record numbers; health plan beneficiary numbers; account numbers; certificate/license numbers; vehicle identifiers and serial numbers; device identifiers and serial numbers; web Universal Resource Locators (URLs); internet protocol (IP) address numbers; biometric identifiers, including finger and voice prints; and full face photographic images and any comparable images. An LDS may contain, for example: dates of birth, dates of death; dates of service; town or city; state; or zip code or any combination of only those elements.

3.104 Limited IRB Review: For certain research activities to be exempt from 45 CFR 46 requirements, a Limited IRB Review is required to ensure that there are adequate privacy safeguards for identifiable private information and identifiable biospecimens in the proposed research. This review process may be conducted via non-committee review (i.e., one or more IRB members).

3.105 Local Context (also known as "Local Considerations"): Requirements of any applicable state or local laws (including tribal law passed by the official governing body of an American Indian or Alaska Native tribe), regulations, institutional policies, standards or other local factors, including local ancillary reviews, relevant to an instance of research.

3.106 Long-Term Follow-Up: Includes research interactions that involve no more than minimal risk to subjects (e.g., quality of life surveys) and/or collection of follow-up data from procedures or interventions that would have been done as part of routine clinical practice to monitor a subject for disease progression or recurrence, regardless of whether the procedures or interventions are described in the research protocol.

3.107 Mean: The mean is defined by adding up all the values for a given variable and then dividing the sum by the number of values included. The mean is one type of measure of central tendency.

3.108 Median: The median literally is the value in the middle of a set of values. The median is defined by lining up the values, from largest to smallest. The one in the dead-center is the median. The median is one type of measure of central tendency.

3.109 Medical Experiment (per California Health and Safety Code 24178):

- The severance or penetration or damaging of tissues of a human subject or the use of a drug or device, electromagnetic radiation, heat or cold, or a biological substance or organism, in or upon a human subject in the practice or research of medicine in a manner not reasonably related to maintaining or improving the health of the subject or otherwise directly benefiting the subject; or
- The investigational use of a drug or device; or
- Withholding medical treatment from a human subject for any purpose other than maintenance or improvement of the health of the subject; and
- The medical experiments relate to the cognitive impairment, lack of capacity or serious or life-threatening diseases and conditions of research participants.

3.110 Minimal Risk: A risk is minimal when the probability of magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in the participant's daily life or during the performance of routine physical or psychological examinations or tests.

- For research involving prisoners, the definition of minimal risk refers to the probability and magnitude of physical or psychological harm that is normally encountered in the daily lives, or in the routine medical, dental or psychological examination of healthy persons.

3.111 Minor: A person less than 18 years of age, whether or not they meet the federal definition for a "child."

- Minors Who May Consent as Adults: In California, certain people under 18 years of age are legally able to consent for treatments or procedures involved in research, such as "Emancipated" or "Self-Sufficient," and certain "Un-emancipated" Minors.

3.112 Minor Modification: Does not materially affect an assessment of the risks and benefits of the study and does not substantially change the specific aims/design of the study.

3.113 Mode: This statistic tells the value that appears the most often for a given variable. It is possible to have more than one mode, and it is possible to have no mode. The mode is one type of measure of central tendency.

3.114 Monitor: A monitor is a type of research auditor, usually employed by the drug/device sponsor, who ensures that research protocols are being followed and documented appropriately. Monitors visit research sites regularly to inspect study documents and medical records and to validate research data.

3.115 Multi-Center Research: A research study conducted at more than one institution (nationally and/or internationally) using the same protocol, each with its own Principal Investigator. Many clinical trials involving drugs/biologics/devices are conducted at more than one center. Also referred to as Multi-Site Study.

3.116 Multi-Site Study (also known as Multi-Center Research): A study that uses the same protocol to conduct non-exempt human subjects' research at more than one site.

- Protocols that address the same research questions, involve the same methodologies, and evaluate the same outcomes are considered to be the "same research protocol." Sites that are accruing research participants for studies that are identical except for variations due to local context consideration would be considered to be conducting the "same research protocol".
- If a study is conducted or supported by any Federal department or agency and involves a separate site for study coordination or coordination of data and statistical analyses and the site is conducting the same protocol as the other participating sites, then all sites would be expected to rely on the designated IRB of Record. The Relying Organizations designate the IRB of Record on its Federalwide Assurance (FWA) with the Federal Office of Human Research Protection (OHRP).

3.117 National Science Foundation (NSF): The NSF is an independent federal agency created by Congress in 1950 "to promote the progress of science; to advance the national health, prosperity, and welfare; to secure the national defense..." NSF is vital because we support basic research and people to create knowledge that transforms the future.

3.118 No Action Indicated (NAI): A classification designated by the FDA after an inspection, which means no objectionable conditions or practices were found during the inspection (or the objectionable conditions found do not justify further regulatory action).

3.119 Non-compliance: Failure to follow the regulations or the requirements or determinations of the IRB.

3.120 Non-Significant Risk (NSR) Device: An investigational device that does not meet the definition of a significant risk device. See *POLICY: Investigational Devices (16509)* and *GUIDANCE: Investigational Devices (HRP-095).*

3.121 Normalizing/Standardizing/Transforming Data: Accurate interpretation of many statistical tests is difficult if a dataset fails to satisfy important assumptions about the data. Adjustment for such violations may be achieved by normalizing/standardizing/transforming a dataset by mathematical means.

3.122 Normative/Normed Data: Data points of a second data set are placed relative to the original data obtained from a large sample for the purpose of comparison. The originally collected sample is typically referred to as the norm group because it is the group upon which the new group's data is compared.

3.123 Not Human Subjects Research (NHSR): An activity that does not meet the definition of "Human Research." Investigators are not permitted to determine if their research is NHSR. Investigators must submit proposed NHSR to the IRB for review and determination. The following activities are deemed not to be "Research as Defined by DHHS":

- Scholarly and journalistic activities (e.g., oral history, journalism, biography, literary criticism, legal research, and historical scholarship), including the collection and use of information, that focus directly on the specific individuals about whom the information is collected.
- Public health surveillance activities, including the collection and testing of information or biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health authority. Such activities are limited to those necessary to allow a public health authority to identify, monitor, assess, or investigate potential public health signals, onsets of disease outbreaks, or conditions of public health importance (including trends, signals, risk factors, patterns in diseases, or increases in injuries from using consumer products). Such activities include those associated with providing timely situational awareness and priority setting during the course of an event or crisis that threatens public health (including natural or man-made disasters).
- Collection and analysis of information, biospecimens, or records by or for a criminal justice agency for activities authorized by law or court order solely for criminal justice or criminal investigative purposes. See *GUIDANCE: Repositories - Banking of Specimens and Data (HRP-086).*
- Authorized operational activities (as determined by each agency) in support of intelligence, homeland security, defense, or other national security missions.

3.124 Official Action Indicated (OAI): A classification designated by the FDA after an inspection, which means regulatory and/or administrative actions will be recommended.

3.125 Original Medical Record: See "Source Documents."

3.126 Outcomes Research: Studies that aim to identify and evaluate effective care processes that improve the quality of patients' lives. See *GUIDANCE: Conducting Outcomes Research at Sharp HealthCare's Outcomes Research Institute (HRP-097)*.

3.127 Participant (also known as subject): See Human Subject as identified by DHHS and Human Subject as identified by FDA in definitions above.

3.128 Physician Extender: A health care provider who is not a physician but who performs medical activities typically performed by a physician. It is most commonly a nurse practitioner or physician assistant.

3.129 Planned Emergency Research: Research involving human subjects who are in need of emergency medical intervention (e.g., comparison of methods for providing cardiopulmonary resuscitation), but who cannot give informed consent because of their life-threatening medical conditions and who do not have an available legally authorized representative.

3.130 Principal Investigator: The investigator is the person responsible for the conduct of the clinical trial. If the clinical trial is conducted by a team of individuals, the principal investigator is the responsible leader of the team.

3.131 Prisoner: Any individual involuntarily confined or detained in a penal institution. The term is intended to encompass individuals sentenced to such an institution under a criminal or civil statute, individuals detained in other facilities by virtue of statutes or commitment procedures which provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing (45 CFR 46.303(c)).

3.132 Prisoner Representative: An individual who is currently or formerly a prisoner or an individual who has a close working knowledge, understanding and appreciation of prison conditions from the perspective of the prisoner (e.g., prison chaplain, prison social worker, prison health care worker).

3.133 Privacy: Privacy refers to the subject and their interest in controlling access of others to themselves. For example, based on their privacy interests, people want to control:

- The time and place where they give information.

- The nature of the information they give.
- The nature of the experiences that are given to them.
- Who receives and can use the information.

3.134 Privacy Board: A review body that may be established to act upon requests for a waiver or an alteration of the Authorization requirement under the Privacy Rule for uses and disclosures of protected health information (PHI) for a research study.

- If a multi-site project also requires a privacy review under the Health Insurance Portability and Accountability Act of 1996 (HIPAA), it may be appropriate for the IRB of Record to serve as the Privacy Board.
- A Privacy Board may waive or alter all or part of the Authorization requirements for a specified research project or protocol. A covered entity may use and disclose PHI, without an Authorization, or with an altered Authorization, if it receives the proper documentation of approval of such alteration or waiver from a Privacy Board.

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

3.136 Profile Documents: Documents for people or organizations which are study agnostic or can be used across multiple studies. Examples include medical licenses, IRB rosters, lab normal ranges.

3.137 Promptly Reportable Information: Any incident, event, or outcome that investigators must promptly report to the IRB per *GUIDANCE: Prompt Reporting Requirements (HRP-027)*, which includes but is not limited to protocol deviations, violations, other incidences of non-compliance, and unanticipated problems. See *GUIDANCE: IRB Review of Reportable Information Items (HRP-024)*, *GUIDANCE: Prompt Reporting Requirements (HRP-027)*, *GUIDANCE: Research Misconduct (HRP-003),* and *FORM: Promptly Reportable Information (HRP-214)*.

3.138 Protected Health Information (PHI) / Personally Identifiable Information (PII): PHI/PII is any information about health status, provision of health care, or payment for health care that can be linked to a specific individual. The HIPAA Privacy Rule permits the use and disclosure of PHI if certain standards are met and the individual signs a PHI Authorization Form.

3.139 Protocol: The formal design of an experiment or research activity. The protocol includes a description of the research methodology, the eligibility requirements for prospective subjects and controls, the treatment regime(s), and the proposed methods of analysis that will be performed on the collected data.

3.140 Protocol Violation: A failure to comply with the study protocol as approved by the SHC IRB. A violation is a serious non-compliance with the protocol that can result in the exclusion of a subject or their results in the study and in some cases a charge of research misconduct. See *GUIDANCE: IRB Review of Reportable Information Items (HRP-024)*, *GUIDANCE: Prompt Reporting Requirements (HRP-027)*, *GUIDANCE: Research Misconduct (HRP-003)* and *FORM: Promptly Reportable Information (HRP-214)* for reporting requirements.

3.141 Public Health Authority: An agency or authority of the United States, a state, a territory, a political subdivision of a state or territory, an Indian tribe, or a foreign government, or a person or entity acting under a grant of authority from or contract with such public agency, including the employees or agents of such public agency or its contractors or persons or entities to whom it has granted authority, that is responsible for public health matters as part of its official mandate (45 CFR 46.102(k)).

3.142 Public Health Service (PHS): The part of the Department of Health and Human Services (HHS) that is responsible for the public health of the US population. Abbreviated USPHS. USPHS administers a number of important health agencies, including the Food and Drug Administration (FDA), the Centers for Disease Control and Prevention (CDC), and the National Institutes of Health (NIH).

3.143 Radiation Safety Officer (RSO): The person within an organization responsible for the safe use of radiation and radioactive materials as well as regulatory compliance. The State of California Department of Health must approve the facility Radiation Safety Officer in writing.

3.144 Range: The range is the mathematical difference between the highest and lowest values for a given variable. It is the simplest measure of variability to calculate but it depends only on the extreme values in the data set and does not use all of the data. The range is one type of measure of variability.

3.145 Regulatory Specialist: The individual responsible for completing the IRB and sponsor regulatory paperwork.

3.146 Reliance Agreement: A formal, written agreement in which the reviewing IRB agrees to serve as the IRB of Record for a Relying Organization. The agreement documents the respective authorities, roles, responsibilities, and communication between an institution/organization providing the ethical review and a participating site relying on the IRB of Record. The agreement satisfies the specific responsibilities of the IRB of Record in satisfying the requirements of 45 CFR 46 and 21 CFR 50, 56. In NIH sponsored research, the coordinating center/awardee is responsible for ensuring Reliance Agreements are in place, and that documentation is maintained. See *TEMPLATE AGREEMENT: IRB Authorization Reliance Agreement (HRP-574).*

- Commonly used Reliance Agreements for organizations include:
  - Memoranda of Understanding (MOU)
  - IRB Authorization Agreements (IRBAA)
  - Master Reliance Agreement (MRA)
  - Collaborative Review Agreement (CRA)

3.147 Relying Organization: The domestic entity in a single or multi-site study that will rely on the IRB of Record to carry out the site's initial and continuing IRB review of human subjects' research for the single or multi-site study. A relying organization has entered into a Reliance Agreement with another organization's IRB.

3.148 Required: HRPP content is requisite information, and the document must be completed and filed appropriately.

3.149 Research: See "Human Research."

3.150 Research Misconduct: Fabrication, falsification, or plagiarism in proposing, performing, or reviewing research, or in reporting research results. Research Misconduct does not include honest error or difference in opinion. See *GUIDANCE: Research Misconduct (HRP-003)*.

- "Fabrication" is making up data or results and recording or reporting them.
- "Falsification" is manipulating research materials, equipment, or processes, or changing or omitting data or results such that the research is not accurately represented in the research record.
- "Plagiarism" is the appropriation of another person's ideas, processes, results, or words without giving appropriate credit.

3.151 Research Records: See "Source Documents."

3.152 Research/Subject Advocate: Individuals who work with research subjects and promote subject rights. Their range of activities can vary. Some advocates may help subjects make an informed decision about research participation by explaining possible risks and benefits.

3.153 Restricted: Investigators who have continuing non-compliance and serious non-compliance concerns or complaints brought against them by the IRB or others may be restricted. See *GUIDANCE: IRB Review of Reportable Information Items (HRP-024)* for a list of possible restrictions.

3.154 Sample Size: The number of subjects participating in the research, typically denoted *N* or *n* in research literature. Generally, different sample sizes lead to different accuracies of measurement.

3.155 Secondary Research Use: Re-using identifiable and non-identifiable information and biospecimens for research purposes that are collected for some other "primary" or "initial" activity.

3.156 Serious Adverse Event (SAE): An undesirable experience associated with the use of a medical product in a patient. The event is serious and should be reported to the FDA and the SHC IRB when the patient outcome is; death, life-threatening, requires initial or prolonged hospitalization, disability or permanent damage, congenital anomaly/birth defect, required intervention to prevent permanent impairment or damage (devices) or other serious medical events (e.g. drug dependence). See *GUIDANCE: IRB Review of Reportable Information Items (HRP-024)*, *GUIDANCE: Prompt Reporting Requirements (HRP-027)*, and *FORM: Promptly Reportable Information (HRP-214)* for reporting requirements.

3.157 Serious Non-Compliance: Noncompliance that may materially adversely affect the rights and welfare of subjects. See *GUIDANCE: IRB Review of Reportable Information Items (HRP-024)*, *GUIDANCE: Prompt Reporting Requirements (HRP-027)*, and *FORM: Promptly Reportable Information (HRP-214)* for reporting requirements.

3.158 Significant-Risk (SR) Device: An investigational device that:

- Is intended as an implant and presents a potential for serious risk to the health, safety or welfare of a subject;
- Is purported or represented to be for use supporting or sustaining human life and presents a potential for serious risk to the health, safety or welfare of a subject;
- Is for a use of substantial importance in diagnosing, curing, mitigating or treating disease or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety or welfare of a subject; or
- Otherwise presents a potential for serious risk to the health, safety or welfare of a subject. See *POLICY: Investigational Devices (16509)* and *GUIDANCE: Investigational Devices (HRP-095)*.

3.159 Single IRB Process (sIRB): Institutions participating in federally funded cooperative research (involving more than one institution) must rely upon approval by a single IRB for the portion of research that is conducted in the U.S. (45 CFR 46.114). While participating institutions are expected to rely on the single IRB, they may conduct their own review in accordance with NIH policy on exceptions from single IRB review. See definition for "Institutional Review Board (IRB) of Record."

3.160 Source Data: All information in original records or certified copies of original records of clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial. Source data are contained in source document (original records or certified copies) and serve to verify the research record.

3.161 Source Documents (also known as "Original Medical Records" or "Research Records"): Original documents, data and records, including; hospital records, clinical and office charts, laboratory notes, memoranda, subjects diaries or questionnaires, evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate and complete, microfiches, photographic negatives, microfilm or magnetic media, x-rays, subject files and records kept at the pharmacy, laboratories and at medico-technical departments involved in conducting the clinical trial. See *GUIDANCE: Source Document Certification (HRP-078).*

3.162 Sponsor: The entity (e.g., pharmaceutical manufacturer) or individual who initiates the clinical trial and is responsible for registering the clinical investigation and submitting clinical trial information to the Clinical Trial Registry Data Bank (www.clinicaltrials.gov). *See GUIDANCE: Clinicaltrials.gov Registration for SHC-Initiated Clinical Trials (HRP-048)*.

3.163 Sponsored/Funded Research: Sponsored or funded research is research that is financially supported by an outside entity. The funding may come from a pharmaceutical company, a foundation, a donor or the government.

3.164 Sponsor-Investigator**:** An individual who both initiates and conducts an investigation, and under whose immediate direction a test article is administered or dispensed, or under whose immediate direction investigational procedures are carried out.

3.165 Standard Deviation: Indicates how tightly all the various data points are clustered around the mean in a set of data. When the data points are tightly bunched together around the mean, the standard deviation is typically small. When the data points are spread apart around the mean, this tells you that you have a relatively large standard deviation. The standard deviation is defined as the square root of the variance. Standard deviation is one type of measure of variability.

3.166 Statistical Significance: Used to assess the probability or error in a study's findings. Tests of statistical significance allow researchers to determine the probability of the results occurring by chance alone. Typically, as the probability level decreases, confidence increases that the results are not due to chance but due to the intervention.

3.167 Subject (also known as "Participant"): See "Human Subject as Defined by DHHS" and "Human Subject as Defined by FDA."

3.168 Subject Identification Code: A unique identifier code that is assigned by the sponsor, investigator or designee to each research subject (participant) to protect the subject's identity and confidentiality in the research file. The Subject Identification Code is used in lieu of the subject's name when the investigator reports adverse events and/or other trial-related data, and on all research documents that go to the sponsor, or outside of SHC.

3.169 Surrogate Consent: The use of a legally authorized representative with reasonable knowledge of the research subject, who shall include any of the persons and/or in descending order of priority, described under California law (Health and Safety Code 24178). See *GUIDANCE: Legally Authorized Representatives (Surrogate Consent) (HRP-013)*

3.170 Suspension of IRB Approval: An action of the IRB, the IRB Chair or Vice Chair, IRB Specialist, the 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. See *GUIDANCE: Suspension or Termination of IRB Approval by Other than the Convened IRB (HRP-026)*

3.171 Systematic Investigation: An activity that involves a prospective plan that incorporates data collection, either quantitative or qualitative, and data analysis to answer a question.

3.172 Termination of IRB Approval: An action of the IRB, Institutional Official or Institutional Official designee to permanently withdraw IRB approval of all research procedures. Terminated studies are permanently closed and no longer need continuing review. See *GUIDANCE: Suspension or Termination of IRB Approval by Other than the Convened IRB (HRP-026)*

3.173 Test Article: See "Investigational Product (IP)."

3.174 Therapeutic Intent: Trials with therapeutic intent must have an objective/aim that assesses the effects of the intervention on patient outcome (i.e., prolongation of life, shrinkage of tumor or improvements in quality of life) and must not be exclusively designed to test toxicity or disease pathophysiology.

3.175 Unanticipated Adverse Device Effect (UADE): Any serious adverse effect on health or safety or 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 investigational plan, or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects. See *FORM: Promptly Reportable Information (HRP-214)*

3.176 Unanticipated Problem: Incident, experience, or outcome that is unanticipated; and related or possibly related to the research; and suggests that the research places the subject or others at increased risk for harm (physical, psychological, criminal or civil liability, damaging to the subject's financial standing, employability, or reputation). *See FORM: Promptly Reportable Information (HRP-214)*

3.177 Unexpected Adverse Drug Experience (also known as "Unanticipated Adverse Drug Event" or "Unanticipated Adverse Drug Reaction"): Any adverse drug experience, the specificity or severity of which is not consistent with the current investigator brochure; or if an investigator brochure is not required or available, the specificity or severity of which is not consistent with the risk information described in the general investigational plan. Unexpected, as used in this definition, refers to an adverse drug experience that has not been previously observed, (e.g., included in the investigator brochure), rather than from the perspective of such experience not anticipated from the pharmacological properties of the pharmaceutical product. See *FORM: Promptly Reportable Information (HRP-214)*

3.178 Unidentified Biospecimens: Biological samples where identifiable personal information is not collected and cannot be retrieved by the investigator. These samples may also be called "anonymous." See *GUIDANCE: IRB Review of Research using Human Biological Materials (HRP-087)*

3.179 Unlinked Biospecimens: Biological samples from which the identifiers are removed and no code or link to the subjects' identities exists. These samples may also be called "anonymized." See *GUIDANCE: IRB Review of Research using Human Biological Materials (HRP-087)*

3.180 Validation of Computer Systems: A process of establishing and documenting that the specified requirements of a computerized system can be consistently fulfilled from design until decommissioning of the system or transition to a new system. The approach to validation should be based on a risk assessment that takes into consideration the intended use of the system and the potential of the system to affect human subject protection and reliability of trial results.

3.181 Variability: This term refers to how spread out the values in a distribution are and it is computed using a variety of measures that are each calculated differently. The greater the spread a dataset displays, the greater variability that dataset shows.

3.182 Variance: A statistic used to define how close values in a distribution are to the middle of the distribution. The mean, median or mode of a distribution may be used as an indication of the middle of the distribution. The variance is defined as the average squared difference of the scores from the measure of central tendency. The variance is one type of measure of variability.

3.183 Voluntary Action Indicated (VAI): A classification designated by the FDA after an inspection, which means objectionable conditions or practices were found but the agency is not prepared to take or recommend any administrative or regulatory action.

3.184 Vulnerable Subjects: 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. 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. Other vulnerable subjects include patients with incurable diseases, persons in nursing homes, unemployed or impoverished persons, patients in emergency situations, ethnic minority groups, homeless persons, nomads, refugees, minors, and those incapable of giving consent.

3.185 Ward: As defined by FDA, a child who is placed in the legal custody of the State or other agency, institution, or entity, consistent with applicable Federal, State, or local law (including tribal law passed by the official governing body of an American Indian or Alaska Native tribe).

3.186 Written, or, in writing: Refers to writing on a tangible medium (e.g., paper) or in an electronic format.

4 RESPONSIBILITIES

4.1 Individuals using policies and procedures are to consult this guidance for the definitions of underlined terms.

5 PROCEDURE

5.1 None.

6 MATERIALS

6.1 None.

7 REFERENCES

7.1 45 CFR §46, §164

7.2 21 CFR §50, §56, §312, §812

7.3 California Health and Safety Code 24178

7.4 E6(R2) Good Clinical Practice: Integrated Addendum to ICH E6(R1) Guidance for Industry

7.5 Federal Food, Drug and Cosmetic Act, Chapter V: Drugs and Devices, Sec. 505(i) & 520(g)

This document is available on www.sharp.com/research, IRBANA or by contacting research@sharp.com.