1 PURPOSE

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

2 REVISION FROM PREVIOUS VERSION

2.1 None.

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 associated with the use of a drug in humans, whether or not considered drug related. An adverse event can arise from any use of the drug (e.g., off-label use, in combination with another drug) and from any route of administration, formulation, or dose, including an overdose.

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: Non-Compliance and other Reportable Unanticipated Problems Involving Risks to Subjects or Others (HRP-024)*.

3.5 Assent: A child's affirmative agreement to participate in research. Mere failure to object is not the same as assent.

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

3.7 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 representatives sign and date this document in addition to providing their signature on the informed consent.

3.8 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)*.

3.9 Case Report (also called Limited Case Series): A description of the clinical characteristics or treatment(s) provided to a single patient or a small group of patients that share a common condition, which did not involve activities defined as research. See *GUIDANCE: Case Reporting Using Existing Data (HRP-094)*.

3.10 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.

3.11 Children: Children means under the following:

3.11.1 DHHS and 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 which the research will be conducted.

3.11.2 California Law: The legal age for consent is generally 18, but there are important exceptions (see Minors who may consent as Adults).

3.12 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.

3.13 Clinical Trial: A biomedical or behavioral research study of human subjects designed to answer specific questions about diagnostic procedures or therapeutic interventions (drugs, treatments, devices, or new ways of using known drugs, treatments, or devices). Clinical trials are used to determine whether new diagnostic procedures or therapeutic interventions are safe, efficacious and effective.

3.14 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.

3.15 Coded Samples: Biological samples 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)*.

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

3.17 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.

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

3.19 Compliance: Adherence to protocol specifications, good clinical practice (GCP) and regulatory requirements. See *GUIDANCE: Non-Compliance and Other Reportable Unanticipated Problems Involving Risks to Subjects or Others (HRP-024)*.

3.20 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.

3.21 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)*.

3.22 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:

- 3.22.1 Involvement in the design, conduct, or reporting of the research.
- 3.22.2 Ownership interest, stock options, or other ownership interest related to the research of any value exclusive of interests in publicly-traded, diversified mutual funds.
- 3.22.3 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.
- 3.22.4 Proprietary interest related to the research including, but not limited to, a patent, trademark, copyright or licensing agreement.
- 3.22.5 Any other reason for which the individual believes that he or she cannot be independent.
- 3.22.6 See *GUIDANCE: Financial Conflicts of Interests (HRP-055).*

3.23 Continuing Non-Compliance: A pattern of non-compliance that suggests the likelihood that, without intervention, instances of non-compliance will recur, a repeated unwillingness to comply, or a persistent lack of knowledge of how to comply. See *GUIDANCE: Non-Compliance and Other Reportable Unanticipated Problems Involving Risks to Subjects or Others (HRP-024)*.

3.24 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: Non-Compliance and Other Reportable Unanticipated Problems Involving Risks to Subjects or Others (HRP-024)*.

3.25 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)*:

3.25.1 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.

3.25.2 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.

3.25.3 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.

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

3.27 Deviation: The term "protocol deviation" is not defined by either the HHS (45 CFR 46) or the FDA (21 CFR 50) human subjects regulations. For SHC IRB purposes, a protocol deviation is a minor or administrative departure from the SHC IRB approved protocol made by the PI or site personnel without prior IRB approval that does not affect the study plan or the rights, safety or welfare of human subjects. See *FORM: Deviation Summary Sheet (HRP-225)*.

3.28 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).*

3.29 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)*.

3.30 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.

3.31 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).*

3.32 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)*.

3.33 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)*.

3.34 Elective: HRPP content is for informational purposes and the document does not need to be completed or retained.

3.35 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: Unanticipated Problem or Event Report (HRP-214)*.

3.36 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. See *GUIDANCE: Emergency Use Review (HRP-023)*.

3.37 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.

3.38 Experimental Subject's Bill of Rights: The California Research Subjects' Bill of Rights should be present at the onset of the consenting process before every California subject participating in the research signs the informed consent form. It is the policy of Sharp HealthCare that all research subjects or their representatives sign and date this document in addition to providing their signature on the informed consent.

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

3.40 Finding of Non-Compliance: Non-compliance in fact. See *GUIDANCE: Non-Compliance and Other Reportable Unanticipated Problems Involving Risks to Subjects or Others (HRP-024)*.

3.41 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.

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

3.42.1 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.

3.42.2 A guardian has the authority to consent on behalf of a child to general medical care. This authority, however, is subject to restrictions.

3.43 Good Clinical Practice (GCP): An international quality standard that is provided by the International Conference on Harmonisation (ICH), an international body that defines standards, which governments can transpose into regulations for clinical trials involving human subjects. These include the protection of human rights as a subject in a clinical trial. They also provide assurance of the safety and efficacy of newly developed investigational drugs and include standards for the design, conduct, performance, monitoring, auditing, recording, analysis and reporting of clinical trials or studies.

3.44 Human Research: Any activity that either:

3.44.1 Is research as defined by Department of Health and Human Services (DHHS) and involves human subjects as defined by DHHS; "a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge."

3.44.1.1 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.

3.44.1.2 Investigations designed to contribute to generalizable knowledge are those designed to draw general conclusions, inform policy, or generalize findings beyond a single individual or an internal program (e.g., publications or policy).

3.44.2 Is research as defined by the U.S. Food and Drug Administration (FDA) and involves human subjects as defined by the FDA, "any experiment that involves a test article or one or more human subjects, and that meets any one of the following:

3.44.2.1 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;

3.44.2.2 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

3.44.2.3 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. "

3.45 Human Subject as Defined by DHHS: A living individual about whom an investigator (whether professional or student) conducting research obtains

3.45.1 Data through intervention or interaction with the individual, or

3.45.2 Information that is both Private Information and Identifiable Information.

For the purpose of this definition:

3.45.2.1 Intervention: 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.

3.45.2.2 Interaction: Communication or interpersonal contact between investigator and subject.

3.45.2.3 Private Information: Information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information 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).

3.45.2.4 Identifiable Information: Information that is individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information).

3.46 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.

3.47 Identifiable Information: Information that is individually identifiable (i.e., the identity of the research participant is or may readily be ascertained by the investigator or associated with the information).

3.48 Identified Biological Samples: Specimens with 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)*.

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

3.50 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 (HRP-508)*.

3.51 Institutional Official (also known as Organization Official): At SHC, the Institutional Official is the Executive Vice President.

3.52 Interaction: Communication or interpersonal contact between an investigator, designee and research participant.

3.53 Intervention: 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.

3.54 Investigational Device: A new, non-FDA approved medical device or procedure which is regulated as part of a research or clinical trials 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)*.

3.55 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)*.

3.56 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)*.

3.57 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)*.

3.58 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)*.

3.59 Investigator (also known as researcher): 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.

3.60 Investigator-Initiated (also known as sponsor-investigator): An individual who both initiates and conducts an investigation, and under whose immediate direction the investigational drug is administered or dispensed.

3.61 Legally Authorized Representative (LAR): 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. See *GUIDANCE: Legally Authorized Representatives (Surrogate Consent) (HRP-013)*.

3.62 Limited Case Series (also called Case Report): A description of the clinical characteristics or treatment(s) provided to a single patient or a small group of patients that share a common condition, which did not involve activities defined as research. See *GUIDANCE: Case Reporting Using Existing Data (HRP-094)*.

3.63 Minor: A person less than 18 years of age, whether or not they meet the federal definition for a "child." In California, certain people under 18 years of age are legally able to consent for treatments or procedures involved in research, such as "Emancipated", "Self-Sufficient," and certain "Un-emancipated" Minors.

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

3.64.1 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

3.64.2 The investigational use of a drug or device; or

3.64.3 Withholding medical treatment from a human subject for any purpose other than maintenance or improvement of the health of the subject; and

3.64.4 The medical experiments relate to the cognitive impairment, lack of capacity or serious or life threatening diseases and conditions of research participants.

3.65 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. Non-compliance: Any action or activity associated with the conduct or oversight of research involving human participants that fails to comply with either the research plan as approved by the SHC IRB, or federal regulations or SHC institutional policies governing human subjects' research.

3.66 Non-compliance: Any action or activity associated with the conduct or oversight of research involving human participants that fails to comply with either the research plan as approved by the SHC IRB, or federal regulations or SHC institutional policies governing human subjects' research.

3.67 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).*

3.68 Not Human Subjects Research (NHSR): A study which uses specimens/data from non-research repositories or databases (the specimens/data have no links to identifiable private data). See *GUIDANCE: Repositories - Banking of Specimens and Data (HRP-086)*.

3.69 Original Medical Record/Source Documents: 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.

3.70 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)*.

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

3.72 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.

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

3.74 Protected Health Information (PHI)/HIPAA Authorization: (PHI) 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

3.75 Protocol Deviation: A minor or administrative departure from the SHC IRB approved protocol that was made by the PI or site personnel without prior IRB approval and does not affect the study plan or the rights, safety or welfare of human subjects. Examples of minor or administrative deviations include; 1) follow-up visits that occurred outside the protocol required time frame because of the participant's schedule or 2) blood samples obtained at times close to but not precisely at the time points specified in the protocol. See *FORM: Deviation Summary Sheet (HRP-225)* for reporting requirements.

3.76 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: Non-Compliance and Other Reportable Unanticipated Problems Involving Risks to Subjects or Others (HRP-024)*, *GUIDANCE: Research Misconduct (HRP-003)* and *FORM: Unanticipated Problem or Event Report (HRP-214)* for reporting requirements.

3.77 Reportable Event: A protocol deviation or violation that is likely to adversely affect the rights and welfare of the research subjects, the safety of the research subjects, or the integrity of the research data. See *GUIDANCE: Non-Compliance and Other Reportable Unanticipated Problems Involving Risks to Subjects or Others (HRP-024)*, *GUIDANCE: Research Misconduct (HRP-003)* and *FORM: Unanticipated Problem or Event Report (HRP-214)* for reporting requirements.

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

3.79 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)*.

- 3.79.1.1 "Fabrication" is making up data or results and recording or reporting them.
- 3.79.1.2 "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.
- 3.79.1.3 "Plagiarism" is the appropriation of another person's ideas, processes, results, or words without giving appropriate credit.

3.80 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: Non-Compliance and Other Reportable Unanticipated Problems Involving Risks to Subjects or Others (HRP-024)* for a list of possible restrictions.

3.81 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: Non-Compliance and Other Reportable Unanticipated Problems Involving Risks to Subjects or Others (HRP-024)* and *FORM: Unanticipated Problem or Event Report (HRP-214)* for reporting requirements.

3.82 Serious Non-Compliance: Non-compliance that adversely affects the rights or welfare of subjects. See *GUIDANCE: Non-Compliance and Other Reportable Unanticipated Problems Involving Risks to Subjects or Others (HRP-024) and FORM: Unanticipated Problem or Event Report (HRP-214)* for reporting requirements.

- 3.82.1 For Department of Defense (DoD) research Serious non-compliance includes failure of a person, group, or institution to act in accordance with DoD Instruction 3216.02 and its references such that the failure could adversely affect the rights, safety or welfare of a human subject; place a human subject at increased risk of harm; cause harm to a human subject; place a human subject at increased risk of harm; cause

harm to a human subject; affect a human subject's willingness to participate in research; or damage or compromise the scientific integrity of the research data.

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

3.83.1 Is intended as an implant and presents a potential for serious risk to the health, safety or welfare of a subject;

3.83.2 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;

3.83.3 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

3.83.4 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)*.

3.84 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.

3.85 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.

3.86 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)*.

3.87 Sponsor-Investigator (same as investigator-initiated)**:** An individual who both initiates and conducts an investigation, and under whose immediate direction the investigational drug is administered or dispensed.

3.88 Subject (also known as participant): See Human Subject as identified by DHHS (3.32) and Human Subject as identified by FDA (3.33) in definitions above.

3.89 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.

3.90 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)*.

3.91 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. See *GUIDANCE: Suspension or Termination of IRB Approval by Other than the Convened IRB (HRP-026)*.

3.92 Termination of IRB Approval: An action of the IRB, IRB designees, 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).

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

3.94 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: Unanticipated Problem or Event Report (HRP-214)*.

3.95 Unanticipated Problem: Events that are; unanticipated; and related or possibly related to the research; and suggest that the research places the subject or others at increased risk for harm (physical, psychological, criminal or civil liability, damaging to the subjects' financial standing, employability, or reputation). *See FORM: Unanticipated Problem or Event Report (HRP-214)*.

For VA research, unanticipated problems that may substantively compromise the effectiveness of the facility's human research protection or oversight programs may also constitute Unanticipated Problems. See *CHECKLIST: Additional Veterans Administrator (VA) Criteria (HRP-432)*.

3.96 Unexpected Adverse Drug Experience (also known as Unanticipated Adverse Drug Event): 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: Unanticipated Problem or Event Report (HRP-214)*.

3.97 Unidentified Biological Samples: 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)*.

3.98 Unlinked Biological Samples: 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)*.

3.99 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.

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 §46.102.

7.2 21 CFR §50.3, 21 CFR §56.102, 21 CFR §312.3, 21 CFR §812.2(a), 21 CFR §812.3(p)

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