

**Louisiana State University Health Sciences Center – Shreveport**

**Human Research Protections Program  
Institutional Review Board**

**Standard Operating Procedures Guidebook**

Revised: November 3, 2017

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## **1. HUMAN RESEARCH PROTECTIONS PROGRAM (HRPP)**

LSUHSC-S has a systematic and comprehensive Human Research Protection Program that affords protections for all research participants. Individuals within the Organization are knowledgeable about and follow the policies and procedures of the Human Research Protection Program. (AAHRPP Standard I-1)

### **1.1 Policy**

Louisiana State University Health Sciences Center-Shreveport (LSUHSC-S) and the affiliated University Health System, hereinafter known as the Institution, its staff, employees, faculty, students and any affiliated institution or individual, fosters a research environment that promotes the rights and welfare of individuals recruited for, or participating in research conducted by, or under the auspices of, the Institution. In the review and conduct of research, actions by the Institution will be guided by the principles set forth by the World Medical Association, the Declaration of Helsinki, and the Belmont Report. The actions of the Institution will also conform to all applicable university, federal, state, and local laws and regulations. In addition, review by the LSUHSC-S IRB is required for all research and related activities involving human beings and/or information and tissue from human beings conducted by LSUHSC-S employees.

To fulfill this policy, the Institution established a Human Research Protection Program (HRPP) which is administered by the Office of the Vice Chancellor for Research. The HRPP consists of this policy, a mission statement, a statement of ethical principles, supporting policies and procedures (SOPs), and institutional agents and committees. This policy document outlines the responsibilities of LSUHSC-S, its researchers and research staff, and its Research Affiliates for the appropriate conduct of Human Subject Research.

### **1.2 Mission**

The mission of the HRPP is to:

- Safeguard and promote the health and welfare of human research subjects by ensuring that their rights, safety and well-being are protected
- Provide ongoing training and education, timely review and monitoring of human research projects
- Facilitate excellence in human subjects research
- Cultivate a culture of consciousness in the research community to ensure the highest level of protections and advocacy for research participants by actively engaging and working cooperatively with the Institutional Official, Institutional Leaders, and all components of the HRPP; by facilitating ethical and scientifically sound research

institutional oversight and Institutional Review Board (IRB) review processes; contributing to the knowledge of investigators and research personnel through education and training programs; communicating with sponsors, and serving as a consistent resource for past, present, and prospective participants.

- Have open communications with Researchers and Research Staff and be responsive to their questions, concerns, and suggestions regarding the HRPP. Researchers are free to contact staff members of HRPP. See <http://www.lsuhsctshreveport.edu/Research/HRPP-Home/index>.
- The HRPP includes mechanisms to:
  - establish a formal process to monitor, evaluate and continually improve the protection of human research participants
  - dedicate resources sufficient to do so
  - exercise oversight of research protection
  - educate IRB Committee members, IRB support staff, investigators and research staff about their ethical responsibility to protect research participants
  - when appropriate, intervene in research and respond directly to concerns of research participants
  - educate research participants and the community

### 1.3 Institutional Authority

LSUHSC-S delegates responsibility for the Human Research Protection Program to an official with sufficient standing, authority, and independence to ensure implementation and maintenance of the program. (AAHRPP Element I.1.B.)

LSUHSC-S has and follows written policies and procedures setting forth the ethical standards and practices of the Human Research Protections Program. Relevant policies and procedures are made available to Sponsors, Researchers, Research Staff, research participants, and the Institutional Review Board, as appropriate. (AAHRPP Element I.1.D)

The Institution's Human Research Protections Program operates under the authority of the Institutional policy "Human Research Protections Program (HRPP)" adopted on August 5, 2008. As stated in that policy, the operating procedures in this document "...serve as the governing procedures for the conduct and review of all human subjects research conducted under the auspices of the Institution."

The HRPP Policy and these operating procedures are made available to investigators, research staff, IRB committee members, IRB support staff, Research Affiliates, sponsors and all components identified under the Institutional Federal Wide Assurance (FWA), and all Assurances relying upon the LSUHSC-S IRB. The HRPP and IRB Standard Operating Procedures are located on the LSUHSC-S HRPP website at <http://www.lsuhsctshreveport.edu/Research/HRPP-Home/index>.

## 1.4 Definitions

Access: means the ability or the means necessary to read, write, modify, or communicate data/information or otherwise use any system resource for the purpose of using, transmitting or receiving private identifiable information.

Administer or administration: means the direct application of a drug to the body of a patient or research subject by injection, inhalation, ingestion, or any other means. (Pharmacy.la.gov)

Administrative Hold: A voluntary action initiated by the principal investigator to temporarily stop some or all approved research activities. Administrative holds are not considered suspensions or terminations. During administrative hold, the research remains subject to continuing review and requirements for reporting non-compliance and unanticipated problems involving risks to subjects or others.

Advocate: An individual who has the background and experience to act in, and agrees to act in, the best interest of the vulnerable participant for the duration of the participant's participation in the clinical investigation. Vulnerable participants may include, but are not limited to children, fetuses, neonates, and adults with intellectual disabilities, prisoners, financially or educationally disadvantaged.

Adverse Event: Any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and that 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), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product. For Veterans Administration (VA) research an adverse event in human subjects research is any untoward physical or psychological occurrence in a human subject participating in research.

Affiliated IRB Member: is an employee or agent of LSU Health Sciences Center (or a member of that person's immediate family). Affiliated members include, but are not limited to individuals who are: Full- or part-time employees; current students; members of any governing panel or board of the institution; paid or unpaid consultants; health care providers holding credentials to practice at the institution; and, volunteers working at the institution on business unrelated to the IRB.

Agent: An individual who is an employee is considered to be an agent of LSUHSC-S if the individual is performing institutionally designated activities or exercising institutionally delegated authority or responsibility. This would include, among others, students or volunteers when interacting with human participants for classroom activities that qualify as human research; employees when conducting research with participants or when using or controlling human participant records; and any individual conducting research with

participants at LSUHSC-S facilities or for whom LSUHSC-S has responsibility.

- An individual who is not an employee is considered an agent of the organization for purposes of engagement in Human Research when that individual has been specifically authorized to conduct research on behalf of the organization. Examples of individuals who would not be considered agents would be employees when conducting human research while on sabbatical through a separate institution; or employees when conducting research for another entity while acting in a consulting role that is not assigned by LSUHSC-S. However, if data derived from consulting work could reasonably be expected to be used later for university related purposes, the employee would be considered an agent. When an LSUHSC-S researcher conducts a consenting process, he/she is then engaged which makes LSUHSC-S engaged.
- Legal counsel has the ultimate authority to determine whether someone is acting as an agent of the organization.

Allegation of Non-Compliance: An unproved assertion of Non-Compliance.

Alternate Member: Alternate members are part of the IRB and may attend convened meetings and perform all the assigned or delegated duties of the primary members. The appointment of alternate members should be based on experience, expertise, background, professional competence, and knowledge comparable to that of the primary IRB voting member whom the alternate would replace. An alternate member may vote only when the regular voting member is absent.

Approval Period (Interval): The period of time between the first day of IRB approval (Start Date) of a protocol and the last day (End Date) of IRB approval of a protocol.

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

Blinded: A study design comparing two or more interventions in which the investigator, the subjects, or some combination thereof, do not know the treatment group assignments of individual subjects; it is sometimes called a masked study design.

Biologic: Any therapeutic serum, toxin, anti-toxin, or analogous microbial drug applicable to the prevention, treatment or cure of disease or injuring.

Case History: A case history is a record of all observations and other data pertinent in the investigation on each research subject. An investigator is required to prepare and maintain adequate and accurate case histories. Case histories include the case report forms and supporting data including signed and dated consent forms, any medical records including, but are not limited to, progress notes of the physician, the individual's hospital chart(s), and nurses' notes. The case history for each individual must document that informed consent was obtained prior to participation in the study.

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. (A series of more than 3 case reports requires IRB review).

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.

Case Series: The external reporting (e.g., publication or poster/verbal presentation) of an interesting clinical situation or medical condition in a series of patients (i.e., more than one patient). Case series usually contain detailed information about each patient and may include demographic information and information on diagnosis, treatment, response to treatment, follow-up after treatment, as well as a discussion of existing relevant literature. The information used in the report must have been originally collected solely for non-research purposes as the result of a clinical experience. A case series of three (3) or more usually meets the definition of a systematic investigation and may be considered human subject research.

Certified Copy: A copy (paper or electronic) of original information that has been verified, as indicated by a dated signature, as an exact copy, having all of the same attributes and information as the original. Source documents are considered to be the original records or certified copies. Use of a certified copy is necessary when the original records are copied to a different media (e.g. electronic records to a pdf file or hard copy). The same person who actually makes the copy from the original is the person who certifies the copy as an accurate and complete representation of the original, having all the same attributes and information. Certification is accomplished by having the person who makes the copy, sign and date the copy to indicate it meets the requirements of a certified copy. Each individual copy of the electronic record shall be signed and dated. When documents are copied in bulk the person who makes the copy is to indicate the number of pages certified next to their signature.

If the printout of the electronic record displays an electronic date and time, stamped by the printer and also prints out the identity of the authorized user (the person making the copy) then this could be considered an acceptable certified copy.

Children: Under the following, children means:

- 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.
- Louisiana Law: Child means a person under eighteen years of age who, prior to juvenile proceedings, has not been judicially emancipated under Civil Code Article 385

or emancipated by marriage under Civil Code Articles 379 through 384.

Classified Research: In the interest of national security, federally funded research can be classified in terms of limited access to data, information, and facilities that may be required to carry out the research or in terms of the limited distribution of the results of the research.

Clinical Investigation: Any experiment that involves a test article and one or more human subjects, and that either must meet the requirements for prior submission to the Food and Drug Administration under section 505(i) or 520(g) of the Federal Food, Drug and Cosmetic Act (FD&C Act), or need not meet the requirements for prior submission to the Food and Drug Administration under these sections of the act, but the results of which are intended to be later submitted to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit. The term does not include experiments that must meet the provisions of part 58, regarding nonclinical laboratory studies. The terms research, clinical research, clinical study, study, and clinical investigation are deemed to be synonymous for purposes of this part. (See 21 CFR 56.102).

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.

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.

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.

Coded Information/Data: Identifying information that would enable the Investigator to readily ascertain the identity of the individual to whom the private information or specimens pertain has been replaced with a number, letter, symbol, or combination thereof and a key to decipher the code exists, enabling linkage of the identifying information to the private information or specimens.

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.

Coercion: Coercion means that a person is forced to some degree, or strongly urged to do something that may not be good for them or against their judgment. In research involving human subjects "under influence" is often used to describe the concept of coercion. It is the practice of using threats, rewards, intimidation, or any other incentive to affect another. Such

actions are used as leverage to force or influence the victim to act in the desired way.

Cognitively Impaired: Individuals that have a psychiatric disorder (e.g., psychosis, neurosis, personality, or behavior disorder), a developmental disorder (e.g., mental retardation/intellectual disabilities) or a neurological disorder that affects cognitive or emotional functions to the extent that capacity for judgment is significantly diminished. These individuals may be considered to have a "Diminished Autonomous Decision Making Capacity". Individuals with cognitive impairment should not automatically be considered unable to provide valid consent or assent. Additionally, individuals may be considered cognitively-impaired or have a diminished autonomous decision-making capacity or have limited decision-making ability because they are under the influence of drugs or alcohol; suffering from degenerative diseases affecting the brain; are terminally ill; or have disabling physical handicaps; or other circumstances temporary or permanent that affect their cognitive abilities.

Combination Product: A product containing a combination of a drug, a device, or a biological product. Studies of combination products are regulated according to the IND or IDE regulations, depending on the components of the product. The FDA determines which of its organizational components has primary jurisdiction for the premarket review and regulation of products that are comprised of any combination of a drug, device, and/or biological. (See 21 CFR 3.2(e))

Common Rule: The Common Rule refers to the "Federal Policy for the Protection of Human Subjects" that provides for the primary source of regulation of research. It has been adopted by a number of federal agencies. Although the Common Rule is codified by each agency separately, the text is identical to Department of Health and Human Services (DHHS) regulations in 45 CFR 46 Subpart A. For the purposes of this document, references to the Common Rule will cite the DHHS regulations and VA regulations at 38 CFR 16.

Compensation: (1) Compensation is payment for participation in research or a way to reimburse a subject for time, travel, parking, and other experiences incurred due to participation. However, payment for participation is not considered a research benefit. Investigators should also make sure that compensation is not used to impart undue influence towards participation in research.

Compensation: (2) Payment of medical care provided to subjects injured in research; does not refer to pay (re-numeration) for participation in research.

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

Confidentiality: Confidentiality is the right of an individual to have personal, identifiable health information kept private; such information should not be disclosed to others unless the individual has given informed consent.

Conflicting Interest: An individual involved in research review is automatically considered to have a conflicting interest when the individual or the individual's spouse, domestic partner, children, and dependents have any of the following interests in the sponsor, product or service being tested, or competitor of the sponsor held by the individual or the individual's immediate family:

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

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.

- For Veterans Administration (VA) research Continuing Non-Compliance includes a persistent failure to adhere to the laws, regulations, or policies governing Human Research.

Continuing Review: Under federal regulations this is periodic review of ongoing research activities by the IRB at intervals appropriate to the degree of risk, but not less than once per year. 45 CFR 46.109(e).

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 or other non-compliance. 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.

Covered Entity: Individuals, organizations and agencies that must comply with HIPAA rules. 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.

Data: Data refers to a collection of organized information, usually the results of experience, observation, testing, analysis or a set of premises. Data may consist of numbers, words, images or specimens. For repository purposes, data/specimens are generally categorized as unidentifiable or identifiable.

Data Safety Monitoring Board: A clinical trial DSMB is a group of individuals with pertinent expertise that reviews on a regular basis accumulating data from one or more ongoing clinical trials. The DSMB advises the sponsor regarding the continuing safety of trial subjects and those yet to be recruited to the trial, as well as the continuing validity and scientific merit of the trial.

Data Safety Monitoring Plan (DSMP): A DSMP plan is a general description of a system for appropriate oversight and monitoring of the data and participant safety in a clinical research study. The plan is developed by the investigator, included in the protocol, and submitted to the IRB for review and approval before the study begins. An appropriate plan is commensurate with the risks, size and complexity of the study. An investigator's DSMP may or may not include a Data and Safety Monitoring Board (DSMB).

Data Use Agreement: An agreement between LSUHSC-S and the recipient of the protected health information (PHI). This agreement establishes who is permitted to use or receive the limited data set; and provides that the limited data set recipient will:

- Not use or further disclose the information other than as permitted by the data use agreement or as otherwise required by law;
- Use appropriate safeguards to prevent use or disclosure of the information other than as provided for by the data use agreement;
- Report to the covered entity any use or disclosure of the information not provided for by its data use agreement of which it becomes aware;
- Ensure that any agents, including a subcontractor, to whom it provides the limited data set agrees to the same restrictions and conditions that apply to the limited data set recipient with respect to such information; and
- Not identify the information or contact the individuals.
- Researchers who will be receiving limited data sets must submit a signed copy of the covered entity's data use agreement to the LSUHSC-S IRB for approval, prior to initiating the research.

Dead Fetus: An un-expelled or delivered fetus that exhibits no heartbeat, spontaneous

respiratory activity, spontaneous movement of voluntary muscles, or pulsation of the umbilical cord (if still attached). 45 CFR 46.203(f) Generally, some organs, tissues and cells (referred to collectively as fetal tissue) remain alive for varying periods of time after the total organism is dead.

De-identified Data: Data that has been stripped of all 18 elements considered by the HIPAA Privacy Rule to be Protected Health Information (PHI) or direct identifiers that could be used to identify the individual or the individual's relatives, employers, or household members. This includes unique identifying numbers, characteristics or codes.

List of 18 Identifiers:

- \*Names
- \*All geographical subdivisions smaller than a state, including street address, city, county, precinct, ZIP code, and their equivalent geographical codes, except for the initial three digits of a ZIP code, if according to the current publicly available data from the Bureau of the Census: (1) The geographic unit formed by combining all ZIP codes with the same three initial digits contains more than 20,000 people; and (2) The initial three digits of a ZIP code for all such geographic units containing 20,000 or fewer people is changed to 000
- All elements of dates (except year) for dates directly related to an individual, including birth date, admission date, discharge date, date of death; and all ages over 89 and all elements of dates (including year) indicative of such age, except that such ages and elements may be aggregated into a single category of age 90 or older
- \*Phone numbers
- \*Fax numbers
- \*Electronic mail addresses
- \*Social Security numbers
- \*Medical record numbers; prescription numbers
- \*Health plan beneficiary numbers
- \*Account numbers
- \*Certificate/license numbers;
- \*Vehicle identifiers and serial numbers, including license plate numbers
- \*Device identifiers and serial numbers
- \*Web Universal Resource Locators (URLs)
- \*Internet Protocol (IP) address numbers
- \*Biometric identifiers, including finger and voice prints
- \*Full face photographic images and any comparable images
- Any other unique identifying number, characteristic, or code (note this does not mean the unique code assigned by the investigator to code the data)
- \*These 16 items must be removed for a limited data set.

Declaration of Helsinki: Statement of ethical principles for human participation in biomedical research. The Declaration was first adopted in 1964 by the World Medical Association. The

Declaration has been revised several times, most recently in 2008. Like the Nuremberg Code that preceded it, the Declaration of Helsinki makes consent a central requirement of ethical research

Deferred: The IRB cannot make one or more of the determinations required for approval by the HHS regulations at 45 CFR 46.111 and, if applicable, subparts B, C, or D of 45 CFR 46. This action is taken if substantial modification or clarification is required, or insufficient information is provided to judge the protocol application adequately the IRB (a) is unable to make the required determinations about research risks and benefits, the adequacy of privacy and confidentiality protections, or the adequacy of the informed consent process because the research protocol provides insufficient information related to these aspects of the research, and (b) is unable to specify changes to the research protocol or consent document that if made would allow the IRB to make these required determinations.

The research may not proceed until the IRB reviews the revised research protocol and approves it at a subsequent convened meeting. When a research protocol is Deferred, the IRB under its authority to require modifications in order for an investigator to secure approval, may require that the investigator (a) make changes to the protocol or informed consent documents, or (b) submit clarifications or additional documents prior to the next review.

In order to receive approval for a research protocol Deferred: The investigator's response, revised research protocol and all requested documents must be submitted for review at a subsequent, convened meeting of the same IRB committee. The HRPP Staff will process the investigator's response, the revised proposal along with the previously submitted proposal. The item will be placed on the agenda for re-review at the next convened meeting.

Delivery: means complete separation of the fetus from the woman by expulsion, extraction, or any other means.

Department of Health and Human Services (DHHS): The United States government's principal agency for protecting the health of all Americans and providing essential human services, especially for those who are least able to help themselves. DHHS has more than 300 programs including FDA, NIH, CMS, OHRP, CDC, and SAMHSA.

Designated Reviewer: The IRB chair or an IRB Member with appropriate scientific or scholarly expertise designated by the IRB chair to conduct Non-Committee Reviews.

Deviations: Departure from, or changes to, the IRB-approved protocol initiated without prior IRB approval.

Device (Medical Device): A device per the FDA is: an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component part, or accessory which is: 1) recognized in the United States Pharmacopeia-

National Formulary, or any supplement to them, 2) intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or 3) intended to affect the structure or any function of the body of man or other animals, and which does not achieve any of its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of any of its primary intended purposes. FD&C Act 210(h).

Dietary Supplement: The Dietary Supplement Health and Education Act of 1994 (DSHEA) established a formal definition of dietary supplement as the following:

- is a product (other than tobacco) that is intended to supplement the diet that bears or contains one or more of the following dietary ingredients: a vitamin, a mineral, an herb or other botanical, an amino acid, a dietary substance for use by man to supplement the diet by increasing the total daily intake, or a concentrate, metabolite, constituent, extract, or combinations of these ingredients,
- is intended for ingestion in pill, capsule, tablet, or liquid form,
- is not represented for use as a conventional food or as the sole item of a meal or diet,
- is labeled as a dietary supplement, includes products such as an approved new drug, certified antibiotic, or licensed biologic that was marketed as a dietary supplement or food before approval, certification, or license (unless the Secretary of Health and Human Services waives this provision).

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

Dispense or dispensing: means the interpretation, evaluation, and implementation of a prescription drug order, including the preparation and delivery of a drug or device to a patient or patient's agent in a suitable container appropriately labeled for subsequent administration to, or use by, a patient. Dispense necessarily includes a transfer of possession of a drug or device to the patient or the patient's agent. (Pharmacy.la.gov)

Distribute or distribution: means the delivery of a drug or device other than by administering or dispensing. (Pharmacy.la.gov)

Double Blinded Design: A double blinded design is a study comparing two or more interventions where neither the investigator nor the subject knows who has received which intervention. This minimizes potential bias or assignment of a particular subject to a specific intervention.

Drug as defined by FDA: (A) articles recognized in the official United States Pharmacopoeia, official Homoeopathic Pharmacopoeia of the United States, or official National Formulary, or any supplement to any of them; and (B) articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals; and (C) articles

(other than food) intended to affect the structure or any function of the body of man or other animals; and (D) articles intended for use as a component of any articles specified in clause (A), (B), or (C).

Drug Dispensing: Louisiana law requires that dispensing may only be done by a licensed pharmacist or a physician who is registered with the Louisiana State Board of Medical Examiners as a dispensing physician in accordance with 46 CFR 65: Subchapter C or 46 CFR 65 (c).

Drug Labeling: The Code of Federal Regulations specifies the following labeling requirements for an investigational new drug:

- The immediate package of an investigational new drug intended for human use shall bear a label with the statement "Caution: New Drug - Limited by Federal (or United States) law to investigational use."
- The label or labeling of an investigational new drug shall not bear any statement that is false or misleading and shall not represent that the investigational new drug is safe or effective for the purposes for which it is being investigated.
- State of Louisiana Regulations and LSUHSC-S policy states that all drugs dispensed shall contain a medication label with the following:
  - a) Patient name, identifier
  - b) Protocol number or name
  - c) Name of prescriber / INVESTIGATOR
  - d) Strength and volume of drug
  - e) Directions for use or administration
  - f) Dose
  - g) Number of units dispensed
  - h) Expiration date
  - i) Initials of preparer
  - j) Initials of pharmacist performing final check
  - k) "Investigational Drug"
  - l) Any auxiliary stickers or warning labels

Emancipated Minor: A legal status conferred upon persons who have not yet attained the age of legal competency as defined by state law (for such purposes as consenting to medical care), but who are entitled to treatment as if they had by virtue of assuming adult responsibilities such as being self-supporting and not living at home, marriage, or procreation.

Emergency Research: Research conducted in participants who are in a life-threatening or emergent situation, where available treatments are unproven or unsatisfactory, and the collection of valid scientific evidence, which may include evidence obtained through randomized placebo-controlled investigation, is necessary to determine the safety and effectiveness of particular interventions.

Emergency Treatment IDE: A mechanism through the FDA for providing eligible participants with investigational devices for the treatment of an immediate serious or life-threatening illness for which there are no satisfactory alternatives. See FDA Guidance for Emergency IDE.

Emergency Treatment IND: A mechanism through the FDA for providing eligible participants with investigational drugs, agents, or biologics for the treatment of an immediate serious or life threatening illness for which there are no satisfactory alternatives. See: FDA Guidance for Emergency IND.

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.

Engaged in Human Subjects Research: In general, an institution is considered engaged in a particular non-exempt human subjects research project when its employees or agents for the purposes of the research project obtain: (1) data about the subjects of the research through intervention or interaction with them; (2) identifiable private information about the subjects of the research; or (3) the informed consent of human subjects for the research. The institution considers private information or specimens to be individually identifiable as defined in 45 CFR 46.102(f) when they can be linked to specific individuals by the investigator(s) either directly or indirectly through coding systems.

Experienced IRB Member: An IRB member is considered experienced if they have been an IRB member for at least one year and the IRB chair considers the IRB member to have sufficient experience in and knowledge of conducting IRB reviews.

Epidemiology: A scientific discipline that studies the factors determining the causes, frequency, and distribution of diseases in a community or specified population.

Exclusion Criteria: The list of elements in a person's medical, psychiatric or social history that would prevent them from participating in a specific research project.

Exempt Research: Certain minimal risk research protocols may meet criteria for exemption if the only involvement of human subjects will be in one or more of the six (6) categories described in the federal regulations. Any research involving prisoners or certain activities with children are not exempt. Only the IRB can make the determination of exemption. 45 CFR 46.101, 38 CFR 16.101(b)

Ex-Officio IRB Member: Ex-officio members on the IRB Committees may include persons who are automatically members by virtue of the position held. These individuals do not have voting privileges and do not count toward quorum.

Expedited Review Procedures for Research: Expedited research is research determined by the IRB to present no more than minimal risk to human subjects and involve only procedures in certain specific categories. Minor changes to previously approved research during the

period for which approval is authorized may also be approved through the expedited process. 38 CFR 16.110(b), 45 CFR 46.110.

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

External Adverse Events: Those adverse events and unanticipated problems experienced by subjects in a clinical trial that are enrolled by investigators at other institutions outside of LSUHSC-S.

Federalwide Assurance (FWA): The Federalwide Assurance (FWA) is the only type of assurance of compliance accepted and approved by OHRP for institutions engaged in non-exempt human subjects research conducted or supported by HHS. Under an FWA, an institution commits to HHS that it will comply with the requirements set forth in 45 CFR part 46, as well as the Terms of Assurance. An institution must have an FWA in order to receive HHS support for research involving human subjects. Each FWA must designate at least one IRB registered with OHRP.

Fetus: The product of conception from the time of implantation until delivery. If the delivered or expelled fetus is viable, it is designated an infant 45 CFR 46.203(c). The term "fetus" generally refers to later phases of development, the term "embryo" as usually used for earlier phases of development.

510(K) Device: A medical device that is considered substantially equivalent to a device that was or is being legally marketed. A Sponsor planning to market such a device must submit notification to the FDA 90 days in advance of placing the device on the market.

Financial Conflict of Interest: Refers to any financial interest that competes with an individual's obligation to protect the integrity of the academic pursuit and especially the rights and welfare of research subjects. While financial interests may not compromise intellectual honesty or institutional integrity, they must not have the appearance of compromising LSUHSC-S values and missions of teaching, research and public service.

Finding of Non-Compliance: Non-Compliance in fact.

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

FDA-Regulated Human Research: Human research is considered FDA regulated when the activity involves an FDA-regulated test article and the activity involves human participants. See FDA 21 CFR 56.102.

Full Committee Review: Review of proposed research at a convened meeting at which a

majority of the membership of the IRB is present, including at least one member whose primary concerns are in scientific areas, at least one member whose primary concerns are in nonscientific areas, at least one member who is unaffiliated, and at least one member who represents the general perspective of subjects. . For the research to be approved, it must receive the approval of a majority of those members present at the meeting. 45 CFR 46.108.

Generalizable Knowledge: An investigation designed to draw general conclusions, inform policy or generalize findings beyond a single individual or an internal program (e.g., publications or presentations). However, research results do not have to be published or presented to qualify the experiment or data gathering as research. The intent to contribute to "generalizable (scholarly) knowledge" makes an experiment or data collection research, regardless of publication. Examples of activities that typically are not generalizable include:

- quality assurance/improvement activities designed to continuously improve the quality or performance of a department or program where it is not the intention to share the results beyond the institution
- classroom exercises solely to fulfill course requirements or to train students in the use of particular methods or devices at the institution

Good Clinical Practice (GCP): is an international ethical and scientific quality 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.

Guardian: An individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care. 45 CFR 46.402 (3). LA ChC 116(12.1)(a)(I)(b)

HIPAA Authorization: A document/form, that gives permission to use specified protected health information (PHI) for a specific purpose, or to disclose PHI to a third party specified by the Investigator other than for treatment, payment or healthcare operations.

Human Research: Any activity that either:

- Is Research as Defined by DHHS and involves Human Subjects as Defined by DHHS: Research means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. Activities which meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program which is considered research for other purposes. For example, some demonstration and service programs may include research activities; or
- Is Research as Defined by FDA and involves Human Subjects as Defined by FDA: Clinical investigation means any experiment that involves a test article and one or more human subjects and that either is subject to requirements for prior submission to the Food and Drug Administration under section 505(i) or 520(g) of the act, or is not subject to requirements for prior submission to the Food and Drug Administration

under these sections of the act, but the results of which are intended to be submitted later to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit. The terms research, clinical research, clinical study, study, and clinical investigation are deemed to be synonymous for purposes of this policy.

Human Research Protections Program (HRPP): An HRPP is a comprehensive system to ensure the protection of human subjects participating in research. The HRPP consist of a variety of individuals and committees. The objective of this program is to assist the Institution in meeting ethical principles and regulatory requirements for the protection of human subjects in research.

Human Subject as Defined by DHHS: A living individual about whom an investigator (whether professional or student) conducting research obtains (1) data through Intervention or Interaction with the individual, or (2) information that is both Private Information and Identifiable Information. For the purpose of this definition:

- 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.
- Interaction: Communication or interpersonal contact between investigator and subject.
- 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).
- 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).

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 with a disease. A human subject includes an individual on whose specimen a medical device is used.

Humanitarian Use Device (HUD): A device that is intended to benefit patients by treating or diagnosing a disease or condition that affects fewer than 4,000 individuals in the United States per year.

Humanitarian device exemption (HDE) application: is submitted to the FDA. A medical device application that is similar to a premarket approval (PMA) application, but exempt from the effectiveness requirements of a PMA. An approved HDE authorizes marketing of a Humanitarian Use Device (HUD).

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).

Identifiable Biological Samples: Specimens with a personal identifier (such as a name, medical record or pathology number) that allows researchers to link the biological information derived from the research directly to the individual from whom the material was obtained.

Incidental Finding: A finding concerning an individual research participant that has potential health or reproductive importance and is discovered in the course of conducting research but is beyond the aims of the study.

Inclusion criteria: The list of elements in a person's medical, psychiatric or social history that is necessary for them to participate in a specific research project

Incompetence: Technically, a legal term meaning inability to manage one's own affairs.

Informed Consent: An individual's voluntary agreement, based upon adequate knowledge and understanding of relevant information, to participate in research. See Informed Consent Requirements 45 CFR 46.116 and 21 CFR 50.25. Note: These policies apply to the use of the Long Form.

Institutional Agent: All individuals performing institutionally designated activities or exercising institutionally delegated authority or responsibility under LSUHSC-S's FWA.

Institutional Official (also known as Organization Official): The Institutional Signatory Official is a senior official who has the authority to commit LSUHSC-S to the legally binding FWA terms and conditions. The IO has the authority to require compliance of the organization and all of its components to the terms of the FWA.

Institutional Review Board (IRB): An IRB is an independent board designated by the Institution to review, to approve the initiation of, and to conduct periodic review of research involving human subjects. The primary purpose of such review is to assure the protection of the rights and welfare of the human subjects. The IRB may be assigned other review functions as deemed appropriate by the Institution. This independent board is composed of medical, scientific, non-scientific and community members.

Internal Adverse Event: Those adverse events or unanticipated problems experienced by subjects enrolled by the investigators at this institution (LSUHSC-S).

Interaction: Communication in any form (for example: verbal, electronic, written) or interpersonal contact between an investigator, designee and research participant.

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.

Investigational Device: means a new medical device that has not been cleared for marketing by the FDA or an existing FDA-approved medical device which is being used for a new purpose in a clinical investigation.

Investigational Device Exemption (IDE): An investigational device exemption (IDE) gives the device manufacturer permission to use the device in a clinical study in order to collect safety and effectiveness data required to support a Premarket Approval (PMA) application or a Premarket Notification [510(k)] submission to FDA.

Investigational Drug: any new drug or biological product that has not been cleared for marketing by the FDA or an existing FDA-approved drug which is being used in a new way not indicated on the approved label or a new purpose in a clinical investigation.

Investigational New Drug (IND) Application: is a request for Food and Drug Administration (FDA) authorization to administer an investigational drug to humans. Such authorization must be secured prior to interstate shipment and administration of any new drug that is not the subject of an approved new drug application.

Investigational Product (IP) (also known as Test Article): Defined by the FDA as any drug (including a biological product for human use), medical device for human use, human food additive, color additive, electronic product, or any other article subject to regulation under the act or under sections 351 and 354-360F of the Public Health Service Act (42 U.S.C. 262 and 263b-263n).

Investigator (also known as researcher): An individual who actually conducts a clinical investigation, or other type of research under whose immediate direction a test article or experiment is administered or dispensed to, or used involving, a human subject. In the event of an investigation conducted by a team of individuals, the principal investigator is responsible leader of that team.

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

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

In Vitro Fertilization: is any fertilization of human ova, which occurs outside the body of a female, either through a mixture of donor human sperm and ova or by any other means.

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

Institutional Review Board (IRB) of Record: An IRB is considered the IRB of Record when it assumes responsibilities for review and continuing oversight of research involving human participants at external sites and other institutions. This relationship must be approved through OHRP.

IRB Records: IRB records include but are not limited to all minutes of IRB meetings, a copy of all proposals reviewed including all amendments, investigator brochures, and any supplemental information including recruitment and informational materials, consent forms, information submitted for continuing review, all correspondences, and IRB membership roster with a CV for each member.

Justice: An ethical principle discussed in the Belmont Report requiring fairness in distribution or what is deserved in relationship to the burdens and benefits of research; this is often expressed in terms of treating persons of similar circumstances or characteristics in a similar manner.

Lapse of Approval: This occurs when continuing review of the research does not occur prior to the end of the approval period specified by the IRB. The IRB approval expires automatically. The study approval ends or expires on the date specified on the approval letter. No research activities can occur after the approval end date. There is no grace period for continuing approval without IRB review and approval prior to the approval end date.

Legal Guardianship: The duty and authority to make important decisions in matters having a permanent effect on the life and development of the child and the responsibility for the child's general welfare until he reaches the age of majority, subject to any residual rights possessed by the child's parents. It shall include but not necessarily be limited to: The authority to consent to marriage, to enlist in the armed forces of the United States, or to major medical, psychiatric, and surgical treatment, to represent the minor in legal actions, to make other decisions of substantial legal significance concerning the minor. The term "legal guardian" means the caretaker in such a relationship. LA ChC 116(12.1)(a)(i)(b)

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

Limited Data Set: Protected health information that is not fully de-identified and retains certain direct patient identifiers. The recipient of a limited data set must get IRB approval and sign a Data Use Agreement. (See page 14 and 15 for list of identifiers)

Major Modification: A major modification is a proposed change in research related activities that include significant protocol changes and may cause subjects to engage in activities not

previously approved; or involves an increased level of risk to the physical, emotional, or psychological well-being of participants; or changes their willingness to participate. Major modifications materially affect an assessment of the risks and benefits of the study and/or substantially change the specific aims or design of the study.

Medical device as defined by the FDA is: an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component part, or accessory which is:

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

Minimal Risk: The probability and magnitude of harm or discomfort anticipated in the research that are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

- For research involving prisoners Minimal Risk is 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.
- When following Department of Defense regulations, the definition of minimal risk based on the phrase “ordinarily encountered in daily life or during the performance of routine physical or physiological examination or tests” shall not be interpreted to include the inherent risks certain categories of human participants face in their everyday life. For example, the risks imposed in research involving human participants focused on a special population should not be evaluated against the inherent risks encountered in their work environment (e.g., emergency responder, pilot, soldier in a combat zone) or having a medical condition (e.g., frequent medical tests or constant pain).

Minor: A person who has not attained the age of majority in a particular jurisdiction.

Minor Modification: A proposed change in research related activities that does not materially affect an assessment of the risks and benefits of the study and does not substantially change the specific aims or design of the study.

Modification: Any change to an IRB-approved study protocol regardless of the level of review it receives initially.

National Institutes of Health (NIH): The National Institutes of Health (NIH) is a part of the U.S. Department of Health and Human Services, and the primary Federal agency for conducting

and supporting medical research. Helping to lead the way toward important medical discoveries that improve people's health and save lives, NIH scientists investigate ways to prevent disease as well as the causes, treatments, and even cures for common and rare diseases. Composed of twenty-seven (27) Institutes and Centers, the NIH provides leadership and financial support to researchers in every state and throughout the world.

National Research Act: In 1974 the U.S. Congress passed Title II, Public Law 93-348 which authorized the creation of the National Commission for Protection of Human Subjects of Biomedical and Behavioral Research. This law established the ethical principles and guidelines for the protection of human subjects in research and mandated review of research studies by institutional review boards.

Neonate: A newborn. For the purposes of DHHS regulations viable neonates are considered children and only require the protections under sections 45 CFR 46 Subpart A and Subpart D whereas neonates of uncertain viability and nonviable neonates require additional protections under Subpart B of 45CFR 46.

Non-Affiliated IRB Member: Any IRB member who is not a current employee or student of LSUHSC-S and who does not have an immediate family who is a current employee or student of LSUHSC-S.

Non-Committee Review: Any of the following:

- Determination of whether an activity is Human Research.
- Determination of whether Human Research is exempt from regulation.
- Reviews of non-exempt research using the expedited procedure.
- Determinations of which subjects can continue in expired research.

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 IRB, or federal regulations or LSUHSC-S institutional policies governing human subjects' research.

- In the case of research funded or conducted by the Department of Defense (DOD), Non-Compliance includes failure of a person, group, or institution to act in accordance with Department of Defense (DOD) instruction 3216.02, its references, or applicable requirements
- In the case of Veterans Administration (VA) research, Non-Compliance includes failure to following the requirements of VHA Handbook.

Non-Financial Conflict of Interest: Non-financial conflicts of interest may exist when an individual serves dual roles, such as healthcare provider and Investigator. Other interests such as publication, promotion or tenure, can also become conflicts of interest that may affect an individual's judgment. Membership in oversight committees such as the IRB as well as positions of authority may pose actual, perceived or potential conflicts of interest. Any position that includes responsibilities for the review and approval of research projects or

contracts may potentially affect the design of, decisions made and/or action taken surrounding a specific study.

Noninvasive as defined by the FDA: when applied to a diagnostic device or procedure, means one that does not by design or intention: (1) Penetrate or pierce the skin or mucous membranes of the body, the ocular cavity, or the urethra, or (2) enter the ear beyond the external auditory canal, the nose beyond the nares, the mouth beyond the pharynx, the anal canal beyond the rectum, or the vagina beyond the cervical os. For purposes of this part, blood sampling that involves simple venipuncture is considered noninvasive, and the use of surplus samples of body fluids or tissues that are left over from samples taken for non-investigational purposes is also considered noninvasive.

Non-Scientific IRB Member: Any IRB member who does not have a terminal degree in a medical or scientific field. The Non-Scientific Member is any IRB Member who has formal education and training in a discipline generally considered to be non-scientific (e.g. humanities, law, business) and/or is engaged in an occupation or role that is generally considered to be non-scientific (e.g. law enforcement, minister).

Non-Significant Risk (NSR) Device: An investigational device that does not meet the definition of a significant risk device.

Nonviable fetus: is a fetus ex utero that, although living, is not able to survive to the point of independently maintaining heart and respiration. In 45 CFR 46 Subpart B, this definition is used as the definition of a non-viable neonate.

Nonviable Neonate: A neonate after delivery that, although living, is not viable.

Nuremberg Code: A code of research ethics developed during the trials of Nazi war criminals following World War II. This code became the first international standard for the conduct of research and began the modern era of protection for human research participants. (See Nuremberg Code)

Off-Label Use: Use of an approved drug, an approved or cleared device, or a licensed biologic for an indication not in the approved labeling. Most research involving off-label uses requires IND or IDE applications. See FDA "Off-Label" and Investigational Use of Marketed Drugs, Biologics and Medical Devices.

Office for Human Research Protections (OHRP): a federal agency that provides leadership in the protection of the rights, welfare, and wellbeing of subjects involved in research conducted or supported by the U.S. Department of Health and Human Services. OHRP helps ensure this by providing clarification and guidance, developing educational programs and materials, maintaining regulatory oversight, and providing advice on ethical and regulatory issues in biomedical and social-behavioral research.

Office of Human Subjects Research (OHSR): The OHSR was established to help NIH Intramural Research Program investigators understand and comply with the ethical guidelines and regulatory requirements for research involving human subjects

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 other medical or technical departments involved in conducting the clinical trial.

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

Parent: A child's biological or adoptive parent.

Periodic Compliance & Quality Review: These reviews are random assessments of the IRB and all investigators or departments involved in the conduct of human subjects research at LSUHSC-S conducted by the HRPP QA/QI Coordinator or other HRPP staff members. These reviews are used to evaluate proper execution and accurate documentation of an IRB approved research project. Internal compliance/quality reviews monitor the adherence to federal regulations, state and local law, LSUHSC-S HRPP policies and procedures, adherence to the study protocol, accurate documentation and reporting of study related activities, and evaluation or observation of the consent process.

Permission: The agreement of parents or guardians to the participation of their child or ward in research.

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

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.

Practitioner: An individual currently licensed, registered, or otherwise authorized by the appropriate licensing board to prescribe and administer drugs in the course of professional practice. (Pharmacy.la.gov)

Pregnancy: Encompasses the period of time from implantation until delivery. A woman shall be assumed to be pregnant if she exhibits any of the pertinent presumptive signs of

pregnancy, such as a missed menses, until the results of a pregnancy test are negative or until delivery.

Preparatory to Research: Any action taken in assessing the research question or hypothesis, such as accessing medical records, querying of databases for any type of individually identifiable health information, or any activity where PHI is accessed to prepare a research protocol.

Principal Investigator (PI): The scientist or scholar with primary responsibility for the design and conduct of a research project. Within VA, a PI is an individual who conducts a research investigation, i.e., under whose immediate direction research is conducted, or, in the event of an investigation conducted by a team of individuals, is the responsible leader of that team. The FDA considers a PI and an investigator to be synonymous.

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.

- For Department of Defense (DOD) research the term includes military personnel in either civilian or military custody.

Privacy Rule: The Health Insurance Portability and Accountability Act of 1996 (HIPAA), mandated the establishment of standards for the privacy of individually identifiable health information. The Privacy Rule created national standards to protect individuals' medical records and other personal health information. Covered entities are required to take reasonable steps to limit the use or disclosure of, and requests for protected health information (PHI) to the minimum necessary to accomplish the intended purpose. Covered entities include most health plans, health care clearinghouses, health care providers and agents of such entities.

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).

Prompt Reporting: LSUHSC-S policy states that prompt reporting of unanticipated problems/events will occur immediately after the PI learns of the event, but in all cases within five (5) working days with the exception of death of a LSUHSC-S study participant. Prompt reporting requirements for a death of a study participant is as soon as the PI becomes aware of the event but no more than five (5) days following the event. Please see HRPP Policy for other events and emergency situations that require prompt reporting.

Proposal: The research proposal includes the complete packet of materials submitted to the

IRB for review, including a description of the research design and methodology as well a complete description of the procedures for the protection of human participants in the research. See Section 4.2 for a listing of materials submitted to the IRB. The proposal includes the protocol.

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

Protocol: A document (including subsequent amendments) that describes the objective(s), design, methodology, statistical considerations, and organization of a trial. The protocol usually also gives the background and rationale for the trial, but these could be provided in other protocol reference documents. Throughout the ICH GCP Guidance, the term protocol refers to protocol and protocol amendments. Good Clinical Practice: Consolidated Guidance (ICH-E6). The protocol should include:

- background information
- rational for performing the study
- objectives or hypothesis
- description of research design
- methodology (schedule of testing, procedures, medications and dosages and any other interventions or interactions with research subjects)
- statistical considerations that will be employed
- number of participants to be enrolled
- inclusion and exclusion criteria
- safety oversight and monitoring
- description of risks and benefits
- informed consent process

Protocol Deviation(s): A protocol deviation is non-adherence to protocol specific study procedures or schedules that does not involve inclusion/exclusion criteria, primary objective variable criteria, and/or Good Clinical Practice (GCP) Guidelines. Deviations are considered minor and do not impact the study. This non-adherence is without prior sponsor and IRB approval and (a) increases the risk or decreases the benefit, and (b) significantly affects the subject's rights, safety or welfare and/or the integrity of the Research data.

The term "protocol deviation" is not defined by either the HHS human subjects regulations (45 CFR 46) Common Rule or the FDA human subjects regulations (21 CFR 50).

Protocol Exception: A protocol exception is an impermanent (temporary) protocol deviation that is pre-approved by the Sponsor or funding agency, (and the FDA if applicable, for investigational device studies) and the IRB prior to implementation. Protocol exceptions are generally for a single subject or, occasionally, a small group of subjects.

Protocol Violation(s): A protocol violation is any significant divergence from the protocol, i.e., non-adherence on the part of the patient, investigator, or the sponsor to protocol-specific inclusion/exclusion criteria, primary objective variable criteria, and/or GCP guidelines without prior sponsor and IRB approval. Protocol Violations generally increase the risk and/or decrease the benefit; affect the subject's rights, safety or welfare and/or the integrity of the Research data. The term "protocol violation" is not defined by either the HHS human subjects regulations (45 CFR 46) Common Rule or the FDA human subjects regulations (21 CFR 50).

Quality Assurance: Systems and procedures designed to ensure that a study is being performed in compliance with applicable federal regulations and guidelines; institutional policies; and that the data being generated is accurate.

Quality Improvement: Routine Quality Improvement (QI) means systematic, data guided activities designed to bring about immediate, positive changes in the delivery of services in particular settings such as healthcare. QI involves deliberate actions to improve care, guided by data reflecting the effects (e.g., types of practical problem solving; an evidence-based management style; the application of science of how to bring about system change; review of aggregate data at the patient/provider/unit/ organizational level to identify a clinical or management change that can be expected to improve care). QI is generally not considered research - however, QI activities can be research if they are also intended to contribute to generalizable knowledge.

Quorum: A quorum is defined as a majority of the voting members as listed on the IRB membership. In the case of the IRB, a quorum must include at least one member whose primary concerns are in non-scientific areas, at least one member whose primary concerns are in scientific areas, at least one unaffiliated member, and at least one member who represents the general perspective of subjects. At meetings of the IRB, a quorum must be established and maintained for the deliberation and vote on all matters requiring a vote.

Randomization: The process by which subjects are assigned by chance to separate groups that compare different treatments or other interventions. Randomization gives each participant an equal chance of being assigned to any of the groups.

Recruitment: The act of selecting and enrolling research participants for a study using protocol specific inclusion and exclusion criteria.

Related to the Research: A financial interest is Related to the Research when the interest is in:

- A sponsor of the research;
- A competitor of the sponsor of the research;
- A product or service being tested; or
- A competitor of the product or service being tested.

Reportable Event / Reportable New Information (RNI): Information items that are 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. Such events or information are to be reported to the IRB within 5 business days.

Repository: The terms data and/or specimen bank, tissue bank, repository, registry and database are often used interchangeably. These all involve the collection, storage and distribution of human data and or biological specimens. Repositories established for research purposes require IRB oversight.

Request for Modification: Investigators must obtain prior approval from the IRB for any modifications of the previously approved research, including modifications to the informed consent process and document, except those necessary to eliminate apparent immediate hazards to subjects as set forth in Federal regulations.

Research as Defined by DHHS: A systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.

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

- Must meet the requirements for prior submission to the Food and Drug Administration 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 Food and Drug Administration 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 Food and Drug Administration as part of an application for a research or marketing permit.

Research Activities: Research activity includes all contact with the research subject, data collection and data analysis. This includes recruiting, enrolling, and any form of intervention or interaction with research subjects.

Research Records: Research records consist of IRB records as well as case histories (also referred to as investigator's research records) or any data gathered for research purposes.

Research under the Auspices of the Institution: Research under the auspices of the Institution includes research conducted at this institution, conducted by or under the direction of any employee or agent of this institution (including students) in connection with his or her institutional responsibilities, conducted by or under the direction of any employee or agent of this institution using any property or facility of this institution, or involving the use of this

institution's non-public information to identify or contact human subjects.

Respect for Persons: Respect for persons incorporates at least two ethical convictions taken from the Belmont Report that discusses the moral requirements to first, acknowledge individuals as autonomous agents in their right to choose or not to choose to participate in research; and second, to protect those with diminished autonomy or decision making capacity.

Restricted: Applies to investigators who are delinquent in meeting IRB requirements.

Risk: The potential harm or injury a subject may incur by participating in research. Risk must be evaluated by considering several components:

- a) Nature of Risk: physical, psychological, social, economic
- b) Probability of Risk: low, moderate, high
- c) Magnitude of Risk: mild, moderate, severe
- d) Duration of Risk: temporary or permanent

Risk/Benefit Analysis: An analysis of the potential risks to participants considered against the potential benefits to the individual or to the research objectives of the study.

Screening: Screening for IRB purposes is considered the activities performed after obtaining consent to ensure subjects are qualified for the study. Screening may not occur prior to Informed Consent. In contrast, "Pre-screening" for IRB purposes is the term used to describe activities prior to obtaining Informed Consent and may not include any research procedures.

Scientific Member: is an individual who has formal education and training as a physician or other medical professional, and M.S. and/or Ph.D. level physical, biological, or social behavioral scientists. Any IRB member who has a terminal degree in a medical or scientific field.

Screen Failure: This is a subject removed from the study during the screening process because they do not meet all inclusion and exclusion criteria, or whatever other requirements must be met for research participation. Subjects who leave the study after randomization or assignment to study intervention should be counted as withdrawals rather than screen failures, even if the subject didn't start the study intervention.

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 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).

Serious Non-Compliance: Non-Compliance that adversely affects the rights or welfare of

subjects.

- For Department of Defense (DOD) research Serious Non-Compliance includes failure of a person, group, or institution to act in accordance with Department of Defense (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; affect a human subject's willingness to participate in research; or damage or compromise the scientific integrity of research data.
- For Veterans Administration (VA) research Serious Non-Compliance includes a failure to adhere to the laws, regulations, or policies governing Human Research that might reasonably be regarded as:
  - Involving substantive harm, or a genuine risk of substantive harm, to the safety, rights, or welfare of human research subjects, research staff, or others
  - Substantively compromising the effectiveness of a Veterans Administration (VA) facility's human research protection or human research oversight programs
- For Veterans Administration (VA) research the unfounded classification of a serious adverse event as anticipated constitutes Serious Non-Compliance.

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
- Otherwise presents a potential for serious risk to the health, safety or welfare of a subject

Single Case Report: The external reporting (e.g., publication or poster/verbal presentation) of an interesting clinical situation or medical condition of a single patient. Case reports normally contain detailed information about an individual patient and may include demographic information and information on diagnosis, treatment, response to treatment, follow-up after treatment, as well as a discussion of existing relevant literature. The patient information used in the report must have been originally collected solely for non-research purposes as the result of a clinical experience. A single case report does not meet the definition of a systematic investigation and may not be human subject research.

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.

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 other medical or technical departments involved in conducting the clinical trial.

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](http://www.clinicaltrials.gov)).

Sponsor-Investigator: A sponsor-investigator is an individual who both initiates and conducts a clinical investigation and under whose immediate direction the investigational drug/device is being administered, used or dispensed. These are considered investigator-initiated or sponsor-investigator IND/IDEs.

Sponsor-Imposed Hold: A determination from the sponsor of the study to place specific research activities on hold. This determination may be made for interim data analysis; inadequate drug availability; response to a DSMB report/recommendation; or a pre-planned stopping point.

Standard of Care: Treatment that is accepted by medical experts as a proper treatment for a certain type of disease and that is widely used by healthcare professionals. Also called best practice, standard medical care, and standard therapy.

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.

Sub-Investigator: Any individual member of the clinical trial team designated and supervised by the investigator at a trial site to perform critical trial-related procedures and/or to make important trial-related decisions.

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 the institution.

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 Louisiana law.

Suspension of IRB Approval: An action of the IRB, IRB designee, Institutional Official, or designee of the Institutional Official to temporarily or permanently withdraw IRB approval of some or all research procedures short of a Termination of IRB Approval. Suspended studies remain open and are subject to continuing review.

- For Veterans Administration (VA) Research Suspension of IRB Approval:
  - Refers to a temporary interruption in the enrollment of new subjects, activities involving previously enrolled subjects, or other research activities.
  - Applies to interruptions related to concerns regarding the safety, rights, or welfare of human subjects, research investigators, research staff, or others.
  - Do not include interruptions in research resulting solely from the expiration of a project approval period, and voluntary interruption of research enrollments, and ongoing research activities by an appropriate VA facility official, research investigator, or sponsor (including the Office of Research and Development (ORD) when ORD is the sponsor).

Termination of IRB Approval: An action of the IRB, IRB designee, Institutional Official, or designee of the Institutional Official to permanently withdraw IRB approval of all research procedures. Terminated studies are permanently closed and no longer require continuing review.

- For Veterans Administration (VA) Research Termination of IRB Approval:
  - Refers to a permanent halt in the enrollment of new subjects, activities involving previously enrolled human subjects, or other research activities.
  - Applies to interruptions related to concerns regarding the safety, rights, or welfare of human subjects, research investigators, research staff, or others.
  - Do not include interruptions in research resulting solely from the expiration of a project approval period, and voluntary interruption of research enrollments, and ongoing research activities by an appropriate VA facility official, research investigator, or sponsor (including the Office of Research and Development (ORD) when ORD is the sponsor).

Test Article: Any drug for human use, biological product for human use, medical device for human use, human food additive, color additive, electronic product, or any other article subject to regulation under the act or under sections 351 or 354-360F of the Public Health Service Act. (See 21 CFR 56.102) Note: This includes but is not limited to food products, medical foods, dietary supplements, and any other substance that is generally recognized as safe (GRAS) for human use; over-the-counter drugs, currently marketed prescription drugs, infant formulas, vaccines, and blood products.

Treatment IDE: A mechanism through the FDA for providing eligible participants with investigational devices for the treatment of a serious or life-threatening illness for which there are no satisfactory alternatives. 21 CFR 812.36.

Treatment IND: A mechanism through the FDA for providing eligible participants with investigational drugs for the treatment of a serious or life-threatening illness for which there are no satisfactory alternatives. 21 CFR 312.34.

Unanticipated: (unexpected) problems/events are those that are not already described as potential risks in the consent form, not listed in the Investigator's Brochure, or not part of an underlying disease. A problem/event is unanticipated when it was unforeseeable at the time of its occurrence. A problem/event is unanticipated when it occurs at an increased frequency or at an increased severity than expected.

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.

Unanticipated Problem Involving Risks to Subjects or Others: Any information that is (1) unanticipated, (2) related to the research, and (3) indicates that subjects or others are at increased risk of harm.

- For Department of Defense (DOD) research the term Unanticipated Problem Involving Risks to Subjects or Others includes any incident, experience, or outcome that meets ALL three of the following conditions:
  - Is unexpected (in terms of nature, severity, or frequency) given the procedures described in the research protocol documents (e.g., the IRB-approved research protocol and informed consent document) and the characteristics of the human subject population being studied.
  - Is related or possibly related to participation in the research (in this Instruction, possibly related means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research).
  - Suggests that the research places human subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized, even if no harm has actually occurred.
- For Veterans Administration (VA) research:
  - The terms unanticipated and unexpected refer to an event or problem that is new or greater than previously known in terms of nature, severity, or frequency, given the procedures described in protocol-related documents and the characteristics of the study population.
  - The term Unanticipated Problem Involving Risks to Subjects or Others includes any event or problem that is serious, unexpected, and related to the research, where related means the event or problem might reasonably be regarded as caused by, or probably caused by, the research.
  - Serious Unanticipated Problems Involving Risks to Subjects or Others includes:

- Interruptions of subject enrollments or other research activities due to concerns about the safety, rights, or welfare of human research subjects, research staff, or others.
- Any work-related injury to personnel involved in human research, or any research-related injury to any other person, that requires more than minor medical intervention (i.e., basic first aid), requires extended surveillance of the affected individual, or leads to serious complications or death.
- Any VA National Pharmacy Benefits Management (PBM) Bulletins or Communications (sometimes referred to as PBM Safety Alerts) relevant to one or more of the VA facility's research projects.
- Any data monitoring committee, data and safety monitoring board, or data and safety monitoring committee report describing a safety problem.
- Any sponsor analysis describing a safety problem for which action at the VA facility level might be warranted.
- Any unanticipated problem involving substantive harm, or a genuine risk of substantive harm, to the safety, rights, or welfare of human research subjects, research staff, or others;
- Any problem reflecting a deficiency that substantively compromises the effectiveness of a VA facility's human research protection or human research oversight programs.

VA Research: is defined as research that is conducted by VA investigators (serving on compensated, work without compensation or Intergovernmental Personnel Agreement appointments) while on VA time, utilizing VA resources, and/or on VA property including space leased to, and used by VA whether funded by VA, by other sponsors or unfunded. VA investigators must follow all VA policies and procedures in the conduct of VA research including VA Handbook 1200.05 entitled "Requirements for the Protection of Human Subjects in Research".

Viable: As it pertains to the neonate, means being able, after delivery, to survive (given the benefit of available medical therapy) to the point of independently maintaining heartbeat and respiration.

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.

Withdrawal: A subject who signed a consent form but does not complete the entire study, regardless of the reason for withdrawal. Subject-initiated withdrawals and investigator or sponsor-initiated withdrawals should be included in the reported number of withdrawals.

1572: The 1572 is the Statement of the Investigator form submitted by the PI to the Sponsor

acknowledging their obligations in the conduct of the research. Principal Investigators on treatment protocols that involve an IND must complete Form FDA 1572. The 1572 is the contract between the clinical investigator and the federal government assuring that he or she will comply with FDA regulations 21 CFR 312.53. In signing the form the investigator assumes full responsibility for the study.

### 1.5 Ethical and Legal Principles Governing Human Subject Research

The Institution is committed to ensuring that all human research in which it is engaged is conducted in accordance with ethical and legal principles. The primary ethical principles applied to research covered by the HRPP, including protocols exempt under federal regulations pertaining to human subject research are set forth in the Belmont Report (<http://www.hhs.gov/ohrp/humansubjects/guidance/belmont.htm>). The Institution holds the conduct of research with the highest regard for the welfare of human subjects. It upholds and adheres to the principles of The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects in Research by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (1979). The three (3) main principles are:

- 1) Respect for Persons, which is ensured by obtaining informed consent, consideration of privacy, confidentiality, and additional protections for vulnerable populations. Individuals should be treated as autonomous agents afforded the right to make decisions themselves. Those with decreased or diminished autonomy such as minors, prisoners, people who are mentally disabled or challenged are entitled to additional protections.
- 2) Beneficence, which is assured by ensuring that possible benefits are maximized and possible risks are minimized to all human subjects. Application of this principle involves a risk/benefit analysis in which the risks to subjects must be reasonable compared to the potential for benefit either to subjects directly or to society. Risk evaluation must include the consideration of both the probability and magnitude of harm, including psychological, physical, legal, social, and economic harm.
- 3) Justice, the equitable selection of subjects. The possibility for benefits and the potential burdens of the research should be equitably distributed among the potential research subjects. Application of this principle requires the close scrutiny of the enrollment process to ensure that particular classes are not selected for their compromised position or convenience to the research investigator. Such classes are welfare patients, racial and ethnic minorities or persons confined to institutions.

All parties involved in the conduct of research are expected to also adhere to the principles of expertise (competent to work) and integrity (faithfully adhere to professional principles). Ethical principles from other sources (e.g., International Conference on Harmonization) may also be applied to research covered by the HRPP, for example:

- To an individual protocol because its particular circumstances raise a type of ethical issue that most other protocols do not

- When they are recognized by the federal or other funding source or the state or country where the research will occur
- When they have been developed for specific areas or types of subjects (e.g., embryos and fetal tissue, illiterate subjects).

Clinical Trials should be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, and that are consistent with Good Clinical Practice ( GCP) and the applicable regulatory requirements(s).

Investigator training on the ethical principles governing human subject research and investigator responsibilities is provided in the CITI tutorial for investigators, IRB Members, and IRB Staff, and in the orientation given to new IRB members.

With respect to sponsored research, LSUHSC-S address the protection of research participants by including in their standard contract language a provision that the sponsor acknowledges and understands that the LSUHSC-S HRPP is applicable to all human participant research.

### 1.5.1 Legal Principles

LSUHSC-S has and follows written policies and procedures that identify applicable laws in the localities where it conducts human research, takes them into account in the review and conduct of research, and resolves differences between federal or national law and local laws. (AAHRPP Element I.1.G.)

The basic legal principles governing human subject research, covered by the HRPP and applicable to individual protocols are:

- Federal Policy for Protection of Human Subjects (Common Rule) in 45 CFR Part 46
- Food and Drug Administration Regulations for the Protection of Human Subjects in 21 CFR Parts 50 and 56
- Standards for Privacy of Individually Identifiable Health Information (HIPAA Privacy Rule) in 45 CFR Parts 160 and 164.
- Department of Veterans Affairs regulations in 38 CFR Part 16 and VHA Handbook 1200.5
- Applicable Louisiana law.

These and other legal principles are addressed when applicable in individual HRPP chapters. The LSUHSC-S Human Research Protections Program (HRPP), in partnership with its research community, is responsible for ensuring the ethical and equitable treatment of all human subjects in research conducted under its auspices.

### 1.5.2 Regulatory Compliance

The HRPP is responsible for ensuring compliance with federal regulations, state law, local law and regulations and institutional policies. The Institution adheres to the following regulations and policies for human subject research activities that fall under its authority;

1. The Federal Policy regulations for the protection of human research subjects (DHHS 45 CFR Part 46; Common Rule: <http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html>)
2. When research involves articles subject to regulation by the FDA, the FDA regulations for the protection of human subjects (21 CFR Parts 50) [Electronic Code of Federal Regulations](#) and Institutional Review Boards (21 CFR Parts 56) [Electronic Code of Federal Regulations](#)
3. Where applicable, other federal, state and local regulations regarding research involving human subjects.
4. Policies and procedures established by the Human Research Protections Program and the IRB, are incorporated in the LSUHSC-S Human Research Protections Program and Institutional Review Board Standard Operating Procedures Manual. The current version of this reference manual may be found on the HRPP web-site at: <http://www.lsuhschreveport.edu/HRPP/HRPPHome.aspx>. All other LSU System and LSUHSC-S Campus policies apply.
5. The provisions of the Federal Wide Assurance Agreements (FWA) for FWA 00000653.
6. All human subject research involving VA investigators and subjects are conducted in compliance with VA federal regulations and requirements including VHA handbook 1200.05 entitled "Requirements for the Protection of Human Subjects in Research", and regulations found in (45 CFR Part 46), the Common Rule, and 21 CFR 50 and 56.

#### **1.6 Federal Wide Assurance (FWA)**

The LSUHSC-S HRPP maintains a Federalwide Assurance (FWA, 00000653) on file with OHRP that, unless exempt, obligates the institution to uphold ethical principles and is applicable whenever research is conducted or supported by any United States federal department or agency that has adopted the policy for the Protection of Human Subjects (also known as the Common Rule). The LSUHSC-S IRB is organized and operates in compliance with Department of Health and Human Services (OHRP) regulations as described in 45 CFR 46, Food and Drug Administration (FDA) regulations as described in 21 CFR Parts 50 and as applicable the International Conference on Harmonization (ICH) E6. The LSUHSC-S IRB is registered with OHRP and the FDA. The IRB registration number is IRB00000178. The parent organization number is IORG0000109.

The LSUHSC-S IRBs shall review all human subject research:

- 1) Sponsored by LSUHSC-S
- 2) Conducted by any LSUHSC-S or agent in connection with his or her institutional duties
- 3) Conducted by any LSUHSC-S agent or employee using any property or facility of LSUHSC-S
- 4) That involves uses of LSUHSC-S's non-public information to identify or contact human research subjects
- 5) Conducted by a research affiliate site or organizations

The Institution assures that whenever it engages in human subjects research conducted or

supported by any federal department or agency that has adopted the Federal Policy for the Protection of Human Subjects, known as the Common Rule the Institution will comply with the terms of the FWA unless the research is otherwise exempt from the requirement of the Common Rule or a department or agency supporting the research. Under 38 CFR 16.102(f), an institution is engaged in human subject research whenever its employees or agents intervene or interact with living individuals for research purposes; or, obtains, release, or access individually-identifiable private information for research purposes.

In its FWA, the Institution has opted to limit the application of the FWA to Research funded by DHHS or Federal agencies that have adopted the Common Rule. While the terms of the FWA are applied to the University only when engaged in federally sponsored research, the policies and procedures in these SOPs apply to all research under the auspices of the Institution involving Human Subjects, regardless of funding source.

Studies involving no greater than minimal risk may be reviewed using Worksheet: Flexibility Policy (HRP-342). The IRB will verify that the research meets all of the following criteria: (1) Not federally funded or supported by federal funds; (2) Minimal Risk; (3) Is not FDA regulated and does not include prisoners. Under no circumstances will federally funded or FDA regulated research be reviewed under this policy. Projects that receive federal support are subject to the terms of the LSUHSC-S Federalwide Assurance. Should the funding status of a study reviewed under this policy change, it is the responsibility of the Principal Investigator to notify the IRB, immediately.

Research projects reviewed outside the scope of the FWA are not subject to the same federal reporting requirements as federally funded projects and will be afforded protections commensurate with risk as determined by the IRB and institutional policy. For projects conducted under the flexibility policy, the LSUHSC-S HRPP and IRB follow internal reporting requirements for serious or continuing non-compliance, suspensions or terminations, or reporting of unanticipated problems involving risk to subjects or others. Determinations of serious or continuing non-compliance, suspensions or terminations, or unanticipated problems involving risk to subjects or others made by the HRPP Compliance Committee or the IRB related to research that falls under the scope of the Flexibility Policy are reported to the LSUHSC-S Institutional Official, Vice Chancellor for Research and the investigator's Department Chair. Corrective measures, restrictions or other requirements for research that requires reporting under this policy will be determined by the LSUHSC-S HRPP, IRB or Institutional leadership. Studies reviewed under this policy will be subject to audit by the HRPP to confirm compliance with institutional policies and that funding status has not changed.

### 1.7 Institutional Official

LSUHSC-S delegates responsibility for the Human Research Protection Program to an official with sufficient standing, authority, and independence to ensure implementation and maintenance of the program. (AAHRPP Element I.1.B.)

The Vice Chancellor for Research for LSUHSC-Shreveport is the Institutional Official. The ultimate responsibility of the HRPP resides with the Institutional Official (IO) of the program. The IO is responsible for ensuring the LSUHSC-S HRPP has the resources and support necessary to comply with all institutional policies and with federal regulations and guidelines that govern human subject research. The IO is legally authorized to represent LSUHSC-S and is the signatory of the FWA and assumes the obligations of the FWA.

The IO:

- Understands the institution's responsibilities under the FWA
- Has the authority to ensure that:
  - Human research subjects are protected
  - Members of the Institutional Review Boards (IRBs) are
    - Knowledgeable about the local research content and
    - Comply with the terms of the FWA
  - All components of the Human Research Protections Program are functioning satisfactorily
  - The LSUHSC-S FWA is updated as necessary and sent to the Office of Human Research Protections within the Department of Health and Human Services (OHRP) for approval
- Supports the independence authority of the IRB as required under federal regulations

The IO also holds ultimate responsibility for 1) oversight of the Institutional Review Boards (IRBs) and all LSUHSC-S investigators; 2) for assuring the IRB members and investigators are appropriately knowledgeable to conduct research in accordance with ethical standards and applicable regulations; and 3) for the development and implementation of an educational plan for IRB members, staff and investigators.

The IO should be an individual of sufficient rank who has the authority to ensure that all obligations of the HRPP are carried out effectively and efficiently (and) should be at a level of responsibility sufficient to allow authorization of necessary administrative or legal action should that be required. The Vice Chancellor for Research is responsible for either retaining this responsibility or delegating it to an institutional officer of appropriate standing with campus-wide jurisdiction.

The IO is responsible for:

- Setting the tone for an institutional culture of respect for human subjects
- Overseeing compliance with all applicable federal regulations and guidance, state law and institutional policies
- Being the signatory authority for the FWA submitted to OHRP
- Serving as a knowledgeable point of contact for OHRP, FDA and other governmental and non-governmental agencies regarding human research protection
- Ensuring effective institution-wide communication and guidance on human subject protection issues

- Overseeing processes to ensure that investigators fulfill their responsibilities under applicable regulations
- Facilitating participation by the LSUHSC-Shreveport research community in human subject protection educational activities
- Designating one or more IRBs that will review research covered by the LSUHSC-Shreveport FWA
- Arrange for sufficient resources, space, and staff to support the IRB's review and record keeping duties
- Appointing the IRB Chairpersons and Vice-Chairperson
- Conducting an annual review of the Human Research Protections Program

### 1.8 Research Covered by the HRPP

LSUHSC-S has and follows written policies and procedures for determining when activities are overseen by the Human Research Protection Program. (AAHRPP Element I.1.A.)

LSUHSC-S conducts or oversees biomedical, social science and behavioral research. Human subject research is covered as stated in the Federal Wide Assurance for LSUHSC-S and any affiliated organization. All research engaged in at LSUHSC-Shreveport is covered by the HRPP. The LSUHSC-S HRPP covers all research involving human subjects that is under the auspices of the Institution regardless of funding. The research may be externally funded, funded from LSUHSC-S sources, or conducted without direct funding.

An activity is covered by the HRPP when:

- It is considered human subject research as defined in any one of the following:
  - FDA regulations
  - DHHS regulations or other Common Rule regulations
  - VA regulations (VA Handbook 1200.5) or
  - Any other applicable state or local regulations, e.g. Louisiana regulations

And

- LSUHSC-S (or its employees or agents) is engaged research - as defined by being involved in one or more of the following activities:
  - Receiving an HHS award for research
  - Intervening with participants for research purposes (invasive or noninvasive)
  - Manipulating the environment
  - Interacting with participants for research purposes
  - Obtaining identifiable private information or identified biological specimens from any source for research purposes, according to the OHRP guidance Engagement of Institutions in Human Subjects Research.  
<http://www.hhs.gov/ohrp/policy/engage08.html>

Agents include all individuals performing institutionally designated activities or exercising institutionally delegated authority or responsibility, including students, faculty, staff, employees or visiting scholars.

LSUHSC-S research affiliate organizations are Biomedical Research Foundation of Northwest Louisiana and University Health Systems.

VA Research - Classified research involving human subjects cannot be approved by a VA IRB or R&D Committee or performed at a VA facility, including space leased to, and used by VA.

See Section 3 of this manual for the policies and procedures for determining when studies meet the regulatory definitions of human subject research.

### **1.8.1 International Research/Transnational Research**

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LSUHSC-S's transnational research activities are consistent with the ethical principles set forth in its Human Research Protection Program and meet equivalent levels of participant protection as research conducted in the Organization's principal location while complying with local laws and taking into account cultural context. (AAHRPP Standard I-3)

The purpose of this policy is to establish guidelines for Louisiana State University Health Sciences Center at Shreveport (LSUHSC-S) or LSUHSC-S affiliates when conducting human subject research, for which one or all of the sites or participants, are located outside the United States (U.S.), regardless of funding.

LSUHSC-S transnational research requirements are consistent with the ethical principles set forth in its Human Research Protection Program (HRPP) and strive to meet equivalent levels of participant protections for research conducted within the United States. For federally funded research, the regulations of the sponsoring agency apply and the required protections must be provided. This policy is to ensure all human subject research, regardless of whether the research is subject to U.S. federal regulations, will be guided by one of the following statements of ethical principles:

- The Belmont Report
- Nuremberg Code
- The World Medical Association's Declaration of Helsinki
- Other appropriate international ethical standards recognized by the U.S. Federal departments and agencies that have adopted the U.S. Federal Policy for the Protection of Human Subjects, known as the Common Rule.

The LSUHSC-S Institutional Review Board (IRB) will review the research in accordance with the applicable Department of Health and Human Services (DHHS) regulations at 45 CFR 46, and the FDA regulations at 21 CFR 50,56,312,600,612, 812 and International Conference on Harmonization (ICH) Guidelines to the extent ICH encompassed in FDA and OHRP regulations. Recognizing the continued growth of international research, the Office of Human Research Protections (OHRP) has developed an International Compilation of Human Subject Research Protections. OHRP provides this compilation of regulations and guidelines that govern human

subject research in other countries, as well as standards from a number of international and regional organizations to support researchers in the conduction of human subject research outside the U.S. The Compilation provides direct web links to each country's key Organizations and laws whenever available. LSUHSC-S HRPP directs researchers to these guidelines and requires their compliance while conducting transnational research.

The document noted below provides an overview of what ethical standards different countries follow and what offices you may need local approval from. To use the compilation, go to page 3 of the document and then click the country of interest.

- See: OHRP <https://archive.hhs.gov/ohrp/international/HSPCompilation.pdf>
- For VA research: VA Handbook 1200.05(1) [Requirements for the Protection of Human Subjects in Research](#), 10P9 - Research and Development

Conflicts arising between federal or national law and other applicable laws are referred to the LSUHSC-S Department of Legal Affairs and Organizational Integrity In House Counsel for guidance and resolution.

### **1.8.2 Principal Investigator Responsibilities for International Research**

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All LSUHSC-S policies and procedures that are applied to research conducted in the U.S. are also applied to research conducted in other countries as appropriate. In addition, Principal Investigators (PI) should ensure that participants outside the U.S. have equivalent protections that participants would be afforded to participants in the U.S.

The PI must obtain LSUHSC-S IRB approval in addition to approval from the local Ethics Committee, should one exist in the host country, in which the research is conducted. If an Ethics Committee or other similar review committee does not exist, then a letter of support from a community leader must be obtained and submitted to the LSUHSC-S IRB. The PI will obtain the letter of support from the facility at which the research is conducted, if applicable.

Investigators are required to be knowledgeable about and comply with local laws while conducting their research and take into account the local customs and cultural context. Care must be taken to ensure that the cultural norms of the host country are respected and that the participants will not suffer adverse consequences from participation, such as being subjected to retaliation from local authorities or local community. The investigator should also consult with researchers familiar with the culture differences of transnational research and become knowledgeable in the different customs, habits, and practices of international study subjects.

Principal Investigators must assist their colleagues from the host country in obtaining a Federal Wide Assurance (FWA) if the research is federally funded and requires that the transnational institution receive an approved FWA from the Office of Human Research Protections (OHRP).

Listed below are additional elements the investigator should address prior to IRB review and

approval:

- The qualifications of collaborator(s) at each site.
- Provide the names and dates of completion of the CITI module on conducting research in an international setting for investigators.
- Is the investigator providing equivalent protections to US regulations and if federally funded, include the FWA number for each research site.
- Investigator must be knowledgeable of local laws and cultural context in all locations where research is conducted.
- Cultural differences that influence study design and the consent process.
- The rationale for conducting the study with an international population.
- Investigator must comply with local laws and adhering to local cultural norms (e.g., customs, socio-economic, political, cultural factors, language and literacy).
- Research methods appropriately minimize the risks to research participants at the selected sites.
- Are there any state department warnings that would prohibit travel? Think about potential risks to the research team. Check early and before leaving the US as political or environmental conditions can change at any time.
- Be sure to allow enough time for additional logistics related to travel (passport, Visas, Immunizations, permits to transport goods into or out of the country).
- Investigator to consider if biological specimens can be brought back into the US. While designing your protocol you may contact LSUHSC-S Safety Office for guidance.
- Meaningful Informed Consent- understand and weigh the implications for cultural differences when trying to obtain informed consent, the informed consent process should be based on local cultural norms and laws, quality of translation, local collaborators to assist in explanation
- Who will translate documents for LSUHSC-S and host country review?
- Is there funding to cover the costs of translations?
- Translator certification will be required for the IRB review.
- English translated documents must be provided to the IRB for IRB review.
- Will a translator be required on-site?
- Have risks been minimized based on the methods implemented? Low risk in the U.S. does not mean low risk in host country. Asking certain questions may be offensive or responses could place the participant at risk.
- Does the host country have provisions for research –related injuries? If clinical studies are conducted, available health care may be minimal or non-existent.
- What is considered Identifiable Data in the U.S. may differ in the host country. Do not collect any data or specimens without knowing the rules. IP addresses are considered identifiable in European countries.
- Have you obtained the appropriate approvals in the host country to conduct research?
- Submit your IRB application to the IRB for IRB review and approval at least 8 to 10 weeks in advance of your planned departure.
- Determine if written agreements are required. Contact the Department of Legal Affairs & Organizational Integrity Contract Coordinator for guidance as needed.

- HIPAA is a U.S. regulation that does not apply in other countries.
- Obtain a description of the host country's ethics review and oversight mechanism for participant protection.
- All federally funded studies must have Federal Wide Assurance (FWA) before the study can begin.

When following VA regulations, International Research includes VA-approved research conducted at international sites not within the United States, its territories, or Commonwealths; and includes research where human tissues are sent outside the United States. For VA purposes, International research does not include studies in which VA is only one of multiple participating sites where the overall study-wide PI is not a VA investigator (i.e. the PI for the study as a whole is not a VA investigator)." The researcher must provide the IRB documentation that the facility director has approved any international research involving the VA.

- Overton Brooks VA Medical Center does not participate in international research.

### **1.8.3 IRB Responsibilities for International Research**

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LSUHSC-S's IRB review of transnational research adheres to the same policies applied to domestic (US) research, when appropriate. The IRB must have knowledge of the local research context. This level of knowledge is in part based upon the level of risk presented by the research. Additional legal or cultural expertise may be consulted by the IRB during its review, and the IRB will make those determinations required by the laws of the countries in which the research is conducted. This knowledge may also be gained from involving legal or cultural expertise as a consultant to the IRB during its review of the research. In addition, the IRB requires documentation that the host country is aware of the research and has agreed for the research to be conducted in that country. When necessary, the IRB will communicate with the host country's Ethics Committee or similar review committee should one exist.

The IRB must review the Informed Consent document which must be translated into the language understandable by the subjects for accuracy and approval. The translated document must be certified or back-translated and major discrepancies with the English version must be addressed. In some circumstances it may be inappropriate to document consent by using the standard written and signed informed consent document. There also may be different laws regarding determination as to who may serve as a Legally Authorized Representative (LAR) which the IRB must take into account.

If subjects participating in transnational research will be compensated for their participation in the research, the IRB must ensure that the amount to be provided to subjects is appropriate and reflective of the standard of living in the country in which the research is being conducted as to not unduly influence subjects to participate.

The IRB is responsible for monitoring the research as with all other human subject research under its purview. Any problems encountered with the research should be communicated to the study sponsor, relevant regulatory bodies, and all reviewing IRBs and Ethic Committees as appropriate. Research that is federally funded and FDA regulated must comply with both DHHS and FDA regulations.

When researchers conduct studies in other countries, the IRB that reviews such research will confirm the following when reviewing and approving transnational research:

- The IRB must have the appropriate expertise and knowledge of the country(ies) either through the IRB membership or consultants.
- The IRB must be knowledgeable about the local laws, regulations, codes, and guidance that govern such research in addition to the cultural context in which the research is conducted. The IRB requires the PI to provide information about the laws and cultural context of other countries in which the research is being conducted.
- The PI must ensure that all of the research procedures described in the IRB application will be conducted at the foreign site for review by the IRB committee and the committee in the host country.
- The PI must provide the qualifications of all of the researchers in the IRB application. The IRB will confirm the qualifications of the researchers and research staff for conducting research in that country.
- When there is a local IRB in the host country where the research is conducted, the researcher and IRBs must agree prior to approval on a process for ensuring that ↓ initial review, continuing review, review of modifications, post-approval monitoring, handling of complaints, non-compliance and unanticipated problems involving risks to subjects or others are conducted. Depending upon the risk level and other factors, the IRB would consider the following options: LSUHSC-S can enter into agreements with the other IRB requiring the other IRB to report problems and complaints or the researcher can describe a process for reporting problems and complaints.
- The IRB must approve the plan provided by the PI regarding informed consent process and document and other language issues
- Coordination and communication with local IRBs or EC when appropriate
- All policies and procedures that are applied to research conducted domestically should be applied to research conducted in other countries, as appropriate.
- The IRB should ensure that equivalent protections are provided to research in other countries. The IRB should make determinations and decisions based on laws and knowledge of the country in which the research will be conducted.

When following VA regulations and guidance in transnational research the IRB ensures the following:

- Permission must be obtained from the chief research and development officer or designee, prior to initiating any VA-approved international research.

- The VA facility director must approve any request for permission to conduct international research prior to forwarding it to the chief research and development officer.
- All international sites must hold an international federalwide assurance, and the research, and the research must be approved by the IRB or Ethics Committee of the participating sites listed on the international federalwide assurance.

#### **1.8.4 Approvals Required Before International Human Subject Research Commences**

IRB approval is required before research activities may commence. In addition to approval from the IRB, depending on the funding source, either contract finalization or departmental approval is required before research involving human participants can commence, as follows:

- Externally funded research (industry-sponsored clinical trials and other clinical research) undergoes a parallel review process but must have an agreed upon agreement in the signature phase prior to IRB submission.
- Other research requires the approval of a Section Chief, Department Chair and Senior Associate Dean for Clinical Affairs, as appropriate, confirming:
  - o Scientific and scholarly validity
  - o Adequacy of resources

Some protocol-specific situations require additional review and approval by other organizational components, or must meet their standards.

#### **1.9 Written Policies and Procedures for all Human Subjects Research**

LSUHSC-S has and follows written policies and procedures for determining when activities are overseen by the Human Research Protection Program. (AAHRPP Element I.1.A.)

The LSUHSC-S HRPP and IRB Standard Operating Policies and Procedures for Human Research Protections, details the policies and regulations governing research with human subjects under the auspices of the Institution and the requirements for submitting research proposals for review by the LSUHSC-S IRB. This is not a static document. The policies and procedures are annually reviewed and revised by the Assistant Vice Chancellor for Research Management (AVCRM) in consultation with applicable Institutional entities, the IO, the Institutional Review Board, and Counsel for the HRPP. The Institutional Official, IO is ultimately responsible for reviewing and approving all recommended revisions to the policies and procedures.

The Assistant Vice Chancellor for Research Management or designee will keep the Institution apprised of new information that may affect the HRPP, including laws, regulations, policies, procedures, and emerging ethical and scientific issues on its website and through campus electronic mailing lists. The policies and procedures will be available on the LSUHSC-S HRPP website and copies will be available upon request.

## 1.10 HRPP Organization

The HRPP is a comprehensive system to ensure the protection of human subjects participating in research. The HRPP consists of a mission statement; ethical principles; policies and supporting SOPs; and various individuals and committees such as: the IO, the Vice Chancellor for Research, the Assistant Vice Chancellor for Research Management, the IRB, other committees or subcommittees addressing human subjects protection (e.g., Bio-safety Committee, Radiation Safety Committee, Pharmacy and Therapeutics Committee, Radioactive Drug Research Committee, Conflict of Interest Committee), investigators, IRB staff, HRPP staff, research staff, health and safety staff (e.g., Hospital Safety Officer Research Compliance Specialist, Privacy Officer) and research pharmacy staff. The objective of this system is to assist the Institution in meeting ethical principles and regulatory requirements for the protection of human subjects in research.

The following officials, administrative units and individuals have primary responsibilities for implementing the HRPP:

### 1.10.1 Chancellor

LSUHSC-S delegates responsibility for the Human Research Protection Program to an official with sufficient standing, authority, and independence to ensure implementation and maintenance of the program. (AAHRPP Element I.1.B.)

The Chancellor is responsible for the overall operations at LSUHSC-S. The Chancellor may retain the responsibilities of IO, or may delegate the ultimate responsibility and authority of the HRPP.

### 1.10.2 Institutional Official (IO)

The ultimate responsibility of the HRPP resides with the Vice Chancellor for Research who serves as the Institutional Official (IO). The IO is responsible for ensuring that the Institution's HRPP has the resources and support necessary to comply with all Institutional policies and with applicable Federal regulations and guidelines that govern human subject research. The IO is legally authorized to represent the Institution and is the signatory of the FWA, and assumes the obligations of the FWA.

### 1.10.3 Assistant Vice Chancellor for Research Management

The Assistant Vice Chancellor for Research Management (AVCRM) reports to the Vice Chancellor for Research and is responsible for the duties below. These duties, or portions thereof, may be delegated to a responsible party as deemed appropriate by the AVCRM, the Vice Chancellor for Research or the IO.

1. Developing, managing and evaluating policies and procedures that ensure compliance

with all state, federal, and local regulations governing research. This includes monitoring changes in regulations and policies that relate to human research protections and overseeing all aspects of the HRPP program.

2. Advising the Institutional Official (IO) on key matters regarding research at the Institution.
3. Implementing the institution's HRPP policy.
4. Submitting, implementing and maintaining an approved FWA through the Institutional Official (IO) and the Department of Health and Human Services Office of Human Research Protections (OHRP)
5. Providing information to the IO regarding the needs and resources required for the HRPP operation.
6. Serving as the primary contact at LSUHSC-S for the Office for Human Research Protections (OHRP) of the U.S. Department of Health and Human Services and other federal regulatory agencies.
7. Assisting the investigators in their efforts to carry out the Institution's research mission.
8. Developing and implementing needed improvements and ensuring follow-up of actions, as appropriate for the purpose of managing risk in the HRPP.

#### **1.10.4 HRPP Staff**

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##### HRPP Medical Director

The Medical Director reports to the Institutional Official (IO) and is Responsible for:

1. Advising the Institutional Official (IO) on key matters regarding research at the Institution.
2. Implementing the institution's HRPP policy.
3. Assisting the investigators in their efforts to carry out the Institution's research mission.
4. Developing and implementing needed improvements and ensuring follow-up of actions, as appropriate for the purpose of managing risk in the HRPP.

##### HRPP Program Manager

The HRPP Program Manager reports directly to the AVCRM and indirectly to the IO. The HRPP Program Manager advises the AVCRM on day to day operations of the HRPP. Additional duties of the HRPP Program Manager are:

1. Ensuring constructive communication concerning HRPP, IRB and Clinical Trial Services (CTS) matters among the officials of the Institution, investigators, clinical care staff, and human subjects as a means of maintaining a high level of awareness regarding the safeguarding of the rights and welfare of the subjects.
2. Assist the AVCRM in developing, managing and evaluating policies and procedures that ensure compliance with all state, federal, and local regulations governing research. This includes monitoring changes in regulations and policies that relate to human research protections and overseeing all aspects of the HRPP program.
3. Assisting investigators in their efforts to carry out the Institution's research mission.
4. Developing and implementing needed improvements and ensuring follow-up of actions, as appropriate, for the purpose of managing risk in the research program.

5. Developing training requirements as required and as appropriate for investigators, subcommittee members and research staff, and ensuring that training is completed on a timely basis.

#### HRPP Educator & Participant Outreach Coordinator

The HRPP Educator & Participant Outreach Coordinator is responsible for:

1. Developing, coordinating, and implementing the LSUHSC-S comprehensive education program for the protection of human participants in research, GCP, investigator responsibilities, IRB and regulatory reporting.
2. Assuring that all components of the education program are in strict compliance with federal and state regulations and Institutional policies governing human research.
3. Assists the HRPP Program Manager and/or AVCRM in determining that all initial and bi-annual certification requirements have been met by all members of the IRB and IRB staff; Investigators and research staff; and students engaged in research involving human subjects.
4. The development and implementation of educational materials (manuals for faculty, staff, and investigators; newsletters; web updates; announcements).
5. The development and implementation of outreach resources and educational materials for research participants, prospective research participants and community members.
6. Participating in the periodic evaluation of community outreach activities.

This Coordinator is supervised by the HRPP Program Manager and evaluated annually as per Institutional policy.

#### HRPP Quality Assurance/Quality Improvement Coordinators (QA/QI Coordinators)

The HRPP Quality Assurance/Quality Improvement Coordinators oversee and ensure that research conducted at the Institution is in compliance with research regulations applicable to human subjects. In this capacity, the QA/QI Coordinators are responsible for (1) developing and implementing policies and procedures to ensure compliance with research regulations and requirements; (2) conducting training and education regarding research compliance topics; and (3) conducting audits and monitoring research activity.

The QA/QI Coordinators serve as ex-officio guests of the IRB to provide information regarding routine or for cause audits, monitoring activities, compliance deviations and violations and assist with corrective measure(s). The QA coordinators meet with the HRPP Program Manager and AVCRM on an ongoing basis to discuss ongoing projects of the HRPP that relate to human subject research. The HRPP Quality Assurance/Quality Improvement Coordinators evaluate and implement measures to improve Human Research Protections in compliance with organizational policies and procedures.

The Coordinators are supervised by the HRPP Program Manager and evaluated annually as per the Institutional policy and Civil Services Guidelines.

When Protocol Exceptions and Deviations are deemed to be serious or continuing, (as defined in Section 10 of this manual), the HRPP Program Manager (or designee) shall report the

Exception or Deviation to the QA Coordinator for review. The coordinator will review/monitor the information and investigate, as needed, and report to the IRB recommendations for a corrective action plan.

The QA Coordinators review and investigate all credible complaints and Allegations of Non-Compliance (as discussed in Section 1.13) that are submitted to the IRB or that have been brought to their attention, and will make a report, as appropriate, to the IRB with recommendation for a corrective action plan.

#### **1.10.5 Institutional Review Board**

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LSUHSC-S has and follows written policies and procedures that allow the Institutional Review Board or Ethics Committee to function independently of other organizational entities in protecting research participants. (AAHRPP Element I.1.C.)

LSUHSC-S has and follows written policies and procedures for reviewing the scientific or scholarly validity of a proposed research study. Such procedures are coordinated with the ethics review process. (AAHRPP Element I.1.F.)

LSUHSC-S IRB has one IRB, appointed by the Institutional Official. The IO retains the authority to create or dissolve IRBs. Members of the IRBs are also appointed by the IO. The IRB is one of five (5) LSUHSC-S Research Assurance Committees. The IRB prospectively and retrospectively reviews and makes decisions concerning all human research conducted at its facilities or by its employees or agents, or under its auspices. The IRB is responsible protecting the rights and welfare of human research subjects involved in research conducted under the auspices of the Institution. It discharges this duty by complying with the requirements of the Common Rule and other applicable federal regulations, state regulations, the FWA; and institutional policies. (See Section 2 for a detailed discussion of the nature, role and duties of the IRB).

The LSUHSC-S IRB serves as the IRB of record for LSUHSC-S; Overton Brooks VA Medical Center; Overton Brooks Research Corporation; Biomedical Research Foundation-Northwest LA; University Health System and any other IRB affiliated sites through agreements.

#### **1.10.6 Counsel for the HRPP**

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LSUHSC-S has and follows written policies and procedures that identify applicable laws in the localities where it conducts human research, takes them into account in the review and conduct of research, and resolves differences between federal or national law and local laws. (AAHRPP Element I.1.G.)

The Institution's Office of Legal Affairs and Organizational Integrity provides advice to the HRPP, the IO and the Institutional Agents, PIs, Investigators, and research staff with respect to laws, regulations, and requirements applicable to Human Subjects Research. This includes

interpretation and application of Federal, State and local laws where research is conducted. Counsel is responsible for addressing all of the legal issues arising out of the activities of LSUHSC-S. A representative of the Office of Legal Affairs and Organizational Integrity is available for consultation on issues regarding human subject research and participant protection.

#### **1.10.7 Department Chair**

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LSUHSC-S ensures that the Human Research Protection Program has resources sufficient to protect the rights and welfare of research participants for the research activities that the Organization conducts or oversees. (AAHRPP Standard I-2)

The Department Chair is responsible for ensuring that the Principal Investigator (PI) is qualified by training and experience to conduct the proposed research. In addition, Department Chairs are responsible for ensuring that the PI has sufficient resources and facilities to conduct the proposed research. Such resources include but are not necessarily limited to personnel, space, equipment and time. For each proposal submitted to the LSUHSC-S IRB for approval, the Department Chair must certify that they accept responsibility for assuring adherence to the federal and state regulations and institutional policies governing the protection of human subject's research, including applicable institutional credentialing requirements. The Department Chair is required to review all proposals before they are submitted to the IRB for review. The signature of the Department Chair indicates that the study is found to be scientifically sound and can reasonably be expected to answer the proposed question.

#### **1.10.8 The Principal Investigator (PI)**

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The Principal Investigator bears the ultimate responsibility for the protection of human subjects who participate in research. The PI is expected to abide by the highest ethical standards for developing a protocol that incorporates the principles of the Belmont Report. He/she is expected to conduct research in accordance with the IRB approved research protocol and to oversee all aspects of the research by providing supervision of support staff, including oversight of the informed consent process. All subjects must provide their informed consent and the investigator must establish and maintain an open line of communication with all research subjects within his/her responsibility. In addition to complying with all the policies and standards of the governing regulatory bodies, the investigator must comply with institutional and administrative requirements for conducting research. The PI is responsible for ensuring that all research staff are appropriately qualified and complete all required training prior to initiating research. When investigational drugs or devices are used, the investigator is responsible for providing written procedures for their storage, security, dispensing and disposal. The PI is ultimately responsible for ensuring that no subject is enrolled before IRB approval is issued and any related sponsor agreement is fully executed.

#### **1.10.9 Other Related Units and Individuals of the HRPP**

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LSUHSC-S has and follows written policies and procedures that allow the Institutional Review Board or Ethics Committee to function independently of other organizational entities in protecting research participants. (AAHRPP Element I.1.C.)
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LSUHSC-S has and follows written policies and procedures to ensure that the handling of investigational or unlicensed test articles conforms to legal and regulatory requirements. (AAHRPP Element I.7.B.)
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#### Office of Sponsored Programs and Technology Transfer

The Office of Sponsored Programs and Technology Transfer (OSPTT) reviews grants and contracts involving human subjects. OSPTT works with departments to secure and document departmental commitments. OSPTT acts as the authorized official and single point of contact for grant applications and awards. When a grant involves human subject research, the grant information will be shared with the IRB.

OSPTT processes determine compliance with state, federal, and institutional policies prior to accepting awards. Federal regulations and institutional commitments can change between time of application and the time of the award. The institution reserves the right to accept or reject awards based on reported levels of financial commitment. This institutional review ensures that all terms of award are in compliance with institutional policies.

When the grant includes human research activities that will be conducted by investigators who are not employees or agents of LSUHSC-S, an agreement or subcontract is executed between LSUHSC-S and the collaborating institution. All agreements and subcontracts are reviewed by the Office of Legal Affairs and Organizational Integrity. The agreement or subcontract includes the requirement for the collaborating institution to assure compliance with federal regulations for the protection of human subjects in research and to provide documentation of current and ongoing IRB approval. The collaborating institution must also ensure that key personnel involved in human subjects' research are in compliance with other appropriate federal agencies policy on education in the protection of human subjects and provide documentation of education of key personnel to LSUHSC-S.

#### Research Pharmacy

All test articles including investigational drugs, devices, biologics and combination products used in human participants research are stored, handled, and dispensed in compliance with regulations or requirements of the FDA, The Joint Commission, Federal and State Boards of Pharmacy, other applicable organizations and in accordance with applicable Hospital, Medical Center and Institutional policies and guidelines. Investigators conducting investigational drug research at Overton Brooks VA Medical Center are responsible for following the VA Research and Investigational Drug Policies and Procedures.

The Research Pharmacy provides services to achieve safe and responsible handling of medications. The main purpose is to maintain control and accountability of medication use in

research subjects in order to provide maximum benefit and safety for those participating in research protocols. Pharmacy staff also serve as collaborators in the planning of research protocols to ensure feasibility of implementation.

Representatives from the Department of Pharmacy serve on the LSUHSC-S IRB, allowing the Pharmacy to have complete information about all IRB approved research that takes place at LSUHSC-S Hospital and under its jurisdiction. The Pharmacist member assures that information about all studies involving drugs used in research is shared with both the Pharmacy Staff as appropriate and that the LSUHSC-S Hospital Pharmacy and Therapeutics Committee is made aware of IRB approved research involving drugs.

#### Ancillary Units Involved in Research

All units involved in research may include but are not limited to Lab, Cardiopulmonary, Radiology, Pharmacy, Nursing, Social Services and Others.

#### Protocol Specific Coordination

For research conducted under the auspices of the LSUHSC-S IRB, protocol-specific coordination must take place. The Principal Investigator must identify services to be provided by ancillary units within the University Health System that are above standard of care. These services will require reimbursement to the hospital. Each department/unit that is to provide the service must be identified in the IRB Initial Application Form and appropriate signatures must be obtained on the Cost Analysis (CA) before IRB approval can be made and services obtained. A copy of the Cost Analysis is located in the document library of the electronic IRB data system (Shields) along with the necessary IRB forms.

The Cost Analysis document must be submitted with every proposal. The CA requires PIs to indicate the Institutional support required for the research. The cost analysis process serves to: 1. identify Medicare Qualifying Trials; 2. identify costs to the institution for conducting the research; 3. provide documentation of specific details for services and procedures from the provider of services in collaboration with LSU Health Shreveport in performing clinical research; and 4. identify and document the funding source for all research procedures.

The CA document details the services, procedures, use of the research pharmacy, use of equipment, procedures to be billed to insurance and professional services needed, if any, and the associated costs. The Investigator Financial Attestation page, completed by the PI, will designate the cost of research covered by either the study sponsor budget or departmental funds. A finalized Cost Analysis will be provided to University Health and/or the applicable Professional Billing Service for billing purposes related to the study by the Clinical Trials Management Team. HRPP will provide notice of IRB approval to LSU Compliance and to UH Compliance in order that Compliance may complete a final sign off and approval of the document. (See Appendix B).

#### Relationship between Components

The IRB functions independently of, but in coordination with, other institutional regulatory committees. The IRB, however, makes its independent determination whether to approve or disapprove a protocol based upon whether or not human subjects are adequately protected. The IRB has review jurisdiction over all research involving human subjects conducted, supported, or otherwise subject to regulation by any federal department or agency that has adopted the human subjects' regulations.

The Institutional Official's Advisory Committee will meet to ensure a dialogue is maintained between the various entities at the Institution. Membership is determined by the Institutional Official, but will include the AVCRM, Office of Legal Affairs and Organizational Integrity, representation from the IRB, among others. The committee will act in an advisory capacity to the IO, monitoring the effectiveness of existing compliance programs, developing new or revised policies as changes in requirements occur, and disseminating updated compliance information to the research community.

Research that has been reviewed and approved by the IRB may be subject to review and disapproval by officials of the Institution. However, those officials may NOT approve research involving Human Subjects if it has been disapproved by the IRB.

## **1.11 HRPP Operations**

LSUHSC-S ensures that the Human Research Protection Program has resources sufficient to protect the rights and welfare of research participants for the research activities that the Organization conducts or oversees. (AAHRPP Standard I-2)

In addition to the leadership structure described above, appropriate support staff members are available to support HRPP functions.

### **1.11.1 HRPP Office**

The LSUHSC-S HRPP Office reports to the AVCRM. The AVCRM has expert knowledge in regulatory issues regarding human subjects and serves as the primary contact at LSUHSC-S for the Office for Human Research Protections, Department of Health and Human Services. The AVCRM may delegate responsibilities to the HRPP Program Manager or other qualified person. The AVCRM, HRPP Program Manager, and HRPP Staff respond to faculty, student, and staff questions about human subject research as well as organizing and documenting the review process. The HRPP Program Manager works closely with the IRB Chairs to develop policy and procedures. The duties and responsibilities for all HRPP staff are found in their respective job descriptions and their performance is evaluated on an annual basis or as dictated by institutional policy.

The HRPP Office is supported by an HRPP Administrative Coordinator responsible for providing administrative and clerical support to functions of the HRPP & IRB as well as scheduling and

coordinating all IRB functions.

The IRB is supported by an adequate number of HRPP staff personnel. At a minimum this shall be the IRB Administrator and 4 IRB Analysts, and 1 IRB Coordinator. The IRB support staff are located in the Clinical Trials Building, with direct access to the HRPP and the Clinical Trial Services group. The LSUHSC-S Research Organization chart can be found on the Office of Research website.

#### IRB Administrator

The IRB Administrator is responsible for all administrative aspects of the IRB throughout the review process of a research proposal involving human subjects. This responsibility includes the review and screening of documents for research proposals prior to review by the IRB, as well as serving as the liaison between the investigators and the IRB. The IRB Administrator reviews the IRB minutes for accuracy and ensures proper documentation of discussions including controverted-discussions and actions taken by IRB during convened meetings.

#### IRB Analysts & IRB Coordinators

The IRB Analyst is responsible for pre-review of research submissions for compliance with applicable federal and state regulations and institutional policies and procedures; provides clear feedback on incomplete and/inaccurate submissions to investigators; prepares reviewer comments or other post approval activities; assists with the coordination of IRB meetings and IRB agendas and minutes.

The IRB Coordinator is responsible for providing administrative and clerical support to the IRB Chairs and IRB Administrator as well as scheduling and coordinating all IRB meetings. The IRB Coordinator is also responsible for IRB record retention and for maintaining complete IRB files as well as Investigator qualification files. The IRB Coordinator shall maintain investigator specific files to include but not limited to CVs, licenses and proof of education.

#### Selection, Supervision and Evaluation of HRPP Supporting Staff

The IRB Administrator, IRB Coordinators and Support staff are selected by the IO or IO designee. The IRB Support Staff are supervised by the IRB Administrator and the IO. The IRB Support Staff are evaluated on an annual basis as per Institutional and Civil Service guidelines.

### **1.12 HRPP Resources**

The LSUHSC-S Institutional Official provides resources to the HRPP and IRB including meeting, office and storage space, and staff for conducting business. The adequacy of personnel and non-personnel resources of the IRB and HRPP is assessed on an annual basis by the AVCRM (or designee) with the HRPP staff and are reviewed and approved by the IO.

Office equipment and supplies, including technical support, file cabinets, computers, internet access, and copy machines, will be made available to the HRPP and IRB staff. The resources

provided for the IRB and HRPP Office will be reviewed during the annual budget review process.

### **1.13 Quality Assurance/Quality Improvement Activities**

LSUHSC-S measures and improves, when necessary, compliance with organizational policies and procedures and applicable laws, regulations, codes, and guidance. The Organization also measures and improves, when necessary, the quality, effectiveness, and efficiency of the Human Research Protection Program. (AAHRPP Standard I-5)

LSUHSC-S conducts audits or surveys or uses other methods to assess compliance with organizational policies and procedures and applicable laws, regulations, codes and guidance. The Organization makes improvements to increase compliance, when necessary. (AAHRPP Element 1.5.A)

LSUHSC-S conducts audits or surveys or uses other methods to assess the quality, efficiency and effectiveness of the Human Research Protections Program. The Organization identifies strengths and weaknesses of the Human Research Protections Program and makes improvements, when necessary, to increase the quality, efficiency and effectiveness of the program. (AAHRPP Element 1.5.B)

LSUHSC-Shreveport is committed to the ongoing improvement of its Human Research Protections Program (HRPP). This commitment is outlined in its Quality Assurance (QA)/Quality Improvement (QI) Program and the ongoing changes, outcomes, and improvement in the HRPP activities on this campus.

Quality Improvement activities emerge from a systematic and organized framework for improvement. This framework, adopted by institutional leadership is understood, accepted and utilized throughout the Institution, as a result of continuous education and involvement of staff at all levels of performance improvement.

The Quality Improvement Program as documented in the QA/QI plan serves as the foundation of the commitment of this institution to continuously assess the compliance of the HRPP. Quality Improvement/Quality Assurance at LSUHSC-S is conducted to assess compliance (regulatory, policy, approved protocol) and to resolve, and to correct problems and discrepancies by improving them on a priority basis.

Continuous Quality Improvement activities involve two primary activities: 1) measuring and assessing the performance of the activities of the HRPP through the collection and analysis of data and 2) conducting quality improvement initiatives and taking action where indicated.

The goal of the Institution's HRPP Quality Assurance (QA)/Quality Improvement (QI) Plan is to design, implement and maintain a program to evaluate and monitor the effectiveness and compliance of the Institution's Human Research Protection Program while improving human

research protections. A primary objective of the HRPP QA/QI Plan is to maintain compliance with organizational policies and procedures and applicable federal, state, and local laws, including adherence to the IRB approved protocol.

In order to assess and measure compliance with organizational policies and procedures and applicable federal, state, and local laws, including adherence to the IRB approved protocol, the HRPP QA/QI plan will conduct audits and administer surveys to the institution's research community. The audits and surveys will be evaluated to identify the strengths and weaknesses of the HRPP and improvements will be made as needed.

### **1.13.1 Standards and Authority - Regulatory Requirements**

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An IRB shall conduct continuing review of research covered by these regulations at intervals appropriate to the degree of risk, but not less than once per year, and shall have authority to observe or have a third party observe the consent process and the research. 21 CFR 56.109 (f).

### **1.13.2 Other Federal Agencies**

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Additional requirements might apply depending on the source of support/funding. See Appendix A - Additional Requirements.

### **1.13.3 Compliance Audits**

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The QA/QI coordinator(s) and other HRPP staff will conduct Post-Approval Monitoring, Directed or For-Cause Reviews, Voluntary Reviews, and Human Research Protections Program Quality Improvement Reviews to monitor and evaluate compliance with applicable federal, state and local laws and Institutional policies and procedures and to identify areas for improvement. Additionally, investigators will use the Checklist: Investigator Quality Improvement Assessment (HRP-430) to monitor, evaluate and make improvements to the conduct of research as part of the QA/QI plan.

- Directed or For-cause Audits/Reviews are conducted by the HRPP QA/QI Coordinator(s) and are initiated upon request by the Institutional Review Board (IRB), IRB Chair, Institutional Official or designee, or the Assistant Vice Chancellor for Research Management. Circumstances where a For-Cause Review may occur include, but are not limited to:
  - due to unusual circumstances
  - significant risks to subjects
  - routine failure of an investigator to comply with federal, state, and/or local institutional requirements
  - allegations or concerns about the conduct of the study brought to the IRB's attention
  - as part of an ongoing corrective action

- or any case requiring further scrutiny as deemed appropriate by the IRB
- Post-Approval Monitoring is conducted for routine post-approval or follow-up monitoring of research activities as needed. The QA Coordinator(s) will review all sponsor monitor follow-up letters, protocol deviations/ violations, unanticipated problems and other documents that are submitted the IRB. A data base of significant information related to the conduct of the studies will be maintained
- Directed or For-cause Reviews are conducted by the HRPP QA/QI Coordinator(s) and are initiated upon request by the Institutional Review Board (IRB), IRB Chair, Institutional Official or designee, or the Assistant Vice Chancellor for Research Management. Circumstances where a For-Cause Review may occur include, but are not limited to:
  - due to unusual circumstances
  - significant risks to subjects
  - routine failure of an investigator to comply with federal, state, and/or local institutional requirements
  - allegations or concerns about the conduct of the study brought to the IRB's attention
  - as part of an ongoing corrective action
  - or any case requiring further scrutiny as deemed appropriate by the IRB
- Voluntary Reviews are conducted upon request of the Principal Investigator to support self-assessment and improvement efforts by the Investigator and the Study Team. Investigators are encouraged to use the Checklist: Investigator Quality Improvement Assessment (HRPP-430) to conduct a voluntary self-assessment. The QA/QI Coordinators educate and suggest corrective actions to the PI for areas in need of improvement. If the results of the review reveal significant deficiencies in protection of human subjects in research, the results will be reported immediately to the Assistant Vice-Chancellor for Research Management, the IRB Chair, and when necessary to the Institutional Official or designee.
- Human Research Protections Program Quality Improvement Reviews are conducted quarterly to track and improve overall satisfaction and compliance with human research protections program requirements. These reviews are conducted by the HRPP QA/QI Coordinator(s) or may be initiated at the discretion of the Assistant Vice-Chancellor for Research Management or the Institutional Official. This may include examination of the IRB records, IRB meeting minutes, notices of committee actions, contract/consent/HIPAA correlation, IRB acknowledgement/approval turn-around times, IRB member performance/qualifications, meetings quorum, etc. The results of such reviews are shared with the Assistant Vice-Chancellor for Research Management and the Institutional Official. The Assistant Vice-Chancellor for Research Management develops a corrective action plan if necessary or provides clarification to the findings, communicates the findings and any corrective actions as appropriate. The results may

impact current practices and may require additional educational activities for the HRPP staff, IRB members, or study personnel.

In addition, the Program Assessment for AAHRPP Accreditation is utilized as a significant component in support of maintaining AAHRPP accreditation. This assessment focuses on maintenance of applicable documentation representing current policy and procedures, utilization of the AAHRPP Self-Evaluation instrument and evaluation of current HRPP practices to ensure appropriate fulfillment of accreditation standards.

Educational programs/announcements are developed for investigators, their research staff, HRPP staff, and IRB members based on the results of the reviews. If/when findings from these reviews are reported to the IRB, the IRB makes a determination whether to report the findings to FDA, OHRP, the study sponsor, the IO, the Assistant Vice-Chancellor for Research Management or other internal departmental faculty/staff.

After a protocol has been selected for review, the QA/QI Coordinator(s) will notify the Principal Investigator, their Department Chair, the Study Coordinator, and the Assistant Vice-Chancellor for Research Management. Timing of notification will vary as a function of the type of review. A written follow-up message from the HRPP confirms the appointment and lists the materials that the investigator should make available for the reviewer, as well as any other issues that need to be specifically addressed.

Post-Approval Monitoring: The PI will be given approximately two (2) weeks' notice for routine post-approval reviews.

Directed (for cause) Reviews: Unless directed to contact the PI sooner, the QA/QI reviewer will contact the investigator by the next business day following receipt of the review request to schedule the review and will work with the investigator and study team to schedule the review within the timeline established by the requestor. The institution recognizes that research personnel may need to be re-directed to comply with the short notice required in a directed or "for cause" review. To allow for subject safety, the notification period will be the minimum necessary time period.

A research study review may include all aspects of the research operation for which the PI is responsible. Additionally, post-approval monitoring will include a review of the study files maintained by the IRB. If the study involves multiple departments or data collection sites, they may be reviewed separately. The findings will be included in the report to the PI.

A study site review may include any or all of the following:

- Discussion with the research staff
- Tour of research offices, labs, clinics, other facilities utilized for the project
- Review of regulatory files on site including:
  - Original IRB protocol approval
  - Amendments/Modifications

- Consent Forms
- IRB Continuing Review materials
- Study Closure Form
- Reportable New Information (including Serious Adverse Events or Unanticipated Problems)
- Sponsor Correspondence
- FDA Form 1572
- Subject Screening and Enrollment Logs
- Investigator Brochure
- Protocol versions
- Monitoring Reports
- Requesting progress reports from researchers
- Examining investigator-held research records
- Contacting research subjects
- Observing research sites where research involving human research subjects and/or the informed consent process is being conducted
- Auditing advertisements and other recruiting materials as deemed appropriate by the IRB
- Reviewing projects to verify from sources other than the researcher that no unapproved changes have occurred since previous review
- Monitoring conflict of interest concerns to assure the consent documents include the appropriate information and disclosure
- Monitoring HIPAA authorizations
- Conducting other monitoring or auditing activities as deemed appropriate by the IRB
- Any other study related documents or processes as needed

Full cooperation of all research and administrative personnel is expected and required; a lack of cooperation may result in the suspension of IRB approval for all research activities or protocols of the investigator and/or research team. Copies of the investigator's pertinent documents will be made by the HRPP QA/QI staff and the documents will be returned to the research staff expeditiously.

#### **1.13.4 Non-Institution Institutional Audits and Compliance Reviews**

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External directed (for-cause audits), post-approval monitoring, and voluntary reviews will be conducted at non-LSUHSC-S Institutional sites, where the Institution's IRB serves as the IRB of Record, to assess compliance with federal, state, and local law, research subject safety, and IRB requirements. Directed audits are implemented in response to identified concerns that require an IRB determination. These reviews may include items listed above.

VA Research: Beginning in FY 2009 Veteran Health Administration (VHA) research facilities must conduct audits of informed consent documents for all research studies annually and audits of regulatory documents are performed every three years.

### 1.13.5 Review Process, Reporting and Disposition

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LSUHSC-S has and follows written policies and procedures for addressing allegations and findings of non-compliance with Human Research Protection Program requirements. LSUHSC-S works with the Institutional Review Board(s) or Ethics Committee when appropriate, to ensure that participants are protected when non-compliance occurs. Such policies and procedures include reporting these actions, when appropriate. (AAHRPP Element I.5.D.)

The QA/QI Coordinator will conduct reviews using the process outlined below:

1. Notification is sent to the PI, Department Chair, and Study Coordinator. The Assistant Vice Chancellor for Research Management and the Institutional Official are copied on the letter.
2. Preliminary documents are prepared and gathered. Requested documents from the PI are reviewed before the site visit.
3. The following documents are reviewed from the IRB files:
  - Protocol
  - Investigator Brochure
  - Initial submission and continuing reviews
  - Informed consent versions
  - Modifications
  - Reportable New Information (including Serious Adverse Events, Unanticipated Problems)
  - Global Safety Reports
  - Research staff mandatory education confirmation
  - Other pertinent records as needed.
4. The visit to the study site is scheduled. The PI will be asked to ensure available space for the reviewer during the review process and access to all study and participant documents.
5. The reviewer visits the site for the review. A tour of the research facility may be requested to verify that records are kept in a secure location or as specified in the study documentation. Afterwards, the QA Coordinator will be left alone to review the study and participant files in the selected location. While the PI does not need to be available during this time, the Study Coordinator or designated staff member familiar with the protocol and participant documents should be available to answer any questions if they arise.

The hospital and/or research pharmacy may be visited to assess investigational product accountability, proper storage of the investigational product, protocol adherence, and maintenance of relevant study documents. If more than 5 subjects have been enrolled, a percentage of the research subjects' files may be selected for a detailed review.

The length of the review is dependent on the study protocol, the materials to be reviewed, and the educational opportunities addressed at that time. In addition to the

review of the study files and documents, a QA review may include an observation of the recruitment process, consent process, and/or the research activity. A QA review may also include an interview or similar contact with selected screened or enrolled participants. A subject consent survey may be sent to subjects as needed.

6. The reviewer will document observations, findings, and any concerns. At the conclusion of the review, the QA/QI reviewer will discuss with the investigator and /or designated study team member(s) the findings, applicable recommendations, and the next steps.
7. The results of reviews and compliance activities are documented and reported to the PI, Department Chair and Study Coordinator. The Assistant Vice-Chancellor for Research Management and the Institutional Official are copied on the letter. If applicable, the letter of findings will request the PI to respond to the IRB with clarifications or corrective actions to prevent deficiencies in the future. The findings are submitted to the IRB as Reportable New Information by the QA/QI Coordinator. Any identified noncompliance will be handled according to institutional policy.
8. If a review finds that subjects in a research project have been exposed to unexpected serious harm, the reviewer will promptly report such findings to the Assistant Vice-Chancellor for Research Management and the Institutional Official.
9. A copy of the findings will be contained in the IRB study file and the report generated by the QA/QI staff will be discussed at a convened meeting of the IRB. After the review is completed, the IRB will notify the principal investigator in writing of the IRB's determination. The Department Chairs and other organizational officials will be copied on the report as needed.
10. All documents and correspondence are reviewed. The review results are placed in the electronic and paper IRB files. The review is closed when all issues have been resolved.

If the QA/QI Coordinator identifies subject exposure to unexpected serious harm or a significant research issue or concern requiring immediate intervention, the reviewer will promptly report such findings to the Assistant Vice-Chancellor for Research Management and the Institutional Official.

In the event the Investigator disagrees with the findings of fact or wishes to provide clarification, the Investigator may provide the rebuttal and/or clarifications, in writing. The provided information and any corrective action plan will be submitted into the electronic IRB submission system (Shields). The investigator is also asked to submit each incident of Reportable New Information found through the audit that has not already been reported to the IRB. Follow-up reviews may be scheduled to confirm ongoing adherence to corrective action recommendation and continued compliance.

Finding types may include, but are not limited to:

- No further action necessary
- Minor administrative issue(s) with best practice or additional education recommendation for corrective action;
- Finding that meets the definition of 'Reportable New Information' with best practice or additional education recommendation for corrective action

- Major finding indicating potential harm or imminent risk of harm to participants' safety and well-being. These findings will be reported immediately by QA/QI auditor to the AVCRM or designee and IRB Chair and when necessary to Institutional Official or designee
- Potential misconduct will also be reported to the Research Integrity Officer in accordance with the LSUHSC-S Policy and Procedures for Dealing with Allegations of Research Fraud

#### **1.13.6 IRB and HRPP Internal Compliance Reviews**

The IRB or EC has qualified leadership (e.g., chair and vice chair) and qualified members and staff. Membership and composition of the IRB or EC are periodically reviewed and adjusted as appropriate. (AAHRPP Element II.1.B)

Human Research Protections Program Quality Improvement Reviews are conducted quarterly. The results may impact current practices and may require additional educational activities. These reviews may include the following along with other areas of concern as they arise:

- Review of the IRB minutes to determine that adequate documentation of the meeting discussion has occurred. This review will include assessing the documentation surrounding the discussion for protections of vulnerable populations as well as other risk/benefit ratio and consent issues that are included in the criteria for approval. Checklist: Minutes Quality Improvement Assessment (HRP-431).
- Assess the IRB minutes to assure that quorum was met and maintained. Worksheet: IRB Composition (HRP-304)
- Assess the unanticipated problem reporting process.
- Assess that privacy provisions have been adequately reviewed, discussed and documented in the IRB minutes.
- Evaluate the continuing review discussions to assure they are substantive and meaningful.
- Monitor the frequency of lapses in IRB approval.
- Observe the IRB meetings or other related activities.
- Review IRB files to assure retention of appropriate documentation and consistent organization of the IRB file according to current policies and procedures.
- Review of evaluations by the IRB members.
- Verification of IRB approvals for collaborating institutions or external performance sites.
- Monitor other activities deemed appropriate.

The Assistant Vice-Chancellor for Research Management will discuss the results of the review with the IRB chair, the Institutional Official (IO) and the HRPP staff as appropriate. The Assistant Vice Chancellor for Research Management develops a corrective action plan if necessary or provides clarification to the findings, communicates the findings and any corrective actions as appropriate. The results may impact current practices and may require additional educational activities for HRPP staff, IRB members, or study personnel.

The Institutional Official or designee will evaluate the following resources provided to the human research protection program and make adjustments as part of the budgeting process:

- Space
- Personnel
- Equipment
- Finances
- Information Technology Systems
- HRPP educational program
- Legal counsel
- Conflicts of interests
- Quality improvement
- Sponsored Programs
- Pharmacy Services

The QA/QI coordinator will obtain updated résumés or curricula vitae from each IRB member or confirmation that there has been no change. The completion of training by IRB members, chairs, vice-chairs, and staff will be assessed along with the knowledge and performance of each IRB member, chair, vice-chair, and staff member. The IRB and organizational registrations will be updated and renewed as necessary.

#### **1.13.7 QA/QI Audit Tools**

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The QA/QI coordinator will utilize various audit tools during the audit process. Depending on the type of audit, QA/QI staff may select any of the following documents, or add additional tools as needed.

- Agenda Quality Improvement Assessment Checklist
- Audit tool – Consenting Process Checklist
- Audit tool – ICF Checklist
- Chart Reviews Checklist
- Contract, Consent, HIPAA Audit
- DOD Reviewer Checklist
- Emergency Use of a Test Article Reviewer Checklist
- Exemption Determination Checklist
- GCP Review
- HRP-410 Checklist: Waiver or Alteration of Consent Process
- HRP-411 Checklist: Waiver of Written Documentation of Consent
- HRP-419 Checklist: Waiver of Consent Process for Emergency Research
- HRP-430 Checklist: Investigator Quality Improvement Assessment
- HRP-431 Checklist: Minutes Quality Improvement Assessment
- HRP-441 Checklist: HIPAA Waiver of Authorization
- IRB Policy and Procedure Evaluation Worksheet
- IRB Files Evaluation

- IRB HRPP Evaluation Quarterly Report
- IRB Notice Assessment
- IRB Quorum and Expertise Checklist
- IRB Submissions History
- Pharmacy GCP Checklist
- Reviewer Checklist for Advertisements
- Subject Specific Consent – Audit Findings
- Visit Review Checklist

### 1.14 Collaborative Research Projects

The IRB or EC has and follows policies and procedures for managing multi-site research by defining the responsibilities of participating sites that are relevant to the protection of research participants, such as reporting of unanticipated problems or interim results. (AAHRPP Element II.2.H.)

In the conduct of cooperative research projects, LSUHSC-S acknowledges that each institution is responsible for safeguarding the rights and welfare of human subjects and for complying with applicable federal and state regulations. When a cooperative agreement exists, LSUHSC-S may enter into a joint review arrangement. A formal relationship must be established between the Institution and the other institution through either a Cooperative Agreement or a Memorandum of Understanding. This relationship must be formalized before the Institution will accept any human research proposals from the other institution.

It is the policy of LSUHSC-S to assure that all facilities participating in a human subjects study receive adequate documentation about the study in order to protect the interests of study participants. Before a study can begin, it must be approved by the IRB(s) of record for each participating facility and, where appropriate, the IRB of record for the coordinating facility.

For collaborative research, the PI must identify all institutions participating in the research, the responsible IRB(s), and the procedures for dissemination of protocol information (IRB initial and continuing approvals, relevant reports of unanticipated problems, protocol modifications, and interim reports) between all participating institutions.

When LSUHSC-S reviews research conducted at another institution, the particular characteristics of each institution's local research context must be considered, either

- through knowledge of its local research context by the LSUHSC-S IRB or
- through subsequent review by appropriate designated institutional officials, such as the Chairperson and/or other IRB members.

When serving as the coordinating institution for the lead principal investigator, the LSUHSC-S IRB is responsible for the review and tracking of information (including but not limited to reportable events, modifications to previously approved research, consent documents and continuing review reports) for approved multi-site research studies involving human subjects.

The LSUHSC-S lead Principal Investigator serves as an agent of LSUHSC-S and is responsible for the receipt and dissemination of all multi-site research study information to all sites considered engaged in the research. If LSUHSC-S is the coordinating facility, the PI must document how the important human subject protection information will be communicated to the other participating facilities engaged in the research study.

The lead LSUHSC-Principal Investigator is responsible for submitting a LSUHSC-S IRB electronic application and providing the following information to the IRB:

- A list of all sites/locations participating in the research study.
- Confirmation of contact information (names, e-mails, addresses) for all sites/locations participating in the research study.
- A plan for the review of each external site's IRB approval correspondence and approved consent documents.
  - The external site's IRB approval correspondence will include the type of review and any conditional approval information.
- When the research study is federally funded or federally regulated, confirmation that each participating site has on file a Federalwide Assurance (FWA) with the Federal Office of Human Research Protections (OHRP).
- Registration of an applicable study on ClinicalTrials.gov.
- A plan to assure that no participating site will begin the research (including recruitment activities) until IRB approval has been granted.
- A method to assure that all sites participating in the research have the most current version of the protocol.
- A method to assure that all sites participating in the research receive, when applicable, protocol amendments.
- A method to assure that all sites participating in the research receive study related communications including reports of adverse outcomes, unanticipated problems, and interim results.
- A plan for the collection and management of data from all sites/locations participating in the research.
- A process for centralized reporting and evaluation of events (and protocol deviations/violations from all sites participating in the research).
- If the external site plans to rely on the LSUHSC-S IRB the lead PI is responsible for consulting with the LSUHSC-S AVCRM or designee who will oversee the completion of the LSUHSC-S IRB Authorization Agreement.
  - The Agreement will specify the roles and responsibilities of LSUHSC-S IRB and the relying organization.
  - The external site will be responsible for updating its FWA to reflect reliance upon the LSUHSC-S IRB as appropriate per DHHS OHRP guidance.
  - The external site and the LSUHSC-S IRB will each maintain one fully executed original of the agreement for inspection by OHRP, as requested.
- IRB submissions (e.g. modifications, continuing review report, reportable events, etc.):
  - If the LSUHSC-S PI's internal application is the mechanism for the initial and

continuing IRB review for any external Relying Organization(s), the lead LSUHSC-S PI is responsible for receiving reports from all participating sites and submitting information to IRB in accordance with LSUHSC-S IRB policies.

- o If an external site application is the mechanism for the initial and continuing LSUHSC-S IRB review for the external Relying Organization, the PI for the external site application is responsible for submitting information to the IRB in accordance with LSUHSC-S IRB policies.

LSUHSC-S IRB Responsibilities: When LSUHSC-S is serving as the coordinating institution for the lead principal investigator, the LSUHSC-S IRB will perform initial review of each research application and all documentation relevant to the protection of human subjects. The LSUHSC-S IRB will conduct IRB review, including, but not limited to review of reportable events, modifications to previously approved research, and continuing review reports.

VA Multi-Site Research: For VA multi-site research, not only the principal investigator, but also all local site investigators, must obtain written approvals from the relevant VA facilities' IRBs of record and all other local committee, subcommittees, and other approvals according to the respective applicable local, VA and other federal requirements. Research cannot be initiated at any given site until the local investigator has obtained written notification that the research can be initiated from the local Chief of Staff for Research and Development. For VA requirements use Worksheet: Additional Federal Criteria (HRP-318) for VA research.

Department of Defense (DoD) Multi-site Research: For multi-site research involving the Department of Defense (DoD), the LSUHSC-S IRB and the lead LSUHSC-S Principal Investigator will adhere to additional responsibilities as set forth in the Department of Defense (DoD) Addendum. The DoD Addendum is a formal agreement between the LSUHSC-S IRB and DoD organizations specifying requirements, roles, and responsibilities. For DoD requirements use Worksheet: Additional Federal Criteria (HRP-318) for DoD research.

### **1.15 Research Community Feedback**

Research participants and community members may contact the HRPP Program Manager or the Education and Outreach Coordinator either directly or through the Research Staff (Investigators, Coordinators). Contact information is available on the HRPP website Participant page, from the Research Staff, the Informed Consent form and from the HRPP Participant Brochure.

All comments, concerns and questions are investigated, tracked and reported to the IRB Chairs and to the QA/QI staff. HRPP will also utilize annual surveys to assess Community Outreach activities. HRPP Policies will be either developed or improved based on community feedback. Investigators and coordinators will be educated on the changes to then educate the participants and the community. Evaluations of activities will be ongoing through the surveys and from participant feedback.

## 2. INSTITUTIONAL REVIEW BOARD

The structure and composition of the IRB or EC are appropriate to the amount and nature of the research reviewed and in accordance with requirements of applicable laws, regulations, codes, and guidance. AAHRPP Standard II-1

### 2.1 Policy

LSUHSC-S has established one (1) Institutional Review Board (IRB) to ensure the protection of human subjects' research under the auspices of the Institution. They include the following:

**Louisiana State University Health Sciences Center-Shreveport IRB 1 (IRB 00000178) (IORG0000109):** This IRB is comprised of members with varying backgrounds to promote complete and adequate review of research activities commonly conducted. IRB approval must be obtained prior to beginning any research activity involving human subjects. The Institution has designated IRB 00000178 as Panel 1. All LSUHSC-S research is reviewed by that panel.

**Through existing MOUs/Agreements the following assurances are linked to Panel 1 (00000178):**

FWA00016205 Overton Brooks Research Corporation  
FWA00002051 Overton Brooks Veterans Affairs Medical Center  
FWA00000640 Biomedical Research Foundation, Northwest Louisiana, University Health Systems  
FWA00009067 Teche Action Board, Inc.  
FWA00013904 Varnado Family Practice  
FWA00017177 Lafayette Health Ventures Inc. dba Cancer Center of Acadiana Research Department

The IRB or EC has and follows written policies and procedures for determining when activities are exempt from applicable laws and regulations, when permitted by law or regulation and exercised by the IRB or EC. Such policies and procedures indicate that exemption determinations are not to be made by Researchers or others who might have a conflict of interest regarding the studies. (AAHRPP Element II.2.A.)

All non-exempt human subjects research conducted under the auspices of the Institution must be reviewed and approved by the LSUHSC-S IRB prior to the initiation of the research. The following describes the authority, role and procedures of the LSUHSC-S IRBs. See section 3.18 for LSUHSC-S policy concerning the use of external IRBs.

## 2.2 IRB Authority

The IRB or EC has and follows written policies and procedures for suspending or terminating IRB or EC approval of research, if warranted, and for reporting these actions, when appropriate.(AAHRPP Element II.2.G)

Under Human Research Protections Program (HRPP), institutional policy, the IRB is authorized:

1. To approve, require modifications to secure approval, or disapprove all human subjects research activities overseen and conducted under the auspices of the LSUHSC-S
2. To suspend or terminate approval of research not being conducted in accordance with the IRB(s) requirements or that has been associated with unexpected serious harm to participants
3. To observe, or have a third party observe, the consent process
4. To observe, or have a third party observe, the conduct of the research

Research that has been reviewed and approved by the IRB may be subject to review and disapproval by officials of the institution. However, those officials may NOT approve research if it has been disapproved by the IRB. Institutional Officials may strengthen requirements and/or conditions, or add other modifications to secure Institutional approval or approval by another Institutional committee. Previously approved research proposals and/or consent forms must be re-approved by the IRB before initiating the changes or modifications. The IRB Chairs make the determination whether the changes require full IRB re-review or expedited review.

VA Research: Through a Memorandum of Understanding (MOU), VA has designated the LSUHSC-S IRB as its IRB of record. The LSUHSC-S IRB is responsible for performing all of the functions required under 38 CFR 16 (Common Rule) for reviewing and approving human subjects research conducted under the auspices of Overton Brooks VAMC(s) FWA #00002051. This includes, but is not limited to, VA supported research or research conducted at a VA facility and research involving VA patients as research subject (hereafter "VA research"). Regulations & Guidance: DHHS 45 CFR § 46.112; FDA 21 CFR § 56.103; 21 CFR§ 56.109; 21 CFR §56.112; and 21 CFR §56.113.

## 2.3 Number of IRB(s)

LSUHSC-S has one (1) on-site Institutional Review Board. The Institutional Official (IO), the AVCRM, and the IRB Chair will review the activity of the IRB on at least an annual basis and make a determination as to the appropriate numbers of IRB(s) that are needed for the institution. This determination will be based on the evaluation of the performance of IRB as described in Section 1.13.6.

The IO or designee can determine the need to form a new internal IRB. The IO or designee will select the new IRB members using Worksheet: IRB Composition (HRP-304) and the criteria described below. Additional criteria may apply for an IRB reviewing VA research. Once training has been completed and the committee members have been added to the electronic

IRB file system, the new IRB will be registered with OHRP before convening.

Similarly, the IO or designee may decide to deactivate an existing IRB. The IO or designee will notify the affected IRB members, unregister the IRB with OHRP, remove the IRB from the Federalwide assurance and update the electronic IRB database.

## **2.4 Roles and Responsibilities**

### **2.4.1 Chairperson of the IRB**

The IRB or EC has qualified leadership (e.g., chair and vice chair) and qualified members and staff. Membership and composition of the IRB or EC are periodically reviewed and adjusted as appropriate. (AAHRPP Element II.1.B)

The LSUHSC-S Institutional Official in consultation with the IRB members, appoints a Chair and Vice-Chair for each IRB to serve for renewable three-year terms. Any change in appointment, including reappointment or removal, requires written notification from the IO. The IRB Chair and Vice-Chair must have previously served as members of the IRB.

The IRB Chair should be a highly respected individual, from within the Institution, fully capable of managing the IRB, and the matters brought before it with fairness and impartiality. The task of making the IRB a respected part of the institutional community will fall primarily on the shoulders of the Chair. The IRB must be perceived to be fair, impartial and immune to pressure by the institution's administration, the investigators whose protocols are brought before it, and other professional and nonprofessional sources.

The criteria used to select an IRB Chair include experience with, and knowledge of, applicable Federal and State laws and regulations and Institutional policies. This individual must be willing to commit to the IRB; must have past experience as an IRB member; and must demonstrate excellent communications skills, along with an understanding of clinical Research. The IRB Chair must also be flexible and demonstrate a thorough understanding of ethical issues involved in clinical Research.

The IRB Chair convenes and chairs the meetings of the IRB and is required to attend a majority of the convened meetings of the IRB. The IRB Chair may conduct or delegate Expedited Review of Research that qualifies for such review; review the responses of Investigators to contingencies of the IRB (to secure IRB approval); and review and approve minor changes in previously approved research during the period covered by the original approval. The IRB Chair may delegate such authority to the authorized IRB Vice Chair or designee as needed.

The IRB Chair plays a leadership role in establishing and implementing IRB policy. The IRB Chair shares authority over all IRB policy and procedures in collaboration with the IO and the

AVCRM. The Chair will represent the Institution in discussions with federal authorities.

It is recommended that the Chair will communicate with other reviewers so that IRB issues are resolved or identified prior to the convened meeting.

The Chair directs the proceedings and discussions of the convened meeting. The Chair is a voting member of the IRB except in situations of declared conflict of interest. The Chair may not review for approval, studies submitted for exempt or expedited review from his/her assigned department.

The Chair should have an in-depth understanding of ethical issues, state law, Institutional policy and federal regulations related to the types of research reviewed by the IRB.

The IRB Chair is responsible for conducting the meetings and is a signatory for correspondence generated by the IRB. The Chair should review all proposals presented to the full committee.

The IRB Chair may designate other IRB members to perform duties, as appropriate, for review, signature authority, and other IRB functions, (e.g., the IRB Vice-Chair or the IRB Administrator.)

The IRB Chair advises the IO or IO designee about IRB member performance and competence. A review of the performance of the IRB Chair will be performed on an annual basis by the IO. Feedback from the evaluation will be provided to the IRB Chair, and their Department Chair if applicable. If the Chair is not acting in accordance with the IRB's mission, not following policies and procedures, has an undue number of absences, or not fulfilling the responsibilities of the Chair, he/she will be removed by the IO and replaced with a suitable alternative.

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#### **2.4.2 Vice-Chair of the IRB**

The IRB Committee has one (1) Vice-Chair appointed for the committee. In the absence of the Chair, the Vice-Chair serves as the Chair. The Vice-Chair has the same qualifications, authority, and duties listed above as the Chair.

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#### **2.4.3 Subcommittees of the IRB**

The Chair, in consultation with the IO, may designate one (1) or more IRB members, i.e. a subcommittee, to perform duties, as appropriate, for review, signature authority, and other IRB functions. The Chair shall also appoint a Chair of the IRB Subcommittee (IRB Subcommittee Chair). The subcommittee must have the appropriate experience for the function delegated.

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#### **2.4.4 Duties of a Subcommittee**

Duties of a subcommittee may include the following:

- Serve as designees by the IRB Chair for the expedited review of new or continuing protocol, and /or the modifications of continuing proposals
- Review and approve the revisions requested by the convened IRB that require only simple concurrence on a proposal given provisional approval, i.e. Deferred for Non-Substantive Issues
- Conduct an inquiry. A subcommittee is appointed consisting of IRB members, and non-members if appropriate, to conduct an inquiry into allegations of noncompliance. The subcommittee is given a charge by the IRB, which can include any or all of the following:
  - o Review of proposal in question
  - o Review of an investigator's FDA audit, or any other audit report generated by an outside agency
  - o Review of any relevant documentation, including consent documents, contractual documents, case report forms, subject's investigation and/or medical files, as they relate to the investigator's execution of his/her study involving human subjects
  - o Interview of appropriate personnel or subjects if necessary
  - o Preparation of either a written or oral report of the findings, which is presented to the fully convened IRB at its next meeting
  - o Recommend appropriate corrective actions as warranted to the IRB
- Conduct on-site review. An onsite review as requested by the IRB might occur or IRB approval may be subject to, an audit of study performance after enrollment of a designated number of subjects.

## 2.5 IRB Membership

The IRB or EC membership permits appropriate representation at the meeting for the types of research under review, and this is reflected on the IRB or EC roster. The IRB or EC has one or more unaffiliated members; one or more members who represent the general perspective of participants; one or more members who do not have scientific expertise; one or more members who have scientific or scholarly expertise; and, when the IRB or EC regularly reviews research that involves vulnerable participants, one or more members who are knowledgeable about or experienced in working with such participants. (AAHRPP Element II.1.A)

The IRB or EC has and follows written policies and procedures requiring research protocols or plans to be reviewed by individuals with appropriate scientific or scholarly expertise and other expertise or knowledge as required to review the research protocol or plan. (AAHRPP Element II.1.E)

The membership of the IRB is based upon Federal policy requirements as described in 45 CFR 46.107.

IRB members are selected based on appropriate diversity, including consideration of race,

gender, cultural backgrounds, and specific community concerns in addition to representation by multiple, diverse professions, knowledge and experience with vulnerable subjects, and inclusion of both scientific and non-scientific members. The structure and composition of the IRB must be appropriate to the amount and nature of the research that is reviewed. Every effort is made to have member representation that has an understanding of the areas of specialty that encompasses most of the research performed at the LSUHSC-S. The LSUHSC-S SOPs has procedures (See Section 4) that specifically outline the requirements of proposal review by individuals with appropriate scientific or scholarly expertise beyond or in addition to that available through the IRB members.

In addition, the IRB will include members who are knowledgeable about and experienced in working with vulnerable populations (e.g., children, prisoners, pregnant women, or physically handicapped or mentally-disabled persons) that typically participate in LSUHSC-S research.

The IRB must promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects; and possess the professional competence necessary to review specific research activities. A member of the IRB may fill multiple membership position requirements for the IRB.

## **2.6 Composition of the IRB**

1. The IRB will have at least five (5) members with varying backgrounds to promote complete and adequate review of research activities commonly conducted by the Institution.
2. The IRB will be sufficiently qualified through the experience and expertise of its members, and the diversity of the members, including consideration of race, gender, and cultural backgrounds and sensitivity to such issues as community attitudes, to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects.
3. In addition to possessing the professional competence necessary to review specific research activities, the IRB will be able to ascertain the acceptability of proposed research in terms of institutional policies and regulations, applicable law, and standards of professional conduct and practice. The IRB will therefore include persons knowledgeable in these areas.
4. If the IRB regularly reviews research that involves a vulnerable category of subjects (e.g., children, prisoners, pregnant women, or physically handicapped or mentally disabled persons), consideration will be given to the inclusion of one (1) or more individuals on the IRB, who are knowledgeable about and experienced in working with these subjects. When protocols involve vulnerable populations, the review process will include one (1) or more individuals who are knowledgeable about or experienced in working with these participants, either as members of the IRB or as consultants (see Section 6.3).
5. Every nondiscriminatory effort will be made to ensure that the IRB does not consist entirely of men or entirely of women, including the institution's consideration of qualified persons of both sexes, so long as no selection is made to the IRB on the basis of gender.
6. The IRB shall not consist entirely of members of one profession.

7. The IRB includes at least one (1) member whose primary concerns are in scientific areas and at least one (1) member whose primary concerns are in nonscientific areas.
8. The IRB includes at least one (1) member who is not otherwise affiliated with the institution and who is not part of the immediate family of a person who is affiliated with the institution.
9. One (1) member may satisfy more than one membership category.
10. The IO and IRB Administrator may be voting members of the IRB.

For VA Research:

11. The IRB includes at least one VA salaried member and alternate, nominated by the VA Medical Center Director (IO) to provide VA representation. At least one VA representative must have scientific expertise. At least one VA representative must be present at any IRB meeting that reviews and approves research performed at the VA.
12. VA Research and Development administration officials including, but not limited to, the Associated Chief of Staff for Research and Development and the Administrative Officer for Research and Development, are prohibited from serving as voting members on the IRB. They may serve as non-voting consultants.
13. Research Compliance Officers (RCO) may act as a consultant to the IRB, but may not serve as a member (voting or nonvoting). The VA Medical Center Director, their administrative staff, Chiefs of Staff, and other local leadership (e.g., members of senior management) may observe IRB meetings, but may not be voting or ex-officio (nonvoting) members of the IRB.
14. The IRB includes two VA employees who hold a minimum of 1/8ths VA-compensated appointments to serve as voting members to each IRB of record. Members appointed to affiliate IRBs may be scientific or non-scientific members. Physicians, dentists, nurses, pharmacists, social workers, other clinicians, statisticians, and allied health professionals are considered scientists.
  - VA facilities with fewer than ten active protocols are only required to appoint one voting member and one alternate voting member.
15. If alternate members are appointed to the facility's IRB, the IRB's written procedures must describe the appointment and function of alternate members, and the IRB membership roster must identify by name the primary member(s) for whom each alternate member may substitute. The alternate members must have qualifications similar to the member they replace" per 1200.05§ 6.I.
16. At least one VA voting member of the IRB must be in attendance when VA research is discussed at a convened meeting.
17. Veterans whose only relationship with the VA facility is receiving care at a VA facility or receiving benefits from the Veterans Benefits Administration are not considered to be affiliated for the purpose of being an IRB member. Individuals who perform occasional volunteer activities without compensation (WOC) are not considered affiliated. However, those who hold a WOC appointment for volunteer activities other than IRB service are considered to be affiliated. Individuals who have retired from the VA and who are receiving VA retirement benefits are considered affiliated.

18. The facility director, administrative staff, chief of staff, other senior administrators such as associate or assistant directors, or chief nurse, may observe IRB meetings but not serve as voting or non-voting members of the facility's IRB. Research office staff including, but not limited to, the associate chief of staff for research and development, the administrative officer for research and development, and IRB administrative staff, may not serve as voting members of the IRB.
19. The privacy officer and information security officer may not serve as voting members, but may serve as non-voting members of the IRB or as consultants. The research compliance officer may not serve as a voting or non-voting member, but may attend meetings of the IRB when requested by the IRB.

## **2.7 Nomination, Appointment and Removal of IRB Members**

The IRB Chair, Vice-Chair and/or the IO, identifies a need for a new and/or replacement member, who may be either a regular or alternate member of the IRB.

New IRB members may be nominated as follows:

- By an IRB member
- By Institutional Department Chair
- By the IRB Chair(s) and/or
- By the IO

The final decision in selecting a new member is made by the IO.

The individual will be asked to submit a resume or CV and a completed Form: IRB Member Information (HRP-202). The IRB Chair and the AVCRM will review all supporting documentation and information submitted to identify those nominees who can provide relevant technical expertise or other pertinent qualifications as needed by the IRB Committee to review the types of research commonly presented to the IRB Committee. All nominations and supporting documents will be forwarded for final selection by the IO.

Documents supporting final appointments along with records of continuing education will become part of the permanent membership records maintained by the Institution HRPP.

Appointments are made for a renewable three-year period of service. Once the appointment letter is signed, the individual will be scheduled for training (if necessary), added to the electronic IRB file database, and included in an update to the registration of the affected IRB with OHRP (within 90 days). Any change in appointment, including reappointment or removal, requires written notification. Members may resign by written notification to the Chair of their assigned Committee.

On an annual basis, the IRB Chair and the AVCRM review the membership and composition of the IRB to determine if it continues to meet regulatory and institutional requirements.

The Institutional Official or designee may remove IRB members, alternate members, IRB chairs, and other officers (e.g., vice chairs) with consultation from the IRB or IRB chair(s). The same process will apply if an IRB member resigns. The IO or designee or HRPP staff will remove the member from the IRB roster, re-evaluate the constitution of the IRB using Worksheet: IRB Composition (HRP-304), update the registration of affected IRB with OHRP (within 90 days), and make the necessary changes to the electronic IRB database.

**VA Representatives** - The Director of the VA will officially appoint VA representatives to the IRB of record in writing. The VA representative will be appointed for a period of three (3) years. They may be re-appointed to new terms of up to three (3) years without a lapse in service at the end of each term.

**Regulatory requirements:** IRB membership, as found in 45 CFR 46.107, require the IRB have sufficient expertise and diversity to evaluate ethical issues therefore committee member selection must be made with the goal of maintaining appropriate IRB diversity, expertise and regulatory compliance.

### **2.7.1 Documentation and Information for New IRB Members**

The IRB or EC maintains a complete set of materials relevant to the research protocol or plan for a period of time sufficient to comply with legal and regulatory requirements, Sponsor requirements, if any, and organizational policies and procedures. Element II.5.A.

Consistent documentation of the following will be required from each member of the IRB at initial appointment and as directed and will be made available as appropriate, upon request for audit.

1. Current (CV), signed as an attestation of its accuracy, initially and upon reappointment.
2. Attendance at an appropriate number of IRB meetings. LSUHSC-S utilizes a primary/alternate system for most “seats” on the Committee. Representation for each seat must occur at a minimum of 70% of the regularly scheduled IRB meetings, though attendance may be divided by those assigned to the seat. The primary member is to contact the IRB Office of any potential absence as far in advance as possible.
3. Participation in the required training and new IRB member orientation must occur prior to review of any research.
4. Documentation of current institutional certification in compliance education in the conduct of human subject research.
5. Documentation of attendance of participation in continuing education opportunity attended throughout the year.

### **2.7.2 Community Members**

LSUHSC-S promotes the involvement of community members, when appropriate, in the design and implementation of research and the dissemination of results. (AAHRPP Element I.4.C.)

45 CFR 46.107 requires representation on the IRB that is sensitive to issues such as community feelings and thoughts. The Community Member serves as a consumer representative and as the ethical conscience of the IRB. The Community Member provides insight in evaluating the Informed Consent Document (ICD) for clarity and understanding. The Community Member functions as an effective link to the IRB, Investigator and the community. The Community Member provides the perspective of the subject.

The regulations at 38 CFR 16.107 require that the IRB have at least one (1) member not otherwise affiliated with the Institution. Community members must attest in writing that neither they, nor a family member, are affiliated with LSUHSC-S or the VA affiliate covered under these assurances. The signed attestation will be maintained in the LSUHSC-S HRPP office membership records for a period of three (3) years beyond the end of the appointment.

**Non-Voting Ex-Officio Members:** Members designated as non-voting ex-officio members are selected and pointed because of their position or area of expertise. Their terms shall be indefinite unless otherwise decided.

### **2.7.3 Alternate members**

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The appointment and function of alternate members is the same as that for primary IRB members, and the alternate's expertise and perspective are comparable to those of the primary member. The area of expertise of the alternates should match that of the regular member such that the federal policy requirements as described in 45 CFR 46.107 are met if a regular member cannot attend an IRB meeting. The role of the alternate member is to serve as a voting member of the IRB when the regular member is unavailable to attend a convened meeting. When an alternate member substitutes for a primary member, the alternate member will receive and review the same materials prior to the IRB meeting that the primary member received or would have received. The IRB roster identifies the primary member(s) for whom each alternate member may substitute. The alternate member will not be counted as a voting member unless the primary member is absent. The IRB minutes will document when an alternate member replaces a primary member. The length of term of the alternate will be the same as the term of the voting member.

### **2.7.4 IRB Member Conflict of Interest**

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The IRB or EC has and follows written policies and procedures so that members and consultants do not participate in the review of research protocols or plans in which they have a conflict of interest, except to provide information requested by the IRB or EC. (AAHRPP Element II.1.D)

No regular, alternate, or ex-officio member may participate in the review (initial, continuing, or modification) of any research project in which the member has a conflict of interest (COI), except to provide information as requested. It is the responsibility of each IRB voting and non-voting member to disclose any COI in a study submitted for review. All recusals by members

with COI are recorded in the minutes. If the Conflict of Interest status of an IRB member changes during the course of a study, the IRB member is required to declare this to the IRB Chairs and/or Administrator of the IRB Office.

All voting, alternate, and ex-officio members of the IRB complete an IRB Member Human Research Conflict of Interest Assessment Form when first appointed and annually thereafter. Matters of financial conflicts of interest are governed by the Institution's policy contained in [Chancellor's Memorandum-23](#) found on the LSU Health website.

Before reviewing research, IRB members are to use Worksheet: IRB Member and Consultant COI (HRP-325) to determine whether they have a conflicting interest with the research. If an IRB member has a conflicting interest for review outside a meeting (e.g., the expedited procedure), he or she is to notify the IRB staff and return all materials so the submission can be re-assigned. If an IRB member has a conflicting interest for review of a submission for which he or she has been assigned as a primary or scientific reviewer, he or she is to notify the IRB staff so the submission can be re-assigned.

The IRB Chairperson will remind the members about COI at each convened meeting. If an IRB member has a conflicting interest for review of research at a meeting, he or she is to notify the meeting chair, stay in the meeting room only to answer questions about the research, and leave the meeting room for discussion and voting regarding that research. IRB staff will record in the meeting minutes the name of the IRB member leaving the room because of a conflict of interest. The IRB member with a conflict of interest will not count towards quorum.

Committee members may find themselves in any of the following conflicts of interest when reviewing research:

1. Where the member or consultant is involved in the design, conduct, and reporting of the research;
1. Where an immediate family member of the member or consultant is involved in the design, conduct, and reporting of the research;
2. Where the member holds significant financial interests (See Section 14 for a definition of significant financial interests) in the research being reviewed; and/or
3. Any other situation where an IRB member believes that another interest conflicts with his or her ability to deliberate objectively on a protocol.

### **2.7.5 Potential Conflict of Interest for IRB Members and Consultants**

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Financial Interest Related to the Research - is defined as financial interest in the sponsor, product or service being tested, or competitor of the sponsor.

Conflict of interest includes:

- Involvement of you or your family in the design, conduct or reporting of the research
- Ownership interest, stock options, or other financial interest related to the research

unless it meets four (4) tests:

- o Does not exceed \$5,000.00 when aggregated for you and your immediate family
- o Publicly traded on a stock exchange
- o Value will not be affected by the outcome of the research
- o Does not exceed 5% interest in any one single entity when aggregated for you and your immediate family
- Compensation related to the research unless it meets two (2) tests:
  - o Does not exceed \$5,000.00 in the past year when aggregated for you and your immediate family
  - o Amount will not be affected by the outcome of the research
- Proprietary interest related to the research including, but not limited to, a patent, trademark, copyright or licensing agreement
- Board or executive relationship related to the research, regardless of compensation
- Any other reason for which you believe you cannot provide an independent review

### **2.7.6 Separation of Competing Business Interests from the IRB Review**

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LSUHSC-S has and follows written policies and procedures to separate competing business interests from ethics review functions. (AAHRPP Element II.1.C)

LSUHSC-S recognizes that officials who administer research programs, and individuals who are responsible for development activities (including raising funds), may represent competing business interests, or be in a position to influence programmatic and budgetary decisions and exert undue influence on IRB's or individual IRB members. To avoid such influence, individuals involved in the business function or in research development (i.e. director of grants and contracting, the dean of research, or those responsible for raising funds for research) may not serve as a member of the IRB, may not be involved in the daily operations of the review process and may not discuss business development with IRB members where the discussions might influence or appear to influence review decisions.

Senior leadership and department chairs that are also IRB members will not be assigned as designated reviewers, participate in the IRB committee discussion, or vote for any research that is submitted by faculty, residents, fellows or students in their departments, divisions or institutes. Department Chairs must identify any personal financial conflict of interest that he or she has in the research sponsor or in an entity that owns or controls the investigational product that is the subject of the research in addition to any other conflict of interest. When the Department Chair is the investigator, the Senior Leadership official responsible for that division will identify any personal financial conflict of interest that he or she has in the research sponsor, or in an entity that owns or controls the investigational product that is the subject of the research, in addition to any other conflict of interest. Department chairs are required to review and sign off on all human subjects research proposals being submitted by faculty, residents, fellows or students in their departments. This review occurs prior to IRB submission and utilizes Form: Administrative Approval (HRP-220). When the Department

Chair is the investigator, the Senior Leadership official responsible for that division will complete HRP-220.

Neither Senior Leadership and Department Chairs, nor any other LSUHSC-S official or committee may approve research that has been deferred or disapproved by the LSUHSC-S IRB, nor apply undue pressure on the LSUHSC-S IRB to reverse a determination. The LSUHSC-S Institutional Conflict of Interest policy describes the policies and procedures designed to ensure that research involving human subjects at LSUHSC-S is conducted without untoward influence resulting from either the University's financial investments or holdings or the personal financial interests or holdings of key institutional leaders.

### **2.7.7 Use of Consultants**

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The IRB or EC has and follows written policies and procedures so that members and consultants do not participate in the review of research protocols or plans in which they have a conflict of interest, except to provide information requested by the IRB or EC. (AAHRPP Element II.1.D)
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The IRB or EC has and follows written policies and procedures requiring research protocols or plans to be reviewed by individuals with appropriate scientific or scholarly expertise and other expertise or knowledge as required to review the research protocol or plan. (AAHRPP Element II.1.E)
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The AVCRM and HRPP Staff are consultants to the IRB. These individuals will assist the IRB in managing and evaluating policies and procedures that ensure compliance with all state, federal, and local regulations governing research.

When necessary, the IRB Chair, the IO or designee may solicit individuals from the Institution or the community with competence in special areas to assist in the review of issues or IRB proposals, which require appropriate scientific or scholarly expertise beyond or in addition to that available on the IRB. The need for an outside reviewer is determined in advance of the meeting by the IRB Administrator, IRB Chair, IO or designee by reviewing the IRB proposals scheduled to be reviewed at the convened meeting. The HRPP Office will ensure that all relevant materials are provided to the outside reviewer prior to the convened meeting.

In the event that additional scientific or scholarly expertise cannot be obtained for a research proposal the IRB Chair, IO or designee will defer the proposal to the next IRB meeting so that appropriate review may be obtained.

When the IRB reviews research that involves categories of participants vulnerable to coercion or undue influence, if there is not at least one (1) member who is knowledgeable or experienced in work with such participants at the meeting, the IRB will defer the research proposal until such expertise can be obtained through the membership or consultation.

Written statements of consultants will be kept in IRB records. Key information provided by

consultants at meetings will be documented in the minutes. Written reviews provided by the outside reviewer will be filed with the protocol.

The IRB Chair, IO or designee reviews the conflict of interest policy for IRB members (See Section 14.1) with consultants. Consultants must verbally confirm to the IRB Chair, IO or designee that they do not have a conflict of interest prior to review. Individuals who have a conflict of interest or whose spouse or family members have a conflict of interest in the research will not be invited to provide consultation.

The consultant's findings will be presented to the full board for consideration either in person or in writing. These individuals do not count for IRB quorum purposes and cannot vote on any issue before the IRB (45 CFR §46.107(f)).

Ad hoc or informal consultations requested by individual members (rather than the full board) will be requested in a manner that protects the researcher's confidentiality and is in compliance with the IRB conflict of interest policy (unless the question raised is generic enough to protect the identity of the particular PI and research proposal).

## **2.8 Duties of IRB Members**

Except for emergency IRB meetings, the agenda, submission materials, proposals, proposed informed consent forms and other appropriate documents are distributed to members at least one (1) week prior to the convened meeting at which the research is scheduled to be discussed. For emergency IRB meetings, these written materials will be submitted as timely as possible in advance of the scheduled IRB meeting date and time. IRB members will treat the IRB proposals, protocols, and supporting data confidentially. All copies of the protocols and supporting data are returned to the IRB staff at the conclusion of the review for document destruction.

The expectations of IRB members reviewing Human Research in advance of a meeting or when serving as a Designated Reviewer are delineated below.

- For review using the expedited (non-committee) procedure, the Designated Reviewer fulfills the roles described for the primary reviewer, and the scientific/scholarly reviewer, or obtains consultation for these roles.
- All IRB members are to treat all oral, written and electronic information obtained as part of the review process as confidential. IRB members must not disclose, use, share or duplicate review documents or confidential information without prior authorization.
- All IRB members are to know the definition of Conflicting Interest.
  - No IRB member may participate in any review (including discussion or voting) in which he or she has a Conflicting Interest, except to provide information requested by the IRB.
  - When reviewing an item each IRB member is to consider whether he or she has a Conflicting Interest and if so, self-identify that Conflicting Interest.

- All IRB members are provided a user account in the electronic IRB submission system for access to review materials.
  - All IRB members are to access all review materials through the electronic system.
  - IRB members attending by video or teleconference are to access all review materials through the electronic system.
  - Any IRB member may request review materials be delivered outside the electronic system by contacting the IRB staff.
- All members assigned as a primary reviewer or scientific/scholarly reviewers are to consider whether they have sufficient expertise to review the submission. A consultant may be retained if additional expertise is required. Sufficient expertise may include:
  - Scientific or scholarly expertise
  - Knowledge of or experience working with vulnerable populations
  - Qualifications as a prisoner representative
  - Knowledge of the country in which the research is conducted
  - Medical licensure for FDA-regulated test articles
- All IRB members review the Pre-Review findings for each submission, if any.
- All IRB members consider the criteria in all applicable worksheets and checklists.
  - Worksheets and checklists are available in the IRB Library through the electronic system or can be made available outside the electronic system by contacting the IRB staff.
  - The primary presenter for each submission is expected to use applicable worksheets and checklists for preliminary judgments as to whether each criterion is met and provide preliminary study-specific findings justifying determinations.
  - The primary presenter leads the discussion.
  - IRB members who are not the primary presenter for a submission do not need to complete any checklists.
  - Worksheet: Criteria for Approval (HRP-314) applies to all non-exempt research.
- For initial review: In advance of the meeting, all IRB members review the following materials to a depth sufficient to determine whether the criteria in applicable worksheets and checklists are met:
  - Application form with local context (Template Protocol - HRP-503)
  - Study Protocol
  - Consent/Assent document(s) and script(s), when applicable
  - HIPAA Authorization
  - Recruitment materials, when applicable
- For review of a modification: In advance of the meeting, all IRB members review the modification, determine which criteria in applicable worksheets and checklists are affected, and criteria are met:
  - Protocol
  - Consent document(s) and script(s), when they exist
  - HIPAA Authorization
  - Recruitment materials, when they exist
- For continuing review: In advance of the meeting, all IRB members review continuing

review progress report and attachments, determine which criteria in applicable worksheets and checklists are affected, and review the following materials as necessary to a depth sufficient to determine whether affected criteria are met:

- o Protocol
  - o Current consent document(s) and script(s), when they exist
  - o Recruitment materials, when they exist
- For review of new information: In advance of the meeting, all IRB members review the new information and attachments, determine which criteria in applicable worksheets and checklists are affected, and review the relevant sections of the following materials to a depth sufficient to determine as necessary whether affected criteria are met:
  - o Protocol
  - o Previously submitted modifications or a summary thereof
  - o Consent document(s) and script(s), when they exist
  - o Written reports of consultants or auditors, when they exist
- The primary presenter reviews all submitted materials for consistency with the materials reviewed by all IRB members, including the following additional documents when they exist:
  - o The complete research protocol including any previously approved protocol modifications
  - o Investigator brochure
  - o Contract or grant application
  - o Model template consent document
  - o New Information reported during the current period of approval for continuing review submissions.
- If the HHS supported research involves prisoners as subjects, the prisoner representative reviews the submitted information to determine whether the criteria in Checklist: Prisoners (HRP-415) are met, be present when the research is reviewed, and provide a review either orally or in writing.
- IRB members or consultants with scientific or scholarly expertise review the submitted information in enough depth to answer the questions in Worksheet: Scientific and Scholarly Review (HRP-320).
- All IRB members review written reports of consultants, if any.
- Any IRB member who needs to access additional information in the IRB records can contact an IRB staff member for assistance.
- A subset of materials that are to be made available for review include Worksheet: Review Materials (HRP-301)
  - o List of protocols approved using the expedited procedure (For Veterans Administration (VA) Research, include the review category.)
  - o List of protocols approved after verification of Modifications Required to Secure Approval for VA Research.
  - o Information for Other Business items
  - o Educational Materials when applicable

## 2.9 Attendance Requirements

Members should attend all meetings for which they are scheduled. If a member is unable to attend a scheduled meeting, they should inform the IRB Chair, Vice-Chair, or an HRPP/IRB staff member at least two (2) weeks prior to the scheduled meeting. In the case of an emergency, members should notify the IRB as soon as possible. If the inability to attend will be prolonged, a request for an alternate to be assigned should be submitted to the IRB Chair or IRB Administrator.

If an IRB member anticipates being absent for an extended period of time, such as for a sabbatical, he or she must notify the IRB at least thirty (30) days in advance so that an appropriate replacement can be obtained. The replacement can be temporary, for the period of absence, or permanent if the member is not returning to the IRB. If the member has a designated alternate, the alternate can serve during the primary member's absence, provided the IRB has been notified in advance.

## 2.10 Training / Ongoing Education of the Chairs and IRB Members

LSUHSC has an education program that contributes to the improvement of the qualifications and expertise of individuals responsible for protecting the rights and welfare of research participants. (AAHRPP Element I.1.E.)

The IRB or EC has qualified leadership (e.g., chair and vice chair) and qualified members and staff. Membership and composition of the IRB or EC are periodically reviewed and adjusted as appropriate. (AAHRPP Element II.1.B)

*Ongoing training and education in regulations and procedures for the IRB Chair and IRB members is a vital component of a comprehensive Human Research Protections Program. LSUHSC-S is committed to providing ongoing training and education for IRB members, IRB staff and the HRPP Office, related to ethical concerns, federal and state regulatory requirements and LSUHSC-S policies for the protection of human subjects. Before the beginning of a new IRB Year (July 1), the HRPP reviews and updates this HRPP education guidance as needed. The HRPP incorporates input received from IRB members, IRB staff, and investigators and from monitoring and evaluation activities. Trends in research at LSUHSC-S are considered and new federal, state, or local regulations (or published guidance) are integrated. Compliance activities (e.g., internal and external audits) also provide input into the education plan.*

### Orientation

*New IRB members, including alternate members will meet with the IRB Chairs, Director of the HRPP Office or HRPP Education Coordinator for an informal orientation session. At the session, the new member will be given an IRB Handbook (binder or electronic) that includes:*

- *LSUHSC-S Federal Wide Assurance (FWA)*
- *LSUHSC-S Policies and Procedures for the Protection of Human Subjects*

- *Reviewer Checklist*
- *DHHS OHRP IRB Guidebook*
- *Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research*
- *Applicable Federal & State regulations including:*
  - *Title 45, part 46 — The Common Rule*
  - *21 CFR part 50 — Protection of Human Subjects*
  - *21 CFR part 56 — Institutional Review Boards*
  - *21 CFR part 312 — Investigational New Drugs*
  - *21 CFR part 812 — Investigational Device Exemptions*
- *FDA Information Sheets Guidance or website address*
- *OHRP Guidance Sheets or website address*

#### *Initial Education*

*New members are required to complete the Initial Education requirement for IRB members before they may serve as Primary Reviewer. IRB members will complete the following web based training:*

- *LSUHSC-S — HIPAA Training (if not already done when hired by institution)*
- *CITI Course in the Protection of Human Subjects Research Basic Courses for Biomedical Researchers and nonmedical research*
- *The CITI IRB Member Module*

#### *Continuing Education*

*To ensure that oversight of human research is ethically grounded and the decisions made by the IRB is consistent with current regulatory and policy requirements, training is continuous for IRB members throughout their service on the IRB. Educational activities include, but are not limited to;*

- *In-service training at IRB meetings; Educational topics, including but not limited to additional bulletins and notices, presented during IRB meetings will be distributed to non-attending members after the meeting through either email, Campus Mail or USPS depending on member's preference.*
- *Collaboration with the VA to present topics consistent with the VA policies and procedures (VHA Handbook 1200.05) during the IRB meetings a minimum of twice a year and as changes occurs related to VA research.*
- *In-services are provided to address specific requirements contained in the Department of Defense regulations and requirements and educated on these requirements when appropriate.*
- *CITI Refresher courses required every three (3) years*
- *Annual training workshops/sessions: Distribution of appropriate publications*
- *Identification and dissemination by the AVCRM, IRB Chair or IRB Administrator of new information that might affect the Human Research Protections Program, including laws, regulations, policies, procedures, and emerging ethical and scientific issues to IRB members via email, mail, or during IRB meetings*

*LSUHSC-S will provide support to send as many members of the IRB as possible to attend the appropriate national and regional conferences on human research protections.*

*When following the Department of Defense (DoD) regulations, initial and continuing research ethics education is required for all personnel who conduct, review, approve, oversee, support, or manage human participants research.*

- *The DoD component may evaluate the education policies to ensure the personnel are qualified to perform the research, based on the complexity and risk of the research.*

#### *The IRB/HRPP Office Professional Staff — Initial Education*

*The HRPP Office Staff will be given an orientation binder or electronic links that includes:*

- *LSUHSC-S — Shreveport's Federal-wide Assurance (FWA)*
- *LSUHSC-S Policies and Procedures for the Protection of Human Subjects*
- *Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research*
- *Applicable Federal and State regulations including:*
  - *Title 45, part 46 — The Common Rule*
  - *21 CFR part 50 — Protection of Human Subjects*
  - *21 CFR part 56 — Institutional Review Boards*
  - *21 CFR part 312- Investigational New Drugs*
  - *21 CFR part 812 — Investigational Device Exemptions*
- *FDA Information Sheets Guidance or website address*
- *OHRP Guidance Sheets or website address*

*Each new staff member is expected to complete and submit the following:*

- *LSUHSC-S - HIPAA Training (if not done upon hire to the institution)*
- *The CITI Human Subjects Research Basic Courses for Biomedical, GCP, HIPS and COI training.*

#### *Continuing Education*

*Continuing training and education is provided on a daily basis through discussions of regulatory and ethical issues that arise during the processing of IRB proposals. Other educational activities include, but are not limited to:*

- *CITI (Collaborative Institutional Training Initiative) Refresher courses required every three (3) years;*
- *At least quarterly attendance of a full IRB meeting;*
- *Annual conferences on human research protections on a rotating basis.*

*Additionally, the IRB/HRPP Office Professional Staff will be encouraged to become CIP certified.*

### *IO, IRB Member and HRPP/IRB Staff Member Training Timeline*

Institutional Official Required Training		
	Course	Timeline
Initial Training	CITI IRB Members Basic	Within 30 days of appointment
	CITI Conflict of Interest	Within 30 days of appointment
	CITI Good Clinical Practice	Within 30 days of appointment
	CITI Health Information Privacy & Security	Within 30 days of appointment
	CITI Institutional/Signatory Official: Human Subject Research	Within 30 days of appointment
Refresher Courses	CITI IRB Members Refresher	Every 3 years
	CITI Conflict of Interest	Every 4 years or upon change
IRB Member Required Training		
	Course	Timeline
Initial Training	CITI IRB Members Basic	Within 45 days of appointment
	CITI Conflict of Interest	Within 45 days of appointment
	CITI Good Clinical Practice	Within 45 days of appointment
	CITI Health Information Privacy & Security	Within 45 days of appointment
	IRB Member Orientation	Prior to voting and review assignments;
Refresher Courses	CITI IRB Members Refresher	Every 3 years
	CITI Conflict of Interest (LSUHSC-S) *	Every 4 years or upon change

HRPP/IRB Staff Required Training		
	Course	Timeline
Initial Training	CITI IRB Members Basic	Within 14 days of employment
	CITI Conflict of Interest	Within 14 days of employment
	CITI Good Clinical Practice	Within 14 days of employment
	CITI Health Information Privacy & Security	Within 14 days of employment
	Clinical Trial Billing Compliance (Required for CTMT Team-only)	Within 14 days of employment
Refresher Courses	CITI IRB Members Refresher	Every 3 years
	CITI Conflict of Interest	Every 4 years or upon change

#### **2.11 Liability Coverage for IRB Members**

The Institution's insurance coverage applies to employees and any other person authorized to act on behalf of the Institution or acts of omissions within the scope of their employment or authorized activity. The institution's legal risk management department should be notified of any potential or actual claims.

#### **2.12 Review of IRB Member Performance**

The IRB or EC has qualified leadership (e.g., chair and vice chair) and qualified members and staff. Membership and composition of the IRB or EC are periodically reviewed and adjusted as appropriate. (AAHRPP Element II.1.B)

The IRB Members' performance will be reviewed on an annual basis by the IRB Chairs and/or

the IO or designee. Performance findings will be provided to the IRB members, Department Chair and the IO. Members who are not acting in accordance with the IRB(s) mission or policies and procedures or who have an undue number of absences will be removed.

### **2.13 Reporting and Investigation of Allegations of Undue Influence**

Undue influence is defined as a real or perceived action that may influence the review of human subjects research outside of the scientific, regulatory and ethical principles that guide review of such research. Such action may include, but is not limited to, attempts to influence decisions based upon financial concerns of the Institution or a department; personnel actions such as denying promotion or tenure; or verbal harassment.

HRPP/IRB staff may explain written procedures to individuals involved in the review process. However, individuals in the Institution may not: 1) Provide information beyond an explanation of written procedures that might influence or appear to influence the review process determinations made as part of the criteria for approval; 2) Communicate the Institution's financial issues regarding specific protocols to individuals responsible for the review process, aside from relevant information regarding conflicts of interest; 3) Answer questions about the Institution's business issues posed by individuals responsible for the review process where the answers might influence or appear to influence review decisions; or, 4) Attempt to influence the review of human subjects research through real or perceived action on any performance review, promotion or tenure decision of any IRB member, IRB staff or any individual involved in the conduct or review of human subjects research.

When the IRB does not follow written procedures, the Institution can require the IRB to re-review the submission and/or disapprove research approved by the IRB. All individuals in the Institution are required to ensure that allegations of undue influence of the HRPP or review process are reported within 5 days of becoming aware of the allegation.

In accordance with Chancellor's Memorandum-23, if an IRB chair, member, or staff person feels that the IRB has been unduly influenced by any party, they shall make a confidential report to the IO or other appropriate official. The official within the institution will conduct a thorough investigation in consultation with the HRPP and IRB Chair(s) as appropriate, to consider whether undue influence exists and make recommendations on what corrective actions will be taken.

During the investigation, the Institution may use methods to gather information can include, but are not limited to:

- Interviews of individuals inside and outside the Institution
- Review of records inside and outside the Institution
- Consultation with internal or external entities

Any findings and recommendations will be reported to the IO for a final decision with a follow-

up report to the IRB. If the report has no basis in fact, the investigator will document the findings and take no further action. If the investigation indicates undue influence occurred, steps will be taken to eliminate the undue influence. These steps may include, but are not limited to:

- No action
- Verbal counseling
- Education
- Reassignment of duties
- Termination of employment
- Evaluate policies and procedures

Allegations of undue influence regarding VA research shall be reported to the Associate Chief of Staff/Research & Development and/or the Medical Center Director at VA for investigation and corrective action.

### 3. IRB REVIEW PROCESS

LSUHSC-S has and follows written policies and procedures for determining when activities are overseen by the Human Research Protection Program. (AAHRPP Element I.1.A.)

The Organization has and follows written policies and procedures that identify applicable laws in the localities where it conducts human research, takes them into account in the review and conduct of research, and resolves differences between federal or national law and local laws. (AAHRPP Element I.1.G.)

The IRB or EC approves each research protocol or plan according to criteria based on applicable laws, regulations, codes, and guidance. (AAHRPP Standard II-3)

#### 3.1 Policy

**Levels of Review:** The IRB/HRPP determines the level of IRB review, not the investigator. Although an investigator may submit an application that anticipates a particular level of review, the responsibility lies with the IRB to determine the appropriate level of IRB review. All research projects submitted to IRB will be processed through one of the following categories of review:

- Not Human Subjects Research
- Exemption Determination
- Expedited Review
- Full Committee Review

The IRB will ensure that the research meets all required ethical and regulatory criteria for initial and continuing review and any modifications of approved research. The following describe the procedures required for the review of research by the IRB.

## 3.2 Definitions

Administrative Hold - When an Investigator or Sponsor wishes to voluntarily interrupt research enrollments and ongoing research activities. An administrative hold must not be used to avoid reporting deficiencies or circumstances that otherwise require reporting by federal agencies. Administrative holds are not suspensions or terminations.

For VA research- Administrative Holds may be requested by an appropriate VA facility official, researcher, or Sponsor (including the ORD when ORD is the sponsor). The term Administrative Hold does not apply to interruptions of VA research related to concerns regarding the safety, rights, or welfare of human subjects research, research investigators, research staff or others.

Modifications Required to Secure Approval - (Conditional Approval) The research requires as a condition of final approval that the investigator (a) makes specified minor changes to the research protocol or informed consent document(s), (b) confirm specific assumptions or understandings on the part of the IRB regarding how the research will be conducted, or (c) submit additional documents, such that, based on the assumption that the conditions are satisfied, the IRB is able to make all of the determinations required for approval under the DHHS regulations at 45 CFR 46.111 and, if applicable, subparts B, C, or D of 45 CFR part 46.

The needed revisions or documents are agreed upon at the IRB meeting. None of the required modifications can be related to the determinations required for approval by the DHHS regulations at 45 CFR 46.111 and, if applicable, subparts B, C, or D of 45 CFR part 46. The requested revisions are presented to the PI for incorporation by simple concurrence. Revisions must be made exactly as designated by the IRB.

Deferred - The IRB cannot make one or more of the determinations required for approval by the HHS regulations at 45 CFR 46.111 and, if applicable, subparts B, C, or D of 45 CFR part 46. This action is taken if substantial modification or clarification is required, or insufficient information is provided to judge the protocol application adequately (the IRB (a) is unable to make the required determinations about research risks and benefits, the adequacy of privacy and confidentiality protections, or the adequacy of the informed consent process because the research protocol provides insufficient information related to these aspects of the research, and (b) is unable to specify changes to the research protocol or consent document that if made would allow the IRB to make these required determinations.

The research may not proceed until the IRB reviews the revised research protocol and approves it at a subsequent convened meeting.

Minimal Risk - Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

Minor Change - A minor change is one which, in the judgment of the IRB reviewer, makes or demonstrates no substantial alteration in:

1. the level of risks to subjects
2. the research design or methodology (adding procedures that are not eligible for expedited review would not be considered a minor change)
3. the number of subjects enrolled in the research (no greater than 10% of the total requested)
4. the qualifications of the research team
5. the facilities available to support safe conduct of the research
6. any other factor which would warrant review of the proposed changes by the convened IRB

Quorum - A quorum of the IRB consists of a simple majority (more than half) of the voting membership, including at least one (1) member whose primary concern is in a non-scientific area as required by 45 CFR 46.108. If research involving an FDA-regulated article is involved, a licensed physician must be included in the quorum.

In addition, for VA research at least one (1) voting VA representative must be present for a quorum.

Suspension of IRB approval - A suspension is a directive of the convened IRB or other authorized individual (e.g., IRB Chairman) (See Section 3.10.1) to temporarily stop some or all previously approved research activities short. Suspended protocols remain open and require continuing review.

Termination of IRB approval - A termination of IRB approval is a directive of the convened IRB to permanently stop some or all activities in a previously approved research protocol. Terminated protocols no longer require continuing review.

### **3.3 IRB Pre-Review**

The IRB pre-review process allows IRB staff to screen submission materials using Worksheet: Pre-Review (HRP-308). This pre-review process applies to all requests for IRB approval (approval of new research, continuing review of research, or modification to previously approved research) or a determination whether an activity is not Human Research or is Human Research that does not engage the Institution.

During Pre-Review, IRB staff will:

- Identify submissions with missing materials or incomplete information
- Identify and document the special determinations that the IRB needs to make to approve research. (For example. waiver of consent, children, prisoners)

- Identify, make, and document regulatory determinations that the institution needs to make to approve research (For example, IND/IDE requirements)
- Identify any relevant local, state, or international requirements
- Arrange for consultation to resolve local, state, or international requirements.
- Identify other special review issues.
- Determine the likely level of review (Committee Review versus Non-committee Review)
- Document Pre-Review determinations in the electronic system or Checklist: Pre-Review (HRP-401).
- Meeting Chair ensures that issues raised by Pre-Review are covered at meetings.

Following the Pre-Review process, the application will be processed using the procedures, worksheets and checklists associated with the relevant research category (as described below). If the submission is incomplete or requires clarification the IRB will contact the investigator by selecting the Request Pre-Review Clarifications Activity within Shields. The investigator will be required to respond to the request for additional information and correct the submission before the review process can continue.

### 3.4 Human Subjects Research Determination

LSUHSC-S has and follows written policies and procedures for determining when activities are overseen by the Human Research Protection Program. (AAHRPP Element I.1.A.)
Researchers and Research Staff know which of the activities they conduct are overseen by the Human Research Protection Program, and they seek guidance when appropriate. (AAHRPP Element III.1.A.)
The IRB or EC has and follows written policies and procedures for determining when activities are exempt from applicable laws and regulations, when permitted by law or regulation and exercised by the IRB or EC. Such policies and procedures indicate that exemption determinations are not to be made by Researchers or others who might have a conflict of interest regarding the studies. AAHRPP Element II.2.A.

Human subject research is defined under 45 CFR 46.102(d) and (f), 21 CFR 50.3 (c) and (j), 45 CFR 46.102(f), 21 CFR 50.3(e). See also [VHA Handbook 1200.05](#). The IRB retains ultimate authority to determine whether an activity meets the definition of human subject research. Upon receipt of written documentation for a human subjects determination the IRB staff reviews the submission, seeks clarification as needed and submits this request to an IRB Chair or designee to make this determination in a timely manner. Notification is provided to the investigator through written IRB correspondence.

All protocols involving both research and human subjects (human subject means interaction or intervention with subjects, or access or use of PHI through records or specimens) must be

reviewed and approved by the IRB before recruitment and data collection may start.

Determinations regarding activities that are either clearly or clearly not human subjects' research, based on the OHRP definition, may be made by the IRB Chair, IO or designee. Determinations regarding less clear-cut activities will be referred to the IRB Chair who may make the determination or refer the matter to the full IRB. If a clear determination cannot be made then, out of an abundance of caution, the activity should be deemed to constitute Human Subjects Research for further review (e.g., Exempt, Expedited or Full IRB Review). Documentation of all Human Subjects Determinations made will be recorded and maintained in the HRPP Office.

#### Activities that Require IRB Review

ACTIVITY	DESCRIPTION	IRB Determination
Cadaver or autopsy material or specimens	Research involving deceased individuals does not require IRB oversight. <b>Note:</b> If using or disclosing decedents PHI see HIPAA Privacy Rule: <a href="https://privacyruleandresearch.nih.gov/pr_08.asp#8f">https://privacyruleandresearch.nih.gov/pr_08.asp#8f</a>	<b>NO</b>
Case Report Studies	<b>Retrospective</b> review of a patient's medical record with intent to document a specific situation or the experience of an individual without intent to form a research hypothesis, draw conclusions or generalize findings. The data will be de-identified.	<b>NO:</b> if using only 1-2 records.  <b>YES:</b> if using 3 or more records.
	<b>Prospective:</b> A single subject study with clear intent, before recruiting or interacting with the participant, to use data that would not ordinarily be collected in the course of treatment. The intent is to report and publish the case study.	<b>YES</b>
Classroom Assignments/ Research Methods Classes	Normal educational activities designed to teach students research methods or demonstrate course concepts. The activities are not intended to create new knowledge or generalize outside the classroom.	<b>NO</b> Faculty/Instructors have an obligation to protect students and others
Clinical Investigations	Experiments using a test article on one or more human subjects that are regulated by the Food and Drug Administration or support applications for research or marketing permits for products regulated by the Food and Drug Administration. Products regulated include foods (dietary supplements that bear a nutrient content claim or a health claim, infant formulas, food and color additives), drugs for human use, medical devices for human use, biological products for human use, and electronic products.	<b>YES</b>
"Compassionate" or Treatment Use of an Investigational Drug or Device	A treating physician determines an <b>unapproved</b> drug or device is the best treatment for a patient, and ALL of the following criteria apply: 1. The patient has a condition that is life-threatening or a serious disease, 2. No comparative or satisfactory alternative treatment is	<b>YES</b>

	available, 3. A controlled, clinical trial of drug/device is ongoing, 4. Sponsor is pursuing marketing approval.	
Planned Emergency Research with a Waiver of Consent	The exception to the consent requirements applies to a limited class of research activities involving individuals who are in need of emergency medical intervention but who cannot give informed consent because of their life-threatening medical condition, and who do not have a legally authorized representative.	<b>YES</b>
Emergency Use of an Investigational Drug or Device	A treating physician determines an unapproved drug or device is the best treatment for a patient, and ALL of the following criteria apply: 1. The test article is used one time per institution to treat a single patient, 2. The patient has a condition that is life-threatening or severely debilitating, 3. No standard treatment is available, 4. There is not sufficient time to obtain IRB review and approval, 5. The emergency use is reported to the IRB within five working days; when possible, the treating physician should consult with the IRB prior to use.	<b>IRB NOTIFICATION REQUIRED WITHIN 5 DAYS OF USE</b>
	Sponsor or manufacturer of the drug/device requires IRB approval before release in an emergency use situation.	<b>YES</b>
Humanitarian Use Device (HUD)	A HUD is a “medical device intended to benefit patients in the treatment or diagnosis of a disease or condition that affects or is manifested in fewer than 4,000 individuals in the U.S. per year [21 CFR 814.3(n)]. They can only be used in a facility after an IRB has approved their use in that facility, except in certain emergencies.	<b>YES</b>
Innovative or Novel Procedures, Treatment, or Instructional Methods	Systematic investigation of innovations in diagnostic, therapeutic procedure or instructional method in multiple participants in order to compare to standard of care or normal procedure. The investigation is designed to test a hypothesis, permit conclusions to be drawn, thus to develop or contribute to generalizable knowledge.	<b>YES</b>
	The use of innovative interventions that are designed solely for therapeutic purposes to enhance the well-being of an individual patient with a reasonable expectation of success. The intent of the intervention is to provide diagnosis, preventive treatment, or therapy to an individual patient. Research is not involved.	<b>NO</b>
Internet Research	Online websites set up for the purposes of collecting data regarding a particular topic. This may include the completion of questionnaires/surveys, personal data, etc.	<b>YES</b>
In Vitro Device Studies	Current FDA guidance indicates that IRB review is required for any IVD study involving human specimens/samples, even when the research involves no identifiers and the biological materials cannot be linked to any identifying information.	<b>YES</b>
Literature Review	An assessment of a body of <b>published</b> research that	<b>NO</b>

	addresses a research question. Identifies or summarizes what is already known about an area of study or may identify questions a body of research does not answer.	
Oral Histories	Oral histories represent a technique that usually involves a series of taped interviews with participants regarding a particular historical event or period. When the focus is a recollection of societal or institutional events rather than the interviewees subjective perceptions then the project is not usually human subjects research.	<b>NO</b>
	Oral histories that involve the testing or confirmation of a hypothesis or the subjective perceptions of the interviewees may be human subjects research.	<b>YES</b>
Pilot Studies	Pilot studies that meet the definition of human research, regardless of the number of subjects enrolled or the duration of the studies.	<b>YES</b>
Professional Recognition	Employees or agents of LSUHSC-S involved in research projects carried out at other locations when the services performed merit professional recognition or publication privileges.	<b>YES</b>
Quality Assurance (QA) and Quality Improvement (QI) Activities	Systematic, data-guided activities designed to implement promising ways to improve patient outcomes, system performance or professional development. The activity usually occurs within standard of care or normal educational or business practices confined to the local setting. Intent is only one element considered. The activity often involves an iterative process that may change over time in response to ongoing feedback. The plan may include mechanisms for assessment, intervention, analysis and implementation. Any risk should be confined to privacy or confidentiality. One-time activities designed to meet personal educational requirements are generally not QA or QI. Since QI and research often overlap all investigator initiated QI/QA projects should be sent to the IRB for a determination.	<b>YES – must have a determination</b>  <b>(All QA/QI activities implemented in a patient or educational setting require oversight by compliance or quality services).</b>
	Proposed QI/QA activities that may have research intent, address a specific deficit in scientific knowledge or are intended to be generalized beyond the local setting require submission to the IRB for a determination.	<b>YES</b>
Repositories, Registries or other specimen or record keeping mechanisms (e.g., data, specimens)	Proposed activity involves accessing a storage site or mechanism by which identifiable human tissue, blood, genetic material, records or data are stored or archived.	<b>YES</b>
	Proposed activity involves accessing stored human tissue, blood, genetic material or data that will be de-identified by study personnel at the time of collection or when the investigator will retain a code or link that enables re-identification of data or specimens.	<b>YES</b>
	Proposed activity involves accessing a controlled repository where the investigator does not receive any PHI or links to the data or specimens, AND the investigator must enter into an agreement with the repository provider that states under no circumstances will the identity of the subjects be released to the investigator.	<b>NO</b>
	Proposed activity involves accessing publicly available specimens or data.	<b>NO</b>
Self - Experimentation	Any research where the investigator is also a subject	<b>YES</b>

	(investigator self-experimentation) requires IRB review and approval.	
Standard Diagnostic or Therapeutic procedures	The collection of data about established and accepted diagnostic, therapeutic procedures, or instructional methods is intended for dissemination or contribution to generalizable knowledge.	<b>YES</b>
	There is an alteration in patient care or assignment for research purposes or the alteration is in a way that standard diagnostic or therapeutic procedures are not completely up to the discretion of a practitioner.	<b>YES</b>
	A diagnostic procedure is added to a standard treatment for the purpose of research.	<b>YES</b>
	An established and accepted diagnostic, therapeutic procedure or instructional method is performed only for the benefit of a patient and not for research purposes.	<b>NO</b>
Student Conducted Research	Thesis or dissertation projects involving human participants conducted to meet the requirements of a graduate degree.	<b>YES</b>
Surveys	Interacting with participants directly or through third party survey administrators to answer a research question requires IRB review even if not collecting identifiable information.	<b>YES</b>

### 3.5 Exempt Studies

The IRB or EC has and follows written policies and procedures for addressing protection of participants in research that is exempt from applicable laws and regulations. These functions may be delegated to an entity other than the IRB or EC. AAHRPP Element II.2.B.

All research using human subjects must be approved by the Institution. Certain categories of research (i.e., exempt research) do not require convened IRB review and approval. Exempt research remains subject to institutional review; its status must be determined and approved by the IRB Chair or designee. Studies determined to meet exemption criteria are communicated to the IRB through the IRB meeting agenda and/or IRB meeting minutes.

Reviewers will use the Exemption Determination Checklist to determine and document whether the protocol meets the exemption criteria. The decision must be communicated in writing to the investigator and the IRB. Documentation must include the specific categories justifying the exemption.

#### Procedures for Exemption Determination

In order to obtain an exemption determination investigators must submit as applicable:

1. a completed Request for Exemption form
2. Human Subjects Determination Form
3. Written Protocol or Research Plan
4. all recruitment materials (letter of invitation, flyer, recruitment script)
5. consent form (when appropriate)

6. all surveys, questionnaires, instruments, etc.
7. letter(s) of permission or an appropriate agreement from each non-University site of performance
8. if sponsored, one copy of the grant application(s) and/or contract
9. verification of current human research protection training for all members of the research team

The IRB Chair or designee reviews all requests for exemptions and determines whether the request meets the criteria for exempt research. The Chair selects designees who are qualified to review this category of submission based upon their expertise of the protocol content and knowledge of the regulations pertaining to the research. Individuals involved in making the determination of an IRB exempt status of a proposed research project cannot be involved in the proposed research. Reviewers cannot have any apparent conflict of interest. Decisions regarding approval of exempt research are made by the IRB Chair or the designee determined by the Chair.

To document the IRB reviewer's determination of the request for exempt research, he/she completes the Exemption Determination Form and documents the category under which it was permitted.

Once institutional review is completed and a determination is made, the IRB staff will send a written notification to the PI of the results of the review.

All requests for an exemption must include a termination date. The exemption is only good until that date or three (3) years, whichever comes first. If the research extends beyond that date then the researcher has to submit a request for an extension or submit a new protocol.

During the approved exemption period, all modifications to the research must be submitted prior to implementation to determine that Exemption Criteria are still met. Investigators must notify the IRB in writing when the project is complete.

OHRP has published decision trees to help in determining whether a research proposal fits the criteria for Exempt review. The chart is available at:

<http://www.hhs.gov/ohrp/policy/checklists/decisioncharts.html>

There are no IRB processing deadlines for submission of projects that meet exemption criteria.

### **3.5.1 Exemption of VA Research**

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VA projects that are determined to be exempt must be reviewed by the VA Research and Development Committee prior to initiation and then they must be included in its annual review of research projects. The exempt status means the research is exempt from the requirements of 38 CFR Part 16 including reviews by the IRB. It does not exempt the research

from other required reviews, such as by the RDC.

### **3.5.2 Limitations on Research Subjects**

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Children: Exemption for research involving survey or interview procedures or observations of public behavior does NOT apply to Research in Children, except for research involving observations of public behavior when the Investigator does not participate in the activities being observed.

Prisoners: Exemptions do NOT apply to Research involving Prisoners. Review is required by either a Convened IRB (with a Prisoner Representative present) or by Expedited Review with review by a Prisoner Representative.

International Research: Exemptions do NOT apply to International Research. Review is required, either by a Convened IRB or, as appropriate, the IRB Chair (or designee).

### **3.5.3 Categories of Exempt Research**

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With the above exceptions, research activities not regulated by the FDA (see Section 3.5.4 for FDA Exemptions) in which the only involvement of human subjects will be in one or more of the following categories are exempt from IRB review, but require institutional review, at LSUHSC-S:

#### **Criteria Allowing Exemption from Federal Regulations**

##### **1. Category 1**

- a. The research is conducted in established or commonly accepted educational settings.
- b. The research involves normal educational practices, such as:
  - i. Research on regular and special education instructional strategies.
  - ii. Research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.
- c. The research does not involve prisoners as participants.
- d. The research is not FDA-regulated.

##### **2. Category 2**

- a. The research involved the use of one or more of the following:
  - i. Educational tests (cognitive, diagnostic, aptitude, achievement).
  - i. Survey procedures.
  - i. Interview procedures.
  - ii. Observation of public behavior.
- b. If any disclosure of the participants' responses outside the research could reasonably place the participants at risk of criminal or civil liability or be damaging to the participants' financial standing, employability, or reputation.
  - i. Information obtained is not recorded in such a manner that participants can be identified, directly or indirectly through identifiers linked to the participants.

- c. If the research is regulated by the Department of Veterans Affairs:
    - i. If any disclosure of the participants' responses outside the research could reasonably place the participants at risk of loss of insurability.
      - Information obtained is not recorded in such a manner that human.
      - Participants can be identified, directly or through identifiers linked to the participants.
  - d. If the research involves children as participants:
    - i. The procedures do not involve any of the following:
      - Survey procedures.
      - Interview procedures.
      - Observation of public behavior where the Researchers participate in the activities being observed.
  - e. The research does not involve prisoners as participants.
  - f. The research is not FDA-regulated.
3. Category 3
- a. The research is not exempt under Category 2.
  - b. Research involving the use of one or more of the following:
    - i. Educational tests (cognitive, diagnostic, aptitude, achievement).
    - ii. Survey procedures.
    - iii. Interview procedures.
    - iv. Observation of public behavior.
  - c. Either of the following is true:
    - i. The participants are elected or appointed public officials or candidates for public office.
    - ii. Federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.
  - d. The research does not involve prisoners as participants.
  - e. The research is not FDA-regulated.
4. Category 4
- a. The research involving the collection or study of existing data, documents, records, pathological specimens or diagnostic specimens.
  - b. Either of the following is true:
    - i. The sources are publicly available.
    - ii. The Researcher records information in such a manner that participants cannot be identified, directly or indirectly through identifiers linked to the participants.
  - c. The research does not involve prisoners as participants.
  - d. The research is not FDA-regulated.
5. Category 5
- a. The project is a research or demonstration project.
  - b. The research is conducted by or subject to the approval of a federal Department or Agency head.

- c. The research is designed to study, evaluate, or otherwise examine one or more of the following:
  - i. Public benefit or service programs.
  - ii. Procedures for obtaining benefits or services under those programs.
  - iii. Possible changes in or alternatives to those programs or procedures.
  - iv. Possible changes in methods or levels of payment for benefits or services under those programs.
- d. The program under study delivers a public benefit (e.g., financial or medical benefits as provided under the Social Security Act) or service (e.g., social, supportive, or nutrition services as provided under the Older Americans Act).
- e. The research is conducted pursuant to specific federal statutory authority.
- f. There is no statutory requirement that an IRB or EC review the research.
- g. The research does not involve significant physical invasions or intrusions upon the privacy of participants.
- h. The research does not involve prisoners as participants.
- i. The research is not FDA-regulated.

For VA research, the determination of exempt status for these research and demonstration projects must be made by the Under Secretary for Health on behalf of the Secretary of Veterans Affairs, after consultation with Office of Research and Development, the Office of Research Oversight, the Office of General Counsel, and other experts, as appropriate.

#### 6. Category 6

- a. The research involves taste and food quality evaluation or is a consumer acceptance study.
- b. Either of the following is true:
  - i. Wholesome foods without additives are consumed.
  - ii. If a food is consumed that contains a food ingredient or an agricultural chemical or environmental contaminant, the food ingredient or agricultural chemical or environmental contaminant is at or below the level and for a use found to be safe by one of the following:
    - The Food and Drug Administration.
    - The Environmental Protection Agency.
    - The Food Safety and Inspection Service of the U.S. Department of Agriculture.
- c. The research does not involve prisoners as participants.

For VA research, the determination of exempt status for these research and demonstration projects must be made by the Under Secretary for Health on behalf of the Secretary of Veterans Affairs, after consultation with Office of Research and Development, the Office of Research Oversight, the Office of General Counsel, and other experts, as appropriate.

**Exemption of VA Research:** VA projects that are determined to be exempt must be reviewed by the VA Research and Development Committee prior to initiation and then they must be included in its annual review of research projects.

### 3.5.4 FDA Exemptions

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The following categories of clinical investigations are exempt from the requirements of IRB review:

1. Emergency use of a test article, provided that such emergency use is reported to the IRB within five (5) working days. Any subsequent use of the test article at the institution is subject to IRB review. (21 CFR 56.104(c))
2. Taste and food quality evaluations and consumer acceptance studies, if wholesome foods without additives are consumed or if a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural, chemical, or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture. (21 CFR 56.104(d))

### 3.5.5 Additional Protections

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The IRB or EC has and follows written policies and procedures for addressing protection of participants in research that is exempt from applicable laws and regulations. These functions may be delegated to an entity other than the IRB or EC. (AAHRPP Element II.2.B)

Although exempt research is not covered by the federal regulations, this research is not exempt from the ethical guidelines of the Belmont Report. The individual making the determination of exemption will determine whether to require additional protections for subjects in keeping with the guidelines of the Belmont Report.

### 3.6 Expedited Review

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The IRB or Ethics Committee has and follows written policies and procedures to conduct reviews by the expedited procedure, if such procedure is used. Element II.2.E.1. – Initial review; Element II.2.E.2. – Continuing review; Element II.2.E.3. – Review of proposed modifications to previously approved research. (AAHRPP Element II.2.E)

Expedited review does not mean that review is less rigorous or happens more quickly than convened review. It refers, instead, to certain types of research considered to involve minimal risk. All protocols processed through Expedited Procedures for Initial Applications, Continuing Review Protocols, or Modifications to previously approved research are subject to the same approval criteria as full board reviews and must adhere to all applicable regulations and policies. Also, a final study closure form is required when the study has ended. OHRP has published decision trees that are available online to help in determining whether a research proposal fits the criteria for expedited review.

An IRB may use the expedited review procedure to review either or both of the following:

1. Some or all of the research appearing on the list of categories of research eligible for expedited review and found by the reviewer(s) to involve no more than minimal risk.
2. Minor changes in previously approved research during the period (of one year or less) for which approval is authorized.

### **3.6.1 Categories of Research Eligible for Expedited Review**

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1. The activities listed below should not be deemed to be of minimal risk simply because they are included on this list. Inclusion on this list merely means that the activity is eligible for review through the expedited review procedure when the specific circumstances of the proposed research involve no more than minimal risk to human subjects.
2. The categories in this list apply regardless of the age of subjects, except as noted.
3. The expedited review procedure may not be used where identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.
4. The expedited review procedure may not be used for classified research involving human subjects. LSUHSC-S does not routinely performed classified research.
5. The standard requirements for informed consent (or its waiver, alteration, or exception) apply regardless of the type of review--expedited or convened--utilized by the IRB.

Research Categories one (1) through seven (7) pertain to both initial and continuing IRB review; Categories (8) and (9) only pertain to continuing review.

1. Clinical studies of drugs and medical devices only when condition (a) or (b) is met.
  - a. Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required. (Note: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.)
  - b. Research on medical devices for which (i) an investigational device exemption application (21 CFR Part 812) is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.
2. Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:
  - a. from healthy, non-pregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week; or
  - b. from other adults and children, considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may

not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week. Children are defined in the DHHS regulations as "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.") (45\_CFR 46.402(a))

3. Prospective collection of biological specimens for research purposes by noninvasive means. Examples:
  - a.* Hair and nail clippings in a non-disfiguring manner
  - b.* Deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction
  - c.* Permanent teeth if routine patient care indicates a need for extraction
  - d.* Excreta and external secretions (including sweat)
  - e.* Uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gum base or wax or by applying a dilute citric solution to the tongue
  - f.* Placenta removed at delivery
  - g.* Amniotic fluid obtained at the time of rupture of the membrane prior to or during labor
  - h.* Supra- and sub-gingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques
  - i.* Mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings
  - j.* Sputum collected after saline mist nebulization
4. Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.) Examples:
  - a.* physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject's privacy;
  - b.* weighing or testing sensory acuity;
  - c.* magnetic resonance imaging;
  - d.* electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, Doppler blood flow, and echocardiography;
  - e.* moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

5. Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for non-research purposes (such as medical treatment or diagnosis). Some research in this category may be exempt from the DHHS regulations for the protection of human subjects. See Exempt Categories and 45 CFR 46.101(b)(4). This listing refers only to research that is not exempt.
6. Collection of data from voice, video, digital, or image recordings made for research purposes.
7. Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies. NOTE: Some research in this category may be exempt from the DHHS regulations for the protection of human subjects. See Exempt Categories and 45 CFR 46.101(b)(2) and (b)(3). This listing refers only to research that is not exempt.
8. Continuing review of research previously approved by the convened IRB as follows:
  - a. where (i) the research is permanently closed to the enrollment of new subjects; (ii) all subjects have completed all research-related interventions; and (iii) the research remains active only for long-term follow-up of subjects; or
  - b. where no subjects have been enrolled and no additional risks have been identified; or
  - c. where the remaining research activities are limited to data analysis.

NOTE: Category (8) identifies three situations in which research that is greater than minimal risk and has been initially reviewed by a convened IRB may undergo subsequent continuing review by the expedited review procedure.

For a multi-center protocol, an expedited review procedure may be used by the IRB at a particular site whenever the conditions of category (8)(a),(b), or (c) are satisfied for that site. However, with respect to category 8(b), while the criterion that "no subjects have been enrolled" is interpreted to mean that no subjects have ever been enrolled at a particular site, the criterion that "no additional risks have been identified" is interpreted to mean that neither the investigator nor the IRB at a particular site has identified any additional risks from any site or other relevant source.

9. Continuing review of research, not conducted under an investigational new drug application or investigational device exemption where categories two (2) through eight (8) do not apply but the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified.

Under Category (9), an expedited review procedure may be used for continuing review of research not conducted under an investigational new drug application or investigational device exemption where categories (2) through (8) do not apply but the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified. The determination that "no additional risks have been identified" does not need to be made by the convened IRB.

### **3.6.2 Expedited Review Procedures**

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Under an expedited review procedure, the review may be carried out by the IRB Chair or by one (1) or more reviewers designated by the Chair from among members of the IRB. IRB members who serve as designees to the IRB Chair for expedited review will be matched as closely as possible with their field of expertise to the study.

The Chairs will designate a list of IRB members eligible to conduct expedited review. The designees must be experienced (having served on the IRB for at least one (1) year) voting members of the IRB. The IRB Staff will select expedited reviewers from that list. Selected reviewers must have the qualifications, experience, and knowledge in the content of the protocol to be reviewed, as well as being knowledgeable of the requirements to approve research under expedited review. IRB members with a conflict of interest in the research (See Section 2.7.4) will not be selected to review the protocol.

When reviewing research under an expedited review procedure, the IRB Chairs, or designated IRB member(s), should receive and review all documentation that would normally be submitted for a full-board review including the complete protocol.

The Continuing Review Form must summarize the research since the previous review and include modifications and unanticipated problems, any notes from the pre-screening conducted by the IRB Office staff and the current consent documents. The Expedited Review Checklist will be used to verify eligibility for review and approval by expedited procedures.

Protocols submitted for Expedited Review will be pre-screened by the HRPP staff to ensure that the submissions are complete. The reviewer(s) conducting initial or continuing review will complete the appropriate Institutional Review Board - Protocol Review Checklist to determine whether the research meets the criteria allowing review using the expedited procedure and if so, whether the research meets the regulatory criteria for approval. If the research does not meet the criteria for expedited review, then the reviewer will indicate the appropriate level of review and whether the research needs full review by the convened IRB. If full board review is required the protocol will be placed on the agenda for the next convened IRB meeting.

In reviewing the research under expedited procedures, the reviewers will follow the Review Procedures described in Sections 3.7 & 3.8 and may exercise all of the authorities of the IRB

except that the reviewers may not disapprove the research. A research activity may be disapproved only after review by the convened board in accordance with the non-expedited procedure set forth below.

Under expedited procedures the reviewer(s) will indicate that the research is eligible for one of the following determinations:

1. Approval
2. Modifications Required
3. Not Human Subjects Research
4. Research Activity must be reviewed by the Convened IRB due to:
  - a. Recommendation for Disapproval
  - b. The activity is not eligible for Expedited Review
  - c. The activity is eligible for Expedited Review but recommend review by the full board.

These actions will be documented on the Reviewer Check sheet and submitted to the HRP staff. If modifications are required the staff will inform the investigator by e-mail or written notification. If the modifications required are minor, the IRB Administrator, IO or designee may determine if the investigator has sufficiently addressed the modifications. If the modifications required are major or if the reviewer(s) has requested to verify the changes, the modified protocol will be sent back to the IRB member(s) for verification.

If the research received a Recommendation for Disapproval by the reviewer(s), the research will be placed on the IRB agenda for review at the next scheduled meeting.

If expedited review is carried out by more than one IRB member and the expedited reviewers disagree, IRB Chair will make a final determination. Upon the discretion of the IRB Chair or designee the protocol will be submitted to the convened IRB for review.

The beginning of the approval period for research reviewed under expedited procedures is the date on which the IRB chairperson or designee has determined that the research protocol and any changes made by the investigator are satisfactory and all criteria for approval have been satisfied under the DHHS regulations at 45 CFR 46.111 and, if applicable, subparts B, C, or D of 45 CFR part 46,

### **3.6.3 Informing the IRB**

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All members of the IRB will be apprised of all research that was approved by the IRB Chair or designated IRB member(s) by expedited procedures by means of a list in the agenda. Any IRB member can request to review the full protocol by contacting the IRB Office.

## **3.7 Convened IRB Meetings**

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The IRB or EC has and follows written policies and procedures for conducting meetings by the convened IRB or EC. (AAHRPP Element II.2.C)

The IRB or Ethics Committee has and follows written policies and procedures to conduct reviews by the convened IRB or Ethics Committee. Element II.2.D.1. – Initial review; Element II.2.D.2. – Continuing review; Element II.2.D.3. – Review of proposed modifications to previously approved research (AAHRPP Element II.2.D)

Except when a submission meets the criteria for expedited review, the IRB will conduct initial and continuing reviews of all research at convened meetings at which a quorum (see below) of the members is present, including at least one (1) member whose primary concerns are in non-scientific areas. In order for the research to be approved, it shall receive the approval of a majority of those members present at the meeting.

### **3.7.1 IRB Meeting Schedule**

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The IRB or EC has and follows written policies and procedures for conducting meetings by the convened IRB or EC. (AAHRPP Element II.2.C)

The IRB meets twice a month, but meetings may vary due to holidays or lack of quorum. The schedule for IRB meetings can be found on the HRPP website. Additionally, this information is available in the HRPP/IRB Office. Whenever possible, the IRB schedules meetings at least 90 days in advance. Special meetings may be called by the Chairs at any time to deal with urgent issues.

### **3.7.2 Preliminary Review**

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The IRB staff will perform a preliminary review of all protocol materials submitted to the IRB for determination of completeness and accuracy. All submissions will be date stamped by the electronic IRB data system (Shields). Only complete submissions will be referred for further consideration (Exempt, Expedited or Full Board review).

The investigator will be informed either by e-mail, phone or in person of missing materials and any deadline to re-submit corrections before further review can take place. It is the investigator's responsibility to provide the IRB/HRPP with the correct contact information.

In the case of a PI who is submitting a protocol for the first time, or an investigator who may not be well-versed in the protocol submission procedures, individualized IRB consultations can be arranged. Specific questions about the IRB policies and procedures, determination of whether a particular protocol is human research or not and what particular forms are required for a particular study can be submitted in writing to the HRPP staff for information and/or clarification. Individual appointments with the IRB Administrator or IRB Analysts can also be arranged and are strongly recommended for first-time submissions.

All sponsored IRB projects considered for IRB review must have an agreed upon Clinical Trial Agreement (CTA). The Contract Coordinator in the Office of Legal Affairs and Organizational Integrity must have released the CTA to the IRB for the project to qualify for IRB review.

### 3.7.3 Primary & Secondary Reviewers

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The IRB or EC has and follows written policies and procedures requiring research protocols or plans to be reviewed by individuals with appropriate scientific or scholarly expertise and other expertise or knowledge as required to review the research protocol or plan. (AAHRPP Element II.1.E)

After it has been determined that the protocol submission is complete, the IRB Chairs, with the assistance of the HRPP staff will assign IRB proposals for review based on the scientific content of the protocol, and the reviewer's area of expertise, and requirements for representation of vulnerable populations involved in the research.

Two reviewers will be assigned to each new protocol on the agenda for initial review. A primary reviewer is assigned to each protocol that requires continuing review and to all modifications to previously approved research that are placed on the meeting agenda.

A reviewer may be assigned multiple items to review at an IRB meeting. When the IRB is presented with a protocol which may be outside of the knowledge base of any of the IRB members, an outside consultant will be sought. Proposals for which appropriate expertise cannot be obtained for a given meeting will be deferred to another meeting.

The primary and secondary reviewers are responsible for:

1. Having a thorough knowledge of all the details of the proposed research.
2. Performing an in-depth review of the proposed research and supporting documents.
3. Leading the discussion of the proposed research at the convened meeting, presenting both positive and negative aspects of the research, and leading the IRB through the regulatory criteria for approval (See Section 3.8).
4. Making suggestions for changes to the proposed research, where applicable.
5. Completing all applicable IRB reviewer forms.

The primary and the secondary reviewers (or consultants) must attend the IRB meetings. If attendance is not possible, the reviewer should notify the Chair as soon as possible. The Chair will decide which action to take. If the primary reviewer is absent from the meeting, the secondary reviewer may act as the primary reviewer or a new reviewer may be assigned, providing the new reviewer has reviewed the materials prior to the meeting. A reviewer may also join the meeting via teleconference or videoconference to present their review if there is a circumstance precluding their attendance at the meeting.

The IRB Chair can add or remove designated reviewers. To add a designated reviewer, the IRB Chair will review the IRB roster and ensure that the proposed individual is an IRB member. The Chair will verify that the IRB member is experienced by having been an IRB member for a period of at least one year. The IRB chair must consider the IRB member to have sufficient experience in and knowledge of the criteria for approval and conducting IRB reviews. There are no criteria to be followed when removing a designated reviewer. The IRB Chair will then notify the IRB or HRPP staff member managing the IRB roster of the decision to add or remove an IRB member and have the staff member update the IRB roster both on paper and in the electronic system.

#### **3.7.4 Pre-Meeting Distribution of Documents**

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IRB members must have sufficient time in advance of an IRB meeting to review documents associated with IRB agenda items. For this reason, all IRB members will receive their research review materials no less than one week before the scheduled meeting to allow sufficient time for the review process. In the case of an emergency IRB meeting, review materials will be distributed with as much advance lead-time as reasonable.

#### **3.7.5 Materials received by the IRB**

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Each IRB member receives and reviews the following documentation, as applicable, for all protocols on the agenda:

1. IRB Initial Application for Approval of Research involving Human Participants or Protocol Summary; including any information on any collaborating investigators or Performance sites;
2. Proposed Consent and Assent Documents including HIPAA Authorization;
3. Recruitment materials.

At least one (1) primary reviewer must receive and review the following documents when they exist for initial research applications:

1. Full Protocol
2. Investigator's Brochure
3. Data collection instruments including surveys and questionnaires
4. FDA form 1572
5. Delegation Log
6. Investigator(s) Education Certification
7. Grant or Contract Information

These documents are available in the IRB electronic data system (Shields). Any IRB member may request any of the material provided to the primary and secondary reviewers by contacting the IRB Office.

If an IRB member requires additional information to complete the review they may contact the investigator directly or may contact the IRB Office to make the request of the investigator. Protocol reviewers will use the Review Worksheet that lists the criteria for approval as a guide.

All IRB members attending the convened meeting are required to review all protocol materials distributed for the meeting, so that they may discuss and vote on each item on the agenda.

### 3.7.6 Quorum - IRB

The IRB or EC membership permits appropriate representation at the meeting for the types of research under review, and this is reflected on the IRB or EC roster. The IRB or EC has one or more unaffiliated members; one or more members who represent the general perspective of participants; one or more members who do not have scientific expertise; one or more members who have scientific or scholarly expertise; and, when the IRB or EC regularly reviews research that involves vulnerable participants, one or more members who are knowledgeable about or experienced in working with such participants. (AAHRPP Element II.1.A)

The IRB or EC has and follows written policies and procedures for conducting meetings by the convened IRB or EC. (AAHRPP Element II.2.C)

A quorum consists of a simple majority (more than 50%) of the voting membership, including at least one (1) member whose primary concern is in a non-scientific area. At least one (1) unaffiliated member and one (1) member who represents the general perspective of subjects will attend 10 out of 12 meetings per fiscal year. The non-scientific member, the unaffiliated member, and the member representing the general perspective of subjects, may be the same person or at times may be represented by two or three different members. If research involving an FDA-regulated article is involved, a licensed physician must be included in the quorum. The IRB Chair, with the assistance of the IRB staff and the Worksheet: Evaluation of Quorum and Expertise (HRP-305), will confirm that an appropriate quorum is present before calling the meeting to order. The IRB Chair will be responsible to ensure that the meetings remain appropriately convened. The meeting minutes will document member attendance and the status of the quorum.

A quorum must be maintained for each vote to occur. Quorum is monitored throughout the meeting by the IRB staff and is reassessed each time a member leaves and enters the meeting room. Quorum will be lost if the only non-scientific member leaves the room, even if half of the members are still present. Quorum may be lost if the only unaffiliated member or only member representing the general perspective of subjects, leaves the room. The IRB staff notifies the Chair immediately if a quorum is lost. If a quorum is not maintained, the research must not be voted on and will be deferred. No official action or vote will be taken by the board if quorum is lost during a meeting.

Members are considered present if participating through teleconferencing or videoconferencing. In this case, the member must have received all pertinent material prior to the meeting and must be able to participate actively and equally in all discussions.

Opinions of absent members that are transmitted by mail, telephone, facsimile or e-mail may be considered by the attending IRB members, but may not be counted as votes or to satisfy the quorum for convened meetings.

For VA Research - At least one (1) VA representative will be present during the review and approval of VA research.

### **3.7.7 Meeting Procedures**

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The IRB or EC has and follows written policies and procedures so that members and consultants do not participate in the review of research protocols or plans in which they have a conflict of interest, except to provide information requested by the IRB or EC. (AAHRPP Element II.1.D)
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The IRB or Ethics Committee has and follows written policies and procedures to conduct reviews by the convened IRB or Ethics Committee. Element II.2.D.1. – Initial review: Element II.2.D.2. – Continuing review; Element II.2.D.3. – Review of proposed modifications to previously approved research (AAHRPP Element II.2.D)
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The IRB Chair, or Vice Chair if the IRB Chair is absent, will call the meeting to order, once it has been determined that a quorum is in place. The Chair or Vice Chair will remind IRB members to recuse themselves from the discussion and vote by leaving the room where there is a conflict of interest.

It is the responsibility of the IRB staff to record the proceedings and minutes of the meeting. After the minutes are transcribed and approved by the board, the audio recordings will be deleted. The IRB will review the IRB Minutes from the prior meeting and determine if there are any revisions/corrections to be made. If there are no changes to be made, the minutes will be accepted as presented and considered final. If it is determined that revisions/corrections are necessary, the minutes will be amended. If the changes are minor administrative errors, the chair may approve the changes. If the changes to the minutes are significant, the revised document will be distributed by email for electronic vote or presented at the next convened IRB meeting.

The IRB reviews all submissions for initial and continuing review, as well as requests for modifications. The Primary Reviewer presents an overview of the research and leads the IRB through a discussion of how the protocol meets the criteria for approval. All members present at a convened meeting have full voting rights, except in the case of a conflict of interest (see below). For the research to be approved, it must receive the approval of a majority of those voting members present at the meeting. The recording of the vote will denote the number of

votes for, against, and abstained.

Board members are contacted via email approximately 7-10 days prior to the scheduled meeting date and asked to confirm their planned attendance to ensure appropriate notification of alternates. A quorum worksheet is completed by the IRB/HRPP staff to determine and document whether the IRB meeting is appropriately convened.

#### Consultants for Vulnerable Populations

When reviewing a protocol involving children, the IRB will ensure that appropriate pediatric expertise is available to review the specific research activities. Non-voting consultants may be invited to assist with the review if additional expertise is needed.

When reviewing studies with other Vulnerable Populations, including pregnant women, fetuses, neonates, handicapped and cognitively impaired persons, the IRB will request review by expert consultants, as needed. If the IRB regularly reviews research involving a vulnerable category of subjects, one or more individuals who are knowledgeable about and experienced in working with these subjects should be included as IRB members. For research that involves mentally disabled persons or persons with impaired decision-making capacity, IRB membership must include at least one (1) member who is an expert in the research area.

#### Prisoner Representatives

Prisoner research is not routinely conducted at LSUHSC-S. Consideration of prisoner's research is discussed with the IO or designee before submitting the protocol to the IRB for review. However, when reviewing a protocol in which a prisoner is a subject,

- A majority of the IRB (exclusive of prisoner members or prisoner advocates) must have no association with the prison(s) involved, apart from their membership on the IRB;
- At least one (1) IRB member present at the meeting shall be a prisoner, or a prisoner advocate/representative with appropriate background and experience to serve in that capacity. The prisoner/prisoner representative must be present for the discussion and for the review of any studies (including initial review, continuing review, modification, or report of anticipated problems involving risks to participants and others) that involve prisoners. The prisoner/prisoner representative is a voting member.

### **3.7.8 Guests & Staff**

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The Principal Investigator/Designee (sub-investigator) may attend the IRB meeting to provide information or answer questions about their proposed or ongoing research. The investigator is to inform the IRB staff or the Chair of his/her planned attendance. The Principal Investigator may not be present for the discussion or vote on their research.

Other guests may be permitted to attend IRB meetings at the discretion of the IRB Chair and the Administrator of the IRB Office. Guests may not participate in discussions, unless requested by the IRB and must sign a confidentiality agreement.

Certain individuals (e.g., HRPP staff) regularly attend IRB meetings as guests. While they are not voting members of the IRB, they may participate in the IRB discussion and may provide additional information to the IRB. They only need to sign a confidentiality agreement once.

### 3.8 Criteria for IRB Approval of Research

The IRB or EC approves each research protocol or plan according to criteria based on applicable laws, regulations, codes, and guidance. AAHRPP Standard II-3

The IRB or Ethics Committee has and follows written policies and procedures to conduct reviews by the convened IRB or Ethics Committee. Element II.2.D.1. – Initial review; Element II.2.D.2. – Continuing review; Element II.2.D.3. – Review of proposed modifications to previously approved research (AAHRPP Element II.2.D)

For the IRB to approve human subjects' research at the time of Initial and Continuing Review, it must determine that the following requirements are satisfied:

1. Risks to subjects are minimized:
  - a) by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk
  - b) whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.
2. Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result. In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research). The IRB should not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) among those research risks that fall within the purview of its responsibility.
3. Selection of subjects is equitable. In making this assessment, the IRB should consider the purposes of the research, the setting in which the research will be conducted, and special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons.
4. Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by 45 CFR 46.116.
5. Informed consent will be appropriately documented, in accordance with, and to the extent required by 45 CFR 46.117.
6. When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.
7. When appropriate, there are adequate provisions to protect the privacy of subjects

and to maintain the confidentiality of data.

8. When some or all the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects.

9 and 10 are to be considered for VA research

9. The IRB must ensure that steps to manage, reduce, or eliminate potential or real conflicts of interest (financial, role (investigator/patient relationship), and or institutional) have been taken. All VA investigators must comply with VHA policies and procedures regarding conflict of interest. Specifically, a member with a conflict of interest cannot: (a) contribute to quorum; (b) be present for the discussion of the issue for which they are conflicted, except to answer questions from the committee; or (c) be present for the vote on the issue. Also, concerning disclosing conflicts of interests, this means disclosing to the IRB any potential, actual, or perceived conflict of interest of a financial, professional, or personal nature that may affect any aspect of the research, and complying with all applicable VA and other Federal requirements regarding conflict of interest.
10. The IRB must determine that the PI and all other investigators of the proposed research activity have met all current educational requirements for the protection of human research subjects as mandated by the facility's Assurance, VA Office of Research and Development, funding institutions, and applicable OHRP requirements. The IRB must also determine that the investigator(s) is qualified through education, training, and experience to conduct the research.

For the IRB to approve human subjects research conducted or supported by the Department of Defense (DOD), the IRB must determine that the following criteria are met:

1. Investigator and research staff are aware of the specific requirements of research under the addendum of the Department of Defense and have been educated on these requirements.
2. The research does not involve prisoners of war as subjects. This includes any person captured, detained, held, or otherwise under the control of personnel of the Department of Defense (military and civilian, or contractor employee). Such persons include: Enemy Prisoners, Civilian Internees, Retained Persons, and Lawful and Unlawful Enemy Consultants. Such persons do not include personnel of the Department of Defense being held for law enforcement purposes.
3. Military personnel will not be provided payment for research conducted during duty hours.
4. If research involves interventions or interactions with subjects, the research does not involve a waiver of consent or parental permission unless a waiver is obtained from the Secretary of Defense.
5. If the research involves cognitively impaired adults, there is anticipated direct

benefit to the subject.

6. For research involving more than minimal risk to subject confirm the following: 1) an independent medical monitor has been appointed by name, 2) the medical monitor is a physician, dentist, psychologist, nurse or other healthcare provider capable of overseeing the progress of the research protocol, especially issues of individual subject/patient management and safety 3) the medical monitor is independent of the investigative team 4) the medical monitor possessed sufficient education and professional experience to serve as the subject advocate 5) the medical monitor has the authority to stop a research study in progress, remove individual subjects from a study, and take whatever steps are necessary to protect the safety and well-being of research subjects until the IRB can assess the medical monitor's report.
7. For research involving more than minimal risk and involving military personnel 1) unit officers and non-commissioned officers will not influence the decisions of their subordinates to participate or not to participate as research subjects 2) unit officers and senior non-commissioned officers in the chain of command will not be present at the time of research subject solicitation and consent during any research recruitment sessions in which members of units under their command are afforded the opportunity to participate as research subjects 3) when applicable, officers and non-commissioned so excluded will be afforded the opportunity to participate as research subjects in a separate recruitment session and 4) during recruitment briefings to a unit where a percentage of the unit is being recruited to participate as a group, an ombudsman not connected in any way with the proposed research of the unit will be present to monitor that the voluntary nature of individual subjects is adequately stressed and the information provided about the research is adequate and accurate.
8. The disclosure regarding provisions for research-related injury follows the requirements of the Department of Defense component.
9. When conducting multi-site research, a formal agreement is required to specify the roles and responsibilities of each party including a Statement of Work (SOW) and specific assignment of responsibilities.
10. If the research involves Human Subjects who are not U.S. Citizens or personnel of the DOD, and is conducted outside the United States, and its territories and possessions: the permission of the host country has been obtained, the laws, customs, and practices of the host country and the United States will be followed, and an ethics review by the host country, or local Naval IRB with host country representation, will take place.

### **3.8.1 Risk/Benefit Assessment**

The IRB or EC has and follows written policies and procedures for identifying and analyzing risks and identifying measures to minimize such risks. The analysis of risk includes a determination that the risks to participants are reasonable in relation to the potential benefits

to participants and to society. (AAHRPP Element II.3.A.)

The goal of the assessment is to ensure that the risks to research subjects posed by participation in the research are justified by the anticipated benefits to the subjects or society. The IRB must:

- Judge whether the anticipated benefit, either of new knowledge or of improved health for the research subjects, justifies asking any person to undertake the risks;
- Disapprove research in which the risks are judged unreasonable in relation to the anticipated benefits.

The assessment of the risks and benefits of proposed research - one of the major responsibilities of the IRB - involves a series of steps:

1. Identify the risks associated with the research, as distinguished from the risks of therapies the subjects would receive even if not participating in research
2. Determine whether the risks will be minimized to the extent possible; This can be done, for example by using procedures which are consistent with sound Research design and which do not unnecessarily expose subjects to risk. This also can be accomplished, as appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes
3. Identify the probable benefits to be derived from the research
4. Determine whether the risks are reasonable in relation to the benefits to subjects, if any, and assess the importance of the knowledge to be gained; In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the Research, as distinguished from risks and benefits of therapies subjects would receive even if not participating in the Research. The IRB should not consider possible long-range effects of applying knowledge gained in the Research (e.g., the possible effects of the Research on public policy) as among those Research risks that fall within the purview of its responsibility
5. Ensure that potential subjects will be provided with an accurate and fair description of the risks or discomforts and the anticipated benefits

Based on this assessment, risk associated with the research will be classified as either Minimal Risk or Greater than Minimal Risk.

### **3.8.1.1 Scientific Merit**

LSUHSC-S has and follows written policies and procedures for reviewing the scientific or scholarly validity of a proposed research study. Such procedures are coordinated with the ethics review process. (AAHRPP Element I.1.F.)

To assess the risks and benefits of the proposed research, the IRB examines the research plan, including research design and methodology, to determine that there are no inherent flaws that would place research participants at unnecessary risk.

- The research uses procedures consistent with sound research design including an adequate data monitoring plan, or protecting confidentiality by using coded data.
- The research is not lacking in statistical power such that meaningful results cannot be obtained.
- The research design is sound enough to reasonably expect the research to answer its proposed question; and
- The knowledge expected to result from this research is sufficiently important to justify the risk.
- The review of scientific validity must determine the available nonclinical and clinical information on an investigational product is adequate to support the proposed trial.

In making this determination, the IRB may draw on its own knowledge and disciplinary expertise, or the IRB may draw on the knowledge and disciplinary expertise of others, such as reviews by a funding agency, or Department Chair/Section review.

When following Department of Defense (DOD) regulations, substantive amendments to approved research submitted to the IRB, must undergo scientific review prior to IRB review or be conducted by the IRB.

Scientific review by the Department Chair is documented by the signature of the Department Chair responsible for the investigator's research on new protocol applications. When a Department Chair is the PI for a research proposal the Departmental review is forwarded to the Department Chair's superior for review and approval.

### 3.8.2 Selection of subjects is equitable

The IRB or EC has and follows written policies and procedures to evaluate the equitable selection of participants. (AAHRPP Element II.3.C.)
The IRB or EC has and follows written policies and procedures to review proposed participant recruitment methods, advertising materials, and payment arrangements and determines whether such arrangements are fair, accurate, and appropriate. (AAHRPP Element II.3.C.1.
Researchers and Research Staff recruit participants in a fair and equitable manner. (AAHRPP Element III.1.E.)

By viewing the IRB proposal, the IRB will determine that the selection of subjects is equitable with respect to gender, age, class, etc. The IRB will not approve a study that does not provide adequately for the equitable selection of subjects or has not provided an appropriate scientific and ethical justification for excluding classes of persons who might benefit from the research. In making this determination, the IRB evaluates: the purposes of the research; the setting in which the research occurs; scientific and ethical justification for including vulnerable populations such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons; the scientific and ethical justification for

excluding classes of persons who might benefit from the research; and the inclusion/exclusion criteria.

At the time of the continuing review the IRB will determine that the PI has followed the subject selection criteria that he/she/originally set forth at the time of the initial IRB review and approval.

### **3.8.2.1 Recruitment of Subjects**

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The investigator will provide the IRB with all recruiting materials to be used in identifying participants including recruitment methods, advertisements, and payment arrangements. See Section 3.9.7 for a discussion of IRB review of advertisements, Section 3.9.8 for a discussion of IRB review of payments or reimbursements.

An Investigator may contact potential research subjects for recruitment purposes using the following methods:

- The potential research subject may initiate the contact by responding to an IRB-approved advertisement or similar recruitment notice.
- A treating physician who is also an investigator may talk directly to the patient about recruitment into a research trial.
- If the treating physician is not the investigator, the treating physician must get an authorization to refer the patient to the investigator. The investigator may then rely on the authorization to contact the individual. The investigator will then obtain an additional authorization from the patient to participate in the research.
- An investigator may contact potential research subjects if granted a partial waiver of authorization for recruitment purposes from the IRB/Privacy Board. Investigators outside the covered entity may use this option. The Privacy Rule requirements and conditions for a waiver apply.

An investigator who is not a part of the covered entity may not use the preparatory research provision to contact prospective research subjects. However, the preparatory research provision of the HIPAA Privacy Rule at 45 CFR 164.512(i)(1)(ii) allows an investigator who is not a part of the covered entity to obtain contact information through a Partial Waiver of Authorization. Use Template – Application for Partial Waiver of Authorization – (HRP-502.3).

The Partial Waiver must be approved the IRB or Privacy Board as permitted at 45 CFR 164.512(i)(1)(i). The IRB or Privacy Board waiver of authorization permits the partial waiver of authorization for the purposes of allowing an investigator to obtain protected health information (PHI) as necessary to recruit potential research subjects. For example, even if an IRB does not waive informed consent and individual authorization for the study itself, it may waive such authorization to permit the disclosure of protected health information as necessary for the investigator to be able to contact and recruit individuals into the study. The

investigator must submit the research protocol and include the recruitment plan for IRB review and approval to obtain approval of the Partial Waiver of Authorization.

### 3.8.3 Informed Consent

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The IRB or EC has and follows written policies and procedures to evaluate the consent process and to require that the Researcher appropriately document the consent process. (AAHRPP Element II.3.F.)
See Section 5 for more information on Informed Consent.

Unless waived by the IRB, legally effective informed consent must be obtained from participants or their LARs as a condition for protocol approval. All relevant requirements in OHRP in 45 CFR 46.111 and 46.116, and in the FDA regulations in 21 CFR 50.20, 50.25, 50.27 and 56.111 that are applicable to the consent process and the consent document must be satisfied. The IRB may require revisions to the consent document prior to protocol approval.

To approve research, the IRB must determine that informed consent will be appropriately documented, unless the IRB waives documentation under OHRP or FDA regulations. If a participant lacks the capacity to consent, then consent for research must be obtained from their LAR.

Consent is documented through use of a written consent document signed and dated by the participant or their legally authorized representative that embodies all of the required eight basic required elements and the six additional elements specified in 45 CFR 46.116 and 21 CFR 50.25.

Only the IRB approved informed consent document may be used, and unless the requirement is waived by the IRB the document must be signed by the participant (or the participant's LAR), and a copy must be given to the person signing the form. FDA regulations and institutional policy requires that the signature be dated.

A copy of the informed consent must be placed on the LSUHSC-S patient medical record along with the HIPAA authorization form. The original document remains with the investigator.

The evaluation of compliance is achieved by:

1. IRB review of the informed consent process information and document(s) provided by the investigator.
2. Periodic consent form audits comparing signed and dated consent forms with the IRB approved versions.
3. Observation of the consent process, performed either as a periodic audit function of the HRPP, or as requested by the convened IRB.

### 3.8.4 Data and Safety Monitoring

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The IRB or EC has and follows written policies and procedures for reviewing the plan for data and safety monitoring, when applicable, and determines that the data and safety monitoring plan provides adequate protection for participants. (AAHRPP Element II.3.B.)

All interventional studies involving more than Minimal Risk must include a Data and Safety Monitoring Plan. A DSMP is established to assure that each research study has a system for appropriate oversight and monitoring of the conduct of the study to ensure the safety of participants and the validity and integrity of the data. The DSMP should specify whether there will be an independent Data and Safety Monitoring Board (DSMB).

The primary purpose of an independent DSMB is to protect the research subjects through independent analysis of emerging data from the trial. This differs from adverse event reporting in that the DSMB can review aggregate and un-blinded data as the data accumulate, identify significant issues and trends during the study, and recommend changes in the study including recommending early termination of the study. The DSMB reviews data for both safety and efficacy. The protections afforded by this review apply to both current subjects and future subjects if the DSMB identifies the need to modify or even halt the trial.

In addition to the above, an independent DSMB protects the credibility of the trial by virtue of its independence from the study sponsors, and helps to ensure the validity of study results by reviewing data on subject accrual and conducting interim reviews.

Independent DSMBs are Required in the Following Situations:

- All Phase III studies require a DSMB, except for most minimal risk studies.
- The involvement of a DSMB may still be requested for minimal risk studies if the studies are exceptionally large, long term, and/or involve particularly vulnerable study participants.
- Phase II clinical trials which are multicenter and randomized require a DSMB, except for most minimal risk studies.
- Phase II studies which are high risk require a DSMB.
- High-risk refers to trials or interventions associated with substantial side effects to subjects (e.g., side effects that could result in serious morbidity or death, or are irreversible), trials of diseases associated with high mortality or morbidity, and trials of highly experimental therapies (e.g., gene therapy).
- In general, DSMBs are required for clinical trials of diseases with high mortality or morbidity, for clinical trials involving high risks, and for large, multicenter clinical trials.
- Single-center, open-label, Phase I and II clinical trials may not need an independent DSMB providing the local investigator/sponsor maintains access to all data and can demonstrate the ability to provide sufficient oversight. (However, investigator initiated single-center open-label Phase I and II clinical trials require an adequate Data and Safety Monitoring Plan).

Information that must be included in Data Safety Monitoring Plan:

- Composition: Describe who will monitor the safety of the data and their expertise. This

may include individuals with expertise in biostatistics, bioethics clinical trials, and the disease and treatment being studied.

- Independence: When a DSMB is required, the investigator must confirm that the DSMB members are independent of the study sponsor and will not participate in the study as investigators, nor will they have conflicts of interest regarding the study, the study sponsor, or any study drugs or devices being tested.
- Data: A description of the data that will be reviewed, e.g., data for primary or secondary endpoints (safety and efficacy), data for early termination of trial (stopping rules), adverse events or unanticipated problems.
- Frequency of Review: Description of how often the data will be reviewed, whether based on the calendar or accrual targets. If formal interim analyses are planned, description of when they will occur. If a DSMB is required, how often will it meet?
- Authority: When a DSMB is required, a description of the actions the DSMB is authorized to take must be included. DSMBs should have authority to recommend changes in the study, including discontinuation, if significant trends in safety or efficacy are identified earlier than expected.

Additional Requirements of a Data Safety Monitoring Plan:

- Data Safety Monitoring Reports are required to be submitted to the IRB, promptly.
- The IRB may require the appointment of an independent medical monitor where appropriate.

It is not the role of the IRB to perform data monitoring, but to ensure that appropriate monitoring is taking place, and to review reports from the monitoring entities.

### 3.8.5 Privacy and Confidentiality

The IRB or EC has and follows written policies and procedures to evaluate the proposed arrangements for protecting the privacy interests of research participants, when appropriate, during their involvement in the research. (AAHRPP Element II.3.D)

The IRB or EC has and follows written policies and procedures to evaluate proposed arrangements for maintaining the confidentiality of identifiable data, when appropriate, preliminary to the research, during the research, and after the conclusion of the research. (AAHRPP Element II.3.E)

The IRB will determine whether adequate procedures are in place to protect the privacy of subjects and to maintain the confidentiality of the data.

#### Definitions

Confidentiality - methods used to ensure that information obtained by researchers about their subjects is not improperly divulged.

Identifiable information - information where the identity of the subject is or may readily be

ascertained by the investigator or associated with the information.

Individually Identifiable Private Information - is information where, for Research purposes, the information or specimens can be linked to specific individuals by the investigator(s) either directly or indirectly through coding systems 45 CFR 46,102(f).

Obtain (or Obtaining) - means to receive or access Individually Identifiable Private Information (or identifiable specimens) for Research purposes. This includes an Investigator's use, study, or analysis for Research purposes of Individually Identifiable Private Information (or identifiable specimens) already in the possession of the Investigator.

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

Private information - 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).

#### Privacy

The IRB must determine whether the activities in the research constitute an invasion of privacy. To make that determination, the IRB must obtain information regarding how the investigators are getting access to subjects or subjects' private, identifiable information and the subjects' expectations of privacy in the situation. Investigators must have appropriate authorization to access the subjects' information.

In developing strategies for the protection of subjects' privacy, consideration should be given to:

1. Methods used to identify and contact potential participants
2. Settings in which an individual will be interacting with an investigator
3. Appropriateness of all personnel present for research activities
4. Methods used to obtain information about participants and the nature of the requested information
5. Information that is obtained about individuals other than the target participants, and whether such individuals meet the regulatory definition of human participant (e.g., a subject provides information about a family member for a survey)
6. How to access the minimum amount of information necessary to complete the study.

#### Confidentiality

Confidentiality and anonymity are not the same. If anyone, including the investigator, can readily ascertain the identity of the subjects from the data, then the research is not anonymous and the IRB must determine if appropriate protections are in place to minimize the likelihood that the information will be inappropriately divulged. The level of confidentiality protections should be commensurate with the potential of harm from inappropriate

disclosure. At the time of initial review, the IRB ensures that the privacy and confidentiality of research subjects is protected. The IRB assesses whether there are adequate provisions to protect subject privacy and maintain confidentiality. The IRB does this through the evaluation of the methods used to obtain information:

- a. About subjects
- b. About individuals who may be recruited to participate in studies
- c. The use of personally identifiable records and
- d. The methods to protect the confidentiality of research data

The PI will provide the information regarding the privacy and confidentiality of research subjects at the time of initial review through the completion of the IRB proposal, HIPAA Form, and/or other submitted, applicable materials. The IRB will review all information received from the PI and determine whether the privacy and confidentiality of research subjects is sufficiently protected. In some cases, the IRB may also require that a Certificate of Confidentiality be obtained to additionally protect research data (See Section 17.1).

In reviewing confidentiality protections, the IRB shall consider the nature, probability, and magnitude of harm that would be likely to result from a disclosure of collected information outside the research. It shall evaluate the effectiveness of proposed de-identification techniques, coding systems, encryption methods, storage facilities, access limitations, and other relevant factors in determining the adequacy of confidentiality protections.

### 3.8.6 Vulnerable Populations

The IRB or EC provides additional protections for individuals who are vulnerable to coercion or undue influence and participate in research. AAHRPP Standard II-4:
The IRB or EC has and follows written policies and procedures for determining the risks to prospective participants who are vulnerable to coercion or undue influence and ensuring that additional protections are provided as required by applicable laws, regulations, codes, and guidance. (AAHRPP Element II.4.A.)

At the time of initial review the IRB will consider the scientific and ethical reasons for including vulnerable subjects in research. To approve research involving vulnerable populations, the IRB must determine, where appropriate, that additional safeguards have been included to protect the rights and welfare of participants who are likely to be vulnerable to coercion or undue influence, such as:

- Children (45 CFR 46 Subpart D; 21 CFR 50 Subpart D)
- Prisoners (45 CFR 46 Subpart C)
- Pregnant women, human fetuses, or neonates (45 CFR 46 Subpart B)
- Persons with mental disabilities, cognitively impaired, economically or educationally disadvantaged persons

Additional requirements might apply, depending on the source of support/funding (e.g., Department of Defense or other Federal Agencies).

The IRB includes among its members persons who are knowledgeable about and experienced in working with vulnerable participants. 45 CFR 46.107(a); 21 CFR 56.107(a). When a research study involves a vulnerable population not otherwise covered by these policies, the IRB takes steps to evaluate whether additional safeguards have been included in the research to protect the rights and welfare of participants. For an extensive discussion about the IRB(s) review and approval process for individual populations of vulnerable subjects, please refer to Section 6.

### **3.9 Additional Considerations During IRB Review and Approval of Research**

#### **3.9.1 Determination of Risk**

At the time of initial and continuing review, the IRB will make a determination regarding the risks associated with the research proposals. Risks associated with the research will be classified as either minimal or greater than minimal based on the absolute interpretation of minimal risk. The meeting minutes will reflect the Committee's determination regarding risk levels.

#### **3.9.2 Period of Approval**

At the time of initial review and at continuing review, the IRB will make a determination regarding the frequency of review of the research protocols. All protocols will be reviewed by the IRB at intervals appropriate to the degree of risk. In some circumstances, a shorter review interval (e.g. biannually, quarterly, or after accrual of a specific number of participants) may be required (see below). Exempt research is given a three (3) year approval period. The approval period for non-exempt research will be determined using the Worksheet: Approval Period (Intervals) (HRP-302). The meeting minutes will reflect the IRB determination regarding review frequency.

##### **3.9.2.1 Review More Often Than Annually**

Any research that meets any of the following criteria will be evaluated by the IRB to determine if it requires review more often than annually:

1. Significant risk to research subjects (e.g., death, permanent or long lasting disability or morbidity, severe toxicity) without the possibility of direct benefit to the subjects
2. The involvement of especially vulnerable populations likely to be subject to coercion (e.g., terminally ill)
3. A history of serious or continuing non-compliance on the part of the PI

The following factors will also be considered when determining which studies require review more frequently than on an annual basis:

1. The probability and magnitude of anticipated risks to subjects
2. The likely medical condition of the proposed subjects

3. The overall qualifications of the PI and other members of the research team
4. The specific experience of the PI and other members of the research team in conducting similar research
5. The nature and frequency of adverse events observed in similar research at this and other institutions
6. The novelty of the research making unanticipated adverse events more likely
7. Any other factors that the IRB deems relevant

In specifying an approval period of less than one year, the IRB may define the period with either a time interval or a maximum number of subjects either studied or enrolled. If a maximum number of subjects studied or enrolled is used to define the approval period, it is understood that the approval period in no case can exceed 1 year (12 months) and that the number of subjects studied or enrolled determines the approval period only when that number of subjects is studied or enrolled in less than 1 year.

If an approval period of less than one year is specified by the IRB the reason for more frequent review must be documented.

### **3.9.3 Independent Verification That No Material Changes Have Occurred**

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The IRB recognizes that protecting the rights and welfare of subjects sometimes requires that the IRB verify independently, utilizing sources other than the investigator that no material changes occurred during the IRB-designated approval period. Independent verification from sources other than the investigator may be necessary at times, for example, in cooperative studies, or other multi-center research.

The IRB will determine the need for verification from outside sources on a case-by-case basis and according to the following criteria:

1. Protocols where concern about possible material changes occurring without IRB approval have been raised based on information provided in continuing review reports or from other sources
2. Protocols conducted by Principal Investigators who have previously failed to comply with federal regulations and/or the requirements or determinations of the IRB
3. Protocols randomly selected for internal audit
4. Whenever else the IRB deems verification from outside sources is relevant

The following factors will also be considered when determining which studies require independent verification:

1. The probability and magnitude of anticipated risks to subjects
2. The likely medical condition of the proposed subjects
3. The probable nature and frequency of changes that may ordinarily be expected in the type of research proposed

In making determinations about independent verification, the IRB may prospectively require that such verification take place at predetermined intervals during the approval period, or may

retrospectively require such verification at the time of continuing review, review of amendments and/or adverse events.

If any material changes have occurred without IRB review and approval, the IRB will decide the corrective action to be taken.

#### **3.9.4 Consent Monitoring**

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In reviewing the adequacy of informed consent procedures for proposed research, the IRB may on occasion determine that special monitoring of the consent process by an impartial observer (consent monitor) is required to reduce the possibility of coercion and undue influence. Such monitoring may be particularly warranted where the research presents significant risks to subjects, or if subjects are likely to have difficulty understanding the information to be provided. Monitoring may also be appropriate as a corrective action where the IRB has identified problems associated with an investigator or a research project. See Section 5.7 for a detailed discussion of consent monitoring.

#### **3.9.5 Investigator Conflicts of Interest**

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LSUHSC-S has and follows written policies and procedures to identify, manage, and minimize or eliminate individual financial conflicts of interest of Researchers and Research Staff that could influence the conduct of the research or the integrity of the Human Research Protection Program. LSUHSC-S works with the IRB or EC in ensuring that financial conflicts of interest are managed and minimized or eliminated, when appropriate. (AAHRPP Element I.6.B.)

The research proposal asks protocol-specific questions regarding conflict of interest for the investigators and key personnel. As part of its review process, the IRB will decide whether a conflict of interest exists with regard to the research under review. If a conflict of interest exists, final IRB approval of a protocol cannot be given until an approved conflict management plan that adequately protects the human subjects in the protocol is in place. (See Section 14 for a detailed discussion of Conflict of Interest)

#### **3.9.6 Significant New Findings**

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During the course of research, significant new knowledge or findings about the medication or test article and/or the condition under study may develop. The PI must report any significant new findings to the IRB and the IRB will review them with regard to the impact on the subjects' rights and welfare. Since the new knowledge or findings may affect the risks or benefits to subjects or subjects' willingness to continue in the research, the IRB may require, during the ongoing review process, that the PI contact the currently enrolled subjects to inform them of the new information. The IRB will communicate this to the PI. The informed consent should be

updated and the IRB may require that the currently enrolled subjects be re-consented, acknowledging receipt of this new information and for affirming their continued participation.

### 3.9.7 Advertisements

The IRB or EC has and follows written policies and procedures to review proposed participant recruitment methods, advertising materials, and payment arrangements and determines whether such arrangements are fair, accurate, and appropriate. (AAHRPP Element II.3.C.1.)

The FDA considers direct advertising for study subjects to be the start of the informed consent and subject selection process. Accordingly, they need to be included as part of the IRB initial application and will require IRB approval before use: Worksheet: Advertisements (HRP-502.3). Any subsequent changes to IRB approved recruitment materials must be submitted for IRB review and approval prior to use.

Direct advertising for research subjects includes, but is not limited to: newspaper, radio, TV, bulletin boards, posters, and flyers that are intended to be seen by prospective subjects and to solicit their participation in a study. Communications that are to be seen or heard by health professionals, such as dear doctor letters and doctor-to-doctor letters are not included in this group. The listing of clinical trials on the internet does not require IRB approval when the format of the website limits the information provided to basic trial information, such as: title; purpose of the study protocol summary; basic eligibility criteria; study site location(s); and contact information.

The IRB must approve any and all recruitment materials/advertisements prior to posting and/or distribution for studies that are conducted under the purview of the LSUHSC-S IRB. The IRB will review:

1. The information contained in the advertisement.
2. The mode of its communication.
3. The final copy of printed advertisements prior to posting.
4. The final audio/video taped advertisements.

The IRB reviews the material to assure that the material is accurate and is not coercive or unduly optimistic, creating undue influence to the subject to participate which includes, but is not limited to:

1. Statements implying a certainty of favorable outcome or other benefits beyond what was outlined in the consent document and the protocol.
2. Claims, either explicitly or implicitly, that the drug, biologic or device was safe or effective for the purposes under investigation
3. Claims, either explicitly or implicitly, that the test article was known to be equivalent or superior to any other drug, biologic or device
4. Using terms such as new treatment, new medication, or new drug without explaining that the test article is investigational

5. Promising free medical treatment when the intent was only to say participants will not be charged for taking part in the investigation
6. Emphasis on payment or the amount to be paid, such as bold type or larger font on printed media
7. The inclusion of exculpatory language.
8. Advertisements will not include compensation for participation in a trial offered by a sponsor to involve a coupon good for a discount on the purchase price of the product once it has been approved for marketing.

Any advertisement to recruit subjects should be limited to the information the prospective subjects need to determine their eligibility and interest. When appropriately worded, the following items may be included:

1. The name and address of the clinical investigator and/or research facility.
2. The condition being studied and/or the purpose of the research.
3. In summary form, the criteria that will be used to determine eligibility for the study.
4. The time or other commitment required of the subjects.
5. The location of the research and the person or office to contact for further information.
6. A clear statement that this is research and not treatment.
7. A brief list of potential benefits (e.g. no cost of health exam).

All advertisements are required to include the following information: IRB Project number, the date of original IRB approval of protocol, and the date of IRB approval of the advertisement. Once approved by the IRB, an Advertisement is not to be altered or manipulated in any way without prior IRB approval.

### **3.9.8 Payment to Research Subjects**

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Payment to research subjects may be an incentive for participation or a way to reimburse a subject for time, travel, parking, and other experiences incurred due to participation. However, payment for participation is not considered a research benefit. Rather, it should be considered compensation for time, travel and inconvenience. Regardless of the form of remuneration, investigators must take care to avoid coercion of subjects. Payments should reflect the degree of risk, inconvenience, or discomfort associated with participation. The amount of compensation must be proportional to the risks and inconveniences posed by participation in the study. See Worksheet: Subject Payments (HRP-316).

Investigators who wish to pay research subjects must indicate in their research project application the justification for such payment. Such justification should:

1. Substantiate that proposed payments are reasonable and commensurate with the expected contributions of the subject
2. State the terms of the subject participation agreement and the amount of payment in the informed consent document

3. Substantiate that subject payments are fair and appropriate, and that they do not constitute (or appear to constitute) undue pressure on the patient to volunteer for the research study

The IRB must review both the amount of payment and the proposed method of disbursement to assure that neither entails problems of coercion or undue influence.

Credit for payment should accrue and not be contingent upon the participant completing the entire study. The IRB does not allow the entire payment to be contingent upon completion of the entire study. Any amount paid as bonus for completion of the entire study should not be so great that it becomes coercive.

The consent form must describe the terms of payment and the conditions under which subjects would receive partial payment or no payment (e.g., if they withdraw from the study before their participation is completed).

Unless the study is confidential, the LSUHSC-S Office of Business and Finance requires identifying information to issue checks to subjects. The consent form must inform subjects that they will be asked to provide their Social Security Number to receive payment. For confidential studies, only names and addresses are required by Business and Finance, but the PI MUST keep an identity key in a secure place.

Investigators must submit a completed "Request to Pay Participants in a Research Protocol" form (Form: LSUHSC-S 1144) to the Office of Business and Finance along with a check requisition form S/N 1238N, for reimbursement.

For VA Research

1. VA policy prohibits paying human subjects to participate in research when the research is integrated with a patient's medical care and when it makes no special demands on the patient beyond those of usual medical care.

Payment may be permitted, with IRB approval, in the following circumstances:

- a) No Direct Subject Benefit. When the study to be performed is not directly intended to enhance the diagnosis or treatment of the medical condition for which the volunteer subject is being treated, and when the standard of practice in affiliated non-VA institutions is to pay subjects in this situation.
- b) Others Being Paid. In multi-institutional studies, when human subjects at a collaborating non-VA institution are to be paid for the same participation in the same study, subjects may be paid at a rate comparable to that proposed at the other sites, if deemed reasonable by the IRB.
- c) Comparable Situations. In other comparable situations in which, in the opinion of the IRB, payments of subjects is appropriate.
- d) Transportation Expenses. When transportation expenses are incurred by the

subject that would not be incurred in the normal course of receiving treatment and which are not reimbursed by any other mechanism.

2. The IRB and R & D Committee must review all proposals for payment of subjects to ensure conformity with VA policies. The facility research office is responsible for ensuring that IRB-approved payments to subjects are made from a VA approved funding source for research activities.

Prospective VA investigators who wish to pay research subjects must include in the protocol: (1) Substantiation that proposed payments are reasonable and commensurate with the expected contributions of the subject; (2) the terms of the payment and the amount of payment are in the informed consent document; and (3) substantiation that subject payments are fair and appropriate, and that they do not constitute (or appear to constitute) undue pressure or influence on the prospective research subjects to volunteer for, or to continue to participate in the research study. In addition, the payments do not constitute (or appear to constitute) coercion to participate in or continue to participate in the research study.

LSUHSC-S Employees who participate in clinical research must be aware of the following:

1. Employees must disclose to the research staff their employment status.
2. Attendance of study visits must be during off time, during annual time or on lunch. Break time may not be used.
3. Disclosure of the employees' participation in a clinical trial may be made to your Business Manager or Department Manager.
4. A "Request to Pay Participants in a Research Protocol" form must be completed and submitted with a PER 3 to Human Resources. Compensation will be provided as additional income in your LSUHSC-S payroll.

### **3.9.9 Recruitment Incentives**

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Payment arrangements among sponsors, organizations, investigators, and those referring research participants may place participants at risk of coercion or undue influence or cause inequitable selection. Payment in exchange for referrals of prospective participants from researchers or physicians (finder's fees) is not permitted and may be considered illegal under Federal or State law. Similarly, payments designed to accelerate recruitment that is tied to the rate or timing of enrollment (bonus payments) are also not permitted. Other types of compensation to health care providers, investigators or designees (books, non-cash gifts) are also prohibited.

### **3.9.10 Compliance with all Applicable State and Local Laws**

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LSUHSC-S has and follows written policies and procedures that identify applicable laws in the localities where it conducts human research, takes them into account in the review and
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conduct of research, and resolves differences between federal or national law and local laws. (AAHRPP Element I.1.G.)

The IRB follows and must adhere to all applicable state and local laws in the jurisdictions where the research is taking place. The HRPP and the LSUHSC-S IRB rely on the Counsel for the HRPP for the interpretation and application of Louisiana State law and the laws of any other jurisdiction where research is conducted as they apply to human subject research. All consent forms must be consistent with applicable state and local laws.

### 3.10 Possible IRB Determinations

The IRB or reviewer(s) may arrive at the following decisions:

- Approval (Approved)
- Modifications Required to Secure Approval
- Deferred
- Disapproved
- Approval in Principle
- Suspension or Termination

Approval - the study is approved as submitted. The research may begin once the investigator has received IRB notification of the determination and the approved consent documents. The beginning of the Approval Period is the date of the IRB meeting where the protocol was approved.

Modifications to Secure Approval - (Conditional Approval) The research requires as a condition of final approval that the investigator (a) makes specified minor changes to the research protocol or informed consent document(s), (b) confirm specific assumptions or understandings on the part of the IRB regarding how the research will be conducted, or (c) submit additional documents, such that, based on the assumption that the conditions are satisfied, the IRB is able to make all of the determinations required for approval under the DHHS regulations at 45 CFR 46.111 and, if applicable, subparts B, C, or D of 45 CFR part 46.

The needed revisions or documents are agreed upon at the IRB meeting. None of the required modifications can be related to the determinations required for approval by the DHHS regulations at 45 CFR 46.111 and, if applicable, subparts B, C, or D of 45 CFR part 46. The requested revisions are presented to the PI for incorporation by simple concurrence. Revisions must be made exactly as designated by the IRB. The requested revisions should be sent to the IRB within 30 days of receiving the IRB notice.

Expedited procedures may be used for final approval of a protocol Modifications Required to Secure Approval at a convened meeting. The investigator's response, the revised proposal and

the previously submitted proposal is given to the IRB Chair, Vice Chair, or a designee of the IRB for review. The reviewer(s) may approve the study revisions without further review by the convened IRB.

The outcome of the IRB(s) deliberations and reviewer(s) findings are communicated to the investigator in writing. The investigator may not proceed with the research until an IRB notice of determination for approval of the research has been received.

The IRB(s) determination concerning the requested revision will be documented in the minutes of the next IRB meeting.

Failure to submit a response to IRB stipulated changes or inquiries related to new research protocols "Modifications Required to Secure Approval" within thirty (30) days will result in the study being inactivated by the IRB. The investigator will receive written notification of the inactivation. The research protocol will be placed in an inactive status file and no further processing will take place. Investigators wishing to reactivate their file must update all the research documents, make the stipulated changes and re-apply to the IRB. An extension beyond 30 days may be granted by the IRB if sufficient cause is provided by the investigator in writing.

The beginning of the Approval Period is the date the IRB chairperson or designee has verified and approved the required changes to the protocol or informed consent documents or any other responsive materials from the investigator.

For VA Research - For studies conducted at the VA, the research may not begin until the IRB Chair or designee has approved the changes and the VA Research and Development Committee has approved the study. This means obtaining written approvals(s) before initiating research. Before initiating the research study at the VA, IRB approval must be obtained in writing from the Chair or other voting member of the IRB, and all other committees (e.g., RDC), subcommittees, and other approvals according to applicable local, VA, and other Federal requirements. Research cannot be initiated at the VA until the VA investigator has obtained written notification that the research can be initiated from the VA ACOS/R&D.

Deferred - The IRB cannot make one or more of the determinations required for approval by the HHS regulations at 45 CFR 46.111 and, if applicable, subparts B, C, or D of 45 CFR part 46. This action is taken if substantial modification or clarification is required, or insufficient information is provided to judge the protocol application adequately. The IRB (a) is unable to make the required determinations about research risks and benefits, the adequacy of privacy and confidentiality protections, or the adequacy of the informed consent process because the research protocol provides insufficient information related to these aspects of the research, and (b) is unable to specify changes to the research protocol or consent document that if made would allow the IRB to make these required determinations.

The research may not proceed until the IRB reviews the revised research protocol and approves it at a subsequent convened meeting. When a research protocol is Deferred, the IRB under its authority to require modifications for an investigator to secure approval, may require that the investigator (a) make changes to the protocol or informed consent documents, or (b) submit clarifications or additional documents prior to the next review. To receive approval for a research protocol that has been Deferred, the investigator's response, revised research protocol and all requested documents must be submitted for review at a subsequent, convened meeting of the same IRB committee. The HRPP Staff will process the investigator's response, the revised proposal along with the previously submitted proposal. The item will be placed on the agenda for re-review at the next convened meeting.

IRB approval of the proposal will not be granted and a written approval notice will not be issued until all requested changes have been satisfied in the manner set forth by the IRB.

The IRB determination concerning any research that required modifications for an investigator to secure approval, will be documented in the minutes of the IRB meeting or in the file for expedited review.

Failure to submit a response to IRB stipulated changes or inquires related to new research protocols "deferred " within sixty 60 days will result in the study being inactivated by the IRB. The investigator will receive written notification of the inactivation. The research protocol will be placed in an inactive status file and no further processing will take place. Investigators wishing to reactivate their file must update all the research documents, including all stipulated changes and re-apply to the IRB. An extension beyond 60 days may be granted by the IRB if sufficient cause is provided by the investigator in writing.

Disapproved - The IRB action of Disapproved means that the research protocol cannot be approved as written. The IRB has determined that the research cannot:

- Be conducted on LSUHSC-S premises, or other facilities
- Involve LSUHSC-S patients or participants
- Be conducted by employees or agents of LSUHSC-S
- Otherwise be conducted under the auspices of LSUHSC-S or the LSUHSC-S IRB
- The PI will be provided an explanation for the cause of any disapproval.

Written notification of Disapproval will be issued to the investigator.

Approval in Principle - As per federal regulations, (45CFR46.118), there are two circumstances in which the IRB may grant approval required by a sponsoring agency without having reviewed all the study procedures and consent documents. One is if study procedures are to be developed during the course of the research, but human subject approval is required by the sponsoring agency. The other is if the involvement of human subjects depends on the outcomes of work with animal subjects. The IRB may then grant approval without having reviewed the yet undeveloped recruitment, consent, and intervention materials. However, if the proposal is funded, the PI must submit such materials for approval at least 60 days before

recruiting human subjects into the study, or into any pilot studies or pre-tests. Approval in principle is granted to satisfy sponsoring agency requirements or to allow investigators to have access to funding to begin aspects of the project that do not involve human subjects.

### **3.11 Study Suspension, Termination and (Administrative) Investigator Hold**

#### **3.11.1 Suspension or Termination**

The IRB or EC has and follows written policies and procedures for suspending or terminating IRB or EC approval of research, if warranted, and for reporting these actions, when appropriate.(AAHRPP Element II.2.G)

The IRB may vote to suspend or terminate approval of research not being conducted in accordance with IRB or regulatory requirements or that has been associated with unexpected problems or serious harm to subjects. (See Section 8 for a discussion of unexpected problems and Section 10 for a discussion of non-compliance)

Suspension - of IRB approval is a directive of the convened IRB or IRB Chair or IO or designee either to temporarily stop some or all previously approved research activities to ensure protection of the rights and welfare of study participants or for non-compliance. Suspension directives made by the Chair or IO or designee must be reported to the next convened IRB. Suspended protocols remain open and require continuing review.

Termination - of IRB approval is a directive of the convened IRB to stop permanently some or all activities in previously approved research. If all research activities are terminated, the research no longer require continue review. If the IRB terminates a portion of the protocol (ex: terminate one arm of a clinical trial), the remaining research requires continued review.

The IRB shall notify the PI in writing of such suspensions or terminations and shall include a statement of the reasons for the IRB(s) actions. The investigator shall be provided with an opportunity to respond in person or in writing.

Research may only be terminated by the convened IRB. However, under LSUHSC-S policy the IO, IO designee, IRB Chair or AVCRM may institute a suspension of IRB Approval, when subjects' rights and welfare may be at risk of adverse effects, before action may be considered by the convened IRB. The risk of adverse effects may be due to Non-Compliance with institutional or other regulatory requirements or an Unanticipated Problem Involving Risks to Participants or Others. The individual instituting the Suspension of IRB Approval or a Termination of IRB Approval may withdraw approval for some or all research procedures.

When the study is suspended or terminated the convened IRB or authorized individual will:

1. Have any unanticipated problems reported to the IRB

2. Consider actions to protect the rights and welfare of subjects
3. Consider whether procedures for withdrawal of enrolled subjects consider their rights and welfare
4. Consider informing current subjects of the suspension or termination

Any termination or suspension of research by the IRB related to concerns about the safety, rights, or welfare of human research subjects, research staff, or others must be reported in writing within five business days after the termination or suspension occurs to the Institutional Official. The HRPP/IRB will implement the process below when instituting a Suspension or Termination of IRB approval:

- Notify the investigator of the Suspension of IRB Approval or Termination of IRB Approval along with the reasons for the decision.
- Ask the investigator for a list of Human Subjects currently involved in the research.
- Ask the investigator whether any actions are required to protect those subjects' rights and welfare or to eliminate an apparent immediate hazard.
- Consider whether any additional actions are required to protect those or other subjects rights and welfare or to eliminate an apparent immediate hazard (see section 3.11.3).
- For Veterans Administration (VA) research report the Suspension of IRB Approval or Termination of IRB Approval directly (without intermediaries) in writing to the VA Medical Center Director within five business days with simultaneous copies to the Associate Chief of Staff for Research, the Research and Development Committee, and any other relevant research review committee.
- Refer to the IRB staff to place on the agenda for the next available convened IRB meeting in an IRB with appropriate scope as an item of Suspension of IRB Approval or Termination of IRB Approval.
- Complete and send to the investigator a Template Letter: Suspension or Termination (HRP-515).

When following VA regulations, any termination or suspension of research by the IRB related to concerns about the safety, rights, or welfare of human research subjects, research staff, or others must be reported in writing within five business days after the termination or suspension occurs to the VA Medical Center Director. A copy will be sent to simultaneously to the ACOS/R&D Chair, and any other relevant research review committee. The VA Medical Center Director will report the termination or suspension to the appropriate Office of Research officer within five business days after receiving such notification.

When following Department of Defense (DoD) regulations, any suspension or termination of DoD-supported research must be promptly (no longer than within 30 days) reported to the DoD human research protection officer.

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### **3.11.2 Investigator-Hold**

An investigator or sponsor may request an Investigator-Hold on a protocol when the investigator/sponsor wishes to temporarily or permanently stop some or all approved research activities. Investigator-Holds are not suspensions or terminations, but rather a voluntary interruption of research enrollments and ongoing research activities by the research investigator or sponsor. An Investigator hold cannot be used to extend IRB approval beyond the expiration date of a protocol without approval of continuing review. It must also not be used to avoid reporting deficiencies or circumstances otherwise covered by institutional policies or other regulatory requirements governing research.

#### **3.11.2.1 Procedures**

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1. Investigators must notify the IRB in writing that:
  - a. They are voluntarily placing a study on Investigator-Hold
  - b. Provide a description of the research activities that will be stopped
  - c. Describe proposed actions to be taken to protect current participants
  - d. Actions that will be taken prior to IRB approval of proposed changes to eliminate apparent immediate harm
2. Upon receipt of written notification from the investigator the IRB staff places the research study on the agenda for review
3. The IRB Administrator, IO or Chair, in consultation with the investigators, determines whether any additional procedures need to be followed to protect the rights and welfare of current participants as described in 3.11.3 below
4. The IRB Administrator, IO or Chair, in consultation with the investigators, determines how and when currently enrolled participants will be notified of the investigator hold.
5. Investigators may request a modification of the investigator hold by submitting a request for a modification to previously approved research

#### **3.11.3 Protection of Currently Enrolled Participants**

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Before an investigator-hold, termination, or suspension is put into effect, the convened IRB, IRB Chair or IRB designee considers whether any additional procedures need to be followed to protect the rights and welfare of current participants. Such procedures might include:

- Transferring participants to another investigator
- Making arrangements for clinical care outside the research
- Allowing continuation of some research activities under the supervision of an independent monitor
- Requiring or permitting follow-up of participants for safety reasons
- Requiring adverse events or outcomes to be reported to the IRB and the sponsor
- Notification of current participants
- Notification of former participants

#### **3.12 Protocol Approval Period**

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A The IRB or Ethics Committee has and follows written policies and procedures to conduct reviews by the convened IRB or Ethics Committee. Element II.2.D.1. – Initial review. (AAHRPP Element II.2.D)

LSUHSC-S determination of the protocol approval period and the need for additional supervision and/or participation is made by the IRB on a protocol-by protocol basis. The approval period will not exceed 12 months. For example, for an investigator who is performing particularly risky research, or for an investigator who has recently had a protocol suspended by the IRB due to regulatory concerns, an on-site review by a subcommittee of the IRB might occur or approval might be subject to an audit of study performance after a few months of enrollment, or after enrollment of the first several subjects.

### **3.12.1 Approval Start Date & Expiration Date**

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The IRB will indicate a protocol approval period with an Approval Start Date and an Approval End Date. These two dates will be specified for each initial or continuing protocol approval. IRB approval will lapse at midnight on the end date of the approval period.

The approval period Start Date for an approved research protocol will be assigned as follows:

1. For research Approved as submitted at a convened IRB meeting the start date of the approval period will be the date of the convened IRB meeting;
2. For research determined to need Modifications Required to Secure Approval at a convened IRB meeting, the approval start date is the date that the IRB chairperson or designee has reviewed and accepted the required changes.
3. For research reviewed under Expedited Procedures, the approval start date is the date on which the IRB chairperson or designee has approved the research protocol and any requested changes.

The approval start date and approval end date are clearly noted on IRB correspondence sent back to the investigator for initial and continuing review submissions. Investigators should allow sufficient time for processing continuing reviews.

Review of a modification in research ordinarily does not alter the date by which continuing review must occur. However, if a modification increases the risks to participants, the approval period of the research is subject to change in accordance with the degree of risk.

The regulations make no provision for any grace period extending the conduct of research beyond the approval end date. Therefore, continuing review and re-approval of research must occur by midnight of the date when IRB approval ends.

### **3.12.2 Applying the Version Letter and Version Effective Date to the Consent Document**

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The investigator is to place a Version Letter (A, B, C, etc.) in the footer of each new version of

the consent or assent document that is submitted to the IRB for review and approval. (See Template Consent Document HRP-502).

When documentation of informed consent is required, the investigator will receive a copy of the study's consent document along with the IRB Approval Notice. The IRB staff will stamp the consent document with the Document Approval Date after the new version of the consent or assent form is approved by the IRB. This is the date the investigator may begin using the document. All unsigned informed consent documents are invalid once a new version is approved by the IRB. The investigator is to make copies of the informed consent document that bears the new Document Approval Date. No other copies of the informed consent document may be used for consenting study participants.

### **3.13 Continuing Review**

The IRB or Ethics Committee has and follows written policies and procedures to conduct reviews by the convened IRB or Ethics Committee. Element II.2.D.2. – Continuing review. (AAHRPP Element II.2.D)

The IRB will conduct a continuing review of all ongoing non-exempt research at intervals that are appropriate to the level of risk for each research protocol, but not less than once per year. Continuing review must occur if the research remains active for long-term follow-up of participants, even when the research is permanently closed to the enrollment of new participants and all participants have completed all research-related interventions. Continuing review of research must occur even when the remaining research activities are limited to the analysis of private identifiable information.

#### **3.13.1 Continuing Review Process**

Submission of a protocol for continuing review is required on all non-exempt approved protocols where research activities are ongoing, including but not limited to continuing recruitment and enrollment of participants; research tests, procedures, and other interactions and interventions; review of identifiable information; data analysis; and follow-up of previously enrolled participants.

Continuing review of a study may stop only when:

- The research is permanently closed to the enrollment of new participants
- All participants have completed all research-related interventions
- Collection and analysis of private identifiable information has completed

To assist investigators, IRB staff will generate (automatically via the electronic IRB system Shields) courtesy reminders to investigators 90 days, 60 days and 30 days in advance of the study expiration date so that they timely submit research for continuing review; however, it is the investigator's responsibility to ensure that the continuing review of ongoing research is

approved prior to the expiration date. By federal regulation, no extension to that date can be granted. At least 30 days prior to the study lapse date, IRB Staff will email or send Template Letter: Continuing Review Reminder (HRP-530) to the investigator.

Investigators must submit the following for continuing review:

- The continuing review application
- The current consent document
- Any newly proposed consent document with any proposed changes highlighted, deletions are to be lined through
- The full protocol or a protocol summary containing the relevant information necessary to determine whether the proposed research continues to fulfill the criteria for approval
- A status report on the progress of the research to include a summary since the last IRB review of:
  - Unanticipated problems involving risks to participants or others
  - Serious adverse events where there is a reasonable possibility of being related to study interventions
  - Findings based on information collected by the data and safety monitoring plan including any multicenter trial reports
  - Participant withdrawals
  - The reason for withdrawals
  - Complaints about the research
  - Amendments or modifications.
  - Any relevant recent literature
  - Any interim findings
- The investigator's current risk-potential benefit assessment based on study results.
- The gender and minority status of those entered into the protocol.
- Number of participants considered as members of specific vulnerable populations.
- An assurance that all serious or unexpected adverse events had been reported as required.
- An assurance signed by the investigator certifying that all participants entered onto the master list of participants for the study signed the consent document prior to undergoing any study procedures, unless the IRB has granted a waiver of consent or waiver of consent documentation
- HIPAA Authorization
- Delegation of Authority
- 1572s if applicable

In conducting continuing review of research not eligible for expedited review, all IRB members are provided the continuing review application, which serves as a summary of all relevant findings during the current review period and the consent documents. The Primary Reviewer will receive and review the complete protocol, application, consent documents, safety data and any modifications previously approved by the IRB. The reviewers are given access to the study's complete IRB record. At the meeting, the Primary reviewers lead the IRB through the

completion of the regulatory criteria for approval.

IRB staff attends the convened meetings and will access any additional related materials the IRB members request to facilitate the review process.

Review of currently approved or newly proposed consent documents must occur during the scheduled continuing review of research by the IRB. However, informed consent documents should be reviewed whenever new information becomes available that would require modification of information in the IRB approved informed consent document. Changes to consent documents are modifications and will be reviewed according to the procedures in section 3.14.

### **3.13.2 Expedited Review of Continuing Review**

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The IRB or Ethics Committee has and follows written policies and procedures to conduct reviews by the expedited procedure, if such procedure is used. Element II.2.E.1. – Initial review; Element II.2.E.2. – Continuing review; Element II.2.E.3. – Review of proposed modifications to previously approved research. (AAHRPP Element II.2.E)

In conducting continuing review under expedited review, the reviewer(s) receive access to the complete IRB record in Shields.

The reviewer(s) use the Criteria for Approval Worksheet to determine whether the research meets the criteria allowing continuing review using the expedited procedure, and if so, whether the research continues to meet the regulatory criteria for approval.

Generally, if research did not qualify for expedited review at the time of initial review, it does not qualify for expedited review at the time of continuing review, except in limited circumstances described by expedited review categories (8) and (9) at 63 FR 60364-60367 (see Expedited Review Categories). It is also possible that research activities that previously qualified for expedited review in accordance with 45 CFR 46.110, have changed or will change, such that expedited IRB review would no longer be permitted for continuing review.

### **3.13.3 Lapses in IRB Approval**

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A lapse in IRB approval of research occurs whenever an investigator has failed to provide continuing review information to the IRB or the IRB has not conducted continuing review and re-approved the research — with or without conditions — by the Approval End Date. The electronic IRB system will automatically send the PI the “Notice of Continuing Review Deadline has Passed” and move the study into a lapsed state.

It is the responsibility of the PI to ensure that a lapse in IRB approval does not occur. Therefore, investigators must allow sufficient time for IRB review and approval. Failure to

submit continuing review information on time is considered non-compliance and will be handled according to the non-compliance policy (See Section 10.4).

Unless the IRB finds that it is in the best interests of already enrolled subjects to continue participating in the research activities when a lapse in IRB approval occurs, the investigator must do the following:

- Stop all research activities
- Stop all Enrollment procedures including consent procedures
- Cancel all recruitment activities (media advertisements must be pulled)
- Stop all research related interventions, interactions, and data collection
- Submit to the IRB a list of research subjects for whom suspension of the research would cause harm

Continuation of research interventions or interactions for already enrolled subjects may continue when the IRB or IRB Chair in consultation with the investigator and the Senior Associate Dean for Clinical Affairs & Chief Medical Officer determines that it is in the best interest of the individual subjects to do so. The IRB Office will notify the investigator in writing of the lapse in approval and that all research activities must stop. The OBVAMC research office will also be notified if VA research is involved.

Enrollment of new subjects cannot occur and For VA Research: Continuation of research interventions or interactions in already enrolled subjects should only continue when the IRB or IRB Chair, in consultation with the VA Chief of Staff (COS) finds that it is in the best interest of individual subjects to do so.

Once the approval period has ended, IRB review and re-approval must occur prior to resuming any research related activities. If the study approval has lapsed more than 30 days and the PI has not submitted a continuing review application, the study will be closed by the IRB. (When it can be demonstrated that the investigator is actively working with the IRB to secure re-approval of a study, the IRB may choose not to permanently close the study after 30 days. However, no research activities may occur).

If the IRB requires revisions to obtain continuing review approval and no response has been received from the PI within thirty (30) days following IRB correspondence, the study will be closed unless the IRB determines that study closure will harm subjects. The PI must submit a new application to the IRB for review and approval if a study is closed by the IRB.

### **3.14 Modification of an Approved Protocol**

The IRB or Ethics Committee has and follows written policies and procedures to conduct reviews by the convened IRB or Ethics Committee. Element II.2.D.3. – Review of proposed modifications to previously approved research. (AAHRPP Element II.2.D)

Investigators may wish to modify or amend their approved applications. Investigators must seek IRB approval before making any changes in approved research unless the change is necessary to eliminate an immediate hazard to the subject.

The IRB Chair or designee will determine whether the proposed changes may be approved through an expedited review process, if the changes are minor, or whether the modification warrants full board review. The reviewer(s) using the expedited procedure has the ultimate responsibility to determine that the proposed changes may be approved through the expedited review procedure and, if not, must refer the protocol for full board review.

For VA Research: If an amendment for VA research addresses an issue related to biosafety or radiation safety, the appropriate VA committee or subcommittee must first approve the amendment prior to LSUHSC-S IRB approval of the amendment. If the LSUHSC-S IRB or IRB reviewer evaluating an amendment determines that an amendment may involve biosafety or radiation safety issues, the investigator will be required to submit the amendment to the VA biosafety or radiation committee for their review and approval (as applicable) prior to the further LSUHSC-S IRB review and approval. Please refer to the Overton Brooks Veteran Affairs Medical Center policy and procedure for instructions of submission requirements to the biosafety or radiation committee.

#### **3.14.1 Protocol Modifications**

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Investigators who wish to modify or amend their approved research (regardless of whether the research is minimal risk or greater than minimal risk) must receive IRB approval before making any changes in the research except when the changes are necessary to eliminate an immediate hazard to the subject, in which case the IRB must then be notified at once). This requirement exists even though the changes are planned for the period for which IRB approval has already been given.

Investigators must submit a Request for Modification to the IRB about the changes in the status of the study, including, but not necessarily limited to:

- Revised study protocol including a revision in any of the following - Eligibility or enrollment criteria; dosing procedures, safety labs or tests; data safety monitoring procedures; investigator conflict of interest.
- Revised Investigator Brochure
- Revised approved consent or assent documents
- Change in study personnel
- Any other documentation that would be provided to subjects when such information might relate to their willingness to continue to participate in the study
- Revised or additional recruitment materials
- Any other relevant documents provided by the investigator

VA Research - If an amendment for VA research addresses an issue related to biosafety or

radiation safety, the appropriate VA committee or subcommittee must first approve the amendment prior to LSUHSC-S IRB approval of the amendment. If the LSUHSC-S IRB or IRB reviewer evaluating an amendment determines that an amendment may involve biosafety or radiation safety issues, the investigator will be required to submit the amendment to the VA biosafety or radiation committee for their review and approval (as applicable) prior to the further LSUHSC-S IRB review and approval. Please refer to Overton Brooks VA Medical Center policies and procedures for instructions of submission requirements to the biosafety or radiation committee.

### **3.14.2 Expedited review of Protocol Modification**

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The IRB or Ethics Committee has and follows written policies and procedures to conduct reviews by the expedited procedure, if such procedure is used. Element II.2.E.1. – Initial review; Element II.2.E.2. – Continuing review; Element II.2.E.3. – Review of proposed modifications to previously approved research. (AAHRPP Element II.2.E)

An IRB may use expedited review procedures to review minor changes in ongoing previously-approved research during the period for which approval is authorized. An expedited review may be carried out by the IRB Chair and/or designee(s) among the IRB members.

The reviewer(s) complete the Review checklist to determine whether the modifications meet the criteria allowing review using the expedited procedure, and if so, whether the research with the proposed modifications meets the regulatory criteria for approval.

The reviewer will also consider whether information about those modifications might relate to subjects' willingness to continue to take part in the research and if so, whether to provide that information to subjects.

If the modification changes the review type (expedited or full board) appropriate for the study, the IRB staff will convert the protocol to the appropriate review type. The Chair or IRB reviewer designated makes the final determination of whether changes to the protocol are major or minor.

### **3.14.3 Full Board Review of Protocol Modifications**

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Substantive or major modifications increase the level of risks or discomforts to participants and are subject to full board review. They are assigned by the Chair or designee to a primary reviewer who reviews and presents the protocol changes at the convened meeting. A major modification may include significant changes in any of the following:

- Consent form
- Research Protocol design or methodology
- Investigator Brochure
- The subject population enrolled in the research

- The qualifications of the research team
- The facilities available to support safe conduct of the research
- Any other factor which would warrant review of the proposed changes by the convened IRB.

All IRB members scheduled to attend the meeting (including alternate members) receive and review all the modified documents submitted by the Investigator.

At the meeting, the Primary Reviewer presents an overview of the modifications and leads the IRB through the completion of the regulatory criteria for approval. The IRB will determine whether the research with the proposed modifications continues to meet the regulatory criteria for approval.

When the IRB reviews modifications to previously approved research, the IRB consider whether information about those modifications might relate to participants' willingness to continue to take part in the research and if so, whether to provide that information to participants.

### **3.15 Closure or Withdrawal of Protocols**

By federal regulation, changes in research activity require reporting to the IRB. Study closure is one such activity. As stated by the FDA, “Although subjects will no longer be “at risk” under the study, a final report/notice to the IRB allows it to close its files as well as providing information that may be used by the IRB in the evaluation and approval of related studies.”

Study Closure Forms should be submitted after any close-out monitoring visit scheduled by the sponsor or sponsor's agent. A copy of the report generated by the close-out visit must be submitted to the IRB. The Principal Investigation must report closure of a research study to the IRB immediately or within thirty (30) days

A research study may not be closed and must remain active if any of the following are true:

1. Local enrollment, research-related interventions and/or participant following are ongoing.
2. Use or access of individually identifiable information for analysis or manuscript preparation is ongoing and /or the analysis may indicate new information may be required.
3. Biological specimens containing individually identifiable information in a repository that has been approved as part of the study or upon which analysis or research is ongoing at the local site.
4. Permission from an external sponsor to close the study has not been received.

Investigators are expected to continue to honor confidentiality protections for data and other commitments made to the subject such as notifying the subject of study completion; communicating research results and/or additional significant findings to the subject; providing

compensation to subject; notifying the subject's primary care physician and ensuring appropriate follow-up and treatment, as needed.

Subsequent use of data from closed research, whether by the original investigator or other investigators, may constitute human subjects research requiring IRB approval or a Determination of Exemption of IRB review.

IRB staff will review the closure application for completeness and query the investigator on any outstanding items. Any significant findings will be referred to the Chair or designee for further consideration. After any requests from the IRB have been satisfied, the Study Closure will be acknowledged and reported to the IRB on the next available meeting agenda.

### **3.16 Reporting IRB Determinations**

Barring extraordinary circumstances, all IRB protocol review determinations are communicated to the investigator or designated primary contact person for the protocol, in writing within 5 business days of the determination. Reporting of Serious Non-Compliance; Continuing Non-Compliance; Suspension of IRB Approval; Termination of IRB Approval; and Unanticipated Problem Involving Risks to Subjects or Others to outside agencies is to take place within 30 days from the recognition of a reportable event.

The IRB uses an electronic database to process IRB submissions. As such, there are no handwritten signatures on the approval letters or other notices when communicating the IRB's determinations on research proposals. IRB correspondence will be generated using the electronic database according to the IRB activity or determination as reflected in the table below.

A deferral notification will include any modifications required by the IRB for approval of the research along with the basis for requiring those modifications. A disapproval, termination or suspension of research notification will include the basis for making that decision.

All IRB Determinations and Notices sent to investigators must be filed in the protocol records maintained by the IRB. The IRB reports its official findings and actions to the institution in the form of its minutes. The minutes are stored permanently and securely in the IRB Office and a copy is forwarded to the LSUHSC-S Institutional Official.

For VA Research the IRB notification will be signed by the IRB Chair or designee.

VA Research - For research conducted at the VA, the IRB must notify the PI and the VA RDC in writing of its decision to approve or disapprove a proposed research activity, or of revisions required to secure IRB approval. The notification by the IRB must be signed by the Chair or the voting member of the IRB who reviewed the research. After the IRB has approved a study, it must not be initiated until the investigator has been notified in writing by the ACOS/R&D that

all applicable approvals have been obtained and the study may be initiated. An IRB approved research activity may be disapproved by the VA RDC, the Medical Center Director, or the VA ORD. If a research activity is disapproved by the IRB, the decision cannot be overruled by the VA RDC, or any higher authority. The VA RDC and higher authority may strengthen requirements and/or conditions, or add other modifications to secure VA approval or approval by higher authority. Previously approved research proposals and/or consent forms must be reapproved by the IRB before initiating the changes or modifications before they are initiated.

### **3.17 Appeal of IRB Decisions**

When an IRB protocol presented at a convened meeting is disapproved or deferred and requires modifications to secure approval, the IRB will notify the investigator in writing about the specific deficiencies and the modifications that are necessary for appropriate IRB approval. The IRB shall include in its written notification a statement of the reasons for its decision and give the investigator an opportunity to respond.

If an investigator disagrees with a decision of the IRB, the investigator may submit a written appeal to the IRB Chair within 30 days of being notified of the decision. The appeal should include information supporting any disagreement made in the appeal. For appeals involving research conducted by designated review the appeal is reviewed by the designated reviewer, IRB Chair and IO or designee. For appeals involving research reviewed by the convened board, the appeal is reviewed by the convened board. The investigator may request to address the board at the meeting to provide clarification or additional information to the IRB.

If the investigator does not agree with IRB's decision regarding the appeal, the investigator may submit a written appeal to the Institutional Official or designee within 30 days of being notified of the decision. The IO may organize a meeting to help facilitate discussion between the IRB and the investigator. The IO may provide input and make recommendations for a resolution of the matter. The IO or other LSUHSC-S Senior Leadership may override the IRB's decision to approve research; however, they may not approve the research if it has not been approved by the IRB or overrule other decisions made by the IRB.

### **3.18 Use of an External IRB**

LSUHSC-S may rely on an external IRB to serve as the IRB of Record for certain LSUHSC-S research protocols. For example, LSUHSC-S may rely upon the IRB of another organization when investigators at LSUHSC-S receive a NIH grant or sub-award (or other federal funds) that mandate the use of an external IRB or when the Institution agrees to rely on an external IRB after evaluating the external IRB and the circumstances of the request. When relying on an external IRB, whether it is for a single research project or a portion the institution's research portfolio, the external IRB will meet Federal Agency regulations for the conduct of human subjects research and IRB review. Non-commercial IRBs will have a Federalwide Assurance and will be part of an AAHRPP organization. Commercial IRBs will be registered with OHRP and will

be AAHRPP accredited.

When LSUHSC-S relies on an external IRB to serve as the IRB of record, the external IRB is evaluated by the LSUHSC-S HRPP and IRB to determine if it meets specific criteria for the protection of human research subjects and, if so, written agreements are executed. There will be a formal written agreement between LSUHSC-S and the external IRB delineating the roles and specific responsibilities of each party.

An authorization agreement, initiated by either the external IRB or LSUHSC-S, is used to document the agreement of both parties. The written authorization agreement must outline the responsibilities of the external IRB and LSUHSC-S and the researcher/s. The authorization agreement is kept in the HRPP administrative files and will be made available upon official request.

The investigator seeks approval from the IO or designee to use an external IRB to serve as the IRB of Record and provides justification for reliance on the external IRB. The IO in conjunction with the IRB Chair assesses whether an external IRB is qualified to serve as the IRB of Record for LSUHSC-S human subject research project by verifying the following:

- The organization's Human Research Protection Program is accredited by AAHRPP.
- The non-commercial IRB has an active Federalwide Assurance (FWA) on file with the Federal Office for Human Research Protection.
- The commercial IRB is registered with OHRP.
- The organization or external IRB has not received any recent FDA warning letters or OHRP determination letters within the last year.
- The Board Membership satisfy the requirements of 45 CFR 46.107 and 21 CFR 56.107.
- The external IRB has an adequate process in place to notify the LSUHSC-S IRB and researcher(s) of its approvals, determinations, reportable events, suspensions, and terminations
- In the opinion of LSUHSC-S HRPP and IRB leadership, the external IRB can fulfill its responsibilities as outlined in the written authorization agreement.

If it is determined that the external IRB is qualified to serve as the IRB of Record, a written authorization agreement is initiated, by either the external IRB or LSUHSC-S, which documents the agreement of both parties.

The following information from the external organization is provided to the LSUHSC-S IO, IRB Chair or designee:

- A copy of the non-commercial IRB's Federalwide Assurance (FWA)
- The commercial IRB's Institution/organization (IORG) number
- The contact information for the external IRB's Institutional Official (name, address, telephone number, e-mail address)
- The contact information for the external IRB's Administrator and/or designated point of contact (name, address, telephone number, e-mail address)

#### LSUHSC-S Investigator Responsibilities:

- Comply with the external IRB's requirements, directives per the Authorization Agreement and local institutional requirements.
- Must not enroll individuals in any research protocol prior to the review and approval by the external IRB, and verification of local review requirements and confirmation of the external IRB approval from the LSUHSC-S IRB Administrative Office.
- Ensure the safe and appropriate performance of the research. This includes, but is not limited to ensuring the qualifications of research staff; monitoring protocol compliance; maintaining compliance with state, local or organizational requirements related to the protection of human subjects; providing a mechanism to receive and address concerns from local study subjects and others about the conduct of the research; and investigating, managing, and providing notification to the external IRB and the LSUHSC-S IRB Administrative Office of any study-specific incidence, experience, or outcome that rises to the level of an unanticipated problem and/or serious or continuing non-compliance.
- Provide the external IRB with any local context issues relevant to the research protocol.
- Disclose financial conflicts of interest according to the agreed upon process and comply with any conflict management plans that may result.
- Promptly report to the external IRB any proposed changes in the research. The investigator must not initiate changes in the research (including changes in the consent document) without prior IRB review and approval or LSUHSC-S IRB Administrative Office confirmation, except where necessary to eliminate apparent immediate hazards to the subjects.
- When responsible for enrolling subjects, will obtain, document, and maintain records of consent for each subject or subject's legally authorized representative as stipulated by the IRB. The investigator will utilize the LSUHSC-S consent, assent, and/or HIPAA templates, as appropriate.
- Will provide to the external IRB any data and safety monitoring reports they receive, either at continuing review, upon request by the reviewing IRB, or on an emergent basis, if appropriate.
- Provide updates to the external IRB and LSUHSC-S IRB Administrative Office whenever a principal investigator is no longer the responsible party for a research project under the purview of the external IRB.
- Provide the contact person and contact information for the LSUHSC-S IO or Designee to the external IRB.
- Documenting reliance on the External IRB through the IRB electronic system (Shields).
  - Document the initial request for reliance.
  - Document any updates, continuing reviews and modifications to the research approved by the external IRB including reportable new information (new risks and unanticipated problems, harm experienced by a subject, non-compliance, audits by external agencies, monitoring reports, protocol deviations, breach of confidentiality, un-reviewed changes taken to eliminate apparent immediate harm

to a subject, incarceration of a subject or unresolved subject complaint).

External IRB Responsibilities include, but are not limited to:

- Conduct review of research according to all applicable regulations and laws, including initial review, continuing review, and review of modifications to previously approved research.
- Conduct review of potential unanticipated problems, adverse events, and/or serious or continuing non-compliance.
- Provide notification to researcher staff and relying institution in writing of its determinations and decisions.
- Make available relevant IRB minutes, IRB membership rosters, and standard operating procedures to the relying institution upon request.
- When appropriate, conduct on-site or remote post-approval monitoring or audits, unless delegated to the relying institution.
- Maintain an IRB membership that satisfies the requirements of 45 CFR 46.107 and 21 CFR 56.107 and which provides special expertise as needed to adequately assess all aspects of each study.
- Promptly notify the LSUHSC-S Institutional Official or designee if there is a suspension or termination of the external IRB's authorization to review a study.
- Provide the LSUHSC-S IO or designee, the contact person and contact information for the reviewing IRB.
- Maintain appropriate documentation per record retention policies, including an OHRP-approved Federalwide Assurance (non-commercial IRBs) for human subjects research.
- Notify the LSUHSC-S HRPP of any changes to external IRB's FWA.

### **3.19 Non-Committee Review**

LSUHSC-S IRB/HRPP policy includes a process for a Designated Reviewer to conduct a Non-Committee Review. The Designated Reviewer may not disapprove research. The designated reviewer will be assigned to the following submissions:

**Study Closure:** The designated reviewer will determine if the submission meets the study closure criteria and either close the study and notify the IRB staff or communicate with the investigator and stop processing until the investigator revises the submission. If the investigator will not revise the submission, the study will be returned to the IRB staff member handling the submission for assignment to Committee Review.

**Pre-review:** The designated reviewer will review all materials and determine if any information is missing. Missing information will be requested from the investigator. The reviewer will conduct the pre-review and determine the required level of review:

- Not Human Research: Worksheet – Human Research Determination (HRP-310)
- Human Research not Engaged – Worksheet – Engagement Determination (HRP-311)
- Exempt Human Research - Worksheet – Exemption Determination (HRP-312)

- Human Research approvable using the expedited procedure – Worksheet - Eligibility for Review Using the Expedited Procedure – (HRP-313)
- Human Research that requires review by a convened IRB. If the research requires review by a convened IRB, the submission will be placed on the agenda for a convened IRB meeting.

Approve initial, continuing or modification submissions: The designated reviewer may approve initial, continuing or modification submissions if the submission meets either:

- The criteria in Exemption Determination (HRP-312)
- The criteria in Worksheet - Eligibility for Review Using the Expedited Procedure – (HRP-313) and Worksheet - Criteria for Approval and Additional Consideration (HRP-314) and other applicable worksheets and checklists as determined by the Pre-Review.
- Modifications Required to Secure Determination of Not Human Research: The submission with changes can be determined Not Human Research.
- Modifications Required to Secure Determination of Not Human Research: The submission with changes can be determined Not Human Research.
- For Veterans Administration (VA) research the approval of minor conditions by the IRB chair or designated IRB voting member must be documented in the minutes of the first IRB meeting that takes place after the date of the approval of the minor conditions.

#### 4. DOCUMENTATION AND RECORDS

The IRB or Ethics Committee maintains documentation of its activities. (AAHRPP Standard II-5)

The IRB or EC maintains a complete set of materials relevant to the research protocol or plan for a period of time sufficient to comply with legal and regulatory requirements, Sponsor requirements, if any, and organizational policies and procedures. (AAHRPP Element II.5.A.)

##### 4.1 Policy

LSUHSC-S shall prepare and maintain adequate documentation of the IRB(s) activities. All records must be accessible for inspection and copying by authorized representatives of the FDA, OHRP, sponsors, and other authorized entities at reasonable times and in a reasonable manner.

The official documentation of the IRB (s) includes the approved minutes, the agenda and the IRB Chairs' notes.

For VA Research - As part of its oversight responsibilities, the VA Research and Development Committee must have access to all IRB records and must review all minutes of the IRB(s) reviewing VA protocol.

## 4.2 IRB Records

IRB records include protocol files, minutes for convened meetings and other documentation as applicable. This list includes but is not limited to:

- IRB membership rosters
- IRB member files, including resumes
- IRB member orientation and training records
- Current and previous policies and procedures (checklists, forms, SOPs, template letters, template minutes, worksheets)
- Sponsor materials - Research protocols, Investigators' brochures and amendments; Including DHHS protocols when they exist
- Recruitment materials
- Scientific evaluations (if any) that accompany the proposals
- Approved consent and assent documents, including DHHS-approved sample consent document and protocol, when they exist
- HIPAA Authorization documents
- Records of continuing review activities and progress reports
- Modifications to previously approved research protocols
- Reports of injuries to participants
- Unexpected Problems involving risks to participants or others
- Documentation of protocol violations
- Data Safety Monitoring Reports
- Documentation of non-compliance with applicable regulations
- Significant new findings
- Documentation of Federal Grant and/or Sponsor Contract
- Conflict of Interest (COI) documents
- Copies of correspondence between the IRB and the investigator
- Documentation of actions taken by reviewer including approvals, disapprovals, waivers or alterations of consent or HIPAA authorizations, justification for any Expedited Review procedure or any Exemption Determination
- Frequency of review on Initial Protocols and Continuing Reviews
- Study Closure documents
- Documentation of Emergency Exemption from Prospective IRB Approval. FDA 21 CFR §56.104(c).
- Documentation of Exceptions from Informed Consent Requirements for Emergency Use of a Test Article [(FDA 21 CFR §50.23)].
- Documentation of Convened IRB meetings minutes
- Documentation of Affiliate Agreements or Memoranda of Understanding (MOUs).
- Quality assurance reviews and internal or external audits or inspections.
- Notifications of suspensions or terminations of research
- Various IRB reviewer checklists

IRB records must also document any determinations required by the regulations and protocol-

specific findings supporting those determinations, including:

- Waiver or alteration of the consent process.
- Research involving pregnant women, fetuses, and neonates.
- Research involving prisoners.
- Research involving children.
- Research involving adults unable to consent.
- Significant/non-significant device determinations.

For VA Research:

- Correspondence between the IRB and the Research and Development Committee
- Internal Serious Adverse Events
- Documentation of protocol deviations
- Reports of complaints from subjects
- Records of expedited review activities
- HIPAA authorization documents
- Audit results and documentation of compliance with remediation activities
- All previous IRB membership rosters
- A resume for each IRB member

For Other Research:

- Records for FDA-regulated research are to be accessible for inspection and copying by authorized representatives of FDA at reasonable times and in a reasonable manner.
- Records for research conducted, supported, or otherwise subject to regulation by a federal department or agency are to be accessible for inspection and copying by authorized representatives at reasonable times and in a reasonable manner.
- Records maintained that document compliance or non-compliance with Department of Defense (DOD) regulations shall be made accessible for inspection and copying by representatives of the DOD at reasonable times and in a reasonable manner as determined by the supporting DOD component.

Each protocol file is organized to allow a reconstruction of a complete history of all IRB events related to the review and approval of the protocol. HRPP/IRB staff will ensure that the IRB Records and Protocol files are maintained in the electronic system. In some instances, paper records may be used in addition to electronic files or as a back-up system.

### **4.3 IRB Membership Roster**

A membership list of IRB members must be maintained for each IRB committee. It must identify members sufficiently to describe each member's chief anticipated contributions to IRB deliberations. The list must contain the following information about members:

1. Name
2. Earned degrees
3. Affiliated or non-affiliated status (neither the member nor an immediate family member of the member may be affiliated with the Institution)

4. Employment or other relationship between each IRB member and LSUHSC-S.
5. Status as scientist (physician-scientist, other scientist, non-scientist or social behavioral scientist). For purposes of this roster, IRB members with research experience are designated as scientists (including the student member). Research experience includes training in research (e.g., doctoral degrees with a research-based thesis) and previous or current conduct of research. Students being trained in research fields will be designated as scientists.
6. Indications of experience, such as board certifications or licenses sufficient to describe each member's chief anticipated contributions to IRB deliberations.
7. Representative capacities of each IRB member; which IRB member is a prisoner representative (as required by Subpart C of 45 CFR 46), and which IRB members are knowledgeable about or experienced in working with children, pregnant women, cognitively impaired individuals, and other vulnerable populations locally involved in research.
8. Role in the IRB (Chair, Vice-Chair, etc.)
9. Voting status. Note that all IRB members are, by definition, entitled to vote. Guests and ex-officio guests do not have a right to vote or be counted toward a Quorum.
10. Alternate status, including the member for whom they alternate with. (Alternate members do not vote when the primary is also in attendance).

The HRPP office must keep IRB membership list current. IRB records include a curriculum vitae (CV), license, special certifications and education of each IRB member. The IO or designee must promptly report changes in IRB membership to the Office for Human Research Protections, Departments of Health and Human Services. The LSUHSC-S IRB does not release or make publicly available membership rosters with names of the IRB members. The De-identified IRB Membership Roster is available upon request.

#### 4.4 The IRB Minutes

The IRB or EC documents discussions and decisions relevant to a research protocol or plan in accordance with legal and regulatory requirements, Sponsor requirements, if any, and organizational policies and procedures. (AAHRPP Element II.5.B).

The IRB documents discussions, decisions, and findings either through the IRB minutes or when a protocol meets the criteria for expedited review through documentation in the protocol file or other records.

The IRB minutes document:

- Meeting attendees and guests
- Discussions and actions taken by the IRB and the separate deliberations for each action
- Determinations made by the IRB and the protocol-specific findings that justify those determinations
- Votes for each action recorded as numbers for, against, abstaining, absent, or recused

- Other issues requiring convened IRB review

Proceedings must be written and available for review by the next regularly scheduled IRB meeting date. Once approved by the members at a subsequent IRB meeting, the minutes may not be altered by any persons of authority except by the IRB Chairperson with the concurrence and approval of the convened IRB.

#### **4.4.1 Minutes of an IRB Meeting.**

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Proceedings must be written and available for review within one week of the meeting date.

#### **4.4.2 Attendance at an IRB Convened Meeting**

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Attendance at an IRB convened meeting is recorded in the minutes by documenting:

- The IRB members (voting, non-voting) who are in attendance;
- The IRB members who are not in attendance;
- When an alternate member replaces a primary member in attendance and voting at the convened meeting
- The continued presence of quorum for all votes, including a member whose primary concern is in a nonscientific area, a member whose primary concern is in a scientific area, a member who is unaffiliated, and a member who represents the general perspective of subjects.
- Attendance of members and alternate members who participate through teleconference, and documentation that those members received all pertinent material before the meeting and had the opportunity to actively and equally participate in all discussions
- The IRB members who leave the meeting because of a conflicting interest
- The IRB members who leave the meeting briefly, are not present during a vote, and are not counted as part of the quorum
- The IRB members who arrive late or depart early from the meeting and their arrival or departure times
- The HRPP staff present
- Any others present (e.g., invited guests, investigators invited to address the IRB, and consultants)

#### **4.4.3 Discussions and Actions Taken By the IRB**

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Discussions and actions taken by the IRB, and the separate deliberations and basis for each action are documented in the minutes, such as:

- Discussion of protocol events — initial, continuing review, modifications, reports of unanticipated problems and events and reportable new information requiring prompt review
- Approval of research — including the approval period for research, at initial and

continuing review, (and if appropriate to the degree of risk determination of an approval period of less than one year)

- Any modifications in the research that the IRB requires before the research can secure approval
- Suspensions and terminations of previously approved research
- Disapproval of research
- Discussion of controverted issues and their resolution or disposition
- Requests for consultant review or input from an expert in the field (e.g. requests made during a convened meeting)
- Actions resulting from review of reports of unanticipated problems involving risks to participants or others, or other reportable events and information
- Actions resulting from determinations of serious or continuing non-compliance
- Identification of any research for which there is need for verification from sources other than the investigator that no material changes are made in the research (e.g., Cooperative Studies, or other collaborative research)
- If a protocol is using a DHHS-approved sample consent: The justification of any deletion or substantive modification of information concerning risks or alternative procedures contained in the sample consent document

#### **4.4.4 Determinations made by the IRB**

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Determinations made by the IRB are recorded in the minutes with documentation of the protocol-specific findings justifying those determinations as appropriate, such as:

- Significant risk and non-significant risk device determinations, pursuant to: 21 CFR 812.2(b), 21 CFR 812.150(b)(9) and considering FDA Information Sheet Significant and Non-significant Risk Medical Device Studies at <http://www.fda.gov/oc/ohrt/irbs/devrisk.pdf>
- Approval of waiver or alteration of informed consent, pursuant to: 45 CFR 46.116(c) and 45 CFR 46.116(d)
- Waiver of informed consent documentation, pursuant to: 45 CFR 46.117(c) and 21 CFR 56.109(c)(1)
- Research involving adults unable to consent in VA research (VHA Handbook 1200.05)
- Waiver of HIPAA Authorization, pursuant to 45 CFR 164.512(i)(2)(ii)
- Waiver of HIPAA Authorization for recruitment or screening, pursuant to 45 CFR 164.512(i)(2)(ii)
- Whether or not subjects need to be re-consented to changes or new information
- When research involves children, the following IRB decisions are documented:
  - Appropriate children finding applicable to research: -45 CFR 46.404, 45 CFR 46.405, 45 CFR 46.406, 45 CFR 46.407, 45 CFR 46.408 (OHRP) -21 CFR 50.51, 21 CFR 50.52, 21 CFR 50.53, 21 CFR 50.54, 21 CFR 50.55 (FDA)
  - Whether the permission of one parent/guardian is sufficient or if permission from both parents/guardians is required. (See guidance Parental Permission.)

- How assent is to be solicited or obtained, unless waived.
- The participation of children who are wards of the state is approved under:
  - 45 CFR 46.406, 45 CFR 46.407 only if 45 CFR 46.409(a) is satisfied, or -21 CFR 50.53, 21 CFR 50.54 only if 21 CFR 50.56(a) is satisfied
- Appropriate involvement of pregnant women, fetuses, and neonates pursuant to:
  - 45 CFR 46.204, 45 CFR 46.205, 45 CFR 46.206, and 45 CFR 46.207
- Approval of research involving prisoners as participants under the following regulations:
  - 45 CFR 46.305 and 45 CFR 46.306
- Determination of the level of risk
- Determinations of serious or continuing non-compliance
- For VA research (see VHA Handbook 1200.05) determinations may address:
  - Research involving adults unable to consent
  - Waiver of requirement to maintain a master list of all subjects
  - If recruitment of non-Veterans is justified and appropriate
  - Whether medical record should be flagged to protect the participant's safety by indicating participation in the study and the source of more information on the study.

#### 4.4.5 Other Issues

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Other issues are documented in the minutes, including but not limited to:

- Events and information that require prompt reporting to the IRB
- Approval of minutes of prior convened IRB meetings
- The approval of research by the chair or designee using expedited procedures that was contingent on non-substantive changes, in the minutes of the first IRB meeting
- Presentation of information from an outside consultant or expert as previously requested by the IRB
- Special situations such as use of a test article and humanitarian use devices, other items as applicable

A copy of the IRB-approved minutes for each IRB meeting will be distributed to the IO, and Counsel for the HRPP. The IRB minutes, once approved, may not be altered by any persons of authority except by the IRB Chairperson with the concurrence and approval of the convened IRB.

For VA Research - The Research and Development Committee of the VA must be given a complete (non-redacted) copy of the IRB-approved minutes to review for each VA-designated IRB.

The minutes document the determination of the level of risk and the rationale for the IRB's determinations of the level of risk.

The minutes provide a summary of the discussion when real Social Security Numbers (SSNs),

scrambled SSNs, or the last four digits of SSNs will be used in the study. The summary needs to include the security measures that are in place to protect the SSN instances embedded in the study. This does not apply if the only use of SSNs is on the informed consent form or the HIPAA authorization.

Approval is documented in the minutes of the first IRB meeting that takes place after the approval date.

#### **4.5 Documentation of Exemptions**

Documentation of verified exemptions consists of the reviewer's citation of a specific exemption category and written concurrence that the activity described satisfies the conditions of the cited Exemption category. The Exempt Determination is reported at the next convened IRB meeting and documented in the minutes.

#### **4.6 Documentation of Expedited Reviews**

IRB records for initial and continuing review by the expedited procedure must include:

- the specific permissible category
- a description of action taken by the reviewer
- the approval period
- any determinations required by the regulations including protocol-specific findings supporting those determinations

#### **4.7 Record Retention**

In accordance with the Common Rule and FDA regulations (45 CFR 46.115(b) and 21 CFR 56.115(b)), IRB records are retained for at least three years after the completion of the research, either electronically or as hard copy. Protocol files are to be retained as long as required by law or as stated in clinical trial agreement but no less than 3 years after completion of the research and then destroyed. Protocols in which there was no subject enrollment or no research was conducted are to be retained the same as protocols where research was conducted. In accordance with federal HIPAA privacy regulations, IRB records pertaining to records containing protected health information (PHI) are retained for at least six (6) years after the completion of the research. It is LSUHSC-S policy to retain records for the greatest amount of mandated time. Thus, the IRB retains all research records for at least six years. Sponsored grants and contracts may require additional periods for record retention.

Records pertaining to the following are to be accessible for inspection and copying by authorized representatives of that agency at reasonable times and in a reasonable manner:

- All records for research conducted or funded by a Common Rule department or agency
- Records maintained that document compliance or non-compliance with Department of Defense (DOD) regulations,

- Records for research subject to FDA regulations
- VA records

Records maintained indefinitely in the HRPP office include: IRB approved meeting minutes, A resume or curriculum vitae for each IRB member, and current and previous versions of IRB member rosters.

Records will be destroyed by HRPP using the following procedure:

- Destroy IRB protocol files for Veterans Administration (VA) research when the protocol has been closed, withdrawn, or terminated more than six years unless otherwise required by law.
- Consistent with LSUHSC-S HRPP policy, destroy IRB protocol files for the Department of Defense (DOD) research when the protocol has been closed, withdrawn, or terminated more than three years unless otherwise required by law. The Department of Defense may require that research records be transferred to the DoD component rather than being retained by LSUHSC-S HRPP.
- Destroy all other IRB protocol files when the protocol has been closed, withdrawn, or terminated more than three years unless otherwise required by law.
- In the case of multi-center research, three years is referenced to the organization's involvement in the research, not the entire study.

VA Record Retention: VA required records, including the investigator's research records, must be retained until disposition instructions are approved by the National Archives and Records Administration and are published in VHA's Records Control Schedule (RCS IO-1). Records pertaining to research must be stored securely in the IRB Office. After that time those records will be shredded or otherwise destroyed. When following VA regulations, required records, including the researcher's research records, must be kept for six years. Codes/Keys linking subject data to identifiers must be kept as part of the research protocol for six years. All records must be accessible for inspection and copying by authorized representatives of the OHRP, FDA, sponsors, and other authorized entities at reasonable times and in a reasonable manner. Records are maintained in locked file cabinets and/or locked offices within the main HRPP Office and are available only to IRB members and IRB office staff.

#### **4.7.1 Maintenance of and Access to IRB Records**

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All hard copy IRB records of active protocols are secured in closed filing cabinets in locked buildings with regular security mechanisms and controlled access. Records of closed protocols are boxed and stored in the same manner as above as long there is sufficient space. (An external vendor may be contacted for long-term storage. Access to those materials can be obtained with five days prior notice). Outdated IRB Records will be shredded or otherwise destroyed as permitted by policy.

Research investigators are provided reasonable access to information related to their own

research files. All other access to IRB records is strictly limited to those with a legitimate need for access, such as LSUHSC-S compliance functions.

## **5. INFORMED CONSENT**

The IRB has and follows written policies and procedures to evaluate the consent process and to require that the Researcher appropriately document the consent process. (AAHRPP Element II.3.F)

### **5.1 Policy**

Researchers employ consent processes and methods of documentation appropriate to the type of research and the study population, emphasizing the importance of comprehension and voluntary participation to foster informed decision-making by participants. (AAHRPP Element III.1.F.)

Informed consent is a continuing process whereby the investigator and research participant have an ongoing dialogue about all aspects of a research study that might inform a participant's decision to take part in the study and their decision to continue their involvement as a participant. The purpose of the consent process is to assure knowledgeable decision-making and voluntary participation.

No investigator conducting research under the auspices of the Institution may involve a human being as a subject in research without obtaining the legally effective informed consent of the subject or the subject's legally authorized representative unless a waiver of consent has been approved by the IRB in accordance with Sections 5.8 and 5.9 of this policy. Except as provided in Sections 5.8 and 5.9 of this policy, informed consent must be documented using a written consent form approved by the IRB.

The informed consent process generally includes:

1. Bringing the research study to the notice of potential participants
2. Presentation and explanation of the study activities to the participant or their legally authorized representative (LAR)
3. Documentation of the informed consent by means of a signed and dated written consent document
4. Ongoing discussions between the investigator and the participant regarding continued participation in the study

The informed consent process must:

1. Provide sufficient opportunity for the participant, or the participant's legally authorized representative (LAR), to consider whether to participate
2. Minimize the possibility of coercion or undue influence

3. Not include exculpatory language
4. Be in language understandable to the participant or their representative
5. Be conducted with the subject face-to-face in a private, quiet setting

The IRB also requires that the circumstances of the consent process be culturally and linguistically appropriate for the intended participants. The IRB will evaluate both the consent process and the procedures for documenting informed consent to ensure that adequate informed consent is obtained from participants.

For VA Research: All VA research requiring written informed consent must use the VA Informed Consent and all required elements must be present and completed, and a separate VA HIPAA Document. The requirement to utilize the VA Informed Consent and VA HIPAA Document to document informed consent applies to all VA-approved research including, but not limited to, studies in which VA investigators working on VA research enroll subjects at an affiliate hospital or other sites outside VA (e.g., community centers or shopping malls). The most recent IRB-approved version of the informed consent form contains the IRB approval date on the consent document. All required elements of the Common Rule must be present and completed as well as any additional elements required by the IRB.

## 5.2 Definitions

The Organization has and follows written policies and procedures that identify applicable laws in the localities where it conducts human research, takes them into account in the review and conduct of research, and resolves differences between federal or national law and local laws. (AAHRPP Element 1.1.G)

A legally authorized representative includes not only a person appointed as a health care agent under a Durable Power of Attorney for Health Care (DPAHC), a court appointed guardian, tutor or curator of the person, but also next-of-kin in the following order of priority: spouse, not judicially separated, adult child (18 years of age or older), parent, adult sibling (18 years of age or older), grandparent, or adult grandchild (18 years of age or older).

LA. C.E. 510(5) Representative of a patient is any person who makes or receives a confidential communication for the purpose of effectuating diagnosis or treatment of a patient.

LA. R.S. 44:17(A) (4) Representative of a patient means a person who is a parent, tutor, curator, spouse, trustee, attorney, or other legal agent of the patient and who is authorized, by and on behalf of the patient, to exercise any of the patient's rights or privileges.

Legal guardian - A person appointed by a court of appropriate jurisdiction. A. ChC 116(12.1)(a)(i)(b) Legal Guardianship means the duty and authority to make important decisions in matters having a permanent effect on the life and development of the child and the responsibility for the child's general welfare until he reaches the age of majority, subject to

any residual rights possessed by the child's parents. It shall include but not necessarily be limited to: The authority to consent to marriage, to enlist in the armed forces of the United States, or to major medical, psychiatric, and surgical treatment, to represent the minor in legal actions, to make other decisions of substantial legal significance concerning the minor. The term legal guardian means the caretaker in such a relationship.

### 5.3 Basic Requirements for Informed Consent

The IRB has and follows written policies and procedures to evaluate the consent process and to require that the Researcher appropriately document the consent process. AAHRPP (Element II.3.F)

subject or the subject's legally authorized representative by the investigator prior to entering a subject into a study and/or conducting any study related procedures required by the protocol. All relevant requirements in 45 CFR 46.111 and 46.116 and in the 21 CFR 50.20, 50.25, 50.27, and 56.111 that are applicable to the consent process and the consent document must be satisfied.

Evaluation of Compliance with Informed Consent Requirements is achieved by:

1. IRB review of the informed consent process information and documents provided by the principal investigator.
2. Periodic consent form audits comparing signed and dated consent forms with the IRB approved versions.
3. Observation of the consent process, performed either as a periodic audit function of the HRPP or as requested by the IRB.

#### 5.3.1 Elements of Informed Consent

Legally effective informed consent includes the basic required elements and the additional elements, if applicable to the study, as specified in 45 CFR 46.116 and 21 CFR 50.25.

Basic Elements (must be provided to each subject):

1. A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed and identification of any procedures which are experimental.
2. A description of any reasonably foreseeable material risks or discomforts to the subject. A material risk is a risk that if disclosed to a prospective participant, would have affected the decision of a reasonable person whether to participate.
3. A description of any benefits to the subject or to others which may reasonably be expected from the research.
4. A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject.
5. A statement describing the extent, if any, to which confidentiality of records identifying

the subject will be maintained. For FDA regulated studies, the possibility that the Food and Drug Administration may inspect the records.

6. For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained.
7. An explanation of whom to contact for answers to pertinent questions about the research subjects' rights, and whom to contact in the event of a research-related injury.
8. A statement that participation is voluntary, that refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and that the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

When following ICH-GCP (E6), the IRB determines that the following disclosures are included in the consent document:

- The alternative procedures or treatment that might be available to the subject, and their important potential benefits and risks.
- That the monitor, the auditor, the IRB, and the regulatory authority will be granted direct access to the subject's original medical records for verification of clinical trial procedures or data without violating the confidentiality of the subject, to the extent permitted by the applicable laws and regulations and that, by signing a written consent form, the subject or the subject's legally acceptable representative is authorizing such access.
- The approval of the IRB.

For VA Research the following is required:

9. A statement that in the event of a research-related injury the VA has to provide necessary medical treatment to a subject injured by participation. This includes any research approved by a VA RDC and conducted under the supervision of one (1) or more VA employees. For research involving more than minimal risk, the consent process and document will disclose a statement that in the event of a research-related injury the VA has to provide necessary medical treatment to a subject injured by participation. VA regulations require the VA to provide care for all research-related injuries including those studies that are considered minimal risk even, if a statement is not included in the consent process or document for research involving no greater than minimal risk.
10. A statement that a veteran-subject does not have to pay for care received as a subject in a VA research study except in accordance with federal law.
11. An indication that all regulations pertaining to the participation of veterans as subjects, including requirements for indemnification in case of research-related injury, pertain to non-veterans subjects enrolled in VA-approved research.
12. This does not apply to: (a) treatment for injuries due to non-compliance by a subject with study procedures; or (b) research conducted for VA under a contract with an individual or a non-VA institution.
13. Consent for research must be obtained from each research subject before taking photographs or making voice or video recordings that will be used for research

purposes. Unless the IRB grants a waiver of documentation of the consent process for research, the consent document for research must include a discussion of why photographs, or voice or video recordings are being taken for the research, who will have access to them, and what their disposition will be after the research is completed.

- When the research subject is a patient (either an inpatient or outpatient), the subject must sign VA Form 10-3203 to permit photographs or video and voice recordings that will be used for research purposes even if the IRB has waived the requirement for documentation of consent for research. Photography or recordings cannot occur prior to the patient's granting such permission.
- When the research subject is a patient, the subject's signed and dated VA Form 10-3203 must be placed into the medical record along with, if applicable, the signed and dated VA informed consent document. The signed VA Form 10-3203 must be obtained and placed in the subject's medical record, even if the IRB has waived documentation of consent for research.
- If someone other than the researcher conducts the interview and obtains consent, policies and procedures have the researcher formally and prospectively designate in writing in the protocol or the IRB application, the individual who will have this responsibility. The person so delegated must have received appropriate training to perform this activity. This person must be knowledgeable about the research to be conducted and the consenting process, and must be able to answer questions about the study. This designee must be a member of the research team.

Additional Elements: When appropriate, one or more of the following elements of information must also be provided to each subject:

1. A statement that a treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable.
2. Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent.
3. Any additional costs to the subject that may result from participation in the research.
4. The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject.
5. A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject.
6. The approximate number of subjects involved in the study.
7. For applicable clinical trials, the following statement shall be provided in informed consent documents and processes: "A description of this clinical trial will be available at <http://www.ClinicalTrials.gov>, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time."
8. Informed Consent requirements for vulnerable and other special populations are addressed in Section 6.

### 5.3.2 Statement regarding Mandatory State of Louisiana Reporting requirements

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LSUHSC-S must comply with the State of Louisiana mandatory reporting regulations. The LSUHSC-S IRB requires all Investigators and clinical study staff engaged in research approved by the LSUHSC S IRB to adhere to mandatory reporting requirements specified by state and local law. A physician or other health professional must report certain conditions, circumstances, and diseases to state and local agencies whether they are found in the course of non-research clinical care or as part of a research protocol. This policy relates to research-related findings that present themselves during the conduct of a protocol and must be reported outside the institution. The principal Investigator must also report the event to the IRB only if the condition/circumstances are a serious, unanticipated and study-related adverse consequence of study participation.

Investigators must include in the consent form a statement regarding the intent to disclose information in accordance with the State of Louisiana mandatory reporting requirements where applicable.

When appropriate, the LSUHSC IRB will require the addition of a statement in the consent form to alert research participants to the possibility that information they disclose, or the results of their medical tests, may have to be reported by law to state/local authorities. For example, additional language in a consent form would be appropriate and necessary when HIV testing or Hepatitis A, B, and/or C testing will occur as a part of a protocol. Additional mandatory state reporting requirements may include untreated pulmonary tuberculosis or acute meningococcal meningitis, acute hepatitis virus B infection, a chronic hepatitis B carrier, or human immunodeficiency virus and/or each case of Cancer.

The Template: Consent Document (HRP-502) is in the Shields document library and on the HRPP website <http://www.lsuhscreport.edu/Research/HRPP-Home/index>. For research involving children, Template: Assent Document (HRP-500) is also provided.

### 5.3.3 Additional Consent Requirements

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1. Vulnerable and Special Populations: Informed Consent requirements for vulnerable and other special populations are addressed in Section 6.
2. VA-Specific: For VA research, additional consent requirements might apply. Refer to VHA Handbook 1200.05.
3. Health Insurance Portability and Accountability Act (HIPAA): If the protocol involves protected health information (PHI) as defined by HIPAA, then HIPAA authorization may be required as part of the consent process. HIPAA authorization is an authorization to use or disclose PHI and must be executed by a separate signature. The Shields document library and the HRPP website contains the LSU Health HIPAA Authorization HRP-502.1. HIPAA is addressed in Section 16.
4. Genetic Testing: Risks specific to this type of testing must be disclosed to the subject. This

is addressed in Section 17.

5. Other Federal Agencies: Additional requirements might apply if research is funded, supported by, or otherwise subject to certain federal agencies or agreements and could be subject to additional requirements to those in the Common Rule. (e.g., Department of Defense, Department of Justice, Bureau of Prisons).

#### 5.3.4 General Requirements:

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Informed consent must be obtained by the investigator prior to entering a subject into a study and/or conducting any study related procedures required by the protocol, unless consent is waived by the IRB.

Investigators are individuals who conduct human subject projects, including individuals directly involved in seeking the voluntary informed consent of the potential subjects. Investigators can include physicians, scientists, nurses, administrative staff, teachers, and students. Investigators must be included on the (1) form 1572 for research with investigational drugs, (2) IRB application request page and (3) Delegation log.

If someone other than the principal investigator conducts the interview and obtains consent from a patient, the investigator needs to formally delegate this responsibility in writing in the protocol or the IRB application, and the person so delegated must have received appropriate training to perform this activity. The person so delegated must be knowledgeable about the research to be conducted and the consenting process and must be able to answer questions about the study.

Prior to a participant's participation in a trial, the written consent document should be signed and personally dated by the person who conducted the informed consent discussion.

The role of a witness on a consent document is to observe and verify that the signature of the subject is original. This witness must not be a member of the research team. The witness is not attesting that the explanation given by the investigator or that the information in the consent form covered all the significant points. The witness is not attesting that the prospective subject appeared to understand. The role of the witness is only to document that they were present when the consent was obtained. Consent is obtained when the informed consent document is signed by all parties. The witness should sign and personally date the consent document.

When a participant withdraws from a study, the data collected on the participant to the point of withdrawal remains part of the study database and may not be removed. The consent document cannot give the participant the option of having data removed.

A Researcher may ask a participant who is withdrawing whether the participant wishes to provide continued follow-up and further data collection after their withdrawal from the

interventional portion of the study. Under this circumstance, the discussion with the participant distinguishes between study-related interventions and continued follow-up of associated clinical outcome information (such as medical course or laboratory results obtained through non-invasive chart review) and addresses the maintenance of privacy and confidentiality of the participant's information.

The Researcher must obtain the participant's consent for this limited participation in the study (assuming such a situation was not described in the original consent document). The IRB must approve the consent document.

If a participant withdraws from the interventional portion of a study and does not consent to continued follow-up of associated clinical outcome information, the Researcher must not access for purposes related to the study the participant's medical record or other confidential records requiring the participant's consent. However, a Researcher may review study data related to the participant collected prior to the participant's withdrawal from the study and may consult public records, such as those establishing survival status.

### **5.3.5 Master List of Subjects**

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The investigator must maintain a master list of subjects for any given study where informed consent is required and documentation of consent is required. This list must be readily available at any given time. The IRB may waive the requirement for the investigator to maintain a master list if the following conditions are met:

1. The IRB has waived the requirement to obtain informed consent; or
2. The IRB has waived documentation of the consent process and such a master list poses a risk to the participants from a breach of confidentiality.

When the IRB waives the requirement for the investigator to maintain a master list for a given study, the IRB must provide written documentation in the IRB minutes or IRB protocol file justifying the waiver.

## **5.4 Short Form**

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Federal regulations permit the use of a short form consent process (45 CFR 46.117 (b) (2) with the prior approval of the IRB. However, the IRB encourages the use of a full consent form translated into the participant's language whenever possible.

When reviewing the short form of consent documentation, the IRB must determine:

- The consent document states that the elements of disclosure required by regulations have been presented orally to the subject or the subject's legally authorized representative.
- A written summary embodies the basic and required additional elements of disclosure.
- There will be a witness to the oral presentation.

- For subjects who do not speak English, the witness is conversant in both English and the language of the subject.
- The subject or the subject's legally authorized representative will sign the consent document.
- The witness will sign both the short form and a copy of the summary.
- The person obtaining consent will sign a copy of the summary.
- A copy of the signed short form will be given to the subject or the legally authorized representative.
- A copy of the signed summary will be given to the subject or the legally authorized representative.

When following FDA regulations 21 CFR 50.27 (b) (2), the IRB must determine:

- The consent document states that the elements of disclosure required by regulations have been presented orally to the subject or the subject's legally authorized representative.
- A written summary embodies the basic and required additional elements of disclosure.
- There will be a witness to the oral presentation.
- For subjects who do not speak English, the witness is conversant in both English and the language of the subject.
- The subject or the subject's legally authorized representative will sign the consent document.
- The witness will sign both the short form and a copy of the summary.
- The person obtaining consent will sign a copy of the summary.
- A copy of the signed short form will be given to the subject or the legally authorized representative.
- A copy of the signed summary will be given to the subject or the legally authorized representative.

## 5.5 The Informed Consent Process

Researchers employ consent processes and methods of documentation appropriate to the type of research and the study population, emphasizing the importance of comprehension and voluntary participation to foster informed decision-making by participants. (AAHRPP Element III.1.F.)

The IRB has and follows written policies and procedures to evaluate the consent process and to require that the Researcher appropriately document the consent process. (AAHRPP Element II.3.F)

The HHS regulations at 45 CFR part 46 for the protection of human subjects in research require that an investigator obtain the legally effective informed consent of the subject or the subject's legally authorized representative. When informed consent is required, it must be sought prospectively, and documented to the extent required under HHS regulations at 45 CFR

46.117. The requirement to obtain the legally effective informed consent of individuals before involving them in research is one of the central protections provided for by the regulations and LSUHSC-S HRPP SOPs.

The informed consent process involves three key features: (1) disclosing to the prospective human subject information needed to make an informed decision; (2) facilitating the understanding of what has been disclosed; and (3) promoting the voluntariness of the decision about whether to participate in the research. Informed consent is more than just a signature on a form.

It is a process of information exchange to include reading and signing the informed consent document. The informed consent process is the critical communication link between the prospective human subject and an investigator, beginning with the initial approach of an investigator and continuing through to the completion of the research study.

Investigators must have received the appropriate training and be knowledgeable about the study protocol in order that they may answer questions to help provide understanding to the study participant or potential study participant.

The exchange of information between the investigator and study participant can occur via one or more of the following modes of communication, among others: face to face contact, mail, telephone, or fax. However, informed consent must be obtained face to face between the investigator and the potential study participant/study participant's legally authorized representative.

Informed consent must be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by Appendix A.9.

### 5.5.1 Requirements

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1. Informed consent may only be obtained from subjects who have the legal and mental capacity to give consent. For subjects without that capacity, consent must be obtained from a legal guardian or a legally authorized representative. In the absence of a parent, permission may be obtained from an individual authorized to consent under applicable law on behalf of a child to general medical care. Generally, the IRB requires assent from children 7 or older but this may vary depending on other factors.
2. The informed consent process shall be sought under circumstances that provide the subject (or legally authorized representative) with sufficient opportunity to consider whether to participate.
3. The informed consent process shall be sought under circumstances that minimize the possibility of coercion or undue influence. Coercion occurs when an overt or implicit threat of harm is intentionally presented by one person to another to obtain compliance. Undue influence, by contrast often occurs through an offer of an excessive or

inappropriate reward or overture to obtain compliance.

4. The informed consent information must be presented in language that is understandable to the subject (or legally authorized representative). To the extent possible, the language should be understandable by a person who is educated to 8<sup>th</sup> grade level and layman's terms shall be used in the description of the research.
5. For subjects whose native language is not English, informed consent must be obtained in a language that is understandable to the subject (or the subject's Legally Authorized Representative). In accordance with this policy, the IRB requires that informed consent conferences include a qualified translator when the prospective subject does not understand the language of the person who is obtaining consent. The Translator must sign and personally date the approved translated consent form as the witness.
6. The informed consent process may not include any exculpatory language through which the subject is made to waive, or appear to waive any of the subject's legal rights or through which the investigator, the sponsor, the Institution or LSUHSC-S employees or agents are released from liability for negligence, or appear to be so released.
7. The Principal Investigator is ultimately responsible for insuring that each prospective subject is adequately informed about all aspects of the research and understands the information provided. However, the HRPP, the research investigators and the research staff all share in the responsibility of ensuring that the informed consent process is adequate.
8. The informed consent process must also be conducted and consent obtained in person in addition to the reading and signing the informed consent document. LSUHSC-S HRPP does not allow for obtaining informed consent over the phone or by mail to ensure subject understanding and to allow for question/answer sessions.
10. In addition to signing the consent, the subject /representative should enter the date of signature on the consent document to permit verification that consent was obtained before the subject began participation in the study. If the consent is obtained on the same day as the subject's involvement in the study begins, the subject's medical records/source documentation should document that consent was obtained prior to participation in the study.
11. A copy of the consent document should be provided to the subject, a copy placed on all the appropriate LSUHSC-S medical records, and the original signed consent document should be retained in the study records. It is not required that the subject's copy be a signed copy, although a photocopy with a signature is preferred.
12. HHS regulations at 45 CFR part 46 do not specify how far in advance of study entry a subject can provide consent. The amount of time required by a subject to decide would presumably depend upon the nature of the study, taking into consideration the degree of risk, potential benefits, alternatives, and desire to consult with family. For the sake of clarification, LSUHSC-S HRPP policy is that consents are current for 30 days but it may be prudent to review information contained in the consent document with the research subject prior to initiating any research procedures.

Translation/Interpreting Services: Services are provided by the Institution using contracted

professional resources that have been identified as able to provide multi-lingual translation/interpreting services. Nursing units shall have a princess phone stored on the unit with a splitter that will be used to access interpreting services. When interpretative services are needed, the extra phone with the splitter will be taken into the room and the phone in the room will be taken out of the wall jack, the splitter inserted into the wall jack and both lines connected to the splitter. This will allow the patient and another person to speak and hear responses without delay. A princess phone line with splitter can be obtained from Telecommunication. These services shall be made available upon request by contacting the Social Services Department. A list of employees that can provide interpretive services is also maintained by Social Services.

## **5.6 Documentation of Informed Consent**

Researchers employ consent processes and methods of documentation appropriate to the type of research and the study population, emphasizing the importance of comprehension and voluntary participation to foster informed decision-making by participants. (AAHRPP Element III.1.F.)

Except as provided in Section 5.9 of this document, informed consent must be documented using a written consent form approved by the IRB. For VA Research, consent will be documented using the VA informed consent.

Documentation requirements for informed consent are specified 45 CFR 46.117(a), (b) and 21 CFR 50.27 (a), (b).

1. Informed consent is documented using a written consent form approved by the IRB and signed and dated by the subject or the subject's legally authorized representative at the time of consent.
2. At the time of consent, the person obtaining consent must signify with their signature and date.
3. At the time of consent, the witness must sign and date the consent form to verify that the signature of the subject or the subject's legal representative is original. The witness must not be a member of the research team.
4. A copy of the consent form must be given to the subject or the subject's Legally Authorized Representative who signed the form. It is not required that the subject's copy, be a signed copy, although a photocopy with a signature is preferred.
5. The consent form may also be documented by either of the following:
  - a. A written consent document that embodies the basic and required additional elements of informed consent may be read to the subject or the subject's legally authorized representative. However, the subject or legally authorized representative must be given adequate opportunity to verbalize understanding before it is signed. After the written consent document and any other written information to be provided is read and explained to the subject or the subject's

legally authorized representative, and after the subject or the subject's legally authorized representative has orally consented to the subject's participation in the trial, and if capable of doing so, has personally signed and dated the consent document, the witness should sign and personally date the consent document.

- b. When the person obtaining consent is assisted by a translator, the translator may serve as the witness. If the witness is attesting to the consenting process, in addition to the authenticity of the subject's or the subject's legally authorized representative's signature, a note to document this is required and is to be placed under the witness's signature line.

VA Research - The informed consent form must be signed and dated by: (1) the subject or the subject's legally authorized representative (LAR); (2) the person obtaining the informed consent, and (3) a witness, if required by IRB (e.g., the IRB may require a witness if the study involves an invasive intervention or an investigational drug or device). A witness is always required when a short form consent is employed. The witness is required to witness only the subject's or subject's LAR's signature, not the informed consent process (e.g., if the subject does not want the witness to know the nature of the research study), unless the sponsor or IRB requires the witness to witness the informed consent process. The witness cannot be the person who obtained informed consent from the subject, but may be another member of the study team or may be a family member. If the subject submits the signed and dated informed consent form to the investigator or designee by facsimile, the person who obtains informed consent must sign and date the facsimile, and then the facsimile can serve as the original informed consent document. If facsimile is used for the informed consent document, measures must be employed to ensure the confidentiality of the information, and the privacy of the subject.

#### **5.6.1 Changes in the Informed Consent Document**

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When a modification makes it necessary to change the Informed Consent document, regardless of whether any participants are enrolled, the changes in the document must be submitted to the IRB for review and approval prior to use. The investigator may inform the subjects of any new information or changes prior to approval when the changes are necessary to eliminate an immediate hazard to the subject.

#### **5.6.2 Flagging a Medical Record**

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For VA research, the IRB needs to determine if the patient's medical record (electronic or paper) must be flagged to protect the subject's safety by indicating the subject's participation in the study, and the source of more information on the study.

The patient health record must be flagged if the subject's participation in the study involves:

- (a) any invasive research procedure (e.g., muscle biopsy or bronchoscopy)
- (b) interventions that will be used in the medical care of the subject, or that could

interfere with other care the subject is receiving or may receive (e.g., administration of a medication, treatment, or use of an investigational device)

- (c) clinical services that will be used in the medical care of the subject (e.g., orders for laboratory tests or x-rays ordered as a part of the study), or that could interfere with other care the subject is receiving or may receive
- (d) the use of a survey or questionnaire that may provoke undue stress or anxiety unless the IRB determines that mandatory flagging is not in the best interests of the subject (e.g., an interview study of victims of sexual assault). There may be additional situations when the IRB determines flagging is necessary

**Flagged VA Record Contents:** If IRB determines and documents that the patient health record must be electronically flagged in the VA Computerized Patient Record System (CPRS) as participating in a research study then, in accordance with VA policy, the health record must:

- (a) identify the investigator, as well as contact information for a member of the research team that would be available at all times [NOTE: The research team must have an appropriate member available (on-call) at all times]; and
- (b) contain information on the research study or identify where this information is available. The duration of flagging will be until study closure if not otherwise specified by the IRB.

## **5.7 Consent Monitoring**

In reviewing the adequacy of informed consent procedures for proposed research, the IRB may on occasion determine that special monitoring of the consent process by an impartial observer (consent monitor) is required to reduce the possibility of coercion and undue influence, ensure that the approved consent process is being followed, or ensure that subjects are truly giving informed consent.

Such monitoring may be particularly warranted for:

1. High risk studies
2. Studies that involve particularly complicated procedures or interventions
3. Studies involving highly vulnerable populations (e.g., ICU patients, children)
4. Studies involving study staff with minimal experience in administering consent to potential study participants
5. Other situations when the IRB has concerns that consent process is not being conducted appropriately

Monitoring may also be appropriate as a corrective action where the IRB has identified problems associated with an investigator or a research project or there have been allegations or findings of non-compliance.

If the IRB determines that consent monitoring is required, the IRB Chair and the IO or designee will develop a monitoring plan and submit it to the IRB for approval. The consent monitoring

may be conducted by IRB staff, IRB members or another party, either affiliated or not with the institution. The PI will be notified of the IRB(s) determination and the reasons for the determination. Arrangements will be made with the PI for the monitoring of the consent process for a specified number of subjects.

When observing the consent process, the monitor will determine:

- Whether the informed consent process was appropriately completed and documented
- Whether the participant had sufficient time to consider study participation
- Whether the consent process involved coercion or undue influence
- Whether the information was accurate and conveyed in understandable language
- Whether the subject appeared to understand the information and gave their voluntary consent

Documentation of the observation will be provided to the IRB using the Worksheet: Audit Tool: Consent Process (HRP-336). Following the monitoring, a report of the findings will be submitted to the IRB, which will determine the appropriate action to be taken.

VA Research: Beginning in 2009, VA research facilities were mandated to conduct complete audits of 100% of the informed consent documents for all research studies, one third of the active studies must have regulatory audits, and all closed studies must have informed consent document and regulatory audits done.

## **5.8 Waiver or Alteration of Informed Consent**

The IRB has and follows written policies and procedures for approving waivers or alterations of the consent process and waivers of consent documentation. (AAHRPP Element II.3.G)

FDA regulations do not provide for waivers of informed consent except in emergency situations (See Section 7.9). Therefore, the information below applies only to non-FDA regulated research.

Under 45 CFR 46.116 I, and (d), IRBs have authority to alter or waive the requirement to obtain informed consent.

Under 45 CFR 46.116 (d), the IRB may approve a consent procedure that does not include, or that alters, some or all the elements of informed consent set forth above; or waive the requirements to obtain informed consent, provided the IRB finds and documents that:

- a. The research involves no more than minimal risk to the subjects;
- b. The waiver or alteration will not adversely affect the rights and welfare of the subjects;
- c. The research could not practicably be carried out without the waiver or alteration; and
- d. Whenever appropriate, the subjects must be provided with additional pertinent

information after participation.

In addition, under 45 CFR 46.116 I, the IRB may approve a consent procedure that does not include, or that alters, some or all of the elements of informed consent; or waive the requirements to obtain informed consent, provided the IRB finds and documents that:

- a. The research or demonstration project is to be conducted by or subject to the approval of state or local government officials and is designed to study, evaluate, or otherwise examine:
  1. Public benefit or service programs
  2. Procedures for obtaining benefits or services under those programs
  3. Possible changes in or alternatives to those programs or procedures
  4. Possible changes in methods or levels of payment for benefits or services under those programs
- b. The research could not practicably be carried out without the waiver or alteration.

In research involving deception, the investigator may, with protocol-specific justification, request an alteration of the consent process. The IRB may approve the research including the request to alter the requirement for informed consent if the investigator demonstrates that deception or incomplete disclosure is necessary and addresses concerns relating to participant protection; e.g., debriefing.

To request a waiver or alteration of the informed consent process the investigator must demonstrate that each of the criteria under Section 46.116I or (d) is met for the given protocol. The investigator is required to enter this information in the Protocol Application.

Other Federal Agencies: Additional requirements might apply if research is funded, supported by, or otherwise subject to certain federal agencies or agreements and could be subject to additional requirements to those in the Common Rule. (e.g., Department of Defense, Department of Justice, Bureau of Prisons). See Appendix A.

## **5.9 Waiver of Documentation of Informed Consent**

The IRB has and follows written policies and procedures for approving waivers or alterations of the consent process and waivers of consent documentation. (AAHRPP Element II.3.G)

As allowed by 45 CFR 46.117 I and 21 CFR 56.109 I, the IRB may waive the requirement to obtain written documentation of informed consent.

The IRB may waive the requirement for the investigator to obtain a signed consent form for some or all subjects if it finds either that the:

1. Only record linking the subject and the research would be the consent document and the principle risk would be potential harm resulting from a breach of confidentiality;
  - Subjects must be asked whether they want documentation linking them with the research, and their wishes must govern. (Example: domestic violence research where the primary risk is discovery by the abuser that the subject is talking to researchers.)
  - To waive written documentation of consent where the only record linking the participant and the research would be the consent document, the IRB must determine that the research was not FDA-regulated.
2. The research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.
  - Procedures such as non-sensitive surveys, questionnaires and interviews generally do not require written consent.

The investigator is required to demonstrate why the research meets the criteria for the waiver of written documentation and must enter this information in the Protocol Application. In cases in which the documentation requirement is waived, the IRB requires the investigator to provide in the application materials a written summary of the information to be communicated to the subject. The IRB will consider whether to require the investigator to provide subjects with a written statement regarding the research.

VA Research - The IRB will document the reason when it waives the requirement to obtain written documentation of the consent process.

Other Federal Agencies - Additional requirements might apply depending on the source of support/funding (e.g., Department of Defense, Department of Justice, Bureau of Prisons). See Appendix A.

## 6. VULNERABLE SUBJECTS IN RESEARCH

Standard II-4: The IRB or EC provides additional protections for individuals who are vulnerable to coercion or undue influence and participate in research.

The IRB or EC has and follows written policies and procedures for determining the risks to prospective participants who are vulnerable to coercion or undue influence and ensuring that additional protections are provided as required by applicable laws, regulations, codes, and guidance. (AAHRP Element II.4.A.)

### 6.1 Policy

The LSUHSC-S HRPP policies and procedures give special consideration to protecting privacy, confidentiality and the welfare of vulnerable participants such as children, prisoners, pregnant women, fetuses, and mentally disabled persons, handicapped persons, or economically or

educationally disadvantaged persons.

Prior to approving research, the LSUHSC-S IRB must ensure that all the regulatory requirements for the protection of vulnerable subjects are met and that appropriate additional protections for vulnerable subjects are in place. The research must include additional safeguards to protect the rights and welfare of these participants who are likely to be vulnerable to coercion or undue influence or have diminished decision-making capacity, as required for 45 CFR 46 Subpart B, Pregnant women, human fetuses, or neonates, Subpart C, Prisoners, Subpart D, Children; and additionally, for persons with Mental Disabilities or Economically, or Educationally disadvantaged persons.

### 6.1.1 Additional requirements

- Additional requirements may apply depending on the source of support/funding.
- Research funded by other federal agencies will be covered by the subparts as applicable.
- Under the LSUHSC-S FWA the subparts only apply to DHHS-funded research and research funded by other federal agencies that requires compliance with the subparts.
- FDA regulations include subpart D, which applies to all FDA-regulated research.

VA Research - Overton Brooks VA Medical Center does not allow for research involving children or prisoners.

## 6.2 Definitions

Children means under the following:

- 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.
- Louisiana Law: Child means a person under eighteen years of age who, prior to juvenile proceedings, has not been judicially emancipated under civil Code Article 385 or emancipated by marriage under Civil Code Articles 379 through 384.–The general rule is that a person may consent for his or her own medical care at the age of eighteen. Therefore, the LSUHSC-S IRB generally defines children as persons less than eighteen years of age. –Certain statutes and case law, however, provide minors with “majority” status in some circumstances, giving them the right to consent to their own medical care. For example: emancipated minors (Louisiana law enumerates certain categories of individuals who, although under the age of 18, have the right to make medical decisions on their own behalf, such as minors who are married, widowed or divorced, minors who are parents, etc.); or certain minors seeking care for drug addiction, sexually transmitted diseases, emotional disorders, or abortion or mental health treatment. Because Louisiana law does not specifically address consent of children with majority status to research, the LSUHSC-S IRB will review issues of consent related to enrollment of these children in research on a case-by-case basis. Minors may consent to the medical

treatment of their children.

Dead fetus is a fetus which does not exhibit a heartbeat, spontaneous respiratory activity, spontaneous movement of voluntary muscles, nor pulsation of the umbilical cord, if still attached.

Delivery means complete separation of the fetus from the woman by expulsion, extraction, or any other means.

Fetus is the product of conception from the time of implantation until delivery.

Guardian means an individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care. In Louisiana a Guardian of a minor means the duty and authority to act in the best interests of the minor, subject to residual parental rights and responsibilities, to make important decisions in matters having a permanent effect on the life and development of the minor and to be concerned with his or her general welfare.

For the purpose of subpart D, a guardian also means an individual who is authorized to consent on behalf of a child to participate in research.

LA. ChC 116(12.1)(a)(i)(b) Legal Guardianship means the duty and authority to make important decisions in matters having a permanent effect on the life and development of the child and the responsibility for the child's general welfare until he reaches the age of majority, subject to any residual rights possessed by the child's parents. It shall include but not necessarily be limited to: The authority to consent to marriage, to enlist in the armed forces of the United States, or to major medical, psychiatric, and surgical treatment, to represent the minor in legal actions, to make other decisions of substantial legal significance concerning the minor. The term "legal guardian" means the caretaker in such a relationship.

For research conducted in jurisdictions other than Louisiana, the research must comply with the laws regarding guardianship in all relevant jurisdictions. The Counsel for the HRPP will provide assistance with regard to the laws in other jurisdictions.

In vitro Fertilization is any fertilization of human ova, which occurs outside the body of a female, either through a mixture of donor human sperm and ova or by any other means.

Neonate means newborn.

Nonviable fetus is a fetus ex utero that, although living, is not able to survive to the point of independently maintaining heart and respiration. NOTE: In 45 CFR 46 Subpart B, this definition is used as the definition of a non-viable neonate.

Non-viable neonate means the same as a non-viable fetus.

Pregnancy is the period of time from confirmation of implantation (through any of the presumptive signs of pregnancy, such as missed menses, or by a medically acceptable pregnancy test), until expulsion or extraction of the fetus.

Prisoner is any individual involuntarily confined or detained in a penal institution. The term is intended to encompass individuals sentenced to such an institution under a criminal or civil statute, individuals detained in other facilities by virtue of statutes or commitment procedures that provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing.

An individual that is classified as a prisoner according to the above definition must not be enrolled in any research under the auspices of LSUHSC-S. In the event a study participant becomes a prisoner during their participation in a clinical trial the IRB must promptly be notified upon learning of the incarceration. The PI in consultation with the Chair or designee will determine the immediate plan for withdrawal and alternative care if necessary.

For Department of defense (DOD) research the term includes military personnel in either civilian or military custody.

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 Louisiana law.

Viable fetus is now termed a viable neonate.

Viable neonate means being able, after delivery, to survive to the point of being independently maintaining heart and respiration (given the benefit of available medical therapy).

### **6.3 Involvement of Vulnerable Populations**

The IRB takes steps to evaluate if additional safeguards are needed to protect the rights and welfare of all research participants. Special considerations are given to protecting the welfare of vulnerable populations that might be involved in research, including people who are educationally or financially disadvantaged, children, pregnant women, fetuses, neonates, prisoners, economically or educationally disadvantaged, adults who lack the ability to consent, students, employees, or homeless persons.

If the IRB reviews research that involves participants vulnerable to coercion or undue influence, the review process will include one or more individuals who are knowledgeable about or experienced in working with these populations. 45 CFR 46.107a. For example, the IRB will include one or more individuals who are knowledgeable about or experienced in working with children, prisoners, or adults with limited decision-making capacity, when reviewing

research that involves individuals from these populations.

The following protections which are based on the Common Rule Subparts B, C and D, apply to all LSUHSC-S research, as required regardless of funding. The policies and procedures below describe how the Subparts apply to DHHS-funded research.

45 CFR 46, Subparts B, C and D are designed to provide extra protections for vulnerable populations which also have additional requirements for IRB(s).

- Subpart B – Additional Protections for Pregnant Women, Human Fetuses and Neonates Involved in Research
- Subpart C – Additional Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects
- Subpart D – Additional Protections for Children Involved as Subjects in Research

DHHS-funded research that involves any of these populations must comply with the requirements of the relevant subparts. Research funded by other federal agencies will be covered by the subparts as applicable. FDA regulations include subpart D, which applies to all FDA-regulated research.

#### **6.4 Responsibilities**

1. The PI is responsible for identifying the potential for enrolling vulnerable subjects in the research proposal.
2. The PI is responsible for identifying patients who are at risk for impaired decisional making capacity as a consequence of psychiatric illness or any other illness, and who are being asked to participate in a research study with greater than minimal risk.
3. The IRB shall include representation, either as members or ad hoc consultants, individual(s) interested in or who have experience with the vulnerable populations involved in a research proposal.
4. The IRB reviews the PI's justifications for including vulnerable populations in the research to assess appropriateness of the research proposal.
5. The IRB must ensure that additional safeguards have been included in each study to protect the rights and welfare of vulnerable subjects as needed at the time of initial review of the research proposal.
6. The IRB shall continue to review research at intervals appropriate to the degree of risk and determine whether the proposed research continues to fulfill criteria for approval. Information reviewed should include the number of participants considered as members of specific vulnerable populations.
7. An IRB may determine that research that includes individuals who lack consent capacity may fulfill criteria for minimal risk and/or expedited review; the fact that a study includes individuals who lack consent capacity should not, in and of itself, mean that review by the convened IRB is required.
8. For studies that do not have or are not required to have a Data and Safety Monitoring Board (DSMB) or a Data Monitoring Committee and have entered vulnerable subjects,

the IRB needs to carefully review the data and safety monitoring plan.

9. The IRB must be knowledgeable about and experienced in working with populations who are vulnerable to coercion and undue influence. If the IRB requires additional qualification or expertise to review a protocol, it should obtain consultation.

## **6.5 Procedures**

### **6.5.1 Initial Review of Research Proposal**

1. The PI should identify the potential to enroll vulnerable subjects in the proposed research at initial review and provide the justification for their inclusion in the study.
2. The IRB evaluates the proposed plan for consent of the specific vulnerable populations involved. If the research involves adults unable to consent, the IRB evaluates the proposed plan for permission of legally authorized representatives.
3. The IRB evaluates and approves the proposed plan for the assent of participants.
4. The IRB evaluates the research to determine the need for additional protections and consider the use of a data and safety monitoring board or data monitoring committee as appropriate.
5. The PI should provide appropriate safeguards to protect the subject's rights and welfare, which may include the addition of an independent monitor. The independent monitor is a qualified individual not involved in the research study who will determine the subject's capacity to provide voluntary informed consent.
  - Examples of studies that warrant independent monitoring include those involving schizophrenic patients who will be exposed to placebo, and/or drug washout, and/or treatment with agents that are not approved by the Food and Drug Administration (FDA). Populations requiring independent monitoring would include individuals with schizophrenia, other psychotic disorders or conditions characterized by lack of reality testing (i.e., psychosis). Populations not usually requiring independent monitoring would include those with substance use disorders.
6. The IRB assess the adequacy of additional protections for vulnerable populations provided by the PI.

### **6.5.2 Continuing Review and Monitoring**

At the time of Continuing Review the PI should identify the number of vulnerable subjects enrolled and any that needed an independent monitor.

## **6.6 Research Involving Pregnant Women or Human Fetuses and Neonates (Subpart B)**

The following applies to all research regardless of funding source. Since, according to the LSUHSC-S FWA, Subpart B of 45 CFR 46 applies only to DHHS-funded research, the funding-source specific requirements are noted in the appropriate sections.

## **6.6.1 Research Involving Pregnant Women and Fetuses**

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### **6.6.1.1 Research Not Funded by DHHS**

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For research not funded by DHHS, no additional safeguards are required by the regulations and there are no restrictions on the involvement of pregnant women in research where the risk to the fetus is no more than minimal. However, it is the policy of the LSUHSC-S IRB to provide additional protections. The IRB does not allow pregnant women, fetuses, or non-viable neonates to be involved in research without specific approval of their involvement in the research (e.g., consultation with professionals in the field).

Pregnant women or fetuses may be involved in research not funded by DHHS involving more than minimal risk to fetuses if all the following conditions are met:

1. Where scientifically appropriate, pre-clinical studies, including studies on pregnant animals, and clinical studies, including studies on non-pregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses;
2. The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus;
3. Any risk is the least possible for achieving the objectives of the research;
4. If the research holds out the prospect of direct benefit to the pregnant woman, the prospect of a direct benefit both to the pregnant woman and the fetus, then the consent of the pregnant woman is obtained in accord with the provisions for informed consent;
5. If the research holds out the prospect of direct benefit solely to the fetus then the consent of the pregnant woman and the father is obtained in accord with the provisions for informed consent, except that the father's consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity or the pregnancy resulted from rape or incest.
6. Each individual providing consent under paragraph 4 or 5 of this section is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate;
7. For children who are pregnant, assent and permission are obtained in accord with the provisions of permission and assent;
8. No inducements, monetary or otherwise, will be offered to terminate a pregnancy;
9. Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy
10. Individuals engaged in the research will have no part in determining the viability of a neonate.

### **6.6.1.2 Research Funded by DHHS**

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For DHHS-funded research, 45 CFR Subpart B applies to all research involving pregnant

women. According to 45 CFR Subpart B, pregnant women or fetuses may be involved in research funded by DHHS if all the following conditions are met:

1. Where scientifically appropriate, pre-clinical studies, including studies on pregnant animals, and clinical studies, including studies on non-pregnant women, have been conducted and provide data for assessing potential risk to pregnant women and fetuses.
2. The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus or, if there is no such prospect of benefit, the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge which cannot be obtained by any other means;
3. Any risk is the least possible for achieving the objectives of the research;
4. If the research holds out the prospect of direct benefit to the pregnant woman, the prospect of a direct benefit both to the pregnant woman and the fetus, or no prospect of benefit for the woman nor the fetus when risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means, then the consent of the pregnant woman is obtained in accord with the provisions for informed consent.
5. If the research holds out the prospect of direct benefit solely to the fetus then the consent of the pregnant woman and the father is obtained in accord with the provisions for informed consent, except that the father's consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity or the pregnancy resulted from rape or incest.
6. Each individual providing consent under numbers 4 and 5 above is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate;
7. For children who are pregnant, assent and permission are obtained in accord with the provisions of permission and assent
8. No inducements, monetary or otherwise, will be offered to terminate a pregnancy
9. Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy
10. Individuals engaged in the research will have no part in determining the viability of a neonate.

#### VA Research

1. Research in which the subject is a fetus, in-utero or ex-utero (including human fetal tissue) must not be conducted by VA investigators while on official duty, or at VA facilities, or at approved off-site facilities.
2. For research involving the participation of pregnant women as research subjects, the IRB must:
  - (a) Determine that the proposed research meets the requirements outlined in VHA Handbook 1200.05;
  - (b) Determine that adequate provision has been made to monitor the risks to the subject and the fetus; and

- (c) Determine that adequate consideration has been given to the manner in which potential subjects are going to be selected, and that adequate provision has been made to monitor the actual informed consent process such as:
  - i.* Overseeing the actual process by which individual consents required by this appendix are secured either by approving enrollment of each individual into the activity, or by verifying, perhaps through sampling, that approved procedures for enrollment of individuals into the activity are being followed,
  - ii.* Monitoring the progress of the activity and intervening, as necessary, through such steps as visits to the activity site and continuing evaluation to determine if any unanticipated risks have arisen. These determinations must be documented in the IRB minutes.
- 3. General limitations
  - (a) Activities related to pregnant women must not be undertaken unless:
    - 1. Except if appropriate studies on animals and non-pregnant individuals have been completed, and data for assessing potential risks to pregnant women and fetuses is provided.
    - 2. The purpose of the activity is to meet the health needs of the mother or the particular fetus, the risk to the fetus is minimal, and, in all cases, is the least possible risk for achieving the objectives of the activity.
    - 3. Individuals engaged in the activity will have no part in:
      - i.* Any decisions as to the timing, method, and procedures used to terminate the pregnancy; or
      - ii.* Determining the viability of the fetus at the termination of the pregnancy.
      - iii.* Introducing any procedural changes, for research purposes, into the procedures for terminating the pregnancy.
  - (b) No inducements, monetary or otherwise, may be offered to terminate pregnancy or purposes of research activity.
  - (c) No pregnant woman may be involved as a subject in a research activity unless:
    - 1. The purpose of the activity is to meet the health needs of the mother, and the fetus will be placed at risk only to the minimum extent necessary to meet such needs; or
    - 2. The risk to the fetus is minimal.
    - 3. The mother and father are legally competent and have given their informed consent after having been fully informed regarding possible impact on the fetus, except that the father's informed consent need not be secured if:
      - i.* The purpose of the activity is to meet the health needs of the mother,
      - ii.* His identity or whereabouts cannot reasonably be ascertained,
      - iii.* He is not reasonably available, or
      - iv.* The pregnancy resulted from rape.

VA-sponsored research involving pregnant women as subjects is not approved unless the following additional criteria are met:

- Adequate consideration has been given to the manner in which potential subjects are

going to be selected.

- Adequate provision has been made to monitor the actual consent process by procedures such as:
  1. Overseeing the process by which the consent of individuals is obtained either by approving enrollment of each individual or verifying, perhaps through sampling, that approved procedures for enrollment of individuals into the activity are being verified.
  2. Monitoring the progress of the activity and intervening, as necessary, through such steps as visits to the activity site and continuing evaluation to determine if any unanticipated risks have arisen.

### **6.6.2 Research involving neonates**

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Neonates of uncertain viability and nonviable neonates may be involved in research if the IRB determines that all the following conditions are met:

1. Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates.
2. Each individual that's providing consent is fully informed regarding the reasonably foreseeable impact of the research on the neonate.
3. Individuals engaged in the research will have no part in determining the viability of a neonate.
4. The requirements of Neonates of Uncertain Viability or Nonviable Neonates (see below in this section) have been met as applicable.

#### **6.6.2.1 Neonates of Uncertain Viability**

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Until it has been ascertained whether or not a neonate is viable, a neonate may not be involved in research covered by this subpart unless the IRB determines the following additional conditions have been met:

1. The research holds out the prospect of enhancing the probability of survival of the neonate to the point of viability, and any risk is the least possible for achieving that objective;
2. The purpose of the research is the development of important biomedical knowledge which cannot be obtained by other means and there will be no added risk to the neonate resulting from the research
3. The legally effective informed consent of either parent of the neonate or, if neither parent is able to consent because of unavailability, incompetence, or temporary incapacity, the legally effective informed consent of either parent's legally authorized representative is obtained in accord with the provisions of permission and assent, except that the consent of the father or his legally authorized representative need not be obtained if the pregnancy resulted from rape or incest.

#### **6.6.2.2 Nonviable Neonates**

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After delivery, nonviable neonates may not be involved in research covered by this subpart unless all the IRB determines that all the following additional conditions are met:

1. Vital functions of the neonate will not be artificially maintained;
2. The research will not terminate the heartbeat or respiration of the neonate;
3. There will be no added risk to the neonate resulting from the research;
4. The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means;
5. The legally effective informed consent of both parents of the neonate is obtained in accord with the provisions of permission and assent, except that the waiver and alteration of the provisions of permission and assent do not apply
6. However, if either parent is unable to consent because of unavailability, incompetence, or temporary incapacity, the informed consent of one parent of a nonviable neonate will suffice to meet the requirements of this paragraph, except that the consent of the father need not be obtained if the pregnancy resulted from rape or incest. The consent of a legally authorized representative of either or both parents of a nonviable neonate will not suffice to meet the requirements of this paragraph.

#### **6.6.2.3 Viable Neonates**

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A neonate, after delivery, that has been determined to be viable may be included in research only to the extent permitted by and in accord with the requirements of IRB Review Process and Research Involving Children.

#### **6.6.2.4 Research Involving, After Delivery, the Placenta, the Dead Fetus or Fetal Material**

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Research involving, after delivery, the placenta; the dead fetus; macerated fetal material; or cells, tissue, or organs excised from a dead fetus, must be conducted only in accord with any applicable Federal, State, or local laws and regulations regarding such activities.

If information associated with material described above in this section is recorded for research purposes in a manner that living individuals can be identified, directly or through identifiers linked to those individuals, those individuals are research subjects and all pertinent sections of this manual are applicable.

#### **6.6.2.5 Research Not Funded by DHHS**

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If the IRB finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses or neonates; and the research is not approvable under the above provisions, then the IRB will consult with a panel of experts in pertinent disciplines (for example: science, medicine, ethics, law). Based on the recommendation of the panel, the IRB

may approve the research based on either:

1. That the research in fact satisfies the conditions of Section 6.5, as applicable; or
2. The following:
  - a. The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses or neonates;
  - b. The research will be conducted in accordance with sound ethical principles;
  - c. Informed consent will be obtained in accordance with the provisions for informed consent and other applicable sections of this manual.

#### **6.6.2.6 Research Funded by DHHS**

DHHS-funded research that falls in this category must be approved by the Secretary of Health and Human Services. If the IRB finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses or neonates; and the research is not approvable under the above provisions, then the research will be sent to OHRP for DHHS review.

#### **6.7 Research Involving Prisoners (Subpart C)**

Prisoner is defined as any individual involuntarily confined or detained in a penal institution. This includes individuals sentenced to such an institution under a criminal or civil statute, individuals detained in other facilities by virtue of statutes or commitment procedures that provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing.

An individual that is classified as a prisoner according to the above definition must not be enrolled in any research under the auspices of LSUHSC-S.

If a human subject involved in ongoing research becomes a prisoner during the course of the study, and the relevant research proposal was not reviewed and approved by the IRB in accordance with the requirements for research involving prisoners under subpart C of 45 CFR 46, the investigator must promptly notify the IRB. All research interactions and interventions with, and obtaining identifiable private information about, the now- incarcerated prisoner-subject must be suspended immediately, except as noted below. Upon receipt of the investigator's report that a previously enrolled research subject has become a prisoner, if the investigator wishes to have the prisoner subject continue to participate in the research, the IRB must promptly re-review the proposal in accordance with the requirements of subpart C, and the institution(s) engaged in the research involving the prisoner subject must send a certification to OHRP and wait for a letter of authorization in reply. Otherwise, the prisoner subject must stop participating in the research except as noted below.

OHRP allows one important exception to the requirement that all research interactions or interventions with, and obtaining identifiable private information about, the now-incarcerated prisoner-subject must cease until the regulatory requirements for research involving prisoners are met. In special circumstances in which the investigator asserts that it is in the best interests of the subject to remain in the research study while incarcerated, the subject may continue to participate in the research until the requirements of subpart C are satisfied. The investigator must promptly notify the IRB of this occurrence, so that the IRB can re-review the study. Note that in these circumstances, some of the findings required by 45 CFR 46.305(a) may not be applicable; for example, the finding required under 45 CFR 46.305(a)(4) regarding the selection of subjects within the prison may not be applicable, if the subject was recruited outside of an incarcerated context. The IRB should document findings of non-applicability accordingly.

### **6.7.1 Research Involving Prisoners**

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Prisoner research is not routinely conducted at LSUHSC-S; however, in the event prisoner research would be conducted, the IRB will address whether prisoners have any real choice in participation in research, or whether incarceration prohibits free choice.

The following applies to all research involving prisoners, regardless of funding source. The requirements in this section are consistent with Subpart C of 45 CFR 46, which applies to DHHS-funded research.

#### **6.7.1.1 Applicability**

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Even though the IRB may approve a research protocol involving prisoners as subjects according to this policy, investigators are still subject to the Administrative Regulations of the Louisiana Department of Corrections and any other applicable State or local law. [45 CFR 46.301] There are no additional limitations on research in accordance with Louisiana State law.

#### **6.7.1.2 Subpart C: Minimal Risk**

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The definition of minimal risk in the Subpart C is different than in the rest of the federal regulations. According to 45 CFR 46.303, minimal risk is 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.

### **6.7.2 Composition of the IRB**

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In addition to satisfying the general requirements detailed in the IRB section of this manual, when reviewing research involving prisoners, the IRB must also meet the following requirements [45 CFR 46.304]:

- A majority of the IRB (exclusive of prisoner members) must have no association with the

prison(s) involved, apart from their membership on the IRB.

- At least one member of the IRB must be a prisoner, or a prisoner representative with appropriate background and experience to serve in that capacity.

### 6.7.3 Additional Duties of the IRB

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Do any of the Exemption Categories for research apply to prisoner research? None of the exemption categories in the HHS regulations for research involving human subjects at 45 CFR 46.101 applies to research involving prisoners.

Does OHRP allow for the Expedited Review of Research? Research involving prisoners may be approved under expedited review; however, because of the vulnerability of prisoners, OHRP recommends that all research involving prisoners be reviewed by the convened IRB. Therefore it is the policy of this institution for all research involving prisoners to be reviewed by the convened IRB. Review of modifications and continuing review must use the same procedures as the initial review.

In addition, the IRB will review research involving prisoners and approve such research only if it finds that:

1. The research falls into one of the following permitted categories [45 CFR 46.306]:
  - a. study of the possible causes, effects, and processes of incarceration, and of criminal behavior, provided that the study presents no more than minimal risk and no inconvenience to the subjects
  - b. study of prisons as institutional structures or of prisoners as incarcerated persons, provided that the study presents no more than minimal risk and no inconvenience to the subjects
  - c. research on conditions particularly affecting prisoners as a class (for example, research on social and psychological problems such as alcoholism, drug addiction, and sexual assaults
  - d. research on practices, both innovative and accepted, which have the intent and reasonable probability of improving the health or well-being of the subject.
2. Any possible advantages accruing to the prisoner through his or her participation in the research, when compared to the general living conditions, medical care, quality of food, amenities and opportunity for earnings in the prison, are not of such a magnitude that his or her ability to weigh the risks of the research against the value of such advantages in the limited choice environment of the prison is impaired;
3. The risks involved in the research are commensurate with risks that would be accepted by non-prisoner volunteers;
4. Procedures for the selection of subjects within the prison are fair to all prisoners and immune from arbitrary intervention by prison authorities or prisoners. Unless the principal investigator provides to the IRB justification in writing for following some other procedures, control subjects must be selected randomly from the group of

available prisoners who meet the characteristics needed for that particular research project

5. The information is presented in language which is understandable to the subject population
6. Adequate assurance exists that parole board will not take into account a prisoner's participation in the research in making decisions regarding parole, and each prisoner is clearly informed in advance that participation in the research will have no effect on his or her parole
7. Where the IRB finds there may be a need for follow-up examination or care of subjects after the end of their participation, adequate provision has been made for such examination or care, taking into account the varying lengths of individual prisoners' sentences, and for informing subjects of this fact.

VA research involving Prisoners - Overton Brooks VAMC does not allow for research involving prisoners. Therefore, research involving prisoners must not be conducted by VA investigators while on official duty or at VA or approved off-site facilities.

## **6.8 Research Involving Children**

Children: Under the regulations, children are 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.

According to Louisiana State Law, minors are persons under the age of eighteen. The general rule is that a person may consent for his or her own medical care at the age of eighteen. Therefore, the LSUHSC-S IRB generally defines children as persons less than eighteen years of age.

The following applies to all research involving children, regardless of funding source. The requirements in this section are consistent with Subpart D of 45 CFR 46, which applies to DHHS-funded research and Subpart D of 21 CFR 50, which applies to FDA-regulated research involving children.

See guidance: FDA/OHRP for additional safeguards and protections for inclusion of children in clinical investigations and research.

### **6.8.1 Allowable Categories**

Research on children must be reviewed and categorized by the IRB into one of the following groups:

1. Research not involving physical or emotional risk greater than that ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests (i.e., minimal risk).
  - a. Adequate provisions are made for soliciting the assent of children and the

- permission of their parents or guardians as set forth in Section 6.8.2.
2. Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects.
    - a. The risk is justified by the anticipated benefit to the subjects; and
    - b. The relation of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by available alternative approaches; and
    - c. Adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians as set forth in Section 6.8.2.
  3. Research involving greater than minimal risk and no reasonable prospect of direct benefit to the individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition.
    - a. The risk represents a minor increase over minimal risk;
    - b. The intervention or procedure presents experiences to subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations; and
    - c. The intervention or procedure is likely to yield generalizable knowledge about the subjects' disorder or condition which is of vital importance to the understanding of amelioration of the subjects' disorder or condition; and
    - d. Adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians as set forth in section 6.8.2.
  4. Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate serious problems affecting the health or welfare of children.
    - a. Federally-funded research in this category must be approved by the Secretary of Health and Human Services, and requires consent of either both parents, or legal guardian.
    - b. FDA-regulated research in this category must be approved by the Commissioner of Food and Drugs.
    - c. For non-federally-funded research, IRB will consult with a panel of experts in pertinent disciplines (for example: science, medicine, ethics, and law). Based on the recommendation of the panel, the IRB may approve the research based on either:
      1. That the research in fact satisfies the conditions of the previous categories, as applicable;
      2. The following:
        - i. The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children;
        - ii. The research will be conducted in accord with sound ethical principles;
        - iii. Informed consent will be obtained in accord with the provisions for informed consent and other applicable sections of this manual.
    - d. Adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians as set forth in 6.8.2.

## 6.8.2 Parental Permission and Assent

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Parental Permission: The IRB must determine that adequate provisions have been made for soliciting the permission of each child's parent or guardian. Parents or guardians must be provided with the basic elements of consent and any additional elements the IRB deems necessary, as described in Section 5.5.

The IRB may find that the permission of one parent is sufficient for research to be conducted under Categories 1 & 2 above. The IRB determination of whether consent must be obtained from one or both parents will be documented in the consent checklist when a protocol receives expedited review, and in meeting minutes when reviewed by the convened committee.

Consent from both parents is required for research to be conducted under Categories 3 & 4 above unless

1. One parent is deceased, unknown, incompetent, or not reasonably available
2. When only one parent has legal responsibility for the care and custody of the child

For research not covered by the FDA regulations, the IRB may waive the requirement for obtaining consent from a parent or legal guardian if:

1. The research meets the provisions for waiver in Section 5.8 or
2. If the IRB determines that the research protocol is designed for conditions or a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects (for example, neglected or abused children) provided an appropriate mechanism for protecting the children who will participate as subjects in the research is substituted, and that the waiver is not inconsistent with Federal State, or local law. The choice of an appropriate mechanism would depend upon the nature and purpose of the activities described in the protocol, the risk and anticipated benefit to the research subjects, and their age, maturity, status, and condition.

Investigators are responsible for reviewing documentation of the legal authority of each parent/guardian (for example, verifying the identity of the legal custodial parent or guardian where the parents are divorced). The research purpose, research context, and/or subject population may warrant special attention to the verification of the authority of parent(s)/guardian(s).

Where the research purpose, research context, and/or subject population warrant the verification of the legal authority of the parent/guardian, documentation of the parent's/guardian's authority will be reviewed by the investigator and/or copies collected from each parent/guardian (including, but not limited to court orders or guardianship documents).

Investigators are responsible for determining any changes in the legally authorized representative status for children participating in research for all cases with vulnerable

populations.

The investigator must be particularly attentive with wards, since the legally authorized representative may change if the ward is adopted or the parents regain guardianship. The investigator should periodically assess with an adult accompanying the child if there has been a change in guardianship or any other method to ensure prompt notification of a change in guardianship status. Investigators have an ongoing responsibility to immediately notify the IRB when an enrolled subject become a ward of the state while the research is active.

Parental permission may not be waived for research covered by the FDA regulations. Permission from parents or legal guardians must be documented in accordance with and to the extent required by Section 5.

### 6.8.3 Assent from Children

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Because “assent” means a child’s affirmative agreement to participate in research, the child must actively show his or her willingness to participate in the research, rather than just complying with directions to participate and not resisting in any way. When judging whether children are capable of assent, the IRB is charged with taking into account the ages, maturity, and psychological state of the children involved.

For research activities involving adolescents whose capacity to understand resembles that of adults, the assent procedure should likewise include information similar to what would be provided for informed consent by adults or for parental permission. For children, whose age and maturity level limits their ability to fully comprehend the nature of the research activity but who are still capable of being consulted about participation in research, it may be appropriate to focus on conveying an accurate picture of what the actual experience of participation in research is likely to be (for example, what the experience will be, how long it will take, whether it might involve any pain or discomfort). The assent procedure should reflect a reasonable effort to enable the child to understand, to the degree they are capable, what their participation in research would involve.

The IRB presumes that children ages 7 and older should be given an opportunity to provide assent. Generally, oral assent using a script should be obtained from children 7 – 11 years of age. Written assent using a written document for the children to sign may be sought for older children.

At times, there may be inconsistency between parent permission and child assent. Usually a “no” from the child overrides a “yes” from a parent, but a child typically cannot decide to be in research over the objections of a parent. Obviously, there are individual exceptions to these guidelines (such as when the use of an experimental treatment for a life-threatening disease is being considered). The general idea, however, is that children should not be forced to be research subjects, even when their parents’ consent to it.

If the IRB determines that the capability of some or all the children is so limited that they cannot reasonably be consulted or that the intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the children and is available only in the context of the research, the assent of the children is not a necessary condition for proceeding with the research.

Even when the IRB determines that the subjects are capable of assenting, the IRB may still waive the assent requirement under circumstances detailed in the Waiver of Informed Consent section of this manual.

#### **6.8.4 The Assent Form**

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When the IRB determines that assent is required, it shall also determine whether and how assent must be documented.

Researchers should try to draft a form that is age appropriate and study specific, taking into account the typical child's experience and level of understanding, and composing a document that treats the child respectfully and conveys the essential information about the study. The assent form should:

1. tell why the research is being conducted
2. describe what will happen and for how long or how often
3. say it's up to the child to participate and that it's okay to say no
4. explain if it will hurt and if so for how long and how often
5. say what the child's other choices are
6. describe any good things that might happen
7. say whether there is any compensation for participating
8. ask for questions

Researchers and research staff shall provide all the disclosures and follow the requirements pertaining to consent covered by ICH-GCP (E6). See website:

<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm073122.pdf>

For younger children, the document should be limited to one page if possible. Illustrations might be helpful, and larger type makes a form easier for young children to read. Studies involving older children or adolescents should include more information and may use more complex language.

#### **6.8.5 Children who are Wards**

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Children who are wards of the State or any other agency, institution, or entity can be included in research involving greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition, only if such research is:

1. related to their status as wards
2. conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards

If the research meets the condition(s) above, an advocate must be appointed for each child who is a ward (one individual may serve as advocate for more than one child), in addition to any other individual acting on behalf of the child as legal guardian or in loco parentis.

The advocate must be an individual who has the background and experience to act in, and agrees to act in the best interests of the child for the duration of the child's participation in the research. In any case the appointment of the ward should be made by a party or individual with no interest in or affiliation with the research being conducted. The IRB should review and approve the process for appointing advocates. In some cases, it might be a member of the IRB or ombudsman's office, or a case manager, social worker, or counselor responsible for the child's rights and welfare. The child's Legally Authorized Representative may serve as the advocate.

VA Research Involving Children - Overton Brooks VAMC does not allow for research involving children. Therefore, research involving children must not be conducted by VA investigators while on official duty or at VA or approved off-site facilities.

## **6.9 Research Involving Persons with Impaired Decision Making Capacity**

The IRB or EC has and follows written policies and procedures requiring appropriate protections for prospective participants who cannot give consent or whose decision-making capacity is in question. (AAHRPP Element II.4.B.)

Individuals with impaired decision making capacity are those with diminished capacity for judgment, impaired capacity to consent, and impaired reasoning due to a psychiatric, organic, developmental, or other disorder that affect cognitive or emotional functions. Other individuals may be considered persons with impaired decision making capacity or have limited decision making ability, because they are under the influence of or dependent on drugs or alcohol, suffering from degenerative diseases affecting the brain, are terminally ill, or have severely disabling physical handicaps. The IRB reviews the risk-benefit analysis including the possibilities of coercion and undue influence, and must determine whether such participants should be recruited and whether support mechanisms, such as surrogate consent, or obtaining consent from a legally authorized representative are appropriate.

This policy is designed to protect human subject from exploitation and harm and, at the same time, make it possible to conduct essential research on problems that are unique to persons who are incompetent, or who have an impaired decision-making capacity.

When following VA Regulations, Research involving adults who are unable to consent may

occur only when the IRB determines the proposed research:

- Does not present greater than minimal risk, or
- Presents a greater probability of direct benefit to the participant than harm to the participant, or
- Poses greater than minimal risk and no prospect of direct benefit to individual participants, but is likely to yield generalizable knowledge about the participant's disorder or condition that is of vital importance to understand or amelioration of the participant's disorder or condition.
- In addition, the IRB determines the research cannot be performed solely on adults who can consent and the focus of the research is the disorder leading to the lack of decision-making capacity, or
- Where the subject of the research is not directly related to the participant's lack of decision-making capacity, the researcher has presented a compelling reason for including adults unable to consent.

#### **6.9.1 Surrogate Consent**

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Surrogate consent may be obtained from a court appointed guardian of the person or a health care agent appointed by the person in a Durable Power of Attorney for Health Care (DPAHC). Surrogate Consent is consent obtained from a legally authorized representative on behalf of a participant determined to lack decision-making capacity. For example, a subject might have designated an individual to provide consent regarding health care decisions through a durable power of attorney and have specified that the individual also has the power to make health care decisions on entry into research.

#### **6.9.2 Legally authorized representative**

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The IRB or EC has and follows written policies and procedures requiring appropriate protections for prospective participants who cannot give consent or whose decision-making capacity is in question. (AAHRPP Element II.4.B.)

When research is conducted in Louisiana the following individuals are Legally Authorized Representatives:

- A legally authorized representative is an individual or body authorized under Louisiana law to provide permission on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research. For the purposes of this policy, a legally authorized representative includes not only a person appointed as a health care agent under a Durable Power of Attorney for Health Care (DPAHC), a court appointed guardian, tutor or curator of the person, but also next-of-kin in the following order of priority: spouse, not judicially separated; adult child (18 years of age or older); any parent, whether adult or minor, for his/her child; adult sibling (18 years of age or

- older); grandparent, or adult grandchild (18 years of age or older).
  - o LA. C.E. 510(5) Representative of a patient is any person who makes or receives a confidential communication for the purpose of effectuating diagnosis or treatment of a patient.
  - o LA. R.S. 44:17(A) (4) Representative of a patient means a person who is a parent, tutor, curator, spouse, trustee, attorney, or other legal agent of the patient and who is authorized, by and on behalf of the patient, to exercise any of the patient's rights or privileges.
  - o For research outside of Louisiana a determination of who is a legally authorized representative is to be made with consultation from legal counsel.
- When research is conducted in Louisiana, children are individuals under eighteen years of age who, prior to juvenile proceedings, have not been judicially emancipated under Civil Code Article 385 or emancipated by marriage under Civil Code Articles 379 through 384.
  - o For research outside of Louisiana a determination of who is a child is to be made in consultation with Legal Counsel.
  - o Unless the IRB has waived the requirement to obtain consent, when research involves children consent may only be obtained from biologic or adoptive parents or an individual legally authorized to consent on behalf of the child to general medical care. Before obtaining permission from an individual who is not a parent, consult with legal counsel.

When research is conducted in Louisiana the following individuals are Guardians:

- LA ChC 116(12.1)(a)(i)(b) Legal Guardianship means the duty and authority to make important decisions in matters having a permanent effect on the life and development of the child and the responsibility for the child's general welfare until he reaches the age of majority, subject to any residual rights possessed by the child's parents. It shall include but not necessarily be limited to: The authority to consent to marriage, to enlist in the armed forces of the United States, or to major medical, psychiatric, and surgical treatment, to represent the minor in legal actions, to make other decisions of substantial legal significance concerning the minor. The term legal guardian means the caretaker in such a relationship.

### **6.9.3 Approval of Research Involving Persons with Impaired Decision-Making Capability**

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Research involving persons with impaired decision-making capability may only be approved when the following conditions apply:

1. Only incompetent persons or persons with impaired decision making capacity are suitable as research subjects. Competent persons are not suitable for the proposed research. The investigator must demonstrate to the IRB that there is a compelling reason to include

incompetent individuals or persons with impaired decision-making capacity as subjects. Incompetent persons or persons with impaired decision-making capacity must not be subjects in research simply because they are readily available.

2. The proposed research entails no significant risks, tangible or intangible, or if the research presents some probability of harm, there must be at least a greater probability of direct benefit to the participant. Incompetent people or persons with impaired decision-making capacity are not to be subjects of research that imposes a risk of injury, unless that research is intended to benefit that subject and the probability of benefit is greater than the probability of harm.

3. Procedures have been devised to ensure that participant's representatives are well informed regarding their roles and obligations to protect incompetent subjects or persons with impaired decision making capacity. Health care agents (appointed under Power of Attorney for Health Care (PAHC)) and next-of-kin, or guardians, must be given descriptions of both proposed research studies and the obligations of the person's representatives. They must be told that their obligation is to try to determine what the subject would do if competent, or if the subject's wishes cannot be determined, what they think is in the incompetent person's best interest.

In accordance with ICH-GCP (E6) guidelines, when adults are unable to consent, policies and procedures have the IRB determine the following:

- A non-therapeutic clinical trial (i.e. a trial in which there is no anticipated direct clinical benefit to the subject) should be conducted in subjects who personally give consent and who sign and date the written consent document.
- Non-therapeutic clinical trials may be conducted in subjects with consent of a legally acceptable representative provided the following conditions are fulfilled:
  - The objectives of the clinical cannot be met by means of a trial in subjects who can personally give consent.
  - The negative impact on the subject's wellbeing is minimized and low.
  - The clinical trial is not prohibited by law.
  - The opinion of the IRB is expressly sought on the inclusion of such subjects, and the written opinion covers this aspect.
  - Such trials, unless an exception is justified, should be conducted in patients having a disease or condition for which the investigational product is intended. Subjects in these trials should be particularly closely monitored and should be withdrawn if they appear to be unduly distressed.

#### **6.9.4 IRB Members**

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The IRB committee must include at least one member who is an expert in the area of the research. Consideration may be given to adding another member who is a member of the population, a family member of such a person or a representative of an advocacy group for

that population. The IRB may utilize ad hoc members as necessary to ensure appropriate scientific expertise.

#### **6.9.5 Determination of Decision-Making Capacity**

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The decision-making capacity of a potential research subject should be evaluated when there are reasons to believe that the subject may not be capable of making voluntary and informed decisions about research participation. The investigator and research staff must have adequate procedures in place for assessing and ensuring subjects' decisional capacity, understanding, and consent capacity or to give assent. The IRB will evaluate whether the proposed plan to assess capacity to consent is adequate. For research protocols that involve subjects with mental disorders that may affect decision-making capacity, the IRB may determine that capacity assessments are necessary, unless the investigator can justify why such assessments would be unnecessary for a particular group.

For research that poses greater than minimal risk, the IRB may require investigators to use independent and qualified professionals to assess whether potential subjects have the capacity to give voluntary, informed consent. Even in research involving only minimal risk, the IRB may require that the study include a capacity assessment if there are reasons to believe that potential subjects' capacity may be impaired. It is not necessary to require a formal capacity assessment by an independent professional for all potential research subjects with mental disorders.

For research protocols involving subjects who have fluctuating or limited decision making capacity the IRB may ensure that investigators establish and maintain ongoing communication with involved caregivers. Periodic re-consent should be considered in some cases. A re-consenting process with surrogate consent may be necessary. Third party consent monitors may be used during the recruitment and consenting process, or waiting periods may be required to allow more time for the subject to consider the information that has been presented.

It is often possible for investigators and others to enable persons with some decisional impairment to make voluntary and informed decisions to consent or refuse participation in research. Potential measures include repetitive teaching, group sessions, audiovisual presentations, and oral or written recall tests. Other measures might include follow-up questions to assess subject understanding, videotaping or audio-taping of consent interviews, second opinions, use of independent consent observers, interpreter for hearing-impaired subjects, allowing a waiting period before enrollment, or involvement of a trusted family member or friend in the disclosure and decision making process.

Although incompetent to provide informed consent, some persons may resist participating in a research protocol approved by their representatives. Under no circumstances may subjects be forced or coerced to participate.

In the event research participants become incompetent or impaired in decision making capacity after enrollment, the PI is responsible for notifying the IRB and HRPP office. The PI is responsible for developing a monitoring plan which follows the guidelines outlined above for incompetent and impaired decision making research participants.

VA Research - The following applies for mentally disabled person or those persons with impaired decision making capacity as a vulnerable population in research:

- A. Research involving subjects who are mentally ill or subjects with impaired decision-making capacity warrants special attention. Research involving these populations frequently presents greater than minimal risk; may not offer direct medical benefit to the subject; and may include a research design that calls for washout, placebo, or symptom provocation. In addition, these populations are considered to be vulnerable to coercion.
- B. IRB membership must include at least one member who is an expert in the area of research. Consideration may be given to adding another member who is a member of the population, a family member of such person or a representative of an advocacy group for that population. The IRB may utilize ad hoc members as necessary to ensure appropriate expertise.
- C. Research involving persons with impaired decision-making capability may only be approved when the following conditions apply:
  1. Only incompetent persons or persons with impaired decision making capacity are suitable as research subjects. Competent persons are not suitable for the proposed research. The investigators must demonstrate to the IRB that there is a compelling reason to include incompetent individuals or persons with impaired decision-making capacity as subjects. Incompetent persons or persons with impaired decision making capacity must not be subjects in research simply because they are readily available.
  2. The proposed research entails no significant risks, tangible or intangible, or if the research presents some probability of harm, there must be at least a greater probability of direct benefit to the participant. Incompetent people or persons with impaired decision-making capacity are not to be subjects of research that impose a risk of injury, unless that research is intended to benefit that subject and the probability of benefit is greater than the probability of harm.
  3. Procedures have been devised to ensure that participant's representatives are well informed regarding their roles and obligations to protect incompetent subjects or persons with impaired decision making capacity. Health care agents (appointed under Durable Power of Attorney for Health Care (DPAHC) and next-of-kin, or guardians, must be given descriptions of both proposed research studies and the obligation is to try to determine what the subject would do if competent, or if the subject's wishes cannot be determined, what they think is in the incompetent person's best interest.
- D. The IRB must make a determination in writing for the inclusion of incompetent subjects

or subjects with impaired decision-making capacity in research projects on the basis of informed consent from authorized representatives as defined in VA policy.

- E. Both investigators and IRB members must be aware that for some subjects, their decision-making capacity may fluctuate. For subjects with fluctuating decision making capacity or those with decreasing capacity to give consent, a re-consenting process with surrogate consent may be necessary.
- F. The IRB determines when reviewing VA research that involves adults who are not able to consent that:
  - 1. The investigator explains the proposed research to the prospective subjects when feasible even when the subject's legally authorized representative gives consent.
  - 2. The practitioner explains the proposed research to the prospective subjects when feasible.
  - 3. There are appropriate procedures for respecting dissent. Although incompetent to provide informed consent, some persons may resist participating in a research protocol approved by their representatives. Under no circumstances may subjects be forced or coerced to participate in a research study.

#### **6.9.6 Determining Capacity to Consent**

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Decisional capacity in the research context has been interpreted by the American Psychiatric Association as requiring:

- Ability to confirm a choice
- Ability to understand relevant information
- Ability to appreciate the situation and its likely consequences
- Ability to manipulate information rationally

Under Louisiana law, to have capacity to consent, the person must be able to comprehend generally the nature and consequences of his decision.

A range of professionals and methods may be utilized to assess capacity. In general, the consent assessor should be a researcher or consultant familiar with dementias and qualified to assess and monitor capacity and consent in such subjects on an ongoing basis. The IRB will consider the qualifications of the proposed individual(s) and whether he or she is sufficiently independent of the research team and/or institution.

The majority of studies conducted at the LSUHSC-S only allow enrolling subjects who have the capacity to consent. For studies that have been approved for enrolling vulnerable populations who may lack capacity to consent, there must be someone who is able to assess capacity of each potential subject to consent. The PI may determine after appropriate medical evaluation that the prospective research subject lacks decision-making capacity and is unlikely to regain it within a reasonable period of time. Additionally, if the reason for lack of capacity is because of mental illness then a psychiatrist or licensed psychologist must confirm this judgment and document in the individual's medical record in a signed and dated progress note.

A person who has been determined to lack capacity to consent to participate in a research study must be notified of that determination before permission may be sought from his or her legally authorized representative to enroll that person in the study. If permission is given to enroll such a person in the study, the potential subject must then be notified. If the person objects to participating, this objection should be heeded.

VA Research - Determination that a subject is incompetent or has an impaired decision-making capacity will be made by a legal determination or a determination by the practitioner, in consultation with the Chief of Service, or the Chief of Staff after appropriate medical evaluation that the prospective subject lacks decision-making capacity and is unlikely to regain it within a reasonable period of time. VA criteria is an individual is presumed to have decision-making capacity unless any one or more of the following apply: (a) it has been documented by a qualified practitioner in the individual's medical record in assigned and dated progress note that the individual lacks capacity to make the decision to participate in the proposed study (NOTE: The qualified practitioner may be a member of the research team); or (b) the individual has been ruled incompetent by a court of law.

If there is any question as to whether a potential adult subject has decision-making capacity, and there is no documentation in the medical record that the individual lacks decision making capacity, and the individual has not been ruled incompetent by a court of law, the investigator must consult with a qualified practitioner (who may be a member of the research team) about the individual's decision-making capacity before proceeding with the informed consent process. Individuals, who because of a known condition, are at high risk for temporary (e.g., head trauma) or fluctuating (e.g., schizophrenia) lack of decision-making capacity must be evaluated by a qualified practitioner (who may be a member of the research team), to determine the individual's ability to provide informed consent. This evaluation must be performed as described in the IRB-approved protocol. If the individual is deemed to lack decision-making capacity at the time of their participation in the study, a legally authorized representative must provide informed consent. If the subject regains decision-making capacity, the investigator or approved designee must repeat the informed consent process with the subject, and obtain the subject's permission to continue with the study

## **6.10 Other Potentially Vulnerable Participants**

The context of the research is an important consideration for the IRB when reviewing research that involves other potentially vulnerable participants such as research involving homeless persons, members of particular minority groups, or the economically or educationally disadvantaged. Research involving significant monetary compensation may unduly influence certain types of participants and the IRB takes such considerations into account. Research involving these participants is socially important for understanding and eventually improving adverse health and general well-being in these populations.

### **6.10.1 Employees and Students**

Because of the risk of coercion and undue influence the IRB considers employees, students and trainees at LSUHSC-S and affiliate sites as vulnerable participants. The IRB will utilize the same standards for approving research involving these groups.

### **6.11 Informed Consent and Assent**

Whenever the participants have the capacity to give consent (as determined by qualified professionals), informed consent should be obtained and documented in accordance with Section 5. When participants lack the capacity to give consent, investigators may obtain consent from the legally authorized representative of a subject (surrogate consent) as described below.

A person who is incompetent or has been determined to lack capacity to consent to participate in a research study should be informed about the trial to the extent compatible with the subject's understanding and, if possible, the subject should give their assent to participate, sign and date the written informed consent or a separate assent form. If the person objects to participating, this objection should be heeded.

Both investigators and IRB members must be aware that for some subjects, their decision-making capacity may fluctuate. For subjects with fluctuating decision making capacity or those with decreasing capacity to give consent, a re-consenting process with surrogate consent may be necessary. Although incompetent to provide informed consent, some persons may resist participating in a research protocol approved by their representatives. Under no circumstances may subjects be forced or coerced to participate.

#### **6.11.1 Surrogate Consent**

Surrogate consent may be obtained. See section 6.9.1

#### **6.11.2 Legally Authorized Representative:**

See section 6.9.2.

### **6.12 Waiver for Epidemiology Research**

The Secretary of DHHS has waived the applicability of 45 CFR 46.305(a)(1) and 46.306(a)(2) for certain research conducted or supported by DHHS that involves epidemiologic studies that meet the following criteria:

1. In which the sole purposes are:
  - a. To describe the prevalence or incidence of a disease by identifying all cases
  - b. To study potential risk factor associations for a disease
2. Where the IRB has approved the research and fulfilled its duties under 45 CFR

46.305(a) (2)–(7) and determined and documented that

- a. The research presents no more than minimal risk and no more than inconvenience to the prisoner-subjects, and
  - b. Prisoners are not a particular focus of the research.
3. The specific type of epidemiological research subject to the waiver involves no more than minimal risk and no more than inconvenience to the human subject participants. The waiver would allow the conduct of minimal risk research that does not now fall within the categories set out in 45 CFR 46.306(a) (2).
  4. The range of studies to which the waiver would apply includes epidemiological research related to chronic diseases, injuries, and environmental health. This type of research uses epidemiologic methods (such as interviews and collection of biologic specimens) that generally entail no more than minimal risk to the subjects.
  5. In order for a study to be approved under this waiver, the IRB would need to ensure that, among other things, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of the data.

## **7. INVESTIGATIONAL DRUG, DEVICES OR BIOLOGICS IN RESEARCH**

LSUHSC-S has and follows written policies and procedures to ensure that the use of any investigational or unlicensed test article complies with all applicable legal and regulatory requirements. (AAHRPP Standard I-7)

### **7.1 Policy**

FDA regulates clinical investigations (research) “that support applications for research or marketing permits for products regulated by the Food and Drug Administration, including foods, dietary supplements that bear a nutrient content claim or a health claim, infant formulas, food and color additives, drugs for human use, medical devices for human use, biological products for human use, and electronic products.” (See 21 CFR 56.101)

All such investigations must be conducted in accordance with FDA requirements for informed consent and IRB review, regardless of funding source or sponsor.

Research with FDA-regulated test articles will be approved only after the IRB:

- Receives documentation that the research will be conducted under an applicable Investigational New Drug Application (IND) or Investigational Device Exemption (IDE); or
- Formally determines and documents that the proposed use of any investigational device satisfies the FDA criteria for non-significant risk devices; or
- Receives satisfactory documentation or justification from the investigator that the FDA has determined that an IND or IDE is not required.

## 7.2 Definitions

Biologic: Any therapeutic serum, toxin, anti-toxin, or analogous microbial drug applicable to the prevention, treatment or cure of disease or injuring. Studies of unlicensed biologics are regulated according to the IND regulations, except in some cases when the biologic is in a combination product with a medical device. FDA regulates biologics general use and licensing under 21 CFR 600 and 601. (42 U.S.C 262 of the Public Health Service Act.)

Clinical Investigation: Any experiment that involves a test article and one or more human subjects, and that either must meet the requirements for prior submission to the Food and Drug Administration under section 505(i) or 520(g) of the Federal Food, Drug and Cosmetic Act (FD&C Act), or need not meet the requirements for prior submission to the Food and Drug Administration under these sections of the act, but the results of which are intended to be later submitted to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit. The term does not include experiments that must meet the provisions of part 58, regarding nonclinical laboratory studies. The terms research, clinical research, clinical study, study, and clinical investigation are deemed to be synonymous for purposes of this part. (See 21 CFR 56.102)

Combination product: A product containing a combination of a drug, a device, or a biological product. Studies of combination products are regulated according to the IND or IDE regulations, depending on the components of the product. The FDA determines which of its organizational components has primary jurisdiction for the premarket review and regulation of products that are comprised of any combination of a drug, device, and/or biological. (See 21 CFR 3.21)

Dispense or dispensing: means the interpretation, evaluation, and implementation of a prescription drug order, including the preparation and delivery of a drug or device to a patient or patient's agent in a suitable container appropriately labeled for subsequent administration to, or use by, a patient. "Dispense" necessarily includes a transfer of possession of a drug or device to the patient or the patient's agent (Pharmacy.la.gov). Louisiana law requires that dispensing may only be performed by a licensed pharmacist or a physician who is registered with the board as a dispensing physician in accordance with Title 46:Chapter 65:Subchapter C.

Distribute or distribution: means the delivery of a drug or device other than by administering or dispensing.

Drug as defined by FDA:

- (a) articles recognized in the official United States Pharmacopoeia, Official Homeopathic Pharmacopoeia of the United States, or official National Formulary, or any supplement to any of them
- (b) articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals

- (c) articles (other than food) intended to affect the structure or any function of the body of man or other animals
- (d) articles intended for use as a component of any articles specified in clause (A), (B), or (C)

Emergency Use: is defined as the use of an investigational drug, device or biological product in accordance with a treatment/procedure with a human subject in a life-threatening situation in which no standard acceptable treatment is available, and in which there is not sufficient time to obtain IRB approval. This is not to be confused with Planned Emergency Research.

Good Clinical Practice (GCP): An international ethical and scientific quality 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.

HDE Application: To obtain approval for a HUD, a humanitarian device exemption (HDE) application is submitted to FDA.

Human subject as defined by DHHS: A living individual about whom an investigator (whether professional or student) conducting research obtains (1) Data through intervention or interaction with the individual, or (2) Identifiable private information. (See 21 CFR 56.102)  
For the purpose of this definition:

Intervention: Includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.

Interaction: Includes communication or interpersonal contact between investigator and subject.

Private Information: Includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record). Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects.

Human Subject as defined by FDA: An individual who is or becomes a participant 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.

Humanitarian Use Device (HUD): Humanitarian Use Device is a medical device intended to

benefit patients in treating or diagnosing a disease or condition that affects fewer than 4,000 individuals in the United States per year. A HUD is approved for marketing through an HDE application

Investigational Device Exemption (IDE): An exemption issued by the FDA that allows the investigational device to be used in a clinical study in order to collect safety and effectiveness data. (21 CFR 812).

Investigational Device: means a new medical device that has not been cleared for marketing by the FDA or an existing FDA-approved medical device which is being used for a new purpose in a clinical investigation.

Investigational New Drug (IND) Application: is a request for Food and Drug Administration (FDA) authorization to administer an investigational drug to humans. Such authorization must be secured prior to interstate shipment and administration of any new drug that is not the subject of an approved new drug application. (21 CFR Part 312).

Investigational Drug: any new drug or biological product that has not been cleared for marketing by the FDA or an existing FDA-approved drug which is being used in a new way not indicated on the approved label or a new purpose in a clinical investigation.

Investigational Product (IP) (also known as Test Article): means as defined by the FDA any drug (including a biological product for human use), medical device for human use, human food additive, color additive, electronic product, or any other article subject to regulation under the act or under sections 351 and 354-360F of the Public Health Service Act (42 U.S.C. 262 and 263b-263n).

Investigator-Initiated (also known as Sponsor-Initiated Studies): refers to a situation in which the individual investigator is a LSUHSC-S investigator who both initiates and conducts an investigation, is the holder of the IND or IDE and under whose immediate direction the investigational drug or experiment is administered, dispensed or used.

Non-Significant Risk (NSR) Device: An investigational device that does not meet the definition of a significant risk device.

Off-Label Use: Use of an approved drug, an approved or cleared device, or a licensed biologic for an indication not in the approved labeling. Most research involving off-label uses requires IND or IDE applications.

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.

Significant Risk (SR) Device: Significant risk device means an investigational device that:

- (a) Is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject; or
- (b) Is purported or represented to be for a use in supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a subject; or
- (c) 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
- (d) Otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.

Test article: Any drug for human use, biological product for human use, medical device for human use, human food additive, color additive, electronic product, or any other article subject to regulation under the act or under sections 351 or 354-360F of the Public Health Service Act. (See 21 CFR 56.102). This includes but is not limited to food products, medical foods, dietary supplements, and any other substance that is generally recognized as safe (GRAS) for human use; over-the counter drugs, currently marketed prescription drugs, infant formulas, vaccines, and blood products.

### **7.3 Internal Handling of Test Articles – Investigational Drugs, Devices & Biologics**

LSUHSC-S has and follows written policies and procedures to ensure that the handling of investigational or unlicensed test articles conforms to legal and regulatory requirements. (AAHRPP Element I.7.B.)

LSUHSC-S policy requires that the IRB review and approve all research using investigational products/test articles involving human subjects prior to initiation of the study, regardless of whether these studies are conducted with inpatient or outpatient participants.

VA Requirements: Investigators conducting investigational drug research at the Overton Brooks VA Medical Center are responsible for following the VA Research and Investigational Drug Policies and Procedures.

### **7.4 Research Involving Off-Label Use of Approved Drugs or Legally Marketed Devices**

Investigators conducting research involving the use of an approved drug or legally marketed device for an indication not in the approved labeling must comply with all Federal Regulations and Louisiana Laws for record-keeping, labeling, packaging, storage and all other requirements for the dispensing and administration of such drugs or devices.

### **7.5 FDA Exemptions**

The following categories of clinical investigations are exempt from the requirements of FDA regulations for IRB review:

1. Emergency Use of a Test Article, provided that such emergency use is reported to the IRB within five (5) working days. Any subsequent use of the test article at the institution is subject to IRB review. (21 CFR §56.104I) See Section 7.9.
2. Taste and food quality evaluations and consumer acceptance studies, if wholesome foods without additives are consumed or if a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural, chemical, or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture. (21 CFR §56.104(d))

## **7.6 Research with Drugs – IND Requirements**

Clinical investigations of drugs are subject to the Investigational New Drug Application (IND) regulations, 21 CFR 312.

An investigational new drug application (IND) is synonymous with “Notice of Claimed Investigational Exemption for a New Drug.” An investigational drug must have an IND before it can be shipped, unless one of the exemptions outlined in 21 CFR 312.2 is met.

Applications for research on the use of a drug, unless that research is exempt from the IND regulations, must be accompanied by documentation from the FDA that includes a valid IND number. The IND number must either match the number on the sponsor protocol with the same title as the proposed research, or be listed on communication from the sponsor specific to the proposed research, or on communication with the FDA. IND numbers may not be validated with an Investigator Brochure (which may serve multiple INDs).

### **7.6.1 Investigational New Drug Exemption - IND Exemption**

If the research involves drugs and there is no IND, the PI must provide the appropriate waivers or documentation from the FDA or sponsor as to why it is not required.

The IRB will review the application and determine:

1. Whether there is an IND and if so, whether there is appropriate supporting documentation.
2. If the research involves drugs with no IND, and whether the research meets the criteria below.

As stated in 21 CFR 312.2(b), clinical investigation of a drug is exempt from the IND regulations if the drug is lawfully marketed in the United States and all of the following are true:

1. The investigation is not intended to be reported to FDA as a well-controlled study in support of a new indication for use nor intended to be used to support any other

- significant change in the labeling for the drug
2. If the drug that is undergoing investigation is lawfully marketed as a prescription drug product, the investigation is not intended to support a significant change in the advertising for the product
  3. The investigation does not involve a route of administration or dosage level or use in a patient population or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product
  4. The investigation is conducted in compliance with the requirements for institutional review set forth in part 56 and with the requirements for informed consent set forth in part 50
  5. The investigation is conducted in compliance with the requirements of 21 CFR 312.7 (Promotion and charging for investigational drugs).

The following are also exempt from the IND requirements:

- a clinical investigation involving use of a placebo if the investigation does not otherwise require submission of an IND; However, investigators who are planning rigorous, carefully controlled clinical investigations of off-label uses of approved drugs or biologics should consult the FDA regarding obtaining an IND before submitting a protocol to the IRB, even when there is no immediate intent to change product labeling or advertising; and
- a drug intended solely for tests in vitro or in laboratory research animals if shipped in accordance with 21 CFR 312.160.

For clinical investigations involving an in vitro diagnostic biological product, an IND is not necessary if:

- a) It involves one or more of the following: (a) Blood grouping serum, (b) Reagent red blood cells or (c) Anti-human globulin
- b) It is intended to be used in a diagnostic procedure that confirms the diagnosis made by another, medically established, diagnostic product or procedure
- c) It is shipped in compliance with 21 CFR 312.160

## **7.7 Research with Devices**

### **7.7.1 IDE Requirements**

Clinical investigations of devices are subject to the Investigational Device Exemptions (IDE) regulations, 21 CFR 812.

An approved investigational device exemption (IDE) permits a device that is not approved (via premarket authorization, PMA) or cleared to market (via 510(k)) by the FDA to be shipped to conduct clinical investigations of that device. Significant risk investigational devices must have an IDE issued by FDA before they can be shipped. Non-significant risk devices are considered to have an approved IDE when the IRB agrees with the sponsor that the device meets the criteria for a non-significant risk device.

Research with devices falls into three categories:

- Investigations of significant risk devices to determine safety and effectiveness of the device
- Investigations of non-significant risk devices to determine safety and effectiveness of the device
- Investigations exempted from the IDE regulations.

Studies that include medical device use in an incidental way, where the device or the use of the device is not the focus of the research, are generally not considered to be FDA-regulated research or subject to 21 CFR 812, and in some instances are eligible for IRB review according to the expedited procedure.

### **7.7.2 Significant Risk Device Research**

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When research involves investigational or unlicensed test articles, LSUHSC-s confirms that the test articles have appropriate regulatory approval or meet exemptions for such approval. (AAHRPP Element I.7.A)

Applications for research on the use of a significant risk device must be accompanied by documentation from the FDA that includes a valid IDE number. The IDE number must either match the number on the sponsor protocol with the same title as the proposed research, or be listed on communication from the sponsor specific to the proposed research, or on communication with the FDA. IDE numbers may not be validated with a device manual (which may serve multiple IDEs).

### **7.7.3 Non-Significant Risk Device Research**

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When research is conducted to determine the safety or effectiveness of a device, the organization confirms that the device fulfills the requirements for an abbreviated IDE (21 CFR 812.2(b)(1)):

- The device is not a banned device
- The sponsor labels the device in accordance with 21 CFR 812.5
- The sponsor obtains IRB approval of the investigation after presenting the reviewing IRB with a brief explanation of why the device is not a significant risk device, and maintains such approval
- The sponsor ensures that each investigator participating in an investigation of the device obtains from each subject under the investigator's care, consent under 21 CFR 50 and documents it, unless documentation is waived
- The sponsor complies with the requirements of 21 CFR 812.46 with respect to monitoring investigations
- The sponsor maintains the records required under 21 CFR 812.140(b) (4) and (5) and makes the reports required under 21 CFR 812.150(b) (1) through (3) and (5) through (10)

- The sponsor ensures that participating investigators maintain the records required by 21 CFR 812.140(a)(3)(i) and make the reports required under 21 CFR 812.150(a) (1), (2), (5), and (7)
- The sponsor complies with the prohibitions in 21 CFR 812.7 against promotion and other practices

If the investigator applies to the IRB for a non-significant risk determination for a device study, but the IRB determines that the device is significant risk, the IRB shall notify the investigator and the sponsor, if appropriate.

#### **7.7.4 Exempt Device Research**

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Clinical investigations that are exempt from IDE regulations still require IRB review and approval. An investigation of a medical device in human subjects research that is exempt from the IDE regulations must fall into one of the following categories (Criteria in 21 CFR 812.21):

- A device legally marketed in the US that is used or investigated in accordance with the indications in the FDA-approved labeling.
- A diagnostic device (that is, an in vitro diagnostic device) if the testing:
  - Is noninvasive
  - Does not require an invasive sampling procedure that presents significant risk
  - Does not by design or intention introduce energy into a subject
  - Is not used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure
- A device undergoing consumer preference testing, testing of a modification, or testing of a combination of two or more devices in commercial distribution, if the testing is not for the purpose of determining safety or effectiveness and does not put subjects at risk.
- A custom device as defined in 21 CFR 812.3(b), unless the device is being used to determine safety or effectiveness for commercial distribution.
- A device, other than a transitional device, in commercial distribution immediately before May 28, 1976, when used or investigated in accordance with the indications in labeling in effect at that time.
- A device, other than a transitional device, introduced into commercial distribution on or after May 28, 1976, that FDA has determined to be substantially equivalent to a device in commercial distribution immediately before May 28, 1976, and that is used or investigated in accordance with the indications in the labeling FDA reviewed under subpart E of part 807 in determining substantial equivalence.

#### **7.7.5 In Vitro Diagnostic Device Research**

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In vitro diagnostic (IVD) device investigations may be exempt from the IDE requirements of 21 CFR 812 if the devices are properly labeled and meet the criteria set forth in 21 CFR 812.21(3). However, such studies are still subject to the FDA regulations and IRB review requirements if the research is to support an application for research or marketing of the device (see 21 CFR 50.1). This is true regardless of whether the samples to be used are individually identifiable or

not. The FDA regulations define a subject to include a human on whose specimens an investigational device is used (21 CFR 812.3(p)). Thus, an IVD study to support a premarket submission to the FDA is considered a human subject investigation and is subject to IRB review under 21 CFR parts 50 and 56. IVD research may be eligible for expedited review and waiver of informed consent when appropriate.

In addition to the above, FDA Guidance on Informed Consent for In Vitro Diagnostic Device Studies Using Leftover Human Specimens that are Not Individually Identifiable makes clear that IRB review is one of several criteria for IVD studies using left-over specimens that are not individually identifiable.

## **7.7.6 Radiology Devices and Radioactive Materials**

The FDA regulates radiology devices and radioactive materials used in research. Oversight at LSUHSC-S is handled by the Radiation Safety Office in conjunction with the Biomedical Director, Hospital Radiation Safety Chairman, and the Medical School Radiation Safety Officer. Most research involving radiation is covered by an IND or an IDE, and must be approved by the IRB. However, the IRB will not approve any research involving radiology devices or radioactive materials without the approval of the Radiation Safety Office. Therefore, any protocol involving radioactive materials and devices will be reviewed and approved by the Radiation Safety Office prior to submission to the IRB for approval.

The Initial Protocol Application includes the necessary radiological safety questions which are reviewed as outlined above, in accordance with the Radiation Safety Office procedures.

Investigators will notify the Radiation Safety Office when the IRB approves the protocol. Notification must include the protocol number, funding status, approval period and location of the device. In addition, the Radiation Safety Office provides assistance for investigators designing studies with radiation.

## **7.8 Responsibilities for Control of Investigation Products**

### **7.8.1 Dispensing and Record Keeping**

LSUHSC-S has and follows written policies and procedures to ensure that the handling of investigational or unlicensed test articles conforms to legal and regulatory requirements. (AAHRPP Element I.7.B.)

#### **7.8.1.1 Inpatient Studies**

Investigational products or test articles including drugs, devices, biologics or combination products for inpatient research studies are housed and dispensed by the Research Pharmacy. Investigational products or test articles including drugs, devices, biologics or combination

products for inpatient research studies may be dispensed by the Principal Investigator if the Principal Investigator provides adequate justification, submits a detailed accountability plan, and has received prior approval from the LSUHSC-S IRB. To ensure that adequate procedures are in place to be able to maintain and document drug accountability, a consult between the PI and Research Pharmacy Services regarding maintenance and documentation of IP accountability may be sought. The PI is responsible for Drug Accountability.

#### **7.8.1.2 Out-Patient Studies**

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Investigational products or test articles including drugs, devices, biologics or combination products for outpatient research studies, may be housed and dispensed by the Research Pharmacy or by the Principal Investigator if the Principal investigator provides adequate justification, submits a detailed accountability plan, and has received prior approval from the LSUHSC-S IRB. In order to ensure that adequate procedures are in place to be able to maintain and document drug accountability, a consult between the PI and Research Pharmacy Services regarding maintenance and documentation of IP accountability may be sought. The PI is responsible for Drug Accountability.

#### **7.8.1.3 Proper Handling of Investigational Test Articles**

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The Investigator, pharmacist, or any other designated individual will maintain records of the delivery of the investigational product to the site, the inventory, use by each participant, and return to Sponsor or alternative disposition of unused investigational products. The records will include dates, quantities, batch or serial numbers and expiration dates, and the unique code assigned to the investigational products and study participants. ICH-GCP (E6).

#### **7.8.1.4 Good Clinical Practice Guidelines**

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(ICH-GCP (E6) – Investigators are to follow Good Clinical Practice (GCP) guidelines when the research involves (1) FDA regulated approved or unapproved drugs, devices or biologics or any other FDA regulated product; or (2) where the sponsor or funding agency requires the use of GCP guidelines.

### **7.8.2 Investigator and Research Pharmacy Services – Handling of Investigational Product**

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1. Dispensing by investigator – In the event the investigator requests to have control of the investigational product (drug, device or biologic) approval of the accountability plan must first be obtained from the IRB. To be eligible to retain control of the investigational drug product the investigator must be currently registered with the Louisiana State Board of Medical Examiners as a dispensing physician in accordance with Title 46 Chapter 65 Subchapter C.
2. RPS Coordination – The investigator is required to use Research Pharmacy Services as

the coordinating and control center for the investigational product (drug, device or biologic) unless prior approval from the IRB has been granted. As the coordinating and control center, RPS assumes the responsibility for maintaining records of the investigational products delivered to the RPS, inventory of the investigational product, dispensing of investigational product to research subjects, and the return to the sponsor or disposition of unused investigational product. RPS will store and dispense the investigational product as specified by the sponsor and in accordance with applicable regulatory requirements.

- a. For research drugs RPS may initiate or adjust drug therapy and/or order laboratory tests associated with a research protocol when requested to do so by the PI. Any pharmacist participating in such a protocol must be trained and deemed competent to participate by the Investigator or his/her designee. Specific details on the adjustment of drug therapy or ordering of laboratory tests should be reviewed during the protocol initiation visit.
  - b. When RPS is the coordinating and control center for the research drug, RPS will store the returned dispensed investigational drug in a designated return area when a study protocol requires the subject to return the empty investigational drug container or any amount of the unused investigational drug. However, it is the responsibility of the investigator to deliver the returned dispensed investigational drug to RPS when subjects leave the dispensed investigational drug in the PI's department.
  - c. When RPS is coordinating the control of the investigational product, the investigator will forward a copy of the complete research protocol, a copy of the Investigator's brochure, ordering procedures, any special storage, handling or preparation requirements, and any pertinent dispensing or use information to the research pharmacist.
  - d. During the Cost Analysis process, RPS will be asked to provide the cost of locally provided drugs required by the protocol. The mandatory institutional pharmacy fee will be applied to all research involving investigational products.
3. Controlled Substances - The investigator should be aware that controlled substances may not be stored outside the Research Pharmacy.
4. Investigational Devices – If a device is considered Non Significant Risk by the investigator or sponsor, but after review the IRB determines the device to have Significant Risk, upon receipt of written notice the investigator is responsible for notifying the sponsor of the IRB(s) determination. The investigator must provide the IRB with confirmation of this action.
5. Investigator Control of Investigational Product Supply – If the Research Pharmacy is not coordinating the control of the investigational product, as outlined above, then the principal investigator is responsible for the control of the investigational product and must provide a plan at the time of application submission for the adequate storage and

control over the distribution and dispensing or use of an investigational product. (If the investigator is requesting to maintain control of a research drug product, the plan must include a copy of the investigator's registration as a dispensing physician with the Louisiana State Board of Medical Examiners.)

When the investigator retains control of investigational product supplies, the investigator is responsible for ensuring that the research is conducted according to all regulatory guidelines and LSUHSC-S policies and procedures. Other specific responsibilities include:

- a. Investigational Product Accountability Record –The investigator must maintain records of the product's delivery to the study site, the inventory at the site, the use by each subject, and the return to the sponsor or alternative disposition of unused product. These records should include dates, quantities, batch/serial numbers, expiration dates, and the unique code numbers assigned to the investigational product(s) and trial subjects. Investigators should maintain records that document adequately that the subjects were provided the doses specified by the protocol and reconcile all investigational product(s) received from the sponsor.

In regard to the use by each subject, investigators should maintain investigational product accountability records that document adequately which subject(s) received the investigational product; when the subject(s) received the investigational product; the specific dosage or amount the subject(s) received; and any returned amount of the dispensed investigational product;

- b. Storage of Investigational Product – Investigational product(s) should be stored as specified by the sponsor and in accordance with applicable regulatory requirement(s). Storage guidelines include:
  - i. Storage area is large enough for the supply of investigational product.
  - ii. Storage area can be locked.
  - iii. Investigational drug is stored separately from other compounds.
  - iv. Non-dispensed investigational product is stored separately from returned dispensed investigational product.
    - If the study protocol requires the subject to return the empty investigational product container or any amount of the unused investigational product, it is the investigator's responsibility to store the returned dispensed investigational product separately from the non-dispensed investigational product.
    - It is the responsibility of the investigator to deliver the returned dispensed investigational product to the Research Pharmacy if it is the coordinating and control center for the research product.
  - v. Inventory control procedures are used.
  - vi. Any environmental controls are maintained.

- vii. Access is limited to study staff.
- c. Drug Dispensing – Louisiana law requires that dispensing may only be done by a licensed pharmacist or a physician who is registered with the Louisiana State Board of Medical Examiners as a dispensing physician in accordance with Title 46: Chapter 65: Subchapter C.
- d. Drug Labeling – The Code of Federal Regulations specify the following labeling requirements for an investigational new drug:
  1. The immediate package of an investigational new drug intended for human use shall bear a label with the statement “Caution: New Drug – Limited by Federal (or United States) law to investigational use.”
  2. The label or labeling of an investigational new drug shall not bear any statement that is false or misleading and shall not represent that the investigational new drug is safe or effective for the purposes for which it is being investigated.
  3. State of Louisiana Regulations and LSUHSC-S policy states that all drugs dispensed shall contain a medication label with the following:
    - i. Patient name, identifier
    - ii. Protocol number or name
    - iii. Name of prescriber / INVESTIGATOR
    - iv. Strength and volume of drug
    - v. Directions for use or administration
    - vi. Dose
    - vii. Number of units dispensed
    - i. Expiration date
    - ii. Initials of preparer
    - iii. Initials of pharmacist performing final check
    - iv. “Investigational Drug”
    - v. Any auxiliary stickers or warning labels
- e. Investigational Product Administration — Investigational products shall be administered in accordance with any applicable State or Federal Regulations and in accordance with any policies or procedures set forth by LSUHSC-S. An informed consent, signed and dated by the subject and the investigator must be in place before administering the investigational product.
  - i. Only a person licensed within the state of Louisiana and so authorized by their professional scope of practice shall administer an investigational product to a subject. A principal investigator may designate the responsibility of administering the investigational product only after the designee has been given and has demonstrated an understanding of basic pharmacologic information about the drug. This education and delegation of responsibility must be documented.
  - ii. Investigational products are to be administered in accordance with the

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  - v. Directions for use or administration
  - vi. Dose
  - vii. Number of units dispensed
  - i. Expiration date
  - ii. Initials of preparer
  - iii. Initials of pharmacist performing final check
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- ii.* Investigational products are to be administered in accordance with the

research protocol and in accordance with any other hospital or clinic policy pertaining to the administration of investigational products. The researcher will document that the amount provided to the research participant is the amount specified in the approved protocol.

- iii.* An investigator shall administer a drug only to subjects under the investigator's personal supervision or under the supervision of a sub-investigator responsible to the investigator. The investigator shall not supply the investigational drug to any person not authorized to receive it. FDA 21CFR 312.61. AAHRPP 3.2.B.
  - iv.* An investigator can permit use of the investigational device only with subjects under his/her supervision and cannot not supply an investigational device to any person not authorized under the IDE regulation to receive it. FDA 21CFR 812.110; AAHRPP 3.2.B.
6. The investigator shall report all unanticipated problems involving risk to subjects or others to the IRB according to the procedures outlined in Section 8.
7. For research involving investigational products:
- a.* The investigator is required to inform the Research Pharmacy that the IRB has approved the protocol through submission of the IRB approval letters.
  - b.* The investigator must inform the IRB and the Research Pharmacy when a study involving investigational products has been terminated by the sponsor.
  - c.* The investigator will report to the sponsor any adverse effect or adverse device effects that may reasonably be regarded as caused by, or probably caused by, the investigational product (21 CFR 312 (b); 21 CFR 812.140) according to the procedures in the protocol.
  - d.* The investigator will maintain the following:
    - i.* Current curriculum vitae (CV)
    - ii.* For devices statement of the investigator's relevant experience, including the dates, location, extent, and type of experience, where applicable
    - iii.* Protocol
    - iv.* Records of receipt and disposition of investigational product
    - v.* List of any sub-investigators with their curriculum vitae
    - vi.* Certification that all physicians, dentists, and/or nurses responsible in the study have appropriate valid licenses for the duration of the investigation, and
    - vii.* Case histories with particular documentation on evidence of drug effects. Emphasis is on toxicity and possible untoward happenings. All unexpected adverse effects are reportable; even if the investigator considers that the event is not related to the drug. All unexpected adverse effects shall be reported immediately to RPS and the IRB in the manner defined by the protocol and HRPP/IRB policies.
    - viii.* IRB letters of approval.

- ix. Other documents as outlined in the Human Subject Protection Program Standard Operating Procedures.

For VA research

- a. The investigator is responsible for informing the VA Pharmacy Service that IRB and R&D Committee approval has been obtained. This must be through the use of a signed copy of VA Form Informed Consent that must be sent to Pharmacy Service to document each subject's consent to participate in the study. Also VA Form 10-9012, Investigational Drug Information Record, must be provided to the pharmacy by the PI.
  - b. The investigator must inform the Chief, VA Pharmacy Service, and the R&D Committee when a study involving investigational drugs has been closed.
8. Record Retention – An investigator shall retain records in accordance with whichever is the greater of the following: (1) as required by the FDA for a period of two (2) years following the date a marketing application is approved for the drug or device for the indication for which it is being investigated; or, if no application is to be filed or if the application is not approved for such indication, until 2 years after the investigation is discontinued and FDA is notified; or (2) as required by LSUHSC-S policy for a period of six years after study closure at this institution; or (3) as required by the Sponsor's contract.

For VA Research - All research records, including the investigator's research records, are the property of VA and must be maintained within the VA according to disposition instructions approved by the National Archives and Records Administration and published in VHA's Records Control Schedule (RCS 10-1).

9. Quality Assurance Audits – The HRPP or IRB will periodically conduct audits of studies of all IND or IDE studies. However, when the LSUHSC-S INVESTIGATOR is acting as a sponsor and holds an IND or IDE for the test article (Investigator-Initiated Studies) there is an increased chance or increased frequency of being audited by the HRPP Quality Improvement/Assurance Program.

### **7.8.3 Investigator-Sponsor or Investigator Initiated Studies**

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When an investigator files an IND or IDE, the investigator is considered the sponsor and as such is accountable for all of the FDA regulatory responsibilities and reporting obligations of both the investigator and the sponsor, as described in the FDA regulations.

An individual or group of individuals or medical center is considered a sponsor for an investigation if they hold the IND or IDE. At LSUHSC-S these studies are typically called investigator initiated studies when they involve the use an investigational drug or device or use an approved drug or device for investigational purposes.

The sponsors' or the investigator as a Sponsor's responsibilities include the following:

- a. Selecting qualified investigators
- b. Providing all investigators with the information they need to conduct the investigation properly
- c. Ensuring proper monitoring of the investigation. The investigator will include in the Data Safety Monitoring Plan submitted to the IRB the use of a Contract Research Organization (CRO) or other independent body to monitor compliance with the protocol and all applicable regulations
- d. Ensuring that the FDA and (for devices) any reviewing IRB(s) or (for drugs) all participating investigators are promptly informed of significant new information about an investigation
- e. Additionally, if the IND or IDE product will be manufactured or produced at LSUHSC-S, the Principal Investigator must submit documentation that the product preparation and manufacture meets the standards for current Good Manufacturing Practice (GMP), or any modification to those standards approved by the FDA in issuing the IND or IDE
- f. The GMP plan has been approved by the applicable LSUHSC-S Institutional Official
- g. The GMP plan has been reviewed and accepted by LSUHSC-S Risk Management and Compliance Office

## 7.9 EMERGENCY USE OF A TEST ARTICLE

LSUHSC-S has and follows written policies and procedures for compliance with legal and regulatory requirements governing emergency use of an investigational or unlicensed test article. (AAHRPP Element I.7.C.)

The IRB or EC has and follows written policies and procedures for making exceptions to consent requirements for planned emergency research and reviews such exceptions according to applicable laws, regulations, codes, and guidance. (AAHRPP Element II.4.C.)

### 7.9.1 Emergency Exemption from Prospective IRB Approval.

Emergency use: Use of a test article on a human participant in a life-threatening situation in which no standard acceptable treatment is available, and in which there is not sufficient time to obtain IRB approval (21 CFR 56.102(d)).

If all conditions described in 21 CFR 56.102(d) exist then the emergency exemption from prospective IRB approval found at 21 CFR 56.104I may be utilized. The emergency use provision in the FDA regulations (21 CFR 56.104I) allows for one emergency use of a test article without prior review and approval by the IRB review. FDA regulations require any subsequent use of the investigational product at the institution have prospective IRB review and approval. However, the FDA acknowledges that it would be inappropriate to deny emergency treatment to a second individual if the only obstacle is that the IRB has not had sufficient time to convene a meeting to review the issue.

The FDA regards emergency use of a test article as a category of clinical investigation (21 CFR 56.104). However, DHHS states, “emergency care may not be claimed as research, nor may the outcome of such care be included in any report of a research activity.” Thus, a patient receiving an emergency use of a test article under FDA regulations, is not considered a research participant by DHHS regulation, and such emergency use is not research as covered under 45 CFR 46. See OHRP guidance Emergency Medical Care.

### **7.9.2 Prior Notification to the IRB of Emergency Use**

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Prior notification to the IRB of an impending emergency use of a test article by an investigator is permissible. However, such notification should not be construed as, and does not, evidence prior IRB approval of the emergency use. Prior notice of an impending emergency use of a test article will be used by the IRB only to initiate tracking to ensure the investigator submits a report to the IRB within the five day time frame required by 21 CFR 56.104I. The IRB may choose to request additional information.

When investigators provide prior notifications of their intent to use a test article in an emergency or their intent to invoke the exception to the requirement to obtain consent, the IRB Chair or designee will review the notification to determine whether the circumstances follow FDA regulations.

### **7.9.3 Informed Consent Requirement**

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The investigator must obtain the informed consent of the participant (or the participant’s legally authorized representative), unless the requirements of an exception from the informed consent requirement (21 CFR 50.23(a)) are satisfied. In addition to obtaining informed consent, the protocol director must obtain the HIPAA authorization from the participant (or the participant’s legally authorized representative). Exception from the informed consent requirement is discussed below.

VA policy (VHA Handbook 1108.04) allows for the emergent use of an IND in accordance with 21 CFR 312.36 if all appropriate conditions exist. Submissions for institution of treatment are detailed in 21 CFR 312.25 and include a treatment protocol submitted by an IND sponsor or a treatment IND submitted by a licensed practitioner. Informed consent is required unless the conditions for exemption are met. The IRB must be notified within five (5) working days of when an emergency exemption is used.

### **7.9.4 Emergency Waiver of Informed Consent**

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An exception under FDA regulations at 21 CFR 50.23 permits the emergency use of an investigational drug, device, or biologic without informed consent where the investigator and an independent physician who is not otherwise participating in the clinical investigation certify in writing all four (4) of the following specific conditions:

- a. The subject is confronted by a life-threatening situation necessitating the use of the test article;
- b. Informed consent cannot be obtained because of an inability to communicate with, or obtain legally effective consent from, the subject;
- c. Time is not sufficient to obtain consent from the subject's legally authorized representative;
- d. No alternative method of approved or generally recognized therapy is available that provides an equal or greater likelihood of saving the subject's life.

If, in the investigator's opinion, immediate use of the test article is required because the patient is confronted by a life-threatening or severely debilitating situation and if time is not sufficient to obtain the independent physician determination that the four conditions above apply, the protocol director should make the determination and, within five working days after the use of the article, have the determination reviewed and evaluated in writing by an independent physician, and submit that evaluation to the IRB.

#### **7.9.5 Submission and Reporting Requirements – IRB and FDA**

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Written documentation of the emergency use must be submitted to the IRB within five (5) working days after the use of the test article. 21 CFR 56.104I. The investigator must submit the following documents to the IRB.

For Drugs and Biologics:

1. Notification of Emergency Use Form which includes:
  - information about the patient
  - indication of the life-threatening nature of the situation
  - explanation as to why this drug or treatment was necessary
  - and if the emergency use occurred without obtaining prior informed consent, Section E on this form must also be completed: Independent Physician Certification – Emergency Use of a Test Article Without Informed Consent
2. Written permission from the manufacturer for the use of the test article under their IND. Generally the investigator will contact the manufacturer and determine if the drug or biologic can be made available for the emergency use under the company's IND. If the company declines permission or cannot be reached, the investigator should contact the FDA for authorization of the shipment of the drug in advance of the IND submission. In such a case the FDA may authorize shipment of the test article in advance of the IND submission. The IRB may request that the protocol director contact the FDA to obtain an IND.
3. Signed Consent Form, with HIPAA

The HRPP office will check for emergency uses where the IRB is expecting and has not received a report, within 5 days. HRPP will notify or email the investigator of Failure to Submit Emergency Use Report. If the investigator is not working with the IRB to submit the report,

HRPP will process the failure to submit as a Finding of Non-Compliance. The HRPP Office will also check for emergency uses where the IRB is expecting and has not received a standing protocol within 30 calendar days. HRPP will notify or email the investigator of failure to Submit Emergency Use Protocol. If the investigator is not working with the IRB to submit the protocol, HRPP will process the failure to submit as a Finding of Non-Compliance.

#### **7.9.6 IRB Review (Retrospective) of an Emergency Use of a Test Article**

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The Chair or designated IRB member will review the documentation submitted in support of an emergency use of a test article. IRB review includes an assessment of whether the conditions for the emergency use were satisfied. The reviewer completes the Exemption from IRB Review: Emergency Use of a Test Article Check sheet. A copy of this form is sent to the investigator and a copy is placed in the IRB's Emergency Use Log. If the emergency use did not meet the criteria allowing an exemption from prior IRB review and approval, the action will be handled according to the non-compliance policy.

#### **7.10 Access to Investigational Drugs Outside of a Clinical Trial**

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Expanded access, sometimes called compassionate use, is the use of an investigational drug outside of a clinical trial to treat a patient with a serious or immediately life-threatening disease or condition who has no comparable or satisfactory alternative treatment options.

FDA regulations allow access to investigational drugs for treatment purposes on a case-by-case basis for an individual patient, or for intermediate-size groups of patients with similar treatment needs who otherwise do not qualify to participate in a clinical trial. They also permit expanded access for large groups of patients who do not have other treatment options available, once more is known about the safety and potential effectiveness of a drug from ongoing or completed clinical trials.

These investigational drugs have not yet been approved by the FDA as safe and effective. They may be effective in the treatment of a condition, or they may not. They also may have unexpected serious side effects. It is important that clinical investigators consider the possible risks when seeking access to an investigational drug.

##### **7.10.1 IRB Review and Approval**

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Federal law requires that investigational drug use in Expanded Access Programs be reviewed by an Institutional Review Board (IRB) to protect the individuals receiving the drug, including assuring that, in general, the risks are reasonable in light of the potential benefit. However, there may be significant unknown risks. The IRB will require and review an informed consent document to ensure that patients are aware of potential risks and are willing to accept the level of possible risk associated with the drug.

##### **7.10.2 Expanded Access Programs – Treatment Use of Investigational Drugs**

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The following mechanisms expand access to promising therapeutic agents without compromising the protection afforded to human subjects or the thoroughness and scientific integrity of product development and marketing approval.

#### **7.10.2.1 Open Label Protocol or Open Protocol IND**

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These are usually uncontrolled studies, carried out to obtain additional safety data (Phase 3 studies). They are typically used when the controlled trial has ended and treatment is continued so that the subjects and the controls may continue to receive the benefits of the investigational drug until marketing approval is obtained. These studies require prospective Institutional Review Board (IRB) review and informed consent.

#### **7.10.2.2 Treatment IND**

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The treatment IND (21 CFR 312.34 and 312.35) is a mechanism for providing eligible subjects with investigational drugs for the treatment of serious and life-threatening illnesses for which there are no satisfactory alternative treatments. A treatment IND may be granted after sufficient data have been collected to show that the drug “may be effective” and does not have unreasonable risks. Because data related to safety and side effects are collected, treatment INDs also serve to expand the body of knowledge about the drug.

There are four (4) requirements that must be met before a treatment IND can be issued: 1) the drug is intended to treat a serious or immediately life-threatening disease; 2) there is no satisfactory alternative treatment available; 3) the drug is already under investigation, or trials have been completed; and 4) the trial sponsor is actively pursuing marketing approval.

Treatment IND studies require prospective IRB review and informed consent. A sponsor may apply for a waiver of local IRB review under a treatment IND if it can be shown to be in the best interest of the subjects, and if a satisfactory alternate mechanism for assuring the protection of human subjects is available, e.g., review by a central IRB. Such a waiver does not apply to the informed consent requirement. An IRB may still opt to review a study even if FDA has granted a waiver.

Treatment INDs are discussed under the general heading of expanded access to investigational drugs. See FDA publications: [Charging for Investigational Drugs Under an IND](#) and [Expanded Access to Investigational Drugs for Treatment Use](#).

#### **7.10.2.3 Group C Treatment IND**

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The Group C treatment IND was established by agreement between FDA and the National Cancer Institute (NCI). The Group C program is a means for the distribution of investigational agents to oncologists for the treatment of cancer under protocols outside the controlled clinical trial. Group C drugs are generally Phase 3 study drugs that have shown evidence of relative and reproducible efficacy in a specific tumor type. They can generally be administered by properly trained physicians without the need for specialized supportive care facilities.

Group C drugs are distributed only by the National Institutes of Health under NCI protocols. Although treatment is the primary objective and patients treated under Group C guidelines are not part of a clinical trial, safety and effectiveness data are collected. Because administration of Group C drugs is not done with research intent, FDA has generally granted a waiver from the IRB review requirements 21 CFR 56.105. Even though FDA has granted a waiver for these drugs, an IRB may still choose to conduct a review under its policies and procedures. The usage of a Group C drug is described in its accompanying “Guideline Protocol” document. The Guideline Protocol contains an FDA-approved informed consent document which must be used if there has been no local IRB review.

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#### **7.10.2.4 Parallel Track**

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The Agency’s Parallel Track policy 57 FR 13250 permits wider access to promising new drugs for AIDS/HIV related diseases under a separate expanded access protocol that parallels the controlled clinical trials that are essential to establish the safety and effectiveness of new drugs. It provides an administrative system that expands the availability of drugs for treating AIDS/HIV. These studies require prospective IRB review and informed consent.

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#### **7.10.2.5 Emergency Use IND**

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The need for an investigational drug may arise in an emergency that does not allow time for submission of an IND in the usual manner. In such cases, FDA may authorize shipment of the drug for a specified use 21 CFR 312.36. Such authorization is usually conditioned upon the sponsor filing an appropriate application as soon as practicable. Prospective IRB review is required unless the conditions for exemption are met 21 CFR 56.104I and 56.102(d). Informed consent is required unless the conditions for exception are met 21 CFR 50.23.

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#### **7.10.2.6 Treatment IDE**

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Treatment for desperately ill patient with investigational devices before general marketing of the device has begun when (1) the patient has a serious or life threatening condition; (2) there is no comparable alternative available; (3) the device is under investigation or has undergone investigation for the same use; (4) the sponsor is pursuing marketing approval; and (5) the device has an approved IDE.

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### **7.11 Planned Emergency Research**

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Planned research in life-threatening emergent situations where obtaining prospective informed consent has been waived is permitted by 21 CFR 50.24. The waiver authorization applies to a limited class of research activities involving human subjects who need emergency

medical intervention but who cannot give informed consent because of their life-threatening medical condition, and who do not have available a legally authorized representative. The intent of these regulations is to allow research on life-threatening conditions for which available treatments are unproven or unsatisfactory and where it is not possible to obtain informed consent, while establishing additional protections to provide for safe and ethical studies. The research plan must be approved in advance by the FDA and IRB. Investigators who wish to conduct planned emergency research should consult with IRB staff prior to submission of the protocol to the IRB.

The LSUHSC-S IRB reviews and may approve planned emergency research without requiring that informed consent of all subjects be obtained if the LSUHSC-S IRB (with the concurrence of a licensed physician who is a member of the IRB and who is not otherwise participating in the clinical investigation) finds and documents each of the following seven points:

1. The human subjects are in a life-threatening situation, available treatments are unproven or unsatisfactory, and the collection of valid scientific evidence, which may include evidence obtained through randomized placebo-controlled investigations, is necessary to determine the safety and effectiveness of particular interventions.
2. Obtaining informed consent is not feasible because:
  - The subjects will not be able to give their informed consent because of their medical condition.
  - The intervention under investigation must be administered before consent from the subjects' legally authorized representatives is feasible.
  - There is no reasonable way to identify prospectively the individuals likely to become eligible for participation in the clinical investigation.
3. Participation in the research holds out the prospect of direct benefit to the subjects because:
  - Subjects are facing life-threatening situation that necessitates intervention.
  - Appropriate animal and other preclinical studies have been conducted, and the information derived from those studies and related evidence support the potential for the intervention to provide a direct benefit to the individual subjects.
  - Risks associated with the investigation are reasonable in relation to what is known about the medical condition of the potential class of subjects, the risks and benefits of standard therapy, if any, and what is known about the risks and benefits of the proposed intervention or activity.
4. The clinical investigation could not practicably be carried out without the waiver.
5. The proposed investigational plan:
  - Defines the length of the potential therapeutic window based on scientific evidence
  - The investigator has committed to attempting to contact a legally authorized representative for each subject within that window of time, and if feasible, to asking the legally authorized representative contacted for consent within that window rather than proceeding without consent.
  - The investigator will summarize efforts made to contact legally authorized

representatives and make this information available to the IRB at the same time of continuing review. FORM: Continuation Request or Final Closure Report (HRP-212)

6. The IRB has reviewed and approved informed consent procedures and an informed consent document consistent with 21 CFR 50.25. These procedures and the informed consent document are to be used with subjects or their legally authorized representatives in situations where use of such procedures and documents is feasible. The IRB has reviewed and approved procedures and information to be used when providing an opportunity for a family member to object to a subject's participation in the clinical investigation consistent with information below.
7. Additional protections of the rights and welfare of the subjects will be provided, including, at least:
  - Consultation (including, where appropriate, consultation carried out by the IRB) with representatives of the communities in which the clinical investigation will be conducted and from which the subjects will be drawn.
  - Public disclosure to the communities in which the clinical investigation will be conducted and from which the subjects will be drawn, prior to initiation of the clinical investigation, of plans for the investigation and its risks and expected benefits;
  - Public disclosure of sufficient information following completion of the clinical investigation to apprise the community and researchers of the study, including the demographic characteristics of the research population, and its results
  - Establishment of an independent data monitoring committee to exercise oversight of the clinical investigation
  - If obtaining informed consent is not feasible and a legally authorized representative is not reasonably available, the investigator has committed, if feasible, to attempting to contact within the therapeutic window the subject's family member who is not a legally authorized representative, and asking whether he or she objects to the subject's participation in the clinical investigation. The investigator will summarize efforts made to contact family members and make this information available to the IRB at the time of continuing review.
  - Consenting is an ongoing process. All applicable criteria that would trigger re-consenting a subject in any study also apply to subjects whose consent has been provided by a surrogate. See SOP: Legally Authorized Representatives (Surrogate Consent) (HRP-013) for additional information.
  - In addition to the situations described under the section "Legally Authorized Representatives," if the subject is entered into research with waived consent and the subject dies before a legally authorized representative or family member can be contacted, information about the research should be provided to the subject's legally authorized representative or family member, when feasible.

Overton Brooks VAMC does not participate in Planned Emergency Research.

## 7.12 Humanitarian Use Device (HUD)

An HUD is a device that is intended to benefit patients by treating or diagnosing a disease or condition that affects fewer than 4,000 individuals per year in the United States. Only HUDs with approved HDEs may be used at LSUHSC-S. An investigator must apply for and receive IRB review and approval before a HUD may be used, either under a protocol or on a case-by-case basis. The HUD will be used for treatment, diagnosis or research in accordance with the labeling of the device, intended purpose and in the designated population for which the FDA approved its use.

The FDA makes a distinction between use of a HUD and investigational use/ clinical investigation of a HUD. The term use refers to the use of a HUD according to its approved labeling and indication(s). If a HUD is used in a clinical investigation (i.e., collection of safety and effectiveness data), whether for its HDE-approved indication(s) or for a different indication, this is investigational use or a clinical investigation of the HUD. Such investigational use is subject to the same requirements that apply to all FDA-regulated clinical studies. Clinical investigation of a HUD for a different indication must be conducted in compliance with the IDE regulations at 21 CFR Part 812, in addition to requiring IRB approval (21 CFR Part 56) and protection of human subjects (21 CFR Part 50). If the device is a significant risk device, an FDA-approved IDE is required. See 21 CFR 812.1, 812.20. To date, all HUDs have been significant risk devices requiring FDA-approved IDEs.

The patient must be informed that the HUD is a device authorized under Federal law for use; however, the effectiveness of the device for a specific indication has not been demonstrated. The informed consent of the patient or the patient's legally authorized representative will be obtained when the use of the HUD involves research or when it is required by the sponsor and/or the LSUHSC-S Institutional Review Board (IRB). Prospective LSUHSC-S IRB committee review and approval is required – regardless of intended use. The use of an HUD does not constitute research unless the physician or health care provider intends to collect data from its use. If an emergency exists such that it would not be possible to obtain informed consent from the patient prior to the use of the HUD, the physician shall provide the patient with written information about the device following the use or procedure and notify the IRB of such use. Any clinical investigation of a HUD requires an IRB approved Informed Consent Document.

The physician or designee completes applicable sections of the Template: Protocol (HRP 503) and submits the materials to the IRB. The HUD application is reviewed by the IRB committee using Worksheet: Criteria for Approval for HUD (HRP-323). The Physician may not begin using a HUD on patients until after receipt of IRB approval letter.

The Physician or designee is responsible for reporting adverse events and unanticipated problems that result from the use of a HUD. The Physician or designee is also responsible for reporting to the FDA any information received or otherwise made aware of, from any source, that reasonably suggests that a HUD has or may have caused or contributed to the death or

serious injury of a patient. The physician or designee is to report such findings to the FDA as soon as possible, but no later than 10 working days after the physician first learns of the event or problem. This reporting is, in addition to, not a substitute for, FDA and/or manufacturer reporting requirements in accordance with 21 CFR 803.30. In addition, the physician or designee is responsible for submitting any modifications to the HUD or clinical use of an HUD to the IRB.

Use of a HUD in an emergency that cannot wait for LSUHSC-S IRB review and approval should be handled using the criteria in the following section. The HUD may only be used in an emergency if it meets the FDA criteria (21 CFR 56.104 (d)) and the HUD is not used outside its approved labeling.

When the IRB is deciding whether to approve use of a HUD, its review does not include an SR/NSR (significant risk/non-significant risk) determination. As noted above, use of a HUD to treat or diagnose patients is not a clinical investigation; the HUD as such is legally marketed for use within its HDE-approved indication(s).

If the IRB receives a request to review a clinical investigation of a HUD (i.e., collection of safety and effectiveness data), and that clinical investigation concerns the HDE-approved indication(s), then again, the IRB does not have make an SR/NSR determination in its review. FDA considers such investigations exempt from the IDE requirements in 21 CFR Part 812. Nonetheless, the IRB still must approve the clinical investigation under 21 CFR Part 56 and informed consent and additional safeguards for children (if applicable) are required under 21 CFR Part 50, as for all FDA-regulated clinical studies.

In contrast, if the IRB receives a request to review an application for an investigational study of the HDE for a different indication, then the IRB should be alert that this type of clinical investigation is subject to the IDE regulations at 21 CFR Part 812.

#### **7.12.1 Emergency Use of a HUD**

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Whenever possible physicians are required to notify the IRB in advance of a proposed emergency use of a test article (drug, biologic, or device) in a life-threatening situation in advance of the use. The one-time emergency use of a test article is permitted provided a patient is in a life-threatening situation in which no standard acceptable treatment is available, and when there is not sufficient time to obtain IRB review and approval. Any subsequent use of a test article at the institution shall have prospective IRB review and approval. Data obtained from uses covered by this procedure cannot be used in a non-exempt systematic investigation designed to develop or contribute to generalizable knowledge.

Physicians are required to notify the IRB of a proposed compassionate use of an unapproved device without an IDE for a serious condition. In an emergency, if a physician determines that IRB approval cannot be obtained in time to prevent serious harm or death to a patient, a HUD

may be administered without prior approval by the IRB. The physician must report the emergency use to the IRB within five days and include the identification of the patient involved, the date of the use, and the reason for the use. Upon notification, the designated reviewer will use the Worksheet: Emergency Use (HRP-322) to determine whether the circumstances will meet the regulatory requirements or, if the report is received after the emergency use, if the circumstances met the regulatory requirements. The IRB will provide the results of this determination in writing to the physician. The Notification of Emergency Use will be documented in the IRB Emergency Use Log.

## 8. UNANTICIPATED PROBLEMS AND OTHER REPORTABLE NEW INFORMATION

Researchers and Research Staff follow reporting requirements during a research study in accordance with applicable laws, regulations, codes, and guidance; LSUHSC-S policies and procedures; and the IRB's requirements. (DHHS 45 CFR 46.103(b)(5); FDA 21 CFR 56.108(b);) (AAHRPP Element III.2.D)

The IRB or EC has and follows written policies and procedures for addressing unanticipated problems involving risks to participants or others, and for reporting these actions, when appropriate. (AAHRPP Element II.2.F)

### 8.1 Policy

This policy applies to all human subject research under the auspices of LSUHSC-S. It explains events or circumstances that must be reported to the IRB, within five (5) business days, during the conduct of human subject research.

Investigators or other individuals should report any information items that fall into one or more of the following categories to the IRB:

- Information that indicates a new or increased risk, or a new safety issue. For example:
  - New information (e.g., an interim analysis, safety monitoring report, publication in the literature, sponsor correspondence or report, CRO report, or investigator finding) that may indicate an increase in the frequency or magnitude of a previously known risk, or uncovers a new risk.
  - An investigator brochure, package insert, or device labeling is revised to indicate an increase in the frequency or magnitude of a previously known risk, or describe a new risk
  - Withdrawal, restriction, or modification of a marketed approval of a drug, device, or biologic used in a research protocol
  - Protocol deviation/violation that harmed subjects or others or that indicates subjects or others might be at increased risk of harm
  - Complaint of a subject that indicates subjects or others might be at increased risk of harm or at risk of a new harm
  - Any changes significantly affecting the conduct of the research

- Harm experienced by a subject or other individual, which in the opinion of the investigator is unexpected and probably related to the research procedures.
  - A harm is unexpected when its specificity or severity are inconsistent with risk information previously reviewed and approved by the IRB in terms of nature, severity, frequency, and characteristics of the study population.
  - A harm is probably related to the research procedures if in the opinion of the investigator, the research procedures more likely than not caused the harm
- Non-compliance with the federal regulations governing human research or with the requirements or determinations of the IRB or the institution or an allegation of such non-compliance.
- Audit, inspection, or inquiry by a federal agency or any other outside entity and any resulting reports (e.g. FDA Form 483.)
- Written reports of study monitors.
- Failure to follow the protocol due to the action or inaction of the investigator or research staff whether planned or unplanned.
- Change to the protocol taken without prior IRB review to eliminate an apparent immediate hazard to a subject.
- Breach of confidentiality (inappropriate disclosure of or access to confidential information).
- Incarceration of a subject in a study not approved by the IRB to involve prisoners.
- Complaint of a subject that cannot be resolved by the research team.
- Premature suspension or termination of the protocol by the sponsor, investigator, or institution.
- Unanticipated adverse device effect (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 application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.)
- For Veterans Administration (VA) research all local or internal serious adverse events.
- When following VA regulations, the terms “unanticipated” and “unexpected” refer to an event or problem in VA research that is new or greater than previously known in terms of nature, severity, or frequency, given the procedures described in protocol-related documents and the characteristics of the study population.
- When following VA regulations, the report of unanticipated problems involving risks to participants or others is to be sent to: The office of Research and Development, if VA-Funded, and The Regional Office of Research Oversight.
- For serious unanticipated problems involving risks to participants or others, within five business days of becoming aware of any serious unanticipated problem involving risks to participants or others in VA research, members of the VA research community are required to ensure that the problem has been reported in writing to the IRB.
- If the convened IRB or the IRB reviewer determines that the problem or event was serious, unanticipated, and related to the research a simultaneous determination is required

regarding the need for any action (e.g., suspension of activities; notification of participants) necessary to prevent and immediate hazard to participants in accordance with VA regulations.

- If the convened IRB determines that a protocol or consent document modification is warranted, the IRB must also determine and document:
  - Whether previously enrolled participants must be notified of the modification
  - When such notification must take place and how such notification must be documented.
- For DoD regulations, any unanticipated problems involving risks to participants or others for any DoD-Supported research must be promptly (no longer than within 30 days) reported to the DoD human research protection officer.

Reports should be made using the LSUHSC-S IRB electronic submission system (Shields) with the Report New Information action. The report should include:

- The date you became aware of the problem.
- A description of the problem and a determination of the following:
  - Does this information indicate a new or increased risk, or a safety issue?
  - Does the study need revision?
  - Does the consent document need revision?
- A list of all studies related to the reportable new information.
- Supporting documentation and a description of any corrective actions when required.

## 8.2 Definitions

Adverse Device Effect – An Adverse Device Effect (ADE) is any adverse event/effect caused by or associated with the use of a device that is unanticipated and has not been included in the protocol or the Investigator’s Brochure.

Adverse Event – An Adverse Event (AE) is defined as any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and that 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), symptom or disease temporarily associated with the use of a medicinal (investigational) product whether or not related to the medicinal (investigational) product. For Veterans Administration (VA) research an adverse event in human subjects research is any untoward physical or psychological occurrence in a human subject participating in research.

Others – Individuals other than research participants (example: Investigators, research assistants, students, the public, etc.)

Prompt Reporting as defined by the institution – Prompt Reporting is defined as immediately, and regardless of circumstances will be reported no later than five (5) working days following the event.

Related – An event is related if it is likely to have been caused by the research procedures.

Serious Adverse Event – A Serious Adverse Event (SAE) is defined as 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 IRB when the patient outcome is; death; a life-threatening experience; hospitalization (for a person not already hospitalized); prolongation of hospitalization (for a patient already hospitalized); persistent or significant disability or incapacity; congenital anomaly and/or birth defects; or a required intervention to prevent permanent impairment or damage (devices) or other serious medical events (e.g. drug dependence).

Unanticipated – means problems/events are those that are not already described as potential risks in the consent form; and usually not listed in the Investigator Brochure or product label; or not identified in investigational protocol or plan; and not part of an underlying disease.

Unanticipated problem involving risks to participants or others – Any information that is (1) unanticipated, (2) related to the research, and (3) indicates that subjects or others are at increased risk of harm.

For Department of Defense (DOD) research term Unanticipated Problem Involving Risks to Subjects or Others includes any incident, experience, or outcome that meets all the following criteria:

1. unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied;
2. related or possibly related to participation in the research (in this guidance document, possibly related means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.
3. Any unanticipated problems involving risks to participants or other for any DoD-supported research must be promptly (no longer than within 30 days) reported to the DoD human research protection officer.

Unexpected Adverse Event – An Unexpected Adverse Event (UAE) is any adverse event and/or reaction, the specificity or severity of which is not consistent with the informed consent, current investigator brochure or product labeling. Further, it is not consistent with the risk information described in the general investigational plan or proposal.

Unexpected Death – The death of a research subject in which a high risk of death is not

projected as indicated by the written protocol, informed consent form, or sponsor brochure. This definition does not include deaths associated with a terminal condition unless the research intervention clearly hastened the subject's death. A subject's death that is determined to be clearly not associated with the research is also not an "unexpected death" for purposes of the reporting requirements of these procedures.

### **8.3 Investigator Responsibilities**

Investigators are responsible for promptly reporting unanticipated problems involving risks to participants or others and other Reportable Information to the IRB. For industry sponsored projects, investigators are responsible for maintaining contact with the sponsor, and receiving reports from the sponsor, and if applicable, the monitoring entity (e.g., DSMB, DMC) and reporting suspected Unanticipated Problems and other Reportable Information to the IRB. For Sponsor-Investigator (Investigator Initiated) projects, the principal investigator is solely responsible for promptly reporting Unanticipated Problems and other Reportable Information to the IRB.

### **8.4 Prompt Reporting Requirements for Items 1-12**

#### **8.4.1 Events and Reportable Information Requiring Immediate Reporting**

Researchers and Research Staff have a process to address participants' concerns, complaints, or requests for information. (AAHRPP Element III.1.G)

All the following Events and Reportable Information require immediate reporting to the IRB; or within five (5) working days. An exception to this reporting period for the Overton Brooks VA Medical Center is noted below under VA Research.

#### **1) Unanticipated Problems Involving Risks to Participants or Others.**

Internal or External Events (deaths, life-threatening experiences, injuries, breaches of confidentiality, or other) occurring during or after the research study, which in the opinion of the Monitoring Entity, Sponsor or the Investigator meet all (a, b & c) of the following criteria must be reported to the IRB within five (5) working days:

- a) Unexpected in terms of nature, severity, or frequency, given (a) the research procedures described in the protocol-related documents, and informed consent document (b) the characteristics of the subject population being studied
- b) Related to participation in the research or there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research; or if a device is involved, probably caused by, or associated with the device
- c) Harmful suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known

or recognized.

An Unanticipated Problem is a major concern of an investigator and the IRB as it generally requires actions such as modification or immediate suspension of the protocol, or informing subjects; and will generally warrant consideration of substantive changes in the research protocol or informed consent process/document, or other corrective actions, in order to protect the safety, welfare, or rights of subjects or others.

When investigators are trying to determine if an event is an Unanticipated Problem please use the following guidance to see if all three (3) criteria apply:

#### UNEXPECTED

- The event is not mentioned in the protocol-related documents. This refers to the IRB-approved research protocol, informed consent document, investigator brochure, protocol, package insert, or label.
- The event is not a characteristic of the subject population being studied. This refers to the expected natural progression of any underlying disease, disorder, or condition of the subject(s) experiencing the adverse event and the subject's predisposing risk factor profile for the adverse event.

#### RELATEDNESS

- A harm is at least probably related if in general it is determined to be caused: at least partially by the procedures involved in the research it would be considered related to participation in the research;
- A harm would probably be considered unrelated to participation in the research if in general it is determined to be caused: solely by an underlying disease, disorder, or condition of the subject, or other circumstances unrelated to either the research or any underlying disease, disorder, or condition of the subject.

#### HARMFUL

- Adverse events need not be serious to qualify as harmful. However, serious adverse events always meet the Harmful criterion.

Serious adverse event is defined by OHRP as an event that:

- results in death
- is life-threatening (places the subject at immediate risk of death from the event as it occurred)
- results in inpatient hospitalization or prolongation of existing hospitalization
- results in a persistent or significant disability/incapacity
- results in a congenital anomaly/birth defect
- based upon appropriate medical judgment, may jeopardize the subject's health and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition

Not serious adverse events might also be Unanticipated Problems: adverse events that are not serious would also be unanticipated problems if they suggest that the research places subjects or others at a greater risk of physical,

psychological, economic, or social harm than was previously known or recognized.

Internal events are those that occur on LSUHSC-S campuses and involve LSUHSC-S investigators. An Internal event that is determined to meet the criteria for an unanticipated problem involves federal reporting requirements by the LSUHSC-S IRB.

Reports of external events are those that occur at non-LSUHSC-S sites and do not involve LSUHSC-S investigators. These reports usually involve multi-center or international clinical trials and may require analysis from sponsor, coordinating center or DSMB/DMC to support that the event is considered an unanticipated problem. The LSUHSC-S IRB does not have additional federal reporting requirements on reports of External events.

2) Change to the protocol taken without prior IRB approval to eliminate an apparent immediate hazard to a subject or a Protocol violation that harmed subject(s).

Once the IRB has approved a project, it must be carried out as planned. Any changes in subject population, recruitment plans, research procedures, study instruments, study sites, or research personnel must be prospectively approved by the IRB. Enacted changes without prior approval constitute protocol violations. Federal regulations require the IRB to have procedures to ensure that investigators do not implement any protocol changes without prior IRB review and approval, except when necessary to eliminate apparent immediate hazards to subjects.

3) New Information that indicates a new or increased risk, or a safety issue.

- a. New information (e.g., an interim analysis, DSMB or other safety monitoring report, publication in the literature, sponsor report, or investigator finding) indicates an increase in the frequency or magnitude of a previously known risk, or uncovers a new risk
- b. An investigator brochure, package insert, or device labeling that is revised to indicate an increase in the frequency or magnitude of a previously known risk, or describe a new risk
- c. Withdrawal, restriction, or modification of a marketed approval of a drug, device, or biologic used in a research protocol
- d. Any changes significantly affecting the conduct of the research

4) Premature suspension or termination of the research by the sponsor or the investigator.

If a trial is prematurely terminated or suspended for any reason by the sponsor or investigator, then the trial subjects must be promptly notified and appropriate therapy and follow-up must be arranged for the subjects. If the trial is suspended or terminated without the prior agreement of the Sponsor then the principal investigator must inform the Sponsor and any other institutions as agreed, providing a detailed written explanation of the reasons for termination or suspension. The investigator would not be expected to terminate or suspend a trial without prior discussion with the IRB unless in an emergency where there are immediate

safety concerns.

5) Failure to follow the protocol due to the action or inaction of the investigator or research staff.

**Protocol Violations** – A Protocol Violation is a deviation from the IRB approved protocol that may affect the subject’s rights, safety, or well-being and/or the completeness, accuracy, and reliability of the study data. A Protocol Violation is any significant divergence from the protocol, i.e., non-adherence on the part of the patient, investigator, or the sponsor to protocol-specific inclusion/exclusion criteria, primary objective variable criteria, and/or GCP guidelines without approval from the Sponsor and IRB. Protocol Violations generally increase the risk and/or decrease the benefit; affect the subject’s rights, safety, or welfare and/or the completeness, accuracy, integrity, or reliability of the research data.

**Protocol Deviations** – A Protocol Deviation is any change, divergence, or departure from the study design or procedures of a research protocol that may or may not be under the investigator’s control and that has not been approved by the IRB. The term deviation is sometimes used interchangeably with the term “violation”. Protocol Deviations are non-adherence to the approved study plan and occur without prior approval from the sponsor and the IRB.

**Protocol Exceptions** – A Protocol Exception is a temporary Protocol Deviation or Eligibility Waiver that is granted by the Sponsor or funding agency, (and the FDA if applicable, for investigational device studies) and must be approved by the IRB prior to implementation. Protocol Exceptions are generally for a single subject or, occasionally, a small group of subjects.

(See section 9 for additional information)

6) Written Monitoring Reports.

Sponsors are responsible for assuring throughout the clinical investigation that the investigators obligations, as set forth in the regulations, are being met and that the facilities used during the clinical investigation remain acceptable. This is accomplished during interim monitoring visits according to the monitoring plan for the specific study.

Sponsors are also responsible for assuring that the data submitted to FDA in support of the safety and effectiveness of a test article are accurate and complete. This requires the review of individual subject records and other supporting documents comparing them against the study data submitted by the investigator to the sponsor.

The purpose of the interim monitoring visit is to:

- review the progress of the study.
- ensure completeness, accuracy, legibility and validity of clinical trial data.

- ensure compliance of the investigator /site with the written approved protocol and GCP regulations.
- ensure protections are adequate to protect the safety and welfare of subjects.
- monitor proper use of investigational products.
- ensure IRB oversight and approval.
- provide the Sponsor opportunity to initiate corrective actions for non-compliance.

Upon receipt of a written interim monitoring visit report, the investigator must submit an unedited copy of the report to the IRB within five (5) working days.

7) Non-compliance with the federal regulations governing human research or with the requirements or determinations of the IRB, or an allegation of such non-compliance.

**Non-Compliance:** Any action or activity associated with the conduct or oversight or research involving human participants that fails to comply with either the research plan as approved by the IRB or federal regulations or LSUHSC-S institutional policies governing human subject's research.

**Serious Non-Compliance:** Non-Compliance that could adversely affect the rights, safety, or welfare of a human subject; place a human subject at increased risk of harm; cause harm to a human subject; affect a human subject's willingness to participate in research; or damage or compromise the scientific integrity of research data.

**Continuing Non-Compliance:** A pattern of Non-Compliance that suggests the likelihood that without intervention, instances of non-compliance will recur; a repeated willingness to comply; or a persistent lack of knowledge of how to comply. Reporting occurrences or allegations:

- A. Investigators are required to promptly report to the IRB all findings and allegations of apparent serious or continuing noncompliance, including major protocol violations, subject complaints, and changes to the protocol made without IRB approval to eliminate apparent immediate harm to subjects. The timeframe for reporting is within 5 working days of becoming aware of the event.
- B. Non-compliance may be uncovered by the IRB or the HRPP during ongoing review or monitoring of research or through audits or other quality assurance activities
- C. Allegations of non-compliance may also be reported by members of the research team, LSUHSC-S faculty, staff or administrators, sponsors, study participants, participating organizations, or other knowledgeable parties. The complaints or allegations may be provided to the AVCRM, HRPP staff, IRB Chair (or designee) or IO. To facilitate reporting, informed consent documents provide a contact phone number and e-mail to discuss concerns or complaints with the research with HRPP staff. The HRPP website also provides telephone and e-mail contacts for HRPP staff members and including the IO and AVCRM.

(See section 10 for additional information on non-compliance.)

8) Audit, inspection, or inquiry by a federal agency.

Various federal agencies such as the FDA, the NCI and others have the authority to inspect records of patients or subjects involved in research studies in which these agencies have an interest. Investigators must contact the AVCRM or designee and the HRPP staff as soon as they receive notice of an inspection or audit by a federal agency. The written report of any audits findings for an LSUHSC-S study must be reported to the IRB using the Reportable New Information activity in Shields.

9) Incarceration of a subject in a study not approved by the IRB to involve prisoners.

If a human subject involved in ongoing research becomes a prisoner during the course of the study, and the relevant research proposal was not reviewed and approved by the IRB in accordance with the requirements for research involving prisoners under subpart C of 45 CFR part 46, the investigator must promptly notify the IRB. All research interactions and interventions with, and obtaining identifiable private information about, the now-incarcerated prisoner-subject must be suspended immediately, except as noted below. Upon receipt of the investigator's report that a previously enrolled research subject has become a prisoner, if the investigator wishes to have the prisoner subject continue to participate in the research, the IRB must promptly re-review the proposal in accordance with the requirements of subpart C, and the institution(s) engaged in the research involving the prisoner subject must send a certification to OHRP and wait for a letter of authorization in reply. Otherwise, the prisoner subject must stop participating in the research, except as noted below.

OHRP allows one important exception to the requirement that all research interactions or interventions with, and obtaining identifiable private information about, the now-incarcerated prisoner-subject must cease until the regulatory requirements for research involving prisoners are met. In special circumstances in which the investigator asserts that it is in the best interests of the subject to remain in the research study while incarcerated, the subject may continue to participate in the research until the requirements of subpart C are satisfied. The investigator must promptly notify the IRB of this occurrence, so that the IRB can re-review the study. Note that in these circumstances, some of the findings required by 45 CFR 46.305(a) may not be applicable; for example, the finding required under 45 CFR 46.305(a)(4) regarding the selection of subjects within the prison may not be applicable, if the subject was recruited outside of an incarcerated context. The IRB should document findings of non-applicability accordingly.

10) Complaint of a subject that cannot be resolved by the research team.

Unresolved research subject concerns should be reported to the IRB office within 5 days. Researchers and research staff must be open to subject complaints or requests for information. If a research subject voices concerns about your research, you should promptly respond to those concerns and notify the IRB of the issue. When applicable, you should seek assistance from the IRB and HRPP staff. Research subject concerns, regardless of seriousness, must be promptly addressed and the study must be further evaluated to mitigate future concerns of additional participants.

(See section 10 for additional information.)

#### 11) Breach of Confidentiality.

In general, the term breach means the unauthorized acquisition, access, use, or disclosure of protected health information which compromises the security or privacy of such information, except where an unauthorized person to whom such information is disclosed would not reasonably have been able to retain such information.

#### 12) Unanticipated adverse device effect.

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.

VA Research - Any unauthorized use, disclosure, transmission, removal, theft, loss, or destruction of VA research-related Protected Health Information (PHI), individually identifiable private information, or confidential information, as defined by the HIPAA Privacy Rule, the Common Rule, the Privacy Act, or applicable Federal codes, must be reported to the Information Security Officer (ISO), Privacy Officer (PO), and the Associate Chief of Staff for Research and Development (ACOS/R&D) within one hour of the discovery. There is no distinguishing between suspected and confirmed breaches as both must be reported.

### **8.4.2 Submission of Reports**

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Investigators must report possible Unanticipated Problems or Other Reportable New Information to the IRB in writing using the Reportable New Information Form. The written report should contain the following:

- a.* Detailed information about the possible unanticipated problem, or reportable new information including relevant dates.
- b.* Any corrective action, planned or already taken, to ensure that the possible unanticipated problem or event is corrected and will not occur again.
- c.* An assessment of whether any subjects or others were placed at risk as a result of the event or suffered any physical, social, or psychological harm and any plan to address these consequences.
- d.* Any other relevant information.
- e.* Any other information requested by the IRB.

A report of a possible unanticipated problem involving risks to participants or others will be immediately forwarded by IRB staff to the IRB Chair or designee if the staff believes that

immediate intervention may be required to protect participants or others from serious harm.

## **8.5 IRB and Other Institutional Responsibilities**

### **8.5.1 Review by IRB Staff and Chairs**

The IRB staff will screen all submissions of Reportable New Information and forward them to the IRB Chair, qualified designee, or the convened IRB for review. Within five business days after receiving a report of a Serious Unanticipated Problem involving risk to subjects or others, or of a local Unanticipated Serious Adverse Event, the convened IRB or a qualified IRB reviewer must determine and document whether the reported incident was serious and unanticipated and related to the research.

The convened IRB or qualified IRB member will review the report including any applicable protocol, informed consent documents, changes already implemented for immediate safety reasons and those proposed, and determine in consultation with the principal investigator, and IRB Chair, AVCRM or designee or consultant as required, if there is a need for immediate action beyond the action taken/recommended by the principal investigator.

If the convened IRB or qualified IRB reviewer determines that the problem or event was serious, unanticipated, and related to the research or that the research should be suspended to enrollment of new subjects or research activities involving currently enrolled subjects should be suspended, the principal investigator will be notified, immediately. The principal investigator will receive written notification of the decision and the actions to be taken to protect currently enrolled subjects.

All determinations, regardless of the outcome will be reported to the IRB Committee at the next convened meeting. All the pertinent information regarding the event will be reviewed. This information will include the protocol, informed consent and any additional information as required so that the IRB can determine if additional modifications are warranted. The actions or modifications may include but are not limited to any of the following:

- o Revision of the protocol including inclusion/exclusion criteria
- o Incorporation of new information into the informed consent
- o Implementation of additional data monitoring activities
- o Informing currently enrolled participants
- o Suspension of enrollment of new subjects
- o Suspension of research procedures in currently enrolled subjects
- o Notification of previously enrolled subjects of the event and any actions they should take
- o Termination of the research
- o Notification to current participants when such information may relate to participants' willingness to continue to take part in the research

- o Requirement for an appropriate Corrective Action Plan
- o Requirement for additional training of the investigator and/or study staff
- o Referral to other organizational entities (e.g., legal counsel, risk management, institutional official)

If it was determined that the problem or event is serious, unanticipated, and related to the research and requires that the protocol or consent document warrants modification, the IRB must also determine and document:

- o Whether previously enrolled subjects must be notified of the modification; and
- o When such notification must take place how such notification must be documented.

The Board's discussion and required actions will be documented in the IRB minutes. The principal investigator will be notified in writing of the Board's decision and with a request that any modifications, corrective action plan or other additional requirements be submitted to the IRB. The Chair of the investigator's department and/or research unit, and the investigator's supervisor will be copied on this correspondence. The investigator must discuss any findings with the study sponsor as appropriate.

If the IRB determines that the problem or event was serious, unanticipated, and related to the research, the Chair or designee will submit a written report to the Institutional Official and copied to the HRPP Medical Director within five business days after the determination. This report will include:

- o the name of the institution
- o title of the research study
- o the name of the principal investigator
- o number assigned by the IRB and any numbers assigned by another agency/sponsor
- o the IND or IDE number if applicable
- o a detailed description of the event or unanticipated problem
- o actions the principal investigator and the IRB have taken or will implement to address the problem and prevent future occurrences.

The Institutional Official will review the event and discuss the report with the AVCRM or designee and IRB Chair. The Institutional Official will ensure notification is sent to OHRP, the FDA if appropriate, the sponsor, and other agency officials as required within 15 working days of the IRB's determination regarding the Serious Unanticipated Problem involving risk to subjects or others or local Unanticipated Serious Adverse Event.

VA Research - Within five (5) business days after a report of a serious unanticipated problem involving risks to subjects or others, or of a local unanticipated SAE, the IRB must determine and document whether the reported incident was serious and unanticipated and related to the research. (Related meaning: the event or problem may reasonably be regarded as caused by, or probably caused by, the research). If the IRB determines that the problem or event is serious and unanticipated and related to the research, the IRB must report the problem or event directly (without intermediaries) to the VA Medical Center Director with five (5) business days after the determination. The report must be made in writing, with a simultaneous copy to the

ACOS/R&D and RDC Chair.

VA Research - The IRB must review any report of apparent serious or continuing noncompliance and should consult with the VA RCO or ORO if the significance is not clear. Should the IRB determine that the reported incident constitutes serious noncompliance or continuing noncompliance, the IRB must report the determination directly (without intermediaries) to the VA Medical Center Director within five (5) business days after the determination. The IRB Chair's report must be made in writing, with a simultaneous copy to the ACOS/R&D, RDC Chair, and any other relevant research review committee.

For Overton Brooks VAMC research, the VAMC Research Office to be forwarded to the Chief of Staff of the OBVAMC Research and Development Committee and the Regional Office of Research Oversight.

### **8.5.2 Reconsideration of the IRB Decision**

A written notice of the IRB determination will be sent to the investigator. The investigator may request reconsideration or appeal the IRB decision by sending the IRB a written request for reconsideration including the basis of the investigator's request.

- a. If an investigator requests reconsideration, the investigator's written request is considered at the next IRB meeting and the IRB decides whether to uphold, reverse or modify its decision. The IRB notifies the investigator of the outcome.
- b. If the IRB receives a request for reconsideration from the investigator, the IRB should notify the IO or designee of the request and outcome.

### **8.6 Submission of Sponsor IND Safety Reports**

The phrase IND Safety Reports originates in FDA regulations 21 CFR 312 Investigational New Drug Application. The regulations require a sponsor, not a study investigator, to submit IND safety reports to the FDA and to participating investigators.

IRBs are required by FDA and DHHS regulations to review unanticipated problems involving risks to participants or others. The IRB does not require investigators to submit IND safety reports if they do not meet the definition of an unanticipated problem or other reportable events as described in this policy.

## **9. PROTOCOL EXCEPTIONS OR DEVIATIONS**

LSUHSC-S has and follows written policies and procedures for reviewing the scientific or scholarly validity of a proposed research study. Such procedures are coordinated with the ethics review process. (AAHRPP Element I.1.F.)

## 9.1 Policy

It is the policy of LSUHSC-S that researchers are expected to adhere to the protocol, protocol-required procedures and consent documents approved by the Institutional Review Board (IRB) as well as the Louisiana State University Health Sciences Center – Shreveport Human Research Protections Program and Institutional Review Board Standard Operating Procedures. The term Protocol Deviation or Protocol Violation is not defined by either the Health and Human Services human subjects regulations, (45CFR 46) Common Rule or the Food and Drug Administration human subjects regulations (21CFR 50). For the sake of research under the auspices of the Louisiana State University Health Sciences Center the following definitions, policies and procedures apply.

## 9.2 Definitions

Protocol Deviation(s) – A Protocol Deviation is any change, divergence, or departure from the study design or procedures of a research protocol that may or may not be under the investigator’s control and that has not been approved by the IRB. The term deviation is sometimes used interchangeably with the term violation. Protocol Deviations are non-adherence to the approved study plan and occur without prior approval from the sponsor and the IRB.

Protocol Exception (or Exception) - A Protocol Exception is a temporary Protocol Deviation or Eligibility Waiver that is granted by the Sponsor or funding agency, (and the FDA if applicable, for investigational device studies) and must be approved by the IRB prior to implementation. Protocol Exceptions are generally for a single subject or, occasionally, a small group of subjects.

Protocol Violations(s) – A Protocol Violation is a deviation from the IRB approved protocol that may affect the subject’s rights, safety, or well-being and/or the completeness, accuracy, and reliability of the study data. A Protocol Violation is any significant divergence from the protocol, i.e., non-adherence on the part of the patient, investigator, or the sponsor to protocol-specific inclusion/exclusion criteria, primary objective variable criteria, and/or GCP guidelines without approval from the Sponsor and IRB. Protocol Violations generally increase the risk and/or decrease the benefit; affect the subject’s rights, safety, or welfare and/or the completeness, accuracy, integrity, or reliability of the research data.

## 9.3 Planned Changes to the Research Protocol

Prior to the beginning of the study, the PI must sign the Clinical Study Agreement and the Investigator’s Signature Page (in applicable research i.e., FDA regulated) documenting his/her agreement to conduct the study in accordance with the protocol. The Investigator is strongly advised to read and understand the contract terms before signing the agreement. The Investigator must not make any changes or deviate from the protocol, except to protect the life and physical well-being of a patient in an emergency unless the change is a planned change.

There are three (3) types of planned changes to research. The most common planned change to research occurs through the submission of an Amendment to the Protocol. Examples include an increase in subject number, changes in investigators or key personnel, a change to the funding source, changes in procedures, revised consent documents, and revised HIPAA authorization. These all involve planned changes through an amended or modified Protocol and are not Protocol Deviations themselves (although they may result from a Protocol Deviation).

Another type of planned change to the research is called a Protocol Exception or Eligibility Waiver, which requires prior approval from the Sponsor and IRB and is made for a single subject or a small group of subjects, but is not a permanent revision to the protocol.

Protocol Exceptions are a subset of Protocol Deviations. Like an amendment, a Protocol Exception or Eligibility Waiver must be IRB approved prior to its implementation. If the research involves an Investigational Agent (e.g. Drug, Device or Biologic), except in an emergency to eliminate immediate harm, prior approval by the Sponsor is also required. Additionally, when research involves an Investigational Device and the changes or deviations may affect the scientific soundness of the research plan or rights, safety, or welfare of subjects, FDA and IRB pre-approval is required 21 CFR §812.150 (4). Although a Protocol Exception must be prospectively approved by the IRB, because the change does not involve a permanent change to the Research Protocol, the FDA considers it to represent a Protocol Deviation.

The third type of planned change to a Protocol is a change made to eliminate apparent immediate harm to a subject and may be considered an Unanticipated Problem. This type of change can be initiated without prior IRB approval, if it is immediately reported to the IRB and any subsequent change is not implemented before IRB approval is obtained. These planned changes are a subset of Protocol Deviations.

#### **9.4 Unplanned Changes to the Research Protocol**

The next category involves unplanned changes to a Research Protocol not otherwise approved by the IRB. Such unplanned changes are either Protocol Deviations or Protocol Violations. These unplanned changes may include changes of the IRB-approved Research Protocol, Good Clinical Practice (GCP) guidelines, regulatory standards, or LSUHSC-Shreveport's HRPP SOPs. The following unplanned changes to the research protocol are to be submitted according to institutional policy on the Protocol Deviation, Violation and Exception Reporting Form.

#### **9.5 Protocol Deviations**

LSUHSC-S has and follows written policies and procedures for addressing allegations and findings of non-compliance with Human Research Protection Program requirements. LSUHSC-S works with the Institutional Review Board(s) or Ethics Committee, when appropriate, to ensure

that participants are protected when non-compliance occurs. Such policies and procedures include reporting these actions, when appropriate. (AAHRPP Element I.5.D)

A Protocol Deviation includes any change or alteration from the procedures stated in the study Protocol, consent document, recruitment process, or study materials (e.g. questionnaires) originally approved by the IRB (but the change or alteration itself is not IRB approved). Protocol Deviation is a general term and includes, Protocol Exceptions, also referred to as Eligibility Waivers, changes made to avoid immediate harm to subjects, and Protocol Violations. 45 CFR §46.103 (b) (4) (iii), 21 CFR §56.108 (a) (4). Protocol Deviations can be examples of non-compliance or serious non-compliance.

The study shall be conducted as described in the Protocol. It is the responsibility of the investigator not to deviate from the Protocol approved by the IRB, except to avoid an immediate hazard to the participant. The Investigator must submit a Modification Request to the IRB and receive written approval prior to implementation of any change to the protocol.

Deviations that increase risk, have potential to recur, or are undertaken to eliminate an immediate hazard, would be considered an Unanticipated Problem and should be handled according to Section 8.

When a sponsor requests that the IRB be notified of a deviation that has not already been submitted to the IRB, the deviation is to be sent to the IRB immediately according to the LSUHSC-S policy and procedures, with all supporting documentation for review by the IRB.

Repetitive deviations may be ruled by the IRB to constitute non-compliance resulting in suspension or termination of IRB approval. Repeated failure by a PI to not report Protocol Deviations will be viewed as serious non-compliance with the Federal regulations, the guidelines that govern ethical conduct of research, and LSUHSC-S HRPP.

The IRB will review all reports of Protocol Deviations for frequency and will audit any protocol reporting frequent deviations.

## 9.6 Protocol Violations

Protocol Violation(s): A Protocol Violation is a subset of Protocol Deviations. A Protocol Violation includes:

- Any planned or unplanned change or deviation from the IRB approved study protocol, consent document, recruitment process, or study materials that were not approved by the IRB prior to implementation that may affect the subject's rights, safety, or well-being and/or the completeness, accuracy and reliability of the study data.
- Any significant divergence from the protocol, i.e., non-adherence on the part of the patient, investigator, or the sponsor to protocol-specific inclusion/exclusion criteria,

primary objective variable criteria, and/or GCP guidelines without prior sponsor and IRB approval.

- A divergence from the protocol that generally increases the risk and/or decreases the benefits; affect the subject's rights, safety, or welfare and/or the completeness, accuracy, integrity or reliability of the research data.

The investigator will not intentionally deviate from the protocol or the protocol-specified procedures except in cases of medical emergencies without submitting, and receiving approval for an amendment to the study. The investigator may deviate from the protocol without prior approval only when the change is necessary to eliminate an apparent hazard to the subject.

Protocol Violations can create serious situations that require immediate investigation by the IRB Chair/Human Research Protections Program and reporting to the Institutional Official (IO) and/or IO Designee and appropriate external agencies, including the Office of Human Research Protections (OHRP), when warranted.

All departures from the IRB approved protocol are a Protocol Deviation/Violation and they are seen by the reporting Federal agencies as such; however, the Institution has established policy to assist the investigator in determining how to report protocol deviations/violations.

Major Protocol Violation: is a deviation that has an impact on subject safety, may substantially alter risks to subjects, may influence the integrity of the study data, or may affect the subject's willingness to participate in the study. Major Protocol Violations can vary in the degree of the seriousness according to how the changes impact subject safety, the degree of non-compliance with Federal regulations, State laws, the HRPP, LSUHSC-S policies or procedures, and the degree of foreknowledge of the event.

All Major Protocol Violations must be reported to the IRB within five (5) days of learning of the violation. Use the Reportable New Information process to report Major Protocol Violations. If it is necessary to make a permanent change to the study procedures to avoid harm to other subjects, then a Protocol amendment should be submitted as soon as possible by the PI, using a Modification Form. If appropriate to maintain safety of the subjects, new subject enrollment should be temporarily stopped by the PI until the amendment is approved. Regardless of who discovers a Major Protocol Violation (e.g., sponsor or their agent during a monitoring visit), the PI is responsible for reporting it to the IRB. Examples of Major Protocol Violations are listed below:

- Failure to obtain valid informed consent (e.g. verbal consent rather than IRB-required signed informed consent)
- Enrolling a subject who does not meet the inclusion/exclusion criteria
- Continuing research activities after IRB approval has expired
- Any deviations from the investigational plan for an Investigational Device taken to protect the life or physical well-being of a participant in an emergency
- Any Emergency Use of an FDA-regulated Test Article or Humanitarian Use Device (HUD)

prior to IRB approval

- Hospitalization or death caused/contributed by a HUD
- Protocol deviations taken without prior IRB review to eliminate an apparent immediate hazard to subjects
- Any event that requires prompt reporting to the Sponsor
- Failure to perform a required laboratory test or procedure that could impact the safety of the subject; i.e., screening lab, test, physical exam
- Sponsor-imposed suspension for risk
- Breaches in subject confidentiality or privacy that could pose an increased risk to subjects or others
- An investigator deliberately decides to follow a different procedure than that set forth in the Protocol for one or more subjects (other than to eliminate apparent immediate hazards to the subject or others)
- Loss of laptop computer that contained identifiable, private information about subjects
- Accidental distribution of incorrect study medication; or wrong dose or route of study medication
- The Protocol indicates that a research nurse will conduct in-take interviews and review the consent document with subjects. The research nurse leaves, so a non-study clinic nurse does the procedure instead. The protocol requires a physical exam and someone not qualified conducts the exam. i.e. study nurse
- Sponsor believes that study data to date indicates a potential subject could safely participate but does not currently meet approved eligibility criteria (Protocol Exception)
- Incarceration of a participant enrolled in a Protocol not approved to enroll Prisoners

Minor Protocol Violation: is one that does not usually impact subject safety, compromise the integrity of the study data, or affect the subject's willingness to participate in the study. The Minor Protocol Violation is to be reported to the IRB by the PI whether identified by the PI, study staff, or during a monitoring visit.

All Minor Protocol Violations require reporting and should be reported by the PI to the IRB within five (5) working days (or no later than at the time of continuing review) of learning of the violation. Use the Reportable New Information process to report Minor Protocol Violations. Examples of Minor Protocol Violations are listed below:

- Research study visits occurring outside study window not impacting subject safety or research data
- A rescheduled study visit
- Failure to collect an ancillary self-report questionnaire
- Use of unapproved recruitment procedures or materials (e.g. when slightly altered)
- Study visits outside the protocol-prescribed visit window (e.g. the subject is on vacation or late due to an illness)
- Failure of the subject to return unused study medication
- Subject's refusal to complete scheduled research activities, not adversely affected

subject or research data

## **9.7 Protocol Exceptions**

A protocol exception is a temporary protocol deviation or eligibility waiver that is granted by the Sponsor or funding agency, (and the FDA if applicable, for investigational device studies) and the IRB prior to implementation. Protocol exceptions are generally for a single subject or, occasionally, a small group of subjects. If under extraordinary circumstances such action is considered ethically, medically, and scientifically justified for a patient, prior approval from the Sponsor and the IRB, in accordance with the SOP, is required before the patient will be allowed to enter the study.

The Protocol Exception or eligibility waiver is usually evaluated by both the sponsor or funding agency (and FDA, if applicable) and the IRB to determine that it does not increase the risk to the subject(s), or jeopardize the integrity of the research data. Documentation of sponsor (or FDA) pre-approval and IRB approval of the exception should be maintained in the investigator's research study file.

If the Investigator becomes aware of a subject that is enrolled in the study who did not meet protocol eligibility criteria (a protocol violation), the investigator must immediately inform the sponsor and the IRB. Such subjects will be discontinued from the study, except in the rare instance following review and written approval by the sponsor and the IRB that it is in the best interest of the subject to remain in the study in accordance with this SOP.

It is the responsibility of the Investigator to ensure any protocol exceptions or eligibility waivers are approved by both the sponsor and IRB before implementation.

Exceptions may not increase risk or decrease benefit, affect the participant's rights, safety, welfare, or affect the integrity of the resultant data. An example of a Protocol Exception or Eligibility Waiver is listed below:

Enrollment of a research subject who fails to meet all the Protocol eligibility criteria (e.g., the subject may have been evaluated for all other parameters, and it was determined by the Sponsor and the IRB that not meeting this inclusion criteria or laboratory screening value would not cause harm to the subject or alter the validity of the study).

## **9.8 IRB Review Process**

### **9.8.1 Protocol Deviations**

There are several types of deviations (violations, exceptions) that may occur from the IRB

approved protocol. Each type has a different IRB reporting requirement.

Protocol deviations/violations are to be reported to the IRB within five (5) days. Consideration for an exception is to be requested prior to any deviation from the IRB approved protocol. The IRB Chair or designee will review the protocol deviation and determine whether it is eligible for review under expedited procedures or requires convened IRB review.

In addition, all major protocol violations that occur after the initial or most recent continuing review should be summarized in the appropriate section of the Continuing Review Form. Alternatively, copies of the report forms submitted to the IRB may be attached to the Continuing Review Form.

### **9.8.2 Major Protocol Violations**

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Investigator evaluation of Protocol Violation – Investigators report Major Protocol Violations via the Reportable New Information process. Each Protocol violation report should discuss what measures have been put in place to prevent future re-occurrences of the same event. The PI should also evaluate Protocol violations for any trends or patterns that would require additional corrective actions or submission of a Protocol amendment to prevent future violations. Repeated violations of the same or similar nature may by a clear indication that a permanent change (i.e. an amendment) to the study procedures is necessary.

Upon receipt in the IRB, the IRB staff will screen the submission for completeness and identify the appropriate level of review.

When the IRB reviews the submitted protocol deviation/violation via Expedited Review, the designated IRB reviewer will document their findings on the Reportable New Information Reviewer Checklist. The possible determinations allowed through expedited review procedures are as follows:

- This event is an Unanticipated Problem involving Risks to Subjects or Others (Send to Convened Board)
- Suspension or termination of the IRB approval is recommended (Send to Convened Board)
- Serious non-compliance (Send to Convened Board)
- Continuing non-compliance (Send to Convened Board)
- Non-compliance that is neither serious nor continuing
- None of the above
- In addition to the above: Refer events or concerns regarding the research to the HRRP QA staff for non-compliance review (audit).

Major Protocol Violations that require review by the Fully Convened IRB, the assigned member reviewers would document determinations on the Reportable New Information Reviewer Checklist. The potential determinations are as follows:

- This event is an Unanticipated Problem involving Risks to Subjects or Others (Send to Convened Board)
- Suspension or termination of IRB approval is recommended (Send to Convened Board)
- Serious non-compliance (Send to Convened Board)
- Continuing non-compliance that is neither serious nor continuing
- Non-compliance that is neither serious nor continuing
- Acknowledged – no further information or action required
- Modifications or Additional Information Required – Additional information is needed to appropriately evaluate the event or changes to the research that are minor in nature are being required based upon the event
- If there are safety issues or concerns related to the event the IRB may make additional determinations that include, but are not limited to, the following:
  - Require substantive changes of the research protocol and/or informed consent document
  - Implement additional safeguards, such as additional safety monitoring or more frequent safety monitoring
  - Increase the continuing review frequency (i.e. six (6) months or three (3) months)
  - Suspend the research and recommend revision to the research that must be made before the suspension can be lifted
  - Suspend enrollment of new subjects, either temporarily or permanently
  - Discontinue participation of currently enrolled subjects
  - Terminate the research
  - None of the above
- In addition to the above: Refer event or concerns regarding the research to the HRPP QA staff for non-compliance review (audit).

The Fully Convened IRB discusses the event at the meeting and the IRB minutes document the discussion and final determination of the convened IRB.

In accordance with federal and institutional policy the IRB is required to determine whether the Protocol Violation/Deviation constitutes an instance of Non-Compliance, Serious Non-Compliance or Continuing Non-Compliance.

When the violation is an event involving a change in the Protocol to eliminate immediate hazard or harm to subjects, the IRB should verify that the investigator reported the event in the required five (5) day period. Also, the IRB should verify that the PI implemented appropriate measures to alleviate or eliminate the harm to current and future subjects in the research.

The PI will receive notification of determination from the IRB.

### 9.8.3 Minor Protocol Violations

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Investigator Evaluation of Protocol Violation – Each Minor Protocol Violation report should discuss what measures have been put in place to prevent future re-occurrences of the same event. The PI should also evaluate Protocol Violations for any trends or patterns that would require additional corrective actions or submission of a Protocol amendment to prevent future violations. Repeated violations of a similar nature may be a clear indication that a permanent change (i.e. an amendment) to the study procedures is necessary.

Minor Protocol Violations should be reported within five (5) working days of the violation, and may be reported to the IRB in summary form at the time of the next continuing review. All Protocol Violations should be reported to the research sponsor or funding agency in a timely manner and according to that company's or agency's policy. All Protocol Violations should be documented in the investigator's research study files.

Protocol Deviation/Violation Log – It is required that the Investigator keep a log of all Protocol violations for each research study. The log should include the subject study identifier, the date of the violation, an indication of whether the violation was a major or minor violation, a description of the violation, the date of the IRB submission, date of notification from the IRB, date of sponsor notification, and the date of sponsor notification of receipt. Copies of the report sent to the IRB should also be maintained in the research files.

LSUHSC-S investigators are not required to report Protocol Violations to LSUHSC-S IRB that occur at other research sites in multi-center research trials.

#### **9.8.4 Protocol Exceptions**

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It is the responsibility of the investigator and research staff to follow the written protocol as provided by the sponsor and approved by the IRB. However, there are times when deviations to the protocol are identified before they occur. Examples include enrollment of a single individual who does not meet the protocol inclusion criteria or scheduling a study visit outside the protocol required time frame. The investigator may submit a written request for a one-time exception as a protocol modification request to the IRB. Prior written approval from the sponsor must also be obtained.

An exception request applies to a one-time event. Such a request should be rare and justified in terms of serving the best interests of the potential study subject. Any change or deviation from the protocol that does not receive prior IRB review and approval (except when the deviation is performed to eliminate apparent immediate hazards to the subject) will be evaluated according to the IRB's policies and procedures for handling non-compliance and considering whether the deviation constitutes an unanticipated problem involving risks to subjects or others. This is not intended for deviations from the protocol performed to eliminate apparent immediate hazards to the subject in compliance with 45 CFR 46:103(b)(4) and 21 CFR 6108.(a)(3)and (a)(4).

Investigator requests for protocol exceptions or eligibility waivers must be submitted to the IRB

Office as a Reportable New Information along with documentation of Sponsor justification and approval. The IRB Staff will screen the submission for completeness and identify the appropriate level of review. The IRB Office will forward the submission to the IRB Chair or designee for review.

The IRB will review the investigator's Reportable New Information, and document the findings on the Reportable New Information Reviewer Checklist. The Chair may choose to place any exception request on the agenda of the next convened IRB meeting for discussion. The investigator may be asked to appear at that meeting to answer any questions or clarify issues for the IRB.

The Fully Convened IRB discusses the event at the convened meeting and the IRB meeting minutes document the discussion and final determination of the Fully Convened IRB regarding the Protocol Exceptions.

The possible determinations IRB members can make regarding exceptions include:

- Exception approved-no issues
- Exception disapproved
- Modifications required
- Referred for Fully Convened IRB Review
- Deferral-further justification or information required (only for Fully Convened IRB Review)

Once a determination is made by the IRB, the PI will receive a notification of determination from the IRB and documentation of review is placed in the IRB Protocol file. All determinations made by expedited procedures regarding any Protocol Exception Request will be reported to the convened board on the next meeting agenda.

## **10. COMPLAINTS AND NON-COMPLIANCE**

### **10.1 Policy**

As part of its commitment to protecting the rights and welfare of human subjects in research, LSUHSC-S reviews all complaints and allegations of non-compliance and takes any necessary action to ensure the ethical conduct of research. All protocols reviewed by the IRB are subject to audit by the IRB and HRPP personnel. All investigators and other study personnel involved in human subjects research are required to comply with all laws and regulations governing their research activities, as well as with requirements and determinations of the IRB. Study personnel includes the principal investigator and any staff member, resident, fellow, affiliated investigator or other affiliated individual involved in human subjects research being conducted under the auspices of the institution, regardless of the funding source or whether the research is funded or unfunded. The Institution, which includes the IRB, is expected to comply with

Institutional policies as well as all federal regulations and state laws related to the protection of the safety, rights and welfare of human subjects in research. Noncompliance occurs when research involving human subjects is conducted in a manner that disregards or violates federal regulations, the policies or procedures of the Institutional Review Board (IRB), or institutional policies governing human research. Noncompliance with respect to human research participant protection violates the LSUHSC-Shreveport Federalwide Assurance Registration (FWA) with the Office of Human Research Protections (OHRP). Even in the absence of intent, an unapproved or otherwise noncompliant research activity may place a research participant at unnecessary risk.

## 10.2 Definitions

LSUHSC-S has and follows written policies and procedures for addressing allegations and findings of non-compliance with Human Research Protection Program requirements. LSUHSC-S works with the Institutional Review Board(s) or Ethics Committee, when appropriate, to ensure that participants are protected when non-compliance occurs. Such policies and procedures include reporting these actions, when appropriate. (AAHRPP Element I.5.D.)

Allegation of Non-Compliance – Allegation of Non-Compliance is defined as an unproven allegation of non-compliance.

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. For veterans Administration (VA) research Continuing Non-Compliance includes a persistent failure to adhere to the laws, regulations, or policies governing Human Research.

Finding of Non-Compliance – Finding of Non-Compliance is defined as an allegation of non-compliance that is proven true or a report of non-compliance that is clearly true. (For example, a finding on an audit of an unsigned consent document, or an admission of an investigator that the protocol was willfully not followed would represent reports of non-compliance that would require no further action to determine their truth and would therefore represent findings of non-compliance.)

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 IRB or federal regulations or LSUHSC-S Institutional policies governing human subjects' research.

In the case of research funded or conducted by the department of Defense (DOD), Non-Compliance includes failure of a person, group, or institution to act in accordance with Department of Defense (DOD) Instruction 3216.02, its references, or applicable requirements.

In the case of VA research, Non-Compliance includes failure to follow the requirements of VA policies and regulations contained in Veterans Administration (VHA) Handbooks.

Serious non-compliance – Non-Compliance that could adversely affect the rights, safety, or welfare of a human subject; place a human subject at increased risk of harm; -cause harm to a human subject; affect a human subject’s willingness to participate in research; or damage or compromise the scientific integrity of research data. Research being conducted without prior IRB approval is considered serious noncompliance.

For Department of Defense (DOD) research Serious Non-Compliance includes failure of a person, group, or institution to act in accordance with Department of Defense (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; affect a human subject’s willingness to participate in research; or damage or compromise the scientific integrity of research data.

For VA research Serious Non-Compliance includes a failure to adhere to the laws, regulations, or policies governing Human Research that might reasonably be regarded as:

- Involving substantive harm, or a genuine risk of substantive harm, to the safety, rights, or welfare of human research subjects, research staff, or others
- Substantively compromising the effectiveness of a Veterans Administration (VA) facility’s human research protection or human research oversight programs

### 10.3 Complaints

LSUHSC-S responds to the concerns of research participants. (AAHRPP Standard I-4)
LSUHSC-S has and follows written policies and procedures so that Researchers and Research Staff may bring forward to the Organization concerns or suggestions regarding the Human Research Protection Program, including the ethics review process. (AAHRPP Element I.5.C.)
LSUHSC-S has and follows written policies and procedures for addressing allegations and findings of non-compliance with Human Research Protection Program requirements. LSUHSC-S works with the Institutional Review Board(s) or Ethics Committee, when appropriate, to ensure that participants are protected when non-compliance occurs. Such policies and procedures include reporting these actions, when appropriate. (AAHRPP Element I.5.D)

The LSUHSC-S IRB will review all complaints, protocol deviations, allegations of noncompliance, findings of serious or continuing noncompliance, and take any necessary action to ensure that the rights and welfare of human subjects are protected. The Chair of the IRB will promptly handle (or delegate staff to handle), and, if necessary, investigate all complaints, concerns, and appeals received by the IRB. This includes complaints, concerns, and appeals from investigators, research participants and others.

A Reportable New Information (RNI) Report must be submitted to the IRB when an investigator including LSUHSC-S personnel, the research team, faculty, staff, administration, residents, fellows or students become aware of any noncompliance with respect to a specific study. Reports of noncompliance may also result from an audit or a monitoring report. Research participants, participant's family members, and others external to the Institution, including regulatory agencies may report suspected noncompliance to the HRPP, IRB or to the Institutional Official. These reports may be in the form of complaints and may be made anonymously. Reports of research misconduct or Whistleblower reports are subject to different rules and will be referred to the Office of Research or LSUHSC-S Compliance Office if received by the IRB or HRPP.

All complaints, written or verbal (including telephone complaints), and regardless of point of origin, are forwarded to the IRB Chair, the IO or designee. Upon receipt of the complaint, the Chair, IO or designee will make a preliminary assessment whether the complaint warrants immediate suspension of the research project. If the complaint meets the definition of non-compliance, it will be considered an allegation of non-compliance according to section 10.4. If the complaint meets the definition of an unanticipated problem involving risk to subjects or others, it will be handled according to Section 8.

Within three (3) business days of receipt of the complaint, the IRB Chair, IO or designee shall generate a letter to acknowledge that the complaint has been received and is being investigated, providing a follow-up contact name.

#### **10.4 Non-compliance**

LSUHSC-S has and follows written policies and procedures for addressing allegations and findings of non-compliance with Human Research Protection Program requirements. LSUHSC-S works with the Institutional Review Board(s) or Ethics Committee, when appropriate, to ensure that participants are protected when non-compliance occurs. Such policies and procedures include reporting these actions, when appropriate. (AAHRPP Element I.5.D)

Investigators and their study staff are required to report instances of possible non-compliance. The Principal Investigator is responsible for reporting any possible non-compliance by study personnel to the IRB. However, any individual or employee may report observed or apparent instances of non-compliance to the LSUHSC-S IRB. In such cases, the reporting party is responsible for making these reports in good faith, maintaining confidentiality and cooperating with any IRB and/or institutional review of these reports.

If an individual, whether investigator, study staff or other, is uncertain whether there is cause to report noncompliance, he or she may contact the IRB Chair, IO or designee directly to discuss the situation informally.

Reports of non-compliance must be submitted to the HRPP Office within five (5) working days

of discovery of this noncompliance. The report must include a complete description of the non-compliance, the personnel involved and a description of the non-compliance.

When following VA Regulations, reference VHA Handbook 1058.01

The IRB must review a report of apparent serious or continuing non-compliance at the earliest practicable opportunity, not to exceed 30 days after notification. The IRB Chair may take interim action as needed to eliminate apparent immediate hazards to subjects.

Should the IRB determine the reported incident constitutes serious non-compliance or continuing non-compliance, within five days the IRB chair, or designee, must provide a written report of the determination directly to:

- o The VA facility director
- o Associate Chief of Staff for Research
- o Research and Development Committee
- o The RCO, if the apparent serious or continuing non-compliance was identified by an RCO audit, regardless of outcome.

The IRB must reach a determination that serious or continuing non-compliance did (or did not) occur within 30-45 days after receiving a report of apparent non-compliance.

Remedial actions involving a specific study or research team must be completed within 90-120 days after the IRB's determination.

Remedial actions involving programmatic non-compliance must be completed within 120-180 days after the IRB's determination, unless remediation requires substantial renovation, fiscal expenditure, hiring, or legal negotiations.

For additional information reference VA Handbook: 1058.01§6.f, 1058.01§5.c, 1058.01§6.f.(3)(a).

When following Department of Defense regulations, determinations of serious or continuing non-compliance of DoD-supported research must be promptly (within 30 days) reported to the DoD human research protection officer.

#### **10.4.1 Review of Allegations of Non-compliance**

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All allegations of non-compliance will be reviewed by the IRB Chair or HRPP Compliance Committee (HRPPCC). The HRPP Compliance Committee serves in an advisory capacity to the

Institution and the IRB on matters of non-compliance or unanticipated problems involving risks to subjects or others. The Compliance Committee includes IRB members but is not part of the IRB Committee. Campus Counsel from the Office of Legal Affairs and Organizational Integrity also serves as a member of the committee. The function of the Compliance Committee is to review, evaluate, and systematically make recommendations regarding non-Compliance and unanticipated problems in accordance with institutional definitions and provide that information to the IRB and institution as needed. The HRPPCC reports to the Institutional Official.

When the HRPP Compliance Committee is notified of an event that includes an allegation or finding of serious or continuing non-compliance or a possible unanticipated problem involving human subjects research, the HRPPCC will review as appropriate:

1. All documents relevant to the allegation
2. The last approval letter from the IRB
3. The last approved IRB application and protocol
4. The last approved consent document
5. The grant, if applicable
6. Any other pertinent information (e.g., questionnaires, DSMB reports, etc.)

The IRB Chair or HRPP Compliance Committee will review the allegation within five (5) days and make a determination as to the validity of the allegation. HRPPCC members do not participate in the review of any event in which the member has Conflicting Interest. Additional information or an audit of the research in question by the HRPP QA/QI team may be requested.

When it is determined that noncompliance did not occur because the incident was within the limits of an approved protocol for the research involved, the determination is reported in writing to the PI following the review and if applicable the reporting party. The determination letter will be copied to the Institutional Official in cases where the Institutional Official and any other parties had been notified at the outset.

If in the judgment of the IRB Chair or HRPP Compliance Committee, the reported allegation of non-compliance is valid, the non-compliance will be processed according to Section 10.4.2 Review of Findings of Non-compliance.

If it is the judgment that any allegation or findings of non-compliance warrants suspension of the research before completion of any review or investigation to ensure protection of the rights and welfare of participants, the IRB Chair, IRB Vice-Chair, or HRPP Medical Director, IO or designee may suspend the research as described in Section 3.10 with subsequent review by the IRB Committee.

It may be determined that additional expertise or assistance is required to make these determinations. The IRB may form an ad hoc committee to assist with the review and fact

gathering process. When an ad hoc committee assists in the review process, the IRB Chair is responsible for assuring that minutes of the meeting are generated and kept to support any determinations or findings made by the ad hoc committee.

#### **10.4.2 Review of Findings of Non-compliance**

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Non-compliance is not serious or continuing: When the IRB Chair or HRPP Compliance Committee determines that the noncompliance occurred, but the noncompliance does not meet definition of serious or continuing noncompliance, the determination is reported in writing to the PI and if applicable the reporting party. The IRB Chair or HRPP Compliance Committee will work with the PI to develop a corrective action plan to prevent future noncompliance. The report of noncompliance and corrective action is reported to the IRB through the expedited review report in the IRB minutes. If the PI refuses to cooperate with the corrective action plan, the matter is referred to a convened meeting of the IRB with notification to the IO or designee.

Serious or Continuing Non-compliance: When the IRB Chair or HRPP Compliance Committee determines that non-compliance has occurred and that the noncompliance meets the definition of serious or continuing noncompliance, the report of noncompliance is communicated to the IRB at an available meeting. The IRB Chair may use discretion and call an emergency IRB meeting should the circumstances warrant such an urgent meeting. The HRPP Compliance Committee will review and determine an appropriate action to (i.e. direct audit) ensure the protection of human subjects.

Examples of serious non-compliance may include the following: falsifying IRB documents, conducting human subjects research without IRB approval, deviating from the IRB-approved protocol or consent process, modifying the protocol or consent process without prior IRB approval, failing to maintain regulatory documents and inadequately overseeing research.

All findings of serious or continuing non-compliance referred to the IRB will be reviewed at a convened meeting to determine an appropriate corrective action plan. All IRB members will receive as appropriate:

1. All documents relevant to the allegation
2. The last approval letter from the IRB
3. The last approved IRB protocol
4. The last approved consent document

At this stage, the IRB may:

1. Find that there is no issue of non-compliance
2. Find that there is non-compliance that is neither serious nor continuing and an adequate corrective action plan is in place
3. Find that there is serious or continuing non-compliance and approve any changes

proposed by the IRB Chair and/or HRPP Compliance Committee

4. Find that there may be serious or continuing non-compliance and direct that a formal inquiry (described below) be held
5. Request additional information

#### **10.4.3 Inquiry Procedures**

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A determination may be made by the IRB that an inquiry is necessary based on several issues that may include but are not limited to:

1. Subjects' complaint(s) that rights were violated
2. Report(s) that investigator is not following the protocol as approved by the IRB
3. Unusual and/or unexplained adverse events in a study
4. Repeated failure of investigator to report required information to the IRB

A subcommittee is appointed consisting of IRB members, and non-members if appropriate, to ensure fairness and expertise. The subcommittee is given a charge by the IRB, which can include any or all of the following:

1. Review of protocol(s) in question
2. Review of sponsor audit report of the investigator, if appropriate
3. Review of any relevant documentation, including consent documents, case report forms, subject's investigational and/or medical files etc., as they relate to the investigator's execution of her/his study involving human subjects
4. Interview of appropriate personnel if necessary
5. Preparation of either a written or oral report of the findings, which is presented to the full IRB at its next meeting
6. Recommend actions if appropriate

#### **10.4.4 Final Review**

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The results of the inquiry will be reviewed at a convened IRB meeting where the IRB will receive a report from the subcommittee. If the results of the inquiry substantiate the finding of serious or continuing non-compliance, the IRB(s) possible actions could include, but are not limited to:

1. Request a correction action plan from the investigator
2. Verification that participant selection is appropriate and observation of the actual informed consent
3. An increase in data and safety monitoring of the research activity
4. Request a directed audit of targeted areas of concern
5. Request a status report after each participant receives intervention
6. Modify the continuing review cycle
7. Request additional Investigator and staff education
8. Notify current subjects, if the information about the non-compliance might affect their willingness to continue participation
9. Require modification of the protocol

10. Require modification of the information disclosed during the consent process
11. Require current participants to re-consent to participation
12. Suspend the study (See below)
13. Terminate the study (See below)

In cases where the IRB determines that the event of non-compliance also meets the definition of unanticipated problem involving risks to subjects or others, the policy and procedure for review of such events will also be followed.

The investigator is informed of the IRB determination and the basis for the determination in writing and is given a chance to respond. If the IRB determines that the non-compliance was serious or continuing, the results of the final review will be reported as described below in Section 11.

## **11. REPORTING TO REGULATORY AGENCIES AND INSTITUTIONAL OFFICIALS**

LSUHSC-S has and follows written policies and procedures for addressing allegations and findings of non-compliance with Human Research Protection Program requirements. LSUHSC-S works with the Institutional Review Board(s) or Ethics Committee, when appropriate, to ensure that participants are protected when non-compliance occurs. Such policies and procedures include reporting these actions, when appropriate. (AAHRPP Element I.5.D)

The IRB or EC has and follows written policies and procedures for addressing unanticipated problems involving risks to participants or others, and for reporting these actions, when appropriate. (AAHRPP Element II.2.F)

The IRB or EC has and follows written policies and procedures for suspending or terminating IRB or EC approval of research, if warranted, and for reporting these actions, when appropriate. (AAHRPP Element II.2.G)

### **11.1 Policy**

Federal regulations require prompt reporting to appropriate institutional officials, and the department or agency head of (i) any unanticipated problems involving risks to subjects or others or any serious or continuing noncompliance with this policy or the requirements or determinations of the IRB; and (ii) any suspension or termination of IRB approval. The LSUHSC-S HRPP will comply with this requirement and the following procedures describe how these reports are handled.

However, should the IRB determine that the reported incident constitute serious or continuing non-compliance, within five business days after the determination, the IRB Chair, or designee must provide a written report of the determination directly to:

- Institutional Official
- VA Medical Center Director

- Other relevant research review committees

## 11.2 Procedures

1. IRB staff will initiate these procedures as soon as the IRB takes any of the following actions:
  - a. Determines that an event may be considered an unanticipated problem involving risks to participants or others
  - b. Determines that non-compliance was serious or continuing
  - c. Suspends or terminates approval of research
2. The IO or designee is responsible for preparing reports or letters which includes the following information:
  - a. The nature of the event (Unanticipated problem involving risks to participants or others, serious or continuing non-compliance, suspension or termination of approval of research)
  - b. Name of the institution conducting the research
  - c. Title of the research project and/or grant proposal in which the problem occurred
  - d. Name of the principal investigator on the protocol
  - e. Number of the research project assigned by the IRB and the number of any applicable federal award(s) (grant, contract, or cooperative agreement)
  - f. A detailed description of the problem including the findings of the organization and the reasons for the IRB(s) decision
  - g. Actions the institution is taking or plans to take to address the problem (e.g., revise the protocol, suspend subject enrollment, terminate the research, revise the informed consent document, inform enrolled subjects, increase monitoring of subjects, etc.)
  - h. Plans, if any, to send a follow-up or final report by the earlier of
    1. A specific date
    2. When an investigation has been completed or a corrective action plan has been implemented
    3. The IRB Chair, IO or designee will review the letter; modify the letter, sign and report as required.
    4. The IO or designee sends a copy of the signed report within five business days after the determination to:
      - a. The IRB by including the letter in the next agenda packet as an information item
      - b. The Institutional Official, Medical Center Director or other relevant research review committees.
      - c. The following federal agencies:
        - OHRP, if the study is subject to DHHS regulations or subject to a DHHS Federal-wide assurance
        - FDA, if the study is subject to FDA regulations.
        - If the study is conducted or funded by any Federal Agency other than DHHS that is subject to The Common Rule, the report is sent to OHRP or

- the head of the agency as required by the agency
- Reporting to a regulatory agency is not required if the event occurred at a site that was not subject to the direct oversight of the organization, and the agency has been notified of the event by the investigator, sponsor, another organization, or other mechanisms.
- d. Principal investigator
- e. Sponsor, if the study is sponsored
- f. Contract research organization, if the study is overseen by a contract research organization
- g. Department Chair or supervisor of the principal investigator
- h. The Privacy Officer of a covered entity, if the event involved unauthorized use, loss, or disclosure of individually-identifiable patient information from that covered entity
- i. The Information Security Officer of an organization if the event involved violations of information security requirements of that organization
- j. Office of Risk Management, if appropriate
- k. Others as deemed appropriate by the Institutional Official
- l. Office of Legal Affairs and Organizational Integrity
- m. Office of Sponsored Programs and Technology Transfer, when applicable
- n. For Overton Brooks VAMC research, the VAMC Research Office to be forwarded to:
  - The Chief of Staff of the OBVAMC Research and Development Committee
  - The Regional Office of Research Oversight

The IO or designee ensures that all steps of this policy are completed within fifteen (15) working days of the initiating action. For more serious actions, the IO or designee will expedite reporting.

## 12. INVESTIGATOR RESPONSIBILITIES

In addition to following applicable laws and regulations, Researchers and Research Staff adhere to ethical principles and standards appropriate for their discipline. In designing and conducting research studies, Researchers and Research Staff have the protection of the rights and welfare of research participants as a primary concern. (AAHRPP Standard III-1)

Researchers and Research Staff meet requirements for conducting research with participants and comply with all applicable laws, regulations, codes, and guidance; LSUHSC-S's policies and procedures for protecting research participants; and the IRB's or EC's determinations. (AAHRPP Standard III-2)

### 12.1 Policy

Researchers maintain appropriate oversight of each research study, as well as Research Staff and trainees, and appropriately delegate research responsibilities and functions. (AAHRPP Element III.2.B)

According to Health and Human Services Regulations an investigator refers to an individual performing tasks involving the conduct of human subjects research activities such as obtaining information about living individuals by intervening or interacting with them for research purposes; obtaining identifiable private information about living individuals for research purposes; obtaining the voluntary informed consent of individuals to be subjects in research; and studying, interpreting, or analyzing identifiable private information of data for research purposes.

Investigators can include physicians, scientists, nurses, administrative staff, teachers, and students, among others. Some research studies are conducted by one or more investigators, and at LSUHSC-S there will be only one Principal Investigator on a research study. In every human subject's research study, investigators have certain responsibilities regarding the ethical treatment of human subjects.

Principal Investigators are ultimately responsible for the conduct of research. Research must be conducted according to the signed investigator statement, the investigational plan and applicable regulations; for protecting the rights, safety, and welfare of subjects under the PI(s) care. Principal Investigators may delegate research responsibility. However, investigators must maintain oversight and retain ultimate responsibility for the conduct of those to whom they delegate responsibility. Research procedures that are delegated to other members of the research team by the PI are documented on a Delegation of Authority Log. Delegation of Authority Logs is to be submitted with Initial Proposals and at the time of continuing review. In the event of changes to the research staff or changes in the delegated responsibilities, the PI is to submit these changes to the IRB for review and approval.

## 12.2 Investigators

Principal Investigators: Faculty or senior staff may serve as the Principal Investigator on a research project involving human subjects in their field of expertise. Adjunct and Gravis faculty members are approved by the IRB chair IO or designee on a case by case basis in consultation with HRPP Counsel and Human Resources. This process should ensure an appropriate relationship between the institution and the researcher to allow for support and oversight. Protocols that require skills beyond those held by the Principal Investigator must be modified to meet the investigator's skills or have one or more additional qualified faculty as sub-investigator(s).

Student Investigators: This Institution allows students and/or medical residents and fellows to act as Principal Investigators in specific human subject research as follows: investigator initiated retrospective review of data, documents or specimens and minimal risk survey research. They

are required to obtain a Faculty Advisor for guidance. The faculty Advisor is required to be listed as part of the research personnel (staff) of the study and to complete human subject research online training courses. Students, medical residents or fellows may not serve as the principal investigator for any research that is determined to be greater than minimal risk.

Change in Principal Investigator: If there is a change in the Principal Investigator, the outgoing investigator must submit a modification form to notify the IRB that he or she has relinquished the responsibilities of the Principal Investigator to the person named, or will do so on a specific date. The newly named Principal Investigator notifies the IRB that he or she has read the protocol and agrees to accept the responsibilities of the Principal Investigator. In sponsored research, the sponsor must be notified and approve the change in PI through an amendment to the Clinical Trial Agreement (CTA).

### 12.3 Responsibilities

Researchers and Research Staff have a process to address participants' concerns, complaints, or requests for information. (AAHRPP Element III.1.G)
Researchers and Research Staff follow the requirements of the research protocol or plan and adhere to the policies and procedures of LSUHSC-S and to the requirements or determinations of the IRB or EC. (AAHRPP Element III.2.C)
Researchers and Research Staff follow reporting requirements in accordance with applicable laws, regulations, codes, and guidance; LSUHSC-S's policies and procedures; and the IRB's or EC's requirements. (AAHRPP Element III.2.D)
The IRB or EC has and follows written policies and procedures for addressing unanticipated problems involving risks to participants or others, and for reporting these actions, when appropriate. ( AAHRPP Element II.2.F)

Investigator obligations when conducting studies involving human subjects are listed below. This is a general guide and not a comprehensive description of all investigator responsibilities.

Investigators are expected to:

1. Protect the rights and welfare of prospective subjects
2. Assume overall administrative responsibilities for all aspects of each IRB-approved research study, conducting the research according to the IRB-approved protocol, maintaining appropriate oversight of the research study and supervision of the research staff, appropriately delegating research responsibilities (Element III.2.B, Element III.2.C)
3. Assure all key personnel under his/her supervision are adequately trained and supervised in the regulatory requirements regarding the conduct of research and the ethical principles upon which they are based (Element III.2.C). LSUHSC-S employs the

- Collaborative Institutional Training Initiative (CITI) course as its training program
4. Assure that research duties are delegated to individuals who are qualified to perform the assigned tasks and informing research staff of any pertinent changes during the course of the study (Element III.2.B)
  5. Develop and conduct a research plan that is in accordance with the ethical principles in the Belmont Report (Element.2.A)
  6. Develop a research plan that is scientifically sound and in accordance with the standards of their discipline (Element III.1.C). Studies should be in a design that minimizes risks to participants
  7. Follow Good Clinical Practice (GCP) guidelines when conducting any study that meets the definition of human subjects' research and involves (1) FDA regulated approved or unapproved drugs, devices or biologics or any other FDA regulated product; or (2) where the sponsor or funding agency requires the use of GCP guidelines
  8. Ensure that pertinent laws, regulations, and institutional procedures and guidelines are observed by participating investigators and research staff. Investigators must be knowledgeable about and comply with requirements of Common Rule and other federal research laws and regulations, applicable state law, LSUHSC-S FWA, and institutional policies and procedures for protection of human subjects (Element III.2.A)
  9. Maintain contact with the sponsor, the monitoring entity if applicable, and receive reports from the sponsor
  10. Ensure that every investigator discloses any potential conflict of interest (Element III.1.B) (As outlined in Section 14)
  11. Cooperate with evaluations, inspections, and audits performed by authorized internal oversight authorities, such as the IRB, as well as external reviews (e.g., sponsor or government agency such as FDA)
  12. Maintain adequate and accurate records in accordance with 21 CFR 312.62, making those records available for inspection in accordance with 21 CFR 312.68 (See Section 4). An investigator shall retain records in accordance with whichever is the greater of the following: (1) as required by the FDA for a period of 2 years following the date a marketing application is approved for the drug or device for the indication for which it is being investigated; or, if no application is to be filed or if the application is not approved for such indication, until 2 years after the investigation is discontinued and FDA is notified; or (2) as required by LSUHSC-S policy for a period of six years after study closure at this institution; or (3) as required by the Sponsor's contract. For VA research, records will be kept indefinitely.
  13. Make a reasonable effort to ascertain the reason for a participant withdrawal from a clinical trial while fully respecting the participant's rights, although the participant is not obliged to give his or her reasons for withdrawing from a clinical trial.
  14. The researcher informs the subject's primary physician about the subject's participation in the clinical trial if the subject has a primary physician and if the subject agrees to the primary physician being informed.
  15. The researcher will provide evidence of his or her qualifications through up- to-date curriculum vitae or other relevant documentation requested by the sponsor, the IRB, or

the regulatory authority.

16. The researcher is familiar with the appropriate use of the investigational, as described in the protocol, in the current investigator brochure, in the product information, and in other information sources provided by the sponsor.
17. A qualified physician (or dentist when appropriate), who is a researcher or a co-researcher for the clinical trial, is responsible for all clinical trial related medical (or dental) decisions.
18. During and following a subject's participation in a clinical trial, the researcher ensures that adequate medical care is provided to a subject for any adverse events, including significant laboratory values, related to the clinical trial.
19. The researcher ensures the accuracy, completeness, legibility, and timeliness of the data reported to the sponsor.
20. The researcher permits monitoring and auditing by the sponsor and inspection by the appropriate regulatory authority.

Investigators are expected to comply with IRB by:

1. Considering whether their project meets the definition of human subject research or Clinical investigation, understanding which activities are overseen by the HRPP. IRB staff is available to assist investigators to determine if a project needs to be submitted for IRB review. The IRB will make that final determination.
2. Ensuring that all research that qualifies as human subjects research receives IRB review and approval in writing before commencement of research
3. Complying with all IRB decisions, conditions, and requirements
4. Ensuring that protocols receive timely progress reports and continuing IRB reviews and approvals
5. Reporting any unanticipated problems or serious adverse events that require prompt reporting to the IRB (As outlined in Section 8.4.)
6. Reporting deviations or changes in research activity to the IRB (See Section 9)
7. Obtain IRB review and approval in writing before changes are made to approved protocols or consent forms
8. Maintaining a master list of subjects for any given study where informed consent is required and documented, having it readily available at any given time. The IRB may waive this requirement (See Section 5.3.4)
9. Seeking IRB assistance in determining if proposed activities requires IRB review. The IRB makes the final determination.
10. Reporting the notification as well as the outcome of any external investigation, inspection, or other external review to the IRB and to the Department of Legal Affairs and Organizational Integrity upon notification and upon receipt of the outcome.
11. Being aware of LSUHSC-S IRB reporting requirements for research activities and providing to the IRB prompt reports of serious or continuing noncompliance with the protocol, determinations of the IRB, LSUHSC-S HRPP SOPs, federal regulations or ICH guidelines.
12. Investigators must report all serious adverse events (SAEs) to the sponsor, except those

SAEs that the protocol or other document (e.g., Investigator's Brochure) identifies as not needing immediate reporting. The investigator must follow regulatory requirements related to the reporting of unexpected serious drug reactions to the regulatory authority and to the IRB.

13. The investigator must report adverse events or laboratory abnormalities (that occur in subjects in the study) identified in the protocol as critical to safety evaluations to the sponsor according to the reporting requirements and within the time periods specified by the sponsor in the protocol.
14. For reported deaths, the investigator should supply the sponsor and the IRB with any additional requested information (e.g., autopsy reports and terminal medical reports).
15. The investigator provides written reports to the sponsor, IRB, and where applicable, the organization on any changes significantly affecting the conduct of the clinical trial or increasing the risk to subjects.
16. If the investigator terminates or suspends a clinical trial without prior written agreement of the sponsor, the investigator should inform the Organization, sponsor and the IRB. The Investigator should contact the Organization through the Department of Legal Affairs and Organizational Integrity Clinical Trial Agreement Coordinator.
17. If the IRB terminates or suspends approval of the clinical trial, the investigator promptly notifies the sponsor.
18. Upon completion of the clinical trial, the researcher informs the Department of Legal Affairs & Organizational Integrity Clinical Trial Agreement Coordinator and the IRB with a summary of the trial's outcome, and the regulatory authority with any required reports.

Investigators are expected to ensure that risks to subjects are minimized and protect subjects' rights and welfare by:

1. Recruiting participants in a fair and equitable manner, avoiding practices that place participants at risk for coercion or undue influence (Element III.1.E)
2. Obtaining and documenting informed consent of subjects or subjects' legally authorized representatives prior to the subjects' participation in the research (unless these requirements have been waived) as required by the IRB and ensuring that no human subject is involved in the research prior to obtaining their consent (Element III.1.F) (As outlined in Section 5)
3. Using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk
4. Using procedures already being performed on the subjects for diagnostic or treatment purposes, whenever appropriate
5. Having plans to monitor the data collected for the safety of research subjects: Investigators are required to have an appropriate Data Safety Monitoring Plan for all interventional studies that are greater than minimal risk and involve any FDA regulated products (drugs, devices, biologics) invasive procedures or any other study intervention as requested by the IRB. PI's are responsible for establishing a Data Safety Monitoring Board when required (See Section 3.8.4)

6. Protecting the privacy of subjects and protect the confidentiality of personal information (As described in Section 3.8.5)
7. Notifying the subjects' primary physician about the participant's participation in the clinical trial if the participant has a primary physician and if the participant consents to the primary physician being informed of their participation
8. Including additional safeguards in the study to protect the rights and welfare of subjects who are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons.
9. Having sufficient resources necessary to protect human subjects, including (Element III.1.D):
  - a. Sufficient time to conduct and complete the research.
  - b. Adequate numbers of qualified staff.
  - c. Adequate facilities.
  - d. A process to ensure that all persons assisting with the research are adequately informed about the protocol and their research-related duties and functions.
  - e. Availability of medical and psychological resources that subjects might require as a consequence of the research. Assure that all procedures in a study are performed with the appropriate level of supervision and only by individuals who are licensed or other qualified to perform such under the laws of Louisiana and policies of LSUHSC-S.
10. Having a procedure to receive complaints or requests for additional information from subjects and respond appropriately. Investigators should explain to research participants how the Research Staff can be contacted to ask questions, express concerns, or express complaints about the research and seeking guidance from the HRPP or IRB when necessary (Element III.1.G) (As outlined in Section 10.3 and Section 15.5).

#### **12.4 Training / Ongoing Education of Investigators and Research Team**

LSUHSC-S has an education program that contributes to the improvement of the qualifications and expertise of individuals responsible for protecting the rights and welfare of research participants. (AAHRPP Element I.1.E.)

Researchers and Research Staff are qualified by training and experience for their research roles, including knowledge of applicable laws, regulations, codes, and guidance; relevant professional standards; and LSUHSC-S's policies and procedures regarding the protection of research participants. (AAHRPP Element III.2.A)

The LSUHSC-S HRPP offers comprehensive human research protection education to the LSUHSC-S research community and affiliate organizations. Education is offered in many areas of research, including ethical standards, LSUHSC-S policies and procedures, and applicable federal, state, and local law. The foundation of ethical training at LSUHSC-S is the Belmont Report, which is made available through the HRPP website and the Collaborative Institutional

Training Initiative (CITI) website.

IRB members, IRB staff, investigators, and all site research staff involved in the design, conduct, or reporting of research are required to complete initial education and training on human subject protection and refresher courses, as applicable. Research teams consist of anyone working directly with human subjects or with identifiable data or biological specimens for research purposes under LSUHSC-S auspices. This includes investigators, research nurses, coordinators, students, technicians working with identifiable data, and faculty advisors. It is the responsibility of the PI to ensure that the research team is compliant with all initial and ongoing education as required by LSUHSC-S policies and regulatory requirements. IRB staff monitors investigator and site research staff education requirements during the initial IRB review process and during the continuation request process.

Investigators should be qualified by education, training, and experience to assume responsibility for the proper conduct of the trial, should meet all the qualifications specified by the applicable regulatory requirements, and should provide evidence of such qualifications through up-to-date curriculum vitae, CITI training certificates and/or other relevant documentation requested by the sponsor, the IRB, and/or the regulatory authorities. IRB approval (initial and continuation) will not be granted for proposed research in which members of the research team have not completed the required human research protections training.

This requirement is mandatory regardless of funding source. The requirement also applies to research that is considered exempt from IRB review.

When Human Research is conducted or funded by the Department of Defense (DOD), this organization commits to apply the Department of Defense (DOD) Directive 3216.02, which includes the requirement to apply 45 CFR §46 Subparts B,C, and D. Initial and continuing research ethics education is required for all personnel who conduct, review, approve, oversee, support, or manage human subject research. There may be specific DOD educational requirements or certification required. The specific requirements of DOD research is located on the HRPP website and discussed in Appendix I of this document. When research is funded or conducted by the DOD, researchers will be asked to contact the program office funding the research to ask about specific education requirements, and then demonstrate they have been completed.

#### **12.4.1 Orientation**

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All Principal Investigators and members of their research team must review core training documentation including:

- o LSUHSC-S Standard Operating Policies and Procedures for Human Research Protection: <http://www.lsuhschreveport.edu/Research/HRPP-Home/index>
- o LSUHSC-S Federal Wide Assurance (FWA): <https://www.hhs.gov/ohrp/irbs-and->

[assurances.html](#)

- o The “Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research: <https://www.hhs.gov/ohrp/regulations-and-policy/belmont-report/index.html>
- o Applicable Federal and State Regulations
- o Title 45, part 46-The Common Rule: <https://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/index.html>
- o 21 CFR part 50-Protection of Human Subjects and 21 CFR part 56-Institutional Review Boards: [Electronic Code of Federal Regulations](#)
- o VHA 1200.05(1): [https://www.va.gov/vhapublications/ViewPublication.asp?pub\\_ID=3052](https://www.va.gov/vhapublications/ViewPublication.asp?pub_ID=3052)
- o FDA website and Information Sheets Guidance: <http://www.fda.gov/default.htm>  
[Information Sheet Guidance for Institutional Review Boards \(IRBs\), Clinical Investigators, and Sponsors](#)
- o OHRP Guidance: <https://www.hhs.gov/ohrp/regulations-and-policy/guidance/>

#### 12.4.2 Initial and Continuing Education

The PI, key investigators, and all members of the research staff must complete and submit the following required training prior to submitting research protocols for review and approval:

Investigator and Research Staff involved in Clinical Studies (drugs, devices, biologics, invasive procedures) Required Training		
	Course	Timeline
Initial Training	CITI Biomedical Research Basic	Prior to IRB submission of research
	CITI Conflict of Interest	Prior to IRB submission of research
	CITI Good Clinical Practice	Prior to IRB submission of research
	CITI Health Information Privacy & Security	Prior to IRB submission of research
Refresher Courses	CITI Biomedical Research Refresher	Every 3 years
	CITI Conflict of Interest	Every 4 years or upon change

Investigator and Research Staff involved in Non -Clinical Studies (Surveys, Qualitative, Educational, Record Reviews) Required Training		
	Course	Timeline
Initial Training	CITI Biomedical Research Basic, or CITI Social and Behavioral Research Basic	Prior to IRB submission of research
	CITI Conflict of Interest	Prior to IRB submission of research
	CITI Health Information Privacy & Security	Prior to IRB submission of research
Refresher Courses	CITI Biomedical or Social and Behavioral Research Refresher	Every 3 years
	CITI Conflict of Interest	Every 4 years or upon change

In addition, LSUHSC-S HIPAA Training (requirement of all employees of LSUHSC-S and should be done upon hiring. If not done at that time then this training can be done during initial education training.)

The HRPP office will be available to assist Investigators with CITI training. The CITI Program will automatically check for individuals whose CITI Biomedical or Social & Behavioral training will lapse in ninety (90) days and Conflict of Interest training in sixty (60) days and will automatically send an email reminder to those individuals. For individuals on new submissions, IRB staff will check for those whose training has lapsed as part of the pre-review process and notify or email those individuals of failure to complete required education. New submissions will not be processed when training has lapsed for any study team member included on the delegation log. IRB members cannot be assigned reviews until the training has been completed.

New research protocols will not be accepted or receive final approval until all sub-investigators and members of the research team have completed the education requirements. All investigators and members of their research teams must meet LSUHSC-S continuing education requirement every three (3) years after certification of initial education for as long as they are involved in human subject research. There is no exception for this requirement. Appropriate refresher modules at the CITI web-based training site must be completed. Investigators must submit evidence of continuing education prior to the expiration of their training certification. New research protocols will not be accepted from principal investigators who have not submitted satisfactory evidence of continuing education. Investigators who are also IRB Chair, IRB members, or HRPP staff will satisfy the training requirements for IRB members and staff.

If investigators or members of their research team have successfully completed human subject research training equivalent to that required by the LSUHSC-S within the last year at another institution, they can submit proof of completion to waive the initial education requirement. However, all investigators or members of their research team must complete the requirements of Continuing Education or all refresher courses.

As a reminder, all personnel involved in the collection, transfer, shipping or processing of human biological samples are required to complete biosafety training and educational courses, both for their own protection and to maintain compliance with numerous local, state and federal regulations including the Office of Risk Management, the Occupational Safety and Health Administration (OSHA) and/or the National Institutes of Health (NIH).

LSUHSC-S institutional policies allow only medical professionals qualified by licensure or training to obtain blood and other biological samples from human research participants. All personnel are required to have current certificates of completion for courses as applicable to their assigned protocol tasks.

The following courses as well as other related courses are available through the CITI online research training program: <http://www.citiprogram.org>

- Basic BioSafety Training
- OSHA Bloodborne Pathogens
- OSHA Personal Protective Equipment Training

- (IATA) Shipping and Transport of Regulated Biological Materials
- Biohazard Spills and Releases
- Human Gene Transfer Trials
- NIH Recombinant DNA (rDNA) Guidelines

Forms and Checklists to assist in applying for IRB approval can be located on the HRPP/IRB website: <http://www.lsuhschreveport.edu/Research/HRPP-Home/index>

This website includes education requirements, Policy and Procedures, Research Participant information and Community Outreach.

There may be additional protocol-specific educational requirements or certification required for investigators and site research staff based on additional regulations (e.g., Department of Defense [DoD] or sponsor requirements, due to the complexity and risk of the research). When Investigators conducting, reviewing, approving, overseeing, supporting or managing DoD supported research with human subjects (including research that qualifies for exempt status) submit a study to one of the LSUHSC-S IRBs, the DoD requires that the institution meet the following education requirements. In addition to completing the HRPP mandatory CITI education requirements, conduct initial and continuing research ethics education for personnel who are engaged in human subject research. This training must be completed by all study team members initially and on a continuing basis every three years. Documentation of this education must be submitted at the time of the IRB submission.

For the Department of the Navy (DoN). See Department of Navy Human Research Protection Program (DON HRPP) Required Training and References. <https://www.onr.navy.mil/en/About-ONR/compliance-protections/Research-Protections/Research-Protection-Training-References>

Research under the purview of the Under Secretary of State (personnel and Readiness): Requires annual training on human subject protections for investigators and research directly involved in human subject research.

For other military branches (e.g. Army, Air Force), the investigator must contact the program offices for specific instruction about their respective education requirements.

### **12.4.3 Additional Resources**

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The HRPP office will be available for scheduled in-services at departmental meetings. Also, human research protection information will be made available on the HRPP office website <http://www.lsuhschreveport.edu/Research/HRPP-Home/index>, with links to:

- LSUHSC-S policies and procedures
- Federal and state regulatory sites
- Compliance and education offices
- Newsletters
- Training opportunities

## 12.5 Investigator Concerns

LSUHSC-S has and follows written policies and procedures so that Researchers and Research Staff may bring forward to the Organization concerns or suggestions regarding the Human Research Protection Program, including the ethics review process. (AAHRPP Element I.5.C.)

Investigators who have concerns or suggestions regarding LSUHSC-S's Human Research Protections Program should convey them to the HRPP, Institutional Official or designee or other responsible parties regarding the issue, when appropriate. The Institutional Official or designee will research the issue, and when deemed necessary, convene the parties involved to form a response for the investigator or make necessary procedural or policy modifications, as warranted. In addition, the Chair of the IRB, IO or designee will be available to address investigators' questions, concerns and suggestions.

## 13. SPONSORED RESEARCH

LSUHSC-S works with public, industry, and private Sponsors to apply the requirements of the Human Research Protections Program (HRPP) to all participants. (AAHRPP Standard 1-8)

### 13.1 Policy

The HRPP, in collaboration with the LSUHSC-Shreveport Office of Legal Affairs and Organizational Integrity, is responsible for ensuring that negotiations between LSUHSC-Shreveport and Sponsors relative to Clinical Investigations that will take place under the purview of LSUHSC-Shreveport's IRB follow all relevant Federal and State laws, rules and regulations and Institutional policies and procedures. The PI cannot commence research and/or otherwise enroll subjects until the IRB has approved the study and, to the extent that the activity is sponsored, a fully executed sponsor agreement is in place between the Sponsor and the Institution.

The Contract Coordinators of the Human Research Protections Program (HRPP) in collaboration with the Office of Legal Affairs and Organizational Integrity negotiate all contracts for clinical trial research involving human subjects to be conducted at LSUHSC-S. Contracts will not be approved by the Chancellor or designee until all institutional requirements have been satisfied. It is both LSUHSC-S and the Sponsor's obligation to protect human research participants. All Clinical Trial Agreements and Confidential Disclosure Agreements must be reviewed and approved by the institution prior to execution.

### 13.2 Definitions

Self-Sponsored (or "Investigator-Initiated," "Investigator-Sponsored," or "Un-sponsored") -

refers to a situation in which the individual Investigator is a LSUHSC-S Investigator and is conducting research without an extra mural sponsor. This happens in such cases as when the PI is the holder of the IND or IDE and therefore assumes the duties of the Sponsor of the clinical Investigator under the applicable FDA regulations.

Sponsor - Sponsor means the company, institution, individual donor, or organization responsible for the initiation, management or financing of a research study. Sponsor is responsible for registering the clinical investigation and submitting clinical trial information to the Clinical Trial Registry Data Bank ([www.clinicaltrials.gov](http://www.clinicaltrials.gov)).

Sponsored research - Sponsored research means research funded by external entities through a grant or contract that involves a specified statement of work (e.g., the research proposal) with a related transfer of value to the sponsor, including clinical trials involving investigational drugs, devices or biologics.

### **13.3 Office of Legal Affairs and Organizational Integrity Review**

The Office of Legal Affairs and Organizational Integrity is designated as institutional representative and is responsible for securing authorized signatures on agreements with Sponsors. To this end, the Office of Legal Affairs and Organizational Integrity in collaboration with the Project Manager of the Human Research Protections Program serves as the intermediary between a Sponsor and the PI for purposes of negotiation, budget changes, modifications to an agreement, agreement date extensions, and other administrative matters. In consultation with the PI and/or Office of Sponsor Programs and Technology Transfer for grants, the Contract Coordinators of HRPP and the Office of Legal Affairs and Organizational Integrity review the clinical trial agreement terms and conditions and the budget before obtaining authorized signatures. The Office of Legal Affairs and Organizational Integrity and the PI are responsible for ensuring Institutional compliance with the terms and conditions of the agreement, as well as any applicable Federal, State, and Institutional regulations and guidelines.

#### **13.3.1 Elements of Contracts**

Applicable Law - A statement should be included in the standard template or any proposed contract stating all work performed by the Institution under the agreement shall be conducted in accordance with the terms of the Protocol, and consistent with applicable laws and the Institution's policies and procedures.

HIPAA/Protected Health Information (PHI) - Protecting and maintaining the integrity of patient's protected health information is required of the Institution. LSUHSC-S is and will always comply with the Health Insurance Portability and Accountability Act of 1996 ("HIPAA"). A statement reflecting HIPAA compliance should be included in any proposed contract and is in the standard LSUHSC-S template. A statement should also be included by

the sponsor on how they will treat LSUHSC-S patient's protected health information. PHI shall only be disclosed to individuals who agree to the terms of the Agreement and who reasonably require such information for the performance of the agreement. PHI should be kept confidential and not be released for any purpose other than authorized by the patient in the Consent document or HIPAA authorization or enumerated in the Agreement.

Informed Consent/HIPAA Authorization - A statement should be included in the contract stating that a sponsor and IRB approved informed consent form and HIPAA authorization form will be obtained from each study participant, or their legal representative, prior to participation in the Study.

Indemnification - Studies with pharmaceutical sponsors must provide indemnification coverage and defense of LSUHSC-S for performing the study, including its trustees, officers, agents, faculty, and employees for all claims arising from the Institution's conduct of the study that are not due to negligence or willful misconduct on Institution's part. The indemnification terms, must at a minimum, cover claims arising from study subject injury or illness caused by the product or protocol and the Institution's proper conduct of the protocol. Because we are an Institute of the State of Louisiana, the Attorney General of the state shall represent the state and all departments and agencies of state government in all litigation arising out of or involving tort or contract. Language in the contract should state the following:

- "Subject to the statutory duties of the Attorney General of the State of Louisiana, Sponsor, as Indemnitor, shall have the right to select counsel and has sole control over the disposition of such claim or suit, provided, however, that the Sponsor shall sign no settlement of Institution's behalf without first receiving written input from the Institution, and the right to settle any such claim at Sponsor's sole expense provided that any settlement will not include admission of liability on the Indemnities without their prior written consent."

Subject Injury - Prior to the start of any clinical research involving human research participants, arrangements for medical care for research-related injuries are defined within the contract, including who will provide such care and who will be responsible for paying for the care. Also defined is who will determine whether the injury or illness is related to the study drug/procedure.

LSUHSC-S in conjunction with the University Health System will provide the medical treatment and care for any illness or injury caused as a result of study drug/study device.

Investigator will determine, either by himself, or in consultation with the Sponsor/CRO, if the injury or illness was a direct result of the study drug/study device. LSUHSC-S does not expect the Sponsor to pay for subject injury claims if the injury or illness is due to (i) the negligence or malfeasance of the Institution or Investigator (ii) the failure of the Investigator to follow the Protocol, good clinical practices, any applicable laws or regulations, or any IRB approved written

instructions by the Sponsor concerning the study. The Patient Informed Consent form should reflect the contract language.

Insurance: Insurance terms of the Sponsor should be stated in the contract. Sponsor should ensure that it maintains enough insurance to cover any indemnification obligations, product liability or subject injury claims relating to the Agreement. The minimum per occurrence amount and the annual aggregate amount will depend on the risk level of the study. For lower risk studies, the amounts should be \$2,000,000 per occurrence and \$5,000,000 annual aggregate; the higher the risk level for the study, the higher the insurance amounts should be. For evidence of insurance coverage, a certificate of insurance (COI) is requested for each study and the contract will not be sent for final review until the COI has been obtained.

LSUHSC-S (employees, while acting on behalf of the State of Louisiana) is covered by the Office of Risk Management, State of Louisiana Self-Insurance Fund for general liability insurance with limits of \$5,000,000 per occurrence, professional liability insurance with limits of \$5,000,000 per occurrence subject to LA R.S. 40:1237 et seq., and Worker's Compensation Insurance with limits of \$5,000,000. A certificate of insurance is available to Sponsors/CRO's upon request.

Travel Language: In order for Principal Investigator and study coordinator staff to travel, LSUHSC-S travel language must be included in the clinical trial agreement. The language must reflect that any required travel must (i) either be paid directly to or (ii) on behalf of the travelers. This language must be agreed upon prior to PI and/or coordinator traveling (the entire contract does not have to be agreed upon at this time, just the travel language).

Safety Concerns/Data and Safety Monitoring Reports: LSUHSC-S has an obligation to protect the human subjects participating in human subjects research. In order to help protect subjects, LSUHSC-S will need the assistance of the Sponsor/CRO. It is stipulated in the clinical trial agreement that the Sponsor/CRO shall immediately/promptly send reports of any findings of serious or continuing non-compliance detected during the monitoring process to the Institution's Human Research Protection Program/Organization or Researcher that could: (i) affect the safety of participants (ii) affect the participants willingness to continue study participation (iii) influence the conduct of the study and (iv) alter the IRB's approval to continue the study.

Some findings are risks that were not anticipated at the time the study was designed. Participants, past and present, should be notified of these results. The Sponsor/CRO should agree to notify the Investigator and/or the Institution's Human Research Protection Program, who then, will communicate these findings to the participants and IRB as warranted. The Sponsor should be given a time frame after the closure of the study during which they will report such findings to the Institution/Human Research Protection Program.

Contracts or other funding agreements require the Sponsor/CRO to send data and safety monitoring plans and reports to the Organization or Researcher who then provides them to the

IRB for review within five (5) days of receipt. The contract or funding agreement must specify the time frame for providing routine and urgent data and safety monitoring reports to the Organization.

Publications: Sponsor recognizes that the results of the Project must be publishable, and agrees that researcher(s) engaged in the Project shall be permitted to present at symposia, international, national, or regional professional meetings and to publish in journals, theses, or dissertations, or otherwise publish through means of their choosing, methods and results of the Project. Sponsor shall be furnished copies of any proposed publication or presentation at least sixty (60) days in advance of the submission of such proposed publication or presentation to a journal, editor, or other third party and shall have the right to review the documents and make suggestions for appropriate changes. Upon request from the Sponsor, the Institution agrees to delete from publication presentation any “confidential information” owned or provided by the Sponsor. LSUHSC-S shall be given the rights to publish data as a result of the study.

The Sponsor shall recognize under the Institution’s policy that the results of the study must be publishable and agrees that the Principal Investigator engaged in the study shall be permitted to present and publish these results. The Principal Investigator shall furnish a copy of the proposed publication or presentation to the Sponsor for review and comment; the Sponsor will then approve the presentation or publication or request additional time/information at which the Principal Investigator will comply. Each pharmaceutical company has its own stipulations for publication rights.

IRB Fee Schedule: A fee schedule has been developed for the LSU Health Sciences Center – Shreveport Institutional Review Board for Human Research (IRB) for review and approval of study documents. This fee schedule will be reflected either in the body of the contract or in the study budget worksheet.

Pharmacy Fee Schedule: A fee schedule has been developed for the Research Pharmacy for study drug maintenance. This fee schedule will need to be reflected either in the body of the contract or in the study budget worksheet.

Clinical Trial Billing Compliance Fee Scheduled: A fee schedule has been developed for the Clinical Trial Billing Compliance function. This fee schedule will be reflected in either the body of the contract or in the study budget worksheet.

### **13.3.2 Clinical Trial Agreement/Informed Consent Form Review**

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Language contained in the Informed Consent Form Document (ICFD) that is completed for Sponsor initiated Clinical Trials shall not contradict the language negotiated in the Clinical Trial Agreement. Certain elements in the ICFD must reflect contract language. These include: (i) Subject Injury language; (ii) Protected Health Information language (PHI); and (iii) Subject Reimbursement for time and travel. It is the responsibility of the Study Coordinator/Regulatory

Coordinator to ensure that these elements are reflected in the ICFD. The outlined process is listed below:

1. Once negotiations for the Clinical Trial Agreement have begun with the Sponsor, if the Regulatory/Study Coordinator does not have a copy of the sponsor ICFD, the Contract Coordinators of the HRPP will provide the sponsor draft ICFD to them.
2. The Regulatory/Study Coordinator will send the sponsor draft ICFD containing LSUHSC-S required edits to the Contracts Coordinators for review of the following: (i) Subject Injury; (ii) Protected Health Information (PHI); and (iii) Subject Reimbursement. In most cases, the sponsor ICFD will need to be changed to reflect the language proposed for the Clinical Trial Agreement.
3. An email is sent by the Contract Coordinators of the HRPP to the Regulatory/Study Coordinator outlining the draft ICFD language and the proposed contract language. Sections in the draft ICFD language that are not acceptable to the Institution are highlighted or bolded. The Regulatory/Study Coordinator is instructed to use the proposed contract language for the ICFD (making it read in 5<sup>th</sup> grade language). It is the department's responsibility to incorporate the changes in the ICF.

#### **13.4 Clinical Trial Agreement Includes Protections for Research Participants**

LSUHSC-S has and follows written policies and procedures setting forth the ethical standards and practices of the Human Research Protection Program. Relevant policies and procedures are made available to Sponsors, Researchers, Research Staff, research participants, and the Institutional Review Board(s), as appropriate. (AAHRPP Element I.1.D)

In LSUHSC-S sponsored research, LSUHSC-S addresses the protections of research participants by:

- Including in the standard contract templates a provision that the sponsor acknowledges and understands that the LSUHSC-S HRPP is applicable to all human subject research. (See LSUHSC-S Office of Legal Affairs and Organizational Integrity Clinical Study Agreement template)
- Asking for the inclusion of such a provision in any proposed contract that does not use the LSUHSC-S standard template.
- Including in the cover letter accepting and acknowledging the grant an equivalent statement regarding the HRPP in grants to LSUHSC-S.
- Ensuring that relevant policies and procedures are made available to sponsors, researchers, research staff, research participants, and the Institutional Review Board(s) as appropriate.

Additionally, the IRB will review the proposed consent form and delete any provision that requires a participant to waive or appear to waive any legal rights (i.e., exculpatory provisions).

### 13.5 Provision Addressing Medical Care for Participants

LSUHSC-S has a written agreement with the Sponsor that addresses medical care for research participants with a research related injury, when appropriate. (AAHRPP Element I.8.A)

In Sponsored research, medical care for participants is addressed by:

- Including in its standard contract template a provision that the sponsor provides for the cost of diagnosis, care and treatment of any undesirable side effects, adverse reactions, illness or injury to a participant, without regard as to the fault of the Sponsor. All Funding agreements will indicate who will provide care and who is responsible to pay for it.
- Asking for an inclusion of such a provision in any proposed contract that does not use LSUHSC-S Institutional standard template.
- Including the substance of any such provision in the consent form (See LSUHSC-S consent form template).
- Including a statement in the consent form that participants do not waive any liability rights for personal injury by signing consent form.

### 13.6 Communications from Sponsors Affecting IRB Oversight

In studies where Sponsors conduct research site monitoring visits or conduct monitoring activities remotely, LSUHSC-S has a written agreement with the Sponsor that the Sponsor promptly reports to LSUHSC-S findings that could affect the safety of participants or influence the conduct of the study. AAHRPP Element I.8.B

When the Sponsor has the responsibility to conduct data and safety monitoring, LSUHSC-S has a written agreement with the Sponsor that addresses provisions for monitoring the data to ensure the safety of participants and for providing data and safety monitoring reports to LSUHSC-S. (AAHRPP Element I.8.C.)

In LSUHSC-S sponsored research contracts, LSUHSC-S address communication with the sponsors regarding information and findings related to the protocol obtained by the sponsor which could affect the safety of participants or influence the conduct of the study. LSUHSC-S requires Sponsors or its agents to report findings of serious or continuous non-compliance detected during the monitoring process that could affect the safety of participants or influence the conduct of the study. This is accomplished by:

- Including in standard contract templates a provision that the sponsor will notify the Institution or the IBR of:
  - Non-compliance with the protocol or applicable laws, particularly those laws related to participants, that could impact the safety or welfare of the participants
  - Serious adverse events that have been reported to the FDA or other governmental agency in relation to the protocol at LSUHSC-S or any other site

- o Unanticipated problems in the protocol at LSUHSC-S or any other site that could relate to risks to participating participants, and
  - o Circumstances that could affect participant's willingness to continue to participate in the protocol or the IRB's continuing approval of the protocol.
- Ask for the inclusion of such a provision in any proposed contract that does not use their standard template.
- The Institution should receive copies of the monitoring reports that contain findings that could affect the safety of participants or influence the conduct of the study. These findings will be made available to the IRB.
- As outlined in the Institutional SOPs researchers must promptly (within five (5) days) report to the IRB any information that could affect the safety of participants or influence the conduct of the study.

### **13.7 Data and Safety Monitoring (DSM) in Sponsored Agreements**

When the Sponsor has the responsibility to conduct data and safety monitoring, LSUHSC-S has a written agreement with the Sponsor that addresses provisions for monitoring the data to ensure the safety of participants and for providing data and safety monitoring reports to LSUHSC-S (AAHRPP Element 1.8.C)

For sponsored research, LSUHSC-S agreements specify that, as appropriate:

- Provisions are made for monitoring study data which could affect the safety of participants
- The results of this monitoring are reported to the researcher (PI) so that:
  - o Routine monitoring reports will be submitted to the IRB in accordance with Institutional Policy
  - o Urgent reports-Events and Information which require Prompt Reporting to the IRB are submitted according to the Institutional policy outline in Section 8

### **13.8 Publication of Research Results**

Before initiating research, the Institution has a written agreement with the Sponsor about plans for disseminating findings from the research and the roles that Researchers and Sponsors will play in the publication or disclosure of results. (AAHRPP Element 1.8.D)

LSUHSC-S establishes the importance of disseminating research findings. LSUHSC-S shall be given the rights to publish data as a result of the study. The sponsor shall recognize under the Institution's policy that the results of the study may be publishable and agrees that the Principal Investigator engaged in the study shall be permitted to present and publish these results at a mutually agreed upon time. The PI shall furnish a copy of the proposed publication or presentation to the Sponsor for review and comment; the Sponsor will then approve the presentation or publication or request additional time/information at which the Principal Investigator will comply. Each pharmaceutical company has its own stipulations for publication

rights but agrees to provide a copy of the manuscript once accepted for publication.

For Sponsored research, LSUHSC-S implements this policy in agreements concerning sponsored research by:

- Including in its standard template a provision that provides the investigator with a right to publish the research results.
- Revising any provision in any proposed contract that limits an investigator's right to publish research results in a manner that is inconsistent with the policy.

### **13.9 Communicating Study Findings/Results to Participants**

When participant safety could be directly affected by study results after the study has ended LSUHSC-S has a written agreement with the Sponsor that the Researcher or LSUHSC-S will be notified of the results to consider informing participants (AAHRPP Element I.8.E)

For Sponsored research, LSUHSC-S address communication with sponsors regarding the impact of research results on participant health and safety by:

- Including in their standard contract templates a provision that the sponsor will develop a plan of communication with the Principal Investigator that is acceptable with the IRB when new findings or results of the protocol might impact the willingness of subjects to continue to participate in the protocol or directly affect their current or future safety or medical care.
- Ask for the inclusion of such a provision in any proposed contract that does not use the LSUHSC-S standard template.
- Investigators will obtain a copy of the final manuscript from the sponsor and communicate study results to participants in lay language as applicable.

## **14. CONFLICT OF INTEREST IN RESEARCH**

LSUHSC-S has and follows written policies and procedures to ensure that research is conducted so that financial conflicts of interest are identified, managed, and minimized or eliminated. (AAHRPP Standard I-6)

### **14.1 Policy**

LSUHSC-S has and follows written policies and procedures to identify, manage, and minimize or eliminate financial conflicts of interest of LSUHSC-S that could influence the conduct of the research or the integrity of the Human Research Protection Program. (AAHRPP Element I.6.A.)

Researchers and Research Staff identify and disclose financial interests according to organizational policies and regulatory requirements and, with the Organization, manage, minimize, or eliminate financial conflicts of interest. (AAHRPP Element III.1.B.)

The mission of LSUHSC-S is to provide excellence in patient care, to foster the development of future medical, biomedical, and allied health professionals, and to advance medical and scientific research. LSUHSC-S must ensure that service, education, and research are conducted under the highest ethical standards. Procedures outlined in this policy apply to both financial and non-financial conflicts of interest and are guided by Code of Federal Regulations (Title 42 of the Code of Federal Regulations (CFR) Part 50 Subpart F) that promotes objectivity in research to ensure conflict of interests do not adversely affect the protection of participants or the credibility of the LSUHSC-S HRPP.

In response to institutional Clinical Trial financial requirements, the institution implemented the Compliance Financial Policy Committee. This is comprised of individuals representing LSUHSC-S Compliance Department, LSUHSC-S Budget, LSUHSC-S Accounting and the HRPP. The committee includes the Chief Financial Officer, Director of Accounting Service, Director of Compliance, Assistant Director of Compliance, AVCRM, and IO Designee. The Committee is charged with the development of research financial policies and the ongoing oversight and administration of the functions of the Clinical Trial Management Team.

Increasingly, the financial incentives involved in research may lead to Conflicts of Interest, such that financial or other interests compete with the duty to provide and act on unbiased information, and the obligation to protect the rights and welfare of the research subject. The value of the results of research to the health and the economy of the nation must not be compromised by any Investigator's financial interest that could bias the design, conduct or reporting of results. Therefore, it is appropriate that LSUHSC-S adopt the Conflicts of Interest Policy to identify, evaluate, and manage (i.e. reduce or eliminate) any actual, perceived or potential conflicts of interest.

Chancellor's Memorandum-23 defines institutional policy regarding Conflict of Interest, and is consistent with federal regulatory standards, including but not limited to, those of the Food and Drug Administration, National Science Foundation, and Public Health Service (PHS).

For research involving human subjects, everyone involved in research (e.g., research staff listed on the delegation log or 1572, those involved in research oversight, and those responsible for resource allocation) are required to report potential Conflicts of Interest through the Conflict of Interest in Research reporting mechanisms. Each person must report annually, and within thirty (30) days of a change subject to reporting requirements. It should be noted that reporting is required for each individual's immediate household.

If LSUHSC-S carries out the PHS-funded research through sub-grantees, contractors or collaborators, the LSUHSC-S must take reasonable steps to ensure that Investigators working for such entities comply with this subpart, either by requiring those Investigators to comply with LSUHSC-S' policy or by requiring the entities to provide assurances to LSUHSC-S that will enable LSUHSC-S to comply with this subpart (50.604 (a)).

The criteria for disclosing financial interest will not vary by funding source or regulatory oversight.

#### 14.2 Individual Conflicts of Interest

LSUHSC-S has and follows written policies and procedures to identify, manage, and minimize or eliminate individual financial conflicts of interest of Researchers and Research Staff that could influence the conduct of the research or the integrity of the Human Research Protection Program. LSUHSC-S works with the IRB or EC in ensuring that financial conflicts of interest are managed and minimized or eliminated, when appropriate. (AAHRPP Element I.6.B.)

These procedures apply to both financial and non-financial conflicts of interest and are guided by Code of Federal Regulations (Title 42 of the Code of Federal Regulations (CFR) Part 50 Subpart F) that promotes objectivity in research to ensure conflict of interests do not adversely affect the protection of participants or the credibility of the LSUHSC-S HRPP.

For clinical studies involving the use of new human drugs and biological products or medical devices, certifications and disclosure requirements are defined in Food and Drug Administration (FDA) regulations, Title 21 CFR Part 54.

In the environment of research, openness and honesty are indicators of integrity and responsibility, characteristics that promote quality research and can only strengthen the research process. Therefore, conflicts of interest should be eliminated when possible and effectively disclosed and managed when they cannot be eliminated.

#### LOUISIANA CODE OF ETHICS, SECTIONS 1111 A AND 1115

Section 1111 A – No public servant (public employee) shall receive anything of economic value (money or any other thing having economic value), other than the compensation and benefits to which he is entitled from his governmental employer, for the performance of the duties and responsibilities of his office or position.

Section 1115 - No public servant (public employee) shall solicit or accept, directly or indirectly, anything of economic value as a gift or gratuity from any person or from any officer, director, agent, or employee of such person, if such public servant knows or reasonably should know that such person: 1) has or is seeking to obtain a contractual, business or financial relationship with the public servant's agency, or 2) has substantial economic interests which may be substantially affected by the performance or nonperformance of the public employee's official duty.

#### 14.3 Procedures

### 14.3.1 Disclosure of Investigator COI:

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LSUHSC-S has and follows written policies and procedures to identify, manage, and minimize or eliminate individual financial conflicts of interest of Researchers and Research Staff that could influence the conduct of the research or the integrity of the Human Research Protection Program. LSUHSC-S works with the IRB or EC in ensuring that financial conflicts of interest are managed and minimized or eliminated, when appropriate. (AAHRPP Element I.6.B.)

Researchers and Research Staff identify and disclose financial interests according to organizational policies and regulatory requirements and, with the Organization, manage, minimize, or eliminate financial conflicts of interest. (AAHRPP Element III.1.B.)

Individuals are considered to have an institutional responsibility and are subject to this policy when they are involved in any of the following:

- The design, conduct, or reporting of research
- Research consultation
- Teaching
- Professional practice
- Institutional committee memberships
- Service on panels such as Institutional Review Boards or Data and Safety Monitoring Boards

Individuals subject to this policy are required to disclose their institutional responsibility to conduct research and the financial interests Related to the Research through the electronic COI disclosure management system:

- On submission of an initial review.
- At least annually on submission of continuing review.
- Within 30 days of discovering or acquiring (e.g., through purchase, marriage, or inheritance) a new financial interest

Travel disclosures should be made for reimbursed or sponsored travel related to institutional responsibilities. The disclosure should include the purpose of the trip, the identity of the sponsor or organizer, the destination, and the duration. Travel to Investigator meetings for training and education of investigative study staff relative to the research need not be disclosed.

LSUHSC-S defines a significant financial interest as a financial interest consisting of one or more of the following interests of the Investigator (and those of the Investigator's spouse and dependent children) that reasonably appears to be related to the Investigator's institutional responsibilities:

- With regard to any publicly traded entity, a significant financial interest exists if the value of any remuneration received from the entity in the twelve months preceding the disclosure and the value of any equity interest in the entity as of the date of disclosure, when aggregated, exceeds \$5,000. For purposes of this definition,

remuneration includes salary and any payment for services not otherwise identified as salary (e.g., consulting fees, honoraria, paid authorship); equity interest includes any stock, stock option, or other ownership interest, as determined through reference to public prices or other reasonable measures of fair market value;

- With regard to any non-publicly traded entity, a significant financial interest exists if the value of any remuneration received from the entity in the twelve months preceding the disclosure, when aggregated, exceeds \$5,000, or when the Investigator (or the Investigator's spouse or dependent children) holds any equity interest (e.g., stock, stock option, or other ownership interest); or
- Intellectual property rights and interests (e.g., patents, copyrights), upon receipt of income related to such rights and interests.

#### Disclosure Procedures:

1. By the time a research proposal is submitted to the IRB or an application is submitted to a funding agency, all members of the team who are planning to participate in the research (i.e., will be engaged in research, such as those who are listed on the delegation log or on the 1572) shall disclose in accordance with CM-23.
2. All financial disclosures must be updated during the period of the award on an annual basis or as new reportable significant financial interests are obtained.
3. The "Initial Application" form queries the Investigator regarding any potential conflicts of interest. It is the responsibility of the Principal Investigator to ensure that every member of the research team (as described above) discloses any potential conflict of interest.
4. Additionally, the IRB Administrative support staff will verify disclosures and contact the Conflict of Interest Administrator for clarifications.

The criteria for disclosing financial interest will not vary by funding source or regulatory oversight. Members of the research team who have not completed the required financial interests disclosures may not take part in aspects of the research that involve human subjects.

### 14.3.2 Evaluation of COI

Researchers and Research Staff identify and disclose financial interests according to organizational policies and regulatory requirements and, with the Organization, manage, minimize, or eliminate financial conflicts of interest. (AAHRPP Element III.1.B.)

When a potential conflict of interest has been identified, the IRB Administrative Support staff contacts the Conflict of Interest Administrator to determine if a conflict of interest is related to the current research. If the conflict of interest is related to the research, the Conflict of Interest Committee provides the IRB a copy of the Conflict of Interest Management Plan. The IRB reviews the plan along with the protocol. The written management plan should consider the following options:

- Public disclosure of the financial interests.
- Disclosure of the financial interests to subjects.

- Appointment of an independent monitor capable of taking measures to protect the design, conduct, and reporting of the research against bias resulting from the financial conflict of interest.
- Change of personnel or personnel responsibilities, or disqualification of personnel from participation in all or a portion of the research.
- Reduction or elimination of the financial interest (e.g., sale of an equity interest).
- Severance of relationships that create financial conflicts.
- Modification of the research plan.
- Involvement of external individuals in key portions of the protocol
- Use of an external IRB.
- A retrospective review.
- A mitigation report.
- A plan to monitor and enforce the implementation of the management plan.

If the IRB determines that the Management Plan is not sufficient to protect the rights, welfare and safety of the subject, the IRB requires sufficient revision prior to approval. The IRB makes the final decision as to whether the financial interest and its management, if any, allows the research to be approved.

The Office of Legal Affairs and Organizational Integrity and the Conflict of Interest staff will conduct an initial review of all disclosures to determine whether a potential conflict of interest (financial or non-financial) exists. If it is determined that no conflict of interest exists, sufficient information will be provided to the IRB to allow concurrence. If no concurrence is obtained, the matter will follow the procedures below.

If the initial determination is made that there may be a potential for Conflict of interest covered by this policy, then additional information will be requested for review. This information, along with the Disclosure packet will be referred to the Conflict of Interest Committee (COI). The Principal Investigator and disclosing staff will be informed when any disclosures have been forwarded for review.

The review process and mitigation process is described in the Chancellor's Memorandum-23 (CM-23). In summary, the Conflict of Interest Committee will evaluate the potential conflict of interest according to specific criteria and recommend a management plan that ensures the protection of human research subjects and the integrity of the research.

If the proposal is approved through this process, all information about the nature and amount of any potential conflict, along with the committee's findings and recommendations, will be transmitted by the Office of Legal Affairs and Organizational Integrity to the institutional Review Board (IRB). The IRB reviews all information in reviewing the proposal and retains final authority to decide whether the potential conflict of interest and its management (if any) is sufficient to allow approval. Records related to disclosures and management of financial conflicts of interest are to be retained for at least three years from completion of the research.

#### 14.4 Non-Compliance

Whenever an Investigator has violated this policy or the terms of the Chancellor's Memorandum (CM-23) by failing to disclose a conflict of interest, or by failing to adhere to the resolution plan, the COI Committee shall report to the IRB and/or Chancellor, who may explore disciplinary action ranging from a public letter of reprimand, to the loss or restriction of privileges to conduct research, or dismissal and termination of employment. The IRB may, at any time during this process, suspend, require modification to, or otherwise disapprove research activities where appropriate to protect human research subjects.

If the violation results in a collateral proceeding under Health Sciences Center policies regarding misconduct in science, then the COI Committee shall notify the IRB and/or Chancellor; although possible disciplinary action may be delayed until the misconduct allegations have been investigated. During the investigation, it may be necessary to withdraw a pending grant application and/or research application.

If the failure of the Investigator to comply with LSUHSC-S's policy has biased the research, LSUHSC-S must promptly notify the funding agency and any other application agencies of the corrective action taken or to be taken. 42 CFR 50.606(a). If the awarding agency is PHS, LSUHSC-S agrees to make information on conflicting interest available and how those interests have been managed, reduced, or eliminated. 42 CFR 50.606(b). If the funding agency determines that a funded project of clinical research, whose purpose was to evaluate the safety or effectiveness of a drug, medical device, or treatment, was designed, conducted, or reported by an Investigator with a conflicting interest that was not disclosed or managed, LSUHSC-S must require the Investigator to disclose the conflicting interest in each public presentation of the results of the research 42 CFR 50.606(c).

Additionally, the IRB shall consider notification of research subjects, with the presumption that such notification would generally be appropriate.

#### 14.5 Training

Individuals subject to this policy are required to complete financial conflicts of interest training initially, at least every four years, and immediately when:

- Joining the organization
- Financial conflicts policies are revised in a manner that changes investigator requirements
- Non-compliant with financial conflicts policies and procedures

#### 14.6 Institutional Conflict of Interest

LSUHSC-S has and follows written policies and procedures to identify, manage, and minimize or eliminate financial conflicts of interest of the Organization that could influence the conduct of

the research or the integrity of the Human Research Protection Program. (AAHRPP Element I.6.A.)

Institutional Conflicts of Interest arise when the institution or its leadership have interests, financial or otherwise, that conflict with, or may have the appearance of conflicting with, their duty to ensure the credibility of the academic and clinical pursuits occurring under its auspices. Such interests may include licenses, technology transfers, patent interests, investments, gifts or sponsorships, or other financial interests held either by the institution or by its senior administrative leadership (i.e. all individuals whose title includes Chancellor, Dean, Hospital Administrator, Counsel, and others determined by the Chancellor). A faculty member or administrator who has direct authority over personnel appointments, salaries, promotions, and/or allocation of organizational resources (e.g., funding, space, assignment of graduate students, residents, fellows or other trainees) for individuals involved in the design, conduct, reporting, review, or oversight of human subjects research are also required to disclose their financial interests.

The Office for Sponsored Programs and Technology Transfer, Legal Affairs and Organizational Integrity, and Administration and Finance are to disclose any change in the institution's financial holdings not controlled by the institution's investment managers related to Licensing (e.g., licensing or technology transfer agreements), investments of the institution, gifts to the institution when the donor has an interest in the research, financial interests of senior administrative officials and other financial interests.

Consequently, CM-23 describes an analogous process to identify, evaluate and manage institutional Conflicts of Interest. Senior administrative officials must disclose their financial interests using the electronic COI disclosure management system upon joining the Institution, yearly, and when there are changes to their financial interests. Annual Disclosure Certifications and quarterly updates will be provided to the Senior COI Project Manager or COI Project Coordinator within the Office of Legal Affairs and Organizational Integrity.

In summary, the IRB Administrative Support staff will report relevant data fields (e.g., investigational product, sponsor) upon receipt of a new application and at continuing review. If a potential institutional Conflict of Interest is identified, the proposal will not be reviewed by the IRB until the IRB is in receipt of the results of the process below. The evaluation and management of an institutional conflict of interest may not vary by funding or regulatory oversight.

The specific information regarding the institutional Conflict of Interest will be referred to the Dean of the School proposing the academic pursuit, and may decline to advance the proposal. The Conflict of Interest Committee will then review and evaluate the application and potential conflict of interest, and propose a management plan designed to protect human research subjects and assure the integrity of the research. The Chancellor will determine whether or not to grant approval for the management plan for the institutional conflict of interest.

Once approved by the Chancellor, all information about the nature and amount of any potential conflict, along with the committee's findings and recommendations, will be transmitted by the Office of Legal Affairs and Organizational Integrity to the institutional Review Board (IRB). The IRB reviews all information in reviewing the proposal and retains final authority to decide whether the potential Conflict of Interest and its management (if any) is sufficient to allow approval.

If the IRB approves the research, the proposal and results of this process are forwarded to the Institutional Official for review. The Institutional Official may decide to disapprove the research. However, if the IRB disapproves the research, the Institutional Official may not approve the research.

#### **14.7 Conflicts of Interest in VA research**

The VA works with the LSUHSC IRB to identify, evaluate and mitigate Conflicts of Interests, including both institutional and individual. VA researchers are subject to their Research and Development SOP's, part 7. The VA relies on the IRB to evaluate financial Conflicts of Interest and any management plan, in accordance with appropriate regulatory standards. VA personnel listed in an IRB application or engaged in research must submit the VA Conflict of Interest form for review by the RDC and the IRB. The ACOS/R&D is the designated Conflict of Interest Administrator.

VA facilities are not required to follow PHS requirements, even when research is funded by a PHS agency (e.g., NIH).

Researchers must report conflicts of interests using the VA financial conflict of interest form; the IRB must use the VA conflict of interest form, and may not create, redraft, or change this form.

VA SOP's also describe the process for identifying, evaluating and mitigating institutional Conflicts of Interest. The IRB retains the authority for final approval of any management plan.

### **15. PARTICIPANT OUTREACH**

#### **15.1 Policy**

LSUHSC-S is committed to ensuring that educational opportunities are offered to research participants, prospective research participants, and community members, which will enhance their understanding of research involving human participants at LSUHSC-S. The Institution achieves this by involving all departments and sections in outreach to prospective and current research participants through support groups and activities at the Institution as well as off Campus. LSUHSC-S staff, including Research personnel, are encouraged to engage the community in the resources available.

The following procedures describe how LSUHSC-S fulfills that responsibility.

## 15.2 Responsibility

It is the responsibility of the HRPP Education and Outreach Coordinator to implement the procedures outlined below. The HRPP will ensure the availability of information and resources to improve community awareness and involvement with research at LSUHSC-S to comply with the ethical principle of respect for persons participating in research and maximize their involvement in the research process, including proactive outreach activities. In addition, the following responsibilities are designated to the IO and Investigators:

- The Institutional Official is responsible for ensuring the respect for human participants and their awareness of and involvement in LSUHSC-S research protocols.
- Site investigators are responsible for day-to-day assurance of compliance with all aspects of the Human Research Protection Program (HRPP), including participant awareness and outreach activities.
- Investigators involved in human research protocols are responsible for maintaining respectful interactions with participants, involving research participants at every stage, enhancing appropriate safeguards, answering questions in a complete and sensitive manner, and participating in outreach and educational activities for participants and their communities.

## 15.3 Outreach Resources and Educational Materials

LSUHSC-S has and follows written policies and procedures that establish a safe, confidential, and reliable channel for current, prospective, or past research participants or their designated representatives that permits them to discuss problems, concerns, and questions; obtain information; or offer input with an informed individual who is unaffiliated with the specific research protocol or plan. (AAHRPP Element I.4.A.)

Researchers and Research Staff have a process to address participants' concerns, complaints, or requests for information. (AAHRPP Element III.1.G)

The HRPP office dedicates a section of the website to research participants:

<http://www.lsuhschreveport.edu/Research/HRPP-Home/Participants/index>

This website includes:

- Research Participants Rights
- Frequently Asked Questions (FAQs),
- LSUHSC-S participant brochures
- Links to Government websites: OHRP, FDA, NIH
- Opportunity for feedback, concerns or complaints
- Links to local and national clinical trial information

The HRPP brochure HRP-104: Should I Take Part in a Research Study? includes:

- Questions to ask the investigator
- Describes what research is
- Explains the consent process
- Lists the rights of the research participant
- Explains the role of the HRPP and the IRB
- Contact information for questions, concerns or input

#### **15.4 Institutional Activities**

LSUHSC-S conducts activities designed to enhance understanding of human research by participants, prospective participants, or their communities, when appropriate. These activities are evaluated on a regular basis for improvement. (AAHRPP Element I.4.B.)

LSUHSC-S promotes community awareness of research involving human participants and the protections provided by an institutional review board:

The information is distributed through research in-services and presentations to the community. The presentations include:

- Participation in Health Fairs
- Seminars with lectures open to the community
- Partnering with the local libraries to promote consumer health and awareness of research
- Participation in health screenings
- Biomedical research courses in the area school system
- Health related literacy projects targeting vulnerable populations in the local libraries
- Ongoing updates in biomedical research
- Presentations on disease processes related to local clinical trials

LSUHSC-S also sponsors several outreach programs and Support Groups for the Community creating opportunities for the employees to interact with the Community outside the Institution.

Access to institutional and locally sponsored activities can be found on the LSUHC-S websites:

<http://www.lsuhschreveport.edu/About/CommunityOutreach/index>

<http://www.lsuhschreveport.edu/Research/HRPP-Home/Participants/Find-a-Study/index>

LSUHSC-S investigators conducting investigator-initiated research incorporate community input as appropriate in the design (including reducing invasiveness), implementation, and dissemination of research. Based on the type of research, investigators may employ one or more of the following methods, among others:

- Planned community sessions
- Community advisory groups

- Participant advocates
- Partnerships with community-based organizations
- Community-based participant research design methodologies

Community based research is conducted in partnership with researchers and members of the community. There are multiple ways to define a community including but not limited to individuals with a common issue or problem, individuals with a common interest, or individuals in a geographical area. A subset of CBR is Community-Based Participatory Research (CBPR), which is a partnership approach to research that equitably involves community members, organizational representatives, and researchers, in all aspects of the research process and in which partners contribute expertise and share decision making and ownership. The aim of the CBRP 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. When reviewing CBR or CBPR research, the IRB will consider the following:

- Was the community involved in defining the needs for the proposed research?
- Was the community involved in the design of the study protocol and informed consent?
- Is the recruitment plan sensitive and appropriate to the community proposed for the study and has the potential for coercion been minimized?
- Will the community be involved in conducting the research?
- What are the potential risks and benefits for the community with the proposed research?
- How will the outcomes of the research be disseminated within and outside the community?
- Is there a partnership agreement or memorandum of understanding between the researcher and the community partners?

### 15.5 Questions, Concerns, and Complaints

LSUHSC-S conducts activities designed to enhance understanding of human research by participants, prospective participants, or their communities, when appropriate. These activities are evaluated on a regular basis for improvement. (AAHRPP Element I.4.B.)

The HRPP is not affiliated with a specific research study and is available to current, former, and prospective research participants to discuss problems, concerns and questions and to obtain information and to offer input. Informed consent forms (ICF) associated with research activities are reviewed and approved by the LSUHSC-S Institutional Review Board (IRB) to ensure that procedures are in place for research participants to ask questions, express concerns, or voice complaints to the HRPP, IRB, or investigator.

All questions, concerns or complaints received by the HRPP office from any individual through any form of communication (written, verbal, electronic) will be acknowledged and forwarded to

the appropriate official within the institution for handling and follow-up. Complaints will also be forwarded to the HRPP QA/QI Coordinators. While a prompt resolution is expected, the time frame for resolution of complaints is dependent upon the nature and complexity of the issue.

HRPP contact information for reporting concerns or complaints is provided in the Informed Consent Form, Participant Brochure and the HRPP website. Research participants are invited via the LSUHSC-S/HRPP website to contact the HRPP or the IRB staff to provide feedback and/or obtain information about human subjects' research and LSUHSC-S HRPP activities. LSUHSC-S also utilizes the Patient Relations Liaison for concerns and complaints.

## 15.6 Evaluation

LSUHSC-S conducts activities designed to enhance understanding of human research by participants, prospective participants, or their communities, when appropriate. These activities are evaluated on a regular basis for improvement. (AAHRPP Element I.4.B.)

LSUHSC-S periodically evaluates its outreach activities and makes changes when appropriate. These evaluations take place in an informal, ongoing manner. All HRPP and IRB staff, members and Chairs/Vice-Chairs will report both positive and negative feedback about all HRPP outreach activities to the Education and Outreach Coordinator or AVCRM. He/she will then track the input and any changes made to improve outreach activities. He/she will summarize that material annually. To formally evaluate its outreach activities, the Education and Outreach Coordinator will determine:

1. The specific community outreach activities being used.
2. Whether these community outreach activities have an evaluative component, and if so what, if any, changes in the outreach activities have resulted from these Evaluations.

The Education and Outreach Coordinator or AVCRM will administer surveys at least annually to determine the adequacy of outreach activities.

The survey will assess:

1. The scope, the content and the adequacy of outreach activities and resources.
2. Whether the research community is using the HRPP Participant website resource
3. Whether the research community is using other educational materials to inform prospective participants about their rights and welfare as research participants.
4. Whether additional resources are needed to improve participant outreach activities.

The results of the survey will be used to establish both the adequacy of current outreach activities and any additional resources that may be needed to meet the needs of the research community regarding participants outreach.

## 16. HEALTH INSURANCE PORTABILITY AND ACCOUNTABILITY ACT (HIPAA)

### 16.1 Policy

The IRB or EC has and follows written policies and procedures to evaluate proposed arrangements for maintaining the confidentiality of identifiable data, when appropriate, preliminary to the research, during the research, and after the conclusion of the research. (AAHRPP Element II.3.E)

Protected Health Information obtained by LSUHSC-S or a Research Affiliate may not be used internally or disclosed to any outside person or organization for research purposes without prior approval of the IRB. LSUHSC-S researchers must also abide by all LSUHSC-S HIPAA policies regarding HIPAA privacy and security.

### 16.2 Definitions

Access - Access is the mechanism of obtaining or using information electronically, on paper, or other medium for the purpose of performing an official function.

Authorization - An authorization is a written document completed and signed by the individual that allows use and disclosure of protected health information for specified purposes, which are generally other than treatment, payment, or health care operations.

Covered entity - Covered entity is the term applied to institutions that must comply with the Privacy Rule. These include:

- Health plans
- Health care clearinghouses
- Health care providers

Common Rule - Common Rule is a Federal Policy (45 CFR 46) on human subject protection that provides for the primary source of regulation of research.

De-Identified Information - De-Identified information is health information that does not identify an individual and data from which there is no reasonable basis to believe that the information can be used to identify an individual. If information is de-identified, it no longer is subject to the Privacy Rule and exempt from HIPAA.

Deletion - Deletion is the removal, erasing, or expunging information or data from a record.

Disclosure - Disclosure is the release, transfer, access to, or divulging of information in any other manner outside the entity holding the information.

Health Information - Health Information is any information created or received by a health care provider, health plan, public health authority, employer, life insurer, school or university, or health care clearinghouse that relates to the past, present, or future physical or mental health or condition of an individual; the provision of health care to an individual; or payment for the provision of health care to an individual.

Identifiable Health Information - Identifiable Health Information is a subset of health information including demographic information collected from an individual.

Limited Data Set - Refers to PHI that excludes 16 categories of direct identifiers and may be used or disclosed, for purposes of research, public health, or health care operations, without obtaining either an individual's Authorization or a waiver or an alteration of authorization for its use and disclosure, with a data use agreement.

Minimum Necessary - Minimum Necessary refers to the principle that any access should be limited to the minimum amount of information needed to accomplish the intended purpose of the use or disclosure.

Privacy Board - Privacy Board is the term used to describe a board comprised of members of varying backgrounds and appropriate professional competencies, as necessary, to review individual's private rights. It is an alternative to an IRB for privacy issues only. It cannot replace the IRB for Common Rule purposes. The LSUHSC-S Privacy Board is the IRB.

Privacy Act - Privacy Act is an act that provides for the confidentiality of individually identified and retrieved information about living individuals that is maintained in a system of records and permits the disclosure of records only when specifically authorized by the statute. The Act provides that the collection of information about individuals is limited to that which is legally authorized, relevant, and necessary.

Privacy Rule - Privacy Rule provides guidance on the use of protected health information in the conduct of research. It imposes requirements on those involved in research, both individuals and institutions. Privacy refers to a person's desire to control the access of others to themselves. The evaluation of privacy involves consideration of how the investigator will access information from or about participants. The IRB members should know strategies to protect privacy interests relating to contact with potential participants, and access to private information.

Protected Health Information - Protected Health Information is individually identifiable health information transmitted by electronic media, maintained in electronic media, or transmitted or maintained in any other form or medium. The Privacy rule excludes some education records and employment records.

Preparatory Research - Preparatory Research is the method applied to developing or designing a research study.

Waiver of Authorization - The documentation that the covered entity obtains from a researcher or an IRB or a Privacy Board that states that the IRB or Privacy Board has waived or altered the Privacy Rule's requirement that an individual must authorize a covered entity to use or disclose the individual's PHI for research purposes.

### **16.3 Historical Background**

The Health Insurance Portability and Accountability Act of 1996 (HIPAA) required the creation of a Privacy Rule for identifiable health information. The resulting Privacy Rule, finalized in August 2002, set a compliance date of April 14, 2003. While the main impact of the Privacy Rule will be on the routine provision of and billing for health care, the Rule will also affect the conduct and oversight of research. Researchers, IRB staff and members as well as research administration must be aware of these changes.

### **16.4 Effects of HIPAA on Research**

The final Privacy Rule published on August 14, 2002 included a number of changes in how the rule applies to research. The NIH fact sheet in Institutional Review Boards and HIPAA contains additional information on how HIPAA applies to research. See also Impact of the HIPAA Privacy Rules on Academic Research, a white paper published by the American Council on Education.

The Privacy Rule does not make any changes to the Common Rule. However, it does contain several provisions that resemble provisions of the Common Rule and does refer to those provisions. The Common Rule contains specific requirements for a composition of an IRB and the Privacy Rule contains specific requirements for a Privacy Board. The composition of a Privacy Board is similar to that of an IRB.

LSUHSC-S is a covered entity under HIPAA. Researchers who are working with Protected Health Information (PHI) will be required to comply with the rules on HIPAA. The LSUHSC-S IRB acts as the Institution's Privacy Board.

The Privacy Rule permits covered entities to use or disclose protected health information for research purposes when the individual who is the subject of the information authorizes the use or disclosure. For clinical trials, authorization must be sought in addition to informed consent. Authorization must also be sought for other research uses or disclosures of protected health information that do not qualify for an IRB waiver of authorization (discussed below).

The Privacy Rule has several special provisions that apply to research authorizations for uses and disclosures of PHI for research purposes. These requirements are as follows:

1. An authorization for a research purpose may state that the authorization does not expire, that there is no expiration date or event, or that the authorization continues until the end of the research study; and
2. Research authorization forms must be filled out completely and accurately by the investigator, to ensure that all parties who require access to protected health information for the research (including sponsors, CROs, DSMBs, IRB(s), etc.) are identified in the form and may receive the information. The authorization form should be completed by the investigator and submitted to the LSUHSC-S IRB for review and approval.
3. At LSUHSC-S, the authorization for the use or disclosure of PHI is a separate document from the research informed consent form.

VA Research: In accordance with VA Handbook 1058.01, an IRB does not have the authority to approve a HIPAA authorization unless it is incorporated into the informed consent document. Since VA policy requires the HIPAA authorization and the informed consent form to be separate documents, the IRB cannot approve a HIPAA authorization for a VA research study. However, the IRB may waive the requirement for a HIPAA authorization.

## **16.5 Research under HIPAA**

HIPAA defines research as "a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge." This definition is identical with the one used in the "Common Rule", separate federal legislation designed to protect human subjects involved in research. HIPAA describes privacy standards for protecting PHI and so it only applies to research that involves humans' (not animals') health information.

### **16.5.1 Waiver of Authorization for Use or Disclosure of PHI in Research**

Under the Privacy Rule, covered entities are permitted to use and disclose protected health information for research with individual authorization, or without individual authorization under limited circumstances. A covered entity may use or disclose protected health information for research when presented with documentation that an IRB has granted a waiver of authorization (see 45 CFR 164.512(i)(1)(i)). This provision of the Privacy Rule might be used, for example, to conduct records research, epidemiological studies, or other research where de-identified data is unavailable or not suited to the research purpose.

The waiver documentation presented to the covered entity must include the following:

1. Identification of the IRB or Privacy Board and the date on which the alteration or waiver of authorization was approved;
2. A statement that the IRB or Privacy Board has determined that the alteration or waiver of authorization, in whole or in part, satisfies the three criteria in the Rule;
3. A brief description of the protected health information for which use or access has been

determined to be necessary, and without which the research could not practicably be conducted as determined by the IRB or Privacy Board;

4. A statement that the alteration or waiver of authorization has been reviewed and approved under either full or expedited review procedures; and
5. The signature of the IRB chair or other member, as designated by the chair, of the IRB or the Privacy Board, as applicable.

The following criteria must be satisfied for the IRB to approve a waiver of authorization under the Privacy Rule:

1. The use or disclosure of protected health information involves no more than a minimal risk to the privacy of individuals, based on, at least, the presence of the following elements:
  - an adequate plan to protect the identifiers from improper use and disclosure;
  - an adequate plan to destroy the identifiers at the earliest opportunity consistent with conduct of the research, unless there is a health or research justification for retaining the identifiers or such retention is otherwise required by law;
  - adequate written assurances that the protected health information will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research project, or for other research for which the use or disclosure of protected health information would be permitted by this subpart;
2. The research could not practicably be conducted without the waiver or alteration
3. The research could not practicably be conducted without access to and use of the protected health information.

### **16.5.2 Review Preparatory to Research**

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The Privacy Rule permits a covered entity to use or disclose protected health information to a researcher without authorization or waiver for the limited purpose of a “review preparatory to research.” Such reviews may be used to prepare a research protocol, or to determine whether a research site has a sufficient population of potential research subjects. Prior to permitting the researcher to access the protected health information, the covered entity must obtain representations from the researcher that the use or disclosure of the protected health information is solely to prepare a research protocol or for similar purposes preparatory to research, that the researcher will not remove any protected health information from LSUHSC-S, and that protected health information for which access is sought is necessary for the research purpose. Researchers should consult the covered entity regarding any forms or applications necessary to conduct a review preparatory to research.

Researchers conducting a review preparatory to research may not record information in identifiable form, nor may they use the information that they receive to contact potential subjects. Because the Privacy Rule permits a covered entity to disclose protected health information to the individual who is the subject of the information, covered health care providers and patients may continue to discuss the option of enrolling in a clinical trial without

patient authorization. Even when permitted by the Privacy Rule, however, any use of patient information for recruitment must comply with IRB recruitment policies (see discussion below).

1. All human subject research requires IRB review to determine either, (a) exempt status or (b) need for further review.
2. Reviews preparatory to research that are permitted under HIPAA may or may not be human subject research depending on the investigation being conducted.
  - a. Only those reviews of a database by an individual entitled to access that database intended to enumerate an available data set without reviewing PHI and for which no PHI is recorded do not require review. For example: medical records may be queried for information such as: In the year XXXX how many patients had a discharge diagnosis of [indicate disease/diagnosis]. IRB Privacy Board Review is required for all other uses of PHI as indicated.
  - b. If the research involves a de-identified data set, defined as removing the following identifiers, then a de-identified data set certification form must be completed, submitted for administrative review and certified prior to accessing the data set. This activity also requires an IRB determined exemption from review:
    1. Names
    2. Geographic info. (city, state, and zip)
    3. Elements of Dates (except years)
    4. Telephone #s
    5. Fax #s
    6. E-mail address
    7. Social Security#
    8. Medical Record, prescription #s
    9. Health Plan Beneficiary #s
    10. Account #s
    11. Certificate /License #s
    12. VIN and Serial #s, license plate #s.
    13. Device identifiers, serial #s
    14. Web URLs
    15. IP address #s
    16. Biometric identifiers (finger prints)
    17. Full face, comparable photo images
    18. Unique identifying #s

IRB Privacy Board review and approval is required prior to initiating this research. Investigators are not authorized to contact potential research subjects identified in reviews preparatory to research.

### **16.5.3 Research on Protected Health Information of Decedents**

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The protections of the Common Rule apply only to living human beings; by contrast, the Privacy Rule also protects the identifiable health information of deceased persons (decedents). The

Privacy Rule contains an exception to the authorization requirement for research that involves the protected health information of decedents. A covered entity may use or disclose decedents' protected health information for research if the entity obtains representations from the researcher that the use or disclosure being sought is solely for research on the protected health information of decedents, that the protected health information being sought is necessary for the research, and, at the request of the covered entity, documentation of the death of the individuals about whom information is being sought. Researchers should submit the applicable IRB form for IRB approval when they intend to conduct research involving decedents' protected health information.

#### **16.5.4 Limited Data Sets with a Data Use Agreement**

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When a researcher does not need direct identifiers for a study but does require certain data elements that are not permitted in de-identified data, the Privacy Rule permits a covered entity to disclose a limited data set to the researcher without authorization or waiver, provided that the researcher has signed a data use agreement. The limited data set is still considered to be protected health information, but it must exclude only specified direct identifiers of the individual or of relatives, employers, or household members of the individual.

A limited data set is defined as removing the following identifiers:

1. Names
2. Postal address info. (if other than city, state and zip)
3. Telephone numbers
4. Fax numbers
5. Email addresses
6. Social Security #s
7. Medical record, prescription numbers
8. Health plan beneficiary #s
9. Account #s
10. Certificate/license #s
11. Vin and serial #s, license plate #s
12. Device identifiers, serial #s
13. Web URLs
14. IP address #s
15. Biometric identifiers (finger prints)
16. Full face, comparable photo images

The Privacy Rule requires that the data use agreement used in conjunction with the limited data set contain provisions that:

1. Establish the permitted uses and disclosures of the limited data set by the recipient, consistent with the purposes of the research, and which may not include any use or disclosure that would violate the Rule if done by the covered entity;
2. Identify who can use or receive the data
3. Require the recipient to agree to the following:

- a. Not to use or disclose the information other than as permitted by the data use agreement or as otherwise required by law
- b. Use appropriate safeguards to prevent the use or disclosure of the information other than as provided for in the data use agreement
- c. Report to the covered entity any use or disclosure of the information not provided for by the data use agreement of which the recipient becomes aware; Ensure that any agents, including a subcontractor, to whom the recipient provides the limited data set agrees to the same restrictions and conditions that apply to the recipient with respect to the limited data set
- d. Not to identify the information or contact the individual
- e. Researchers who will be receiving limited data sets must submit a signed copy of the covered entity's data use agreement to the LSUHSC-S IRB for approval, prior to initiating the research.

Transition Provisions: The Privacy Rule contains certain grandfathering provisions that permit a covered entity to use and disclose protected health information for research after the Rule's compliance date of April 14, 2003, if the researcher obtained any one of the following prior to the compliance date:

- 1. An authorization or other express legal permission from an individual to use or disclose protected health information for the research
- 2. The informed consent of the individual to participate in the research
- 3. An IRB waiver of informed consent for the research

Even if informed consent or other express legal permission was obtained prior to the compliance date, if new subjects are enrolled or existing subjects are re-consented after the compliance date, the covered entity must obtain the individual's authorization. For example, if there was a temporary waiver of informed consent for emergency research under the FDA's human subject protection regulations, and informed consent was later sought after the compliance date, individual authorization must be sought at the same time.

The transition provisions apply to both uses and disclosures of protected health information for specific research protocols and uses or disclosures to databases or repositories maintained for future research.

## **16.6 HIPAA and Documentation Requirements**

HIPAA documents include an authorization form or a waiver of authorization form. One of these documents must be used whenever PHI is utilized in the research.

## **16.7 Patient Rights and Research**

Under HIPAA, patients have certain rights. Those that may affect research include the right to receive a Notice of Privacy Practices, the right to access, inspect, and receive a copy of one's

own PHI, the right to request an amendment to one's own PHI, and the right to an accounting of certain disclosures of PHI that occur outside the scope of treatment, payment and health care operations that have not been authorized.

## **16.8 HIPAA and Existing Studies**

Any research subject enrolled in a study that uses PHI from a covered entity must sign a HIPAA-compliant authorization form. This form is in addition to the existing Informed Consent document, and is federally required. The LSUHSC-S HIPAA Authorization HRP-502.1 can be found in the Shields document library and on the HRPP website: <http://www.lsuhschreveport.edu/Research/HRPP-Home/index>. This form may not be altered.

## **17. SPECIAL TOPICS**

### **17.1 Certificate of Confidentiality (CoC)**

Certificates of Confidentiality are issued by the federal government to protect identifiable research information from forced disclosure. They allow the investigator and others who have access to research records to refuse to disclose identifying information on research participants in any civil, criminal, administrative, legislative, or other proceeding, whether at the federal, state, or local level. CoCs may be granted for studies collecting information that, if disclosed, could have adverse consequences for subjects or damage their financial standing, employability, insurability, or reputation.

The certificate goes beyond the consent form in ensuring confidentiality and anonymity. Without the certificate, researchers can be required by a court-ordered subpoena to disclose research results (usually as part of a criminal investigation of the subjects).

Any research project that collects personally identifiable, sensitive information and that has been approved by an IRB is eligible for a Certificate. Federal funding is not a prerequisite for a Certificate.

#### **17.1.1 Statutory Basis for Protection**

Protection against compelled disclosure of identifying information about subjects of biomedical, behavioral, clinical, and other research is provided by the Public Health Service Act §301(d), 42 U.S.C. §241(d):

"The Secretary may authorize persons engaged in biomedical, behavioral, clinical, or other research (including research on mental health, including research on the use and effect of alcohol and other psychoactive drugs) to protect the privacy of individuals who are the subject

of such research by withholding from all persons not connected with the conduct of such research the names or other identifying characteristics of such individuals. Persons so authorized to protect the privacy of such individuals may not be compelled in any Federal, State or local civil, criminal, administrative, legislative, or other proceedings to identify such individuals."

### 17.1.2 Usage

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Certificates of Confidentiality may be granted for studies collecting information that, if disclosed, could have adverse consequences for subjects or damage their financial standing, employability, insurability, or reputation. By protecting researchers and institutions from being compelled to disclose information that would identify research subjects, Certificates of Confidentiality help achieve the research objectives and promote participation in studies by assuring confidentiality and privacy to subjects.

Any investigator engaged in research in which sensitive information is gathered from human subjects (or any person who intends to engage in such research) may apply for a Certificate of Confidentiality. Research can be considered sensitive if it involves the collection of:

1. information about sexual attitudes, preferences, practices
2. information about personal use of alcohol, drugs, or other addictive products
3. information about illegal conduct
4. information that could damage an individual's financial standing, employability, or reputation within the community
5. information in a subject's medical record that could lead to social stigmatization or discrimination
6. information about a subject's psychological well-being or mental health

This list is not exhaustive. Researchers contemplating research on a topic that might qualify as sensitive should contact the IRB Office for help in applying for a certificate. In the informed consent form, investigators should tell research subjects that a Certificate is in effect. Subjects should be given a fair and clear explanation of the protection that it affords, including the limitations and exceptions noted above. Every research project that includes human research subjects should explain how identifiable information will be used or disclosed, regardless of whether a Certificate is in effect.

### 17.1.3 Limitations

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The protection offered by a Certificate of Confidentiality is not absolute. A Certificate protects research subjects only from legally compelled disclosure of their identity. It does **not** restrict voluntary disclosures.

For example, a Certificate does not prevent researchers from voluntarily disclosing to appropriate authorities such matters as child abuse, a subject's threatened violence to self or

others, or from reporting a communicable disease. However, if researchers intend to make such disclosures, this should be clearly stated in the informed consent form which research subjects are asked to sign.

In addition, a Certificate of Confidentiality does **not** authorize the person to whom it is issued to refuse to reveal the name or other identifying characteristics of a research subject if:

1. the subject (or, if he or she is legally incompetent, his or her legal guardian) consents, in writing, to the disclosure of such information
2. authorized personnel of the Department of Health and Human Services (DHHS) request such information for audit or program evaluation, or for investigation of DHHS grantees or contractors and their employees
3. release of such information is required by the Federal Food, Drug, and Cosmetic Act or regulations implementing that Act

#### 17.1.4 Application Procedures

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Any person engaged in research collecting sensitive information from human research subjects may apply for a Certificate of Confidentiality. For most research, Certificates are obtained from NIH. If NIH funds the research project, the investigator may apply through the funding Institute. However, even if the research is not supported with NIH funding, the investigator may apply for a Certificate through the NIH Institute or Center funding research in a scientific area similar to the project.

If the research is conducting a sensitive research project that is covered by the Agency for Healthcare Research and Quality (AHRQ) confidentiality statute (42 U.S.C. section 299a-1(c) entitled "limitation on use of certain information") or the Department of Justice confidentiality statute (42 USC section 3789g), then a CoC is not required.

If there is an Investigational New Drug Application (IND) or an Investigational Drug Exemption (IDE), the sponsor can request a CoC from the FDA.

For more information, see the NIH Certificates of Confidentiality Kiosk <https://humansubjects.nih.gov/coc/index>.

#### 17.2 Mandatory Reporting

While any person may make a report if they have reasonable cause to believe that a child or elder was abused or neglected, Louisiana law mandates that certain persons who suspect child or elder abuse or neglect report this to the local or state law enforcement agency, Department of Social Services, Adult Protection Agency, and/or Department of Health and Hospitals.

LSUHSC-S policy requires the solicitation of informed consent from all adult research subjects and assent from children involved as research subjects, in addition to the consent of their parents. In situations where conditions of abuse or neglect might be revealed, mandated

reporters should make themselves known as such to parents of children under age 18, to subjects who are children, and to subjects who are potential victims of abuse or neglect.

According to Louisiana state laws:

1. LA Ch.C. 603 and 609(A)(1)(2) Mandatory and permitted reporting; With respect to mandatory reporters: Notwithstanding any claim of privileged communication, any mandatory reporter who has cause to believe that a child's physical or mental health or welfare is endangered as a result of abuse or neglect or that abuse or neglect was a contributing factor in a child's death shall report in accordance with Article 610. Violation of the duties imposed upon a mandatory reporter subjects the offender to criminal prosecution authorized by R. S. 14:403(A)(1).
2. LA R.S. 14:403(A)(1) and LA R.S. 15:1504-05 Any person who, under Children's Code Article 603 and 609(A), is required to report the abuse or neglect or sexual abuse of a child and knowingly and willfully fails to so report shall be guilty of a misdemeanor and upon conviction shall be fined not more than five hundred dollars or imprisoned for not more than six months, or both.
3. LA R.S.14:403.2(C) Abuse and neglect of adults: Any person, including but not limited to a health, mental health, and social service practitioner, having cause to believe that an adult's physical or mental health or welfare has been or may be further adversely affected by abuse, neglect, or exploitation shall report in accordance with Subsection D of this section.
4. LA R.S. 14:403.2(D)(1) Reports reflecting the reporter's belief that an adult has been abused or neglected shall be made to any adult protection agency or to any local or state law enforcement agency. These reports need not name the persons suspected of the alleged abuse or neglect.
5. LA R.S. 14:403.4 Burn injuries or wounds.
6. LA R.S. 14:403.5 Wounds and injuries caused by firearms.
7. LA R.S. 40:1065 Every case of venereal disease that is attended or examined or for which medication is prescribed or treatment given in accordance with the requirements of the Louisiana Sanitary Code.
8. LA R.S. 40: 1299.23 The existence and circumstances of each case of lead poisoning known and not previously reported.
9. LA R.S. 40: 1299.35.10 Abortion procedures, excluding the name and address of the woman as well as any post abortion care resulting from complications.
10. LA R.S. 40:1299.84 Each case of cancer
11. Infectious diseases, including untreated pulmonary tuberculosis or acute meningococcal meningitis, acute hepatitis virus B infection, a chronic hepatitis B carrier, or human immunodeficiency virus.

Investigators should consult these sources to determine if potential subjects should be advised of mandatory reporting requirements during the informed consent process.

### **17.3 LSUHSC-S Students and Employees as Subjects**

When LSUHSC-S students and/or employees are being recruited as potential subjects, researchers must ensure that there are additional safeguards for these subjects. The voluntary nature of their participation must be primary and without undue influence on their decision. Researchers must emphasize to subjects that neither their academic status or grades, or their employment, will be affected by their participation decision.

To minimize coercion, investigators should avoid, whenever possible, the use of their students and employees in procedures which are neither therapeutic nor diagnostic. In these latter situations, investigators should solicit subjects through means such as bulletin board notices, flyers, advertisements in newspapers, and announcements in classes or laboratories other than their own. When entering a classroom to recruit students and conduct research, e.g. administer a survey, investigators must do so at the end of the class period to allow non-participating students the option of leaving the classroom, thereby alleviating pressure to participate.

## **17.4 Student Research**

### **17.4.1 Human Subjects Research and Course Projects**

Learning how to conduct ethical research is an important part of a student's educational experience. Research activities that are designed as part of a course requirement for purposes of learning experience only and are NOT designed to develop or contribute to generalizable knowledge MAY not require IRB review and approval if all of the following conditions are true:

- Results of the research are viewed only by the course instructor for teaching purposes and discussed within the classroom for teaching and learning purposes.
- Results of the research are not made public through presentation (outside of the classroom) and are not published in paper or electronic format (e.g., cannot be made available on the internet, cannot be published in a journal, etc.).
- Research procedures are no more than minimal risk.
- Vulnerable populations are not targeted (e.g., children under age 18, prisoners, persons who are cognitively impaired, etc.).
- Data collected are recorded in such a manner that the subjects are not identifiable (images in videotapes and photographs and voices on audiotape are identifiable.)
- When appropriate, an informed consent process is in place.

The course instructor is responsible for communicating to the students the ethics of human subjects' research, for ensuring the protection of human subjects (including a process is in place for obtaining voluntary informed consent from research subjects when appropriate), and for monitoring the students' progress.

When designing a project, students should be instructed on the ethical conduct of research and on the preparation of the IRB application when such is required. Instructors and students should:

- Understand the elements of informed consent
- Development appropriate consent document
- Plan appropriate strategies for recruiting subjects
- Identify and minimize potential risks to subjects
- Assess the risk-benefit ratio for the project
- Establish and maintain strict guidelines for protecting confidentiality
- Allow sufficient time for IRB review (if necessary) and completion of the project

In deciding whether a class research project requires IRB review, the instructor is encouraged to err on the side of caution and to contact the IRB office for assistance.

#### **17.4.2 Individual Research Projects Conducted by Students**

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Independent study projects, senior thesis, undergraduate research projects, masters and advanced degree research, and similar exercises must be independently submitted for IRB review, only when they meet the definition of human subjects research. It is important to keep in mind that any human subjects' research activity that will ultimately contribute to part or all a thesis, dissertation, or other type of publication or presentation must go through the IRB review process prior to enrolling subjects and collecting data. IRB review cannot occur after a study has begun.

Student and advisors should contact the IRB office with any questions.

LSUHSC-S policy and procedures, educational module, forms and related information can be found on the LSUHSC-S IRB website at: <http://www.lsuhschreveport.edu/Research/HRPP-Home/index>

\* Minors (individuals under the age of 18) may be included in projects conducted in established or commonly accepted educational settings or involving normal educational practices such as research on instruction strategies, curricula or classroom management methods.

#### **17.4.3 Independent Study, Thesis and Dissertations**

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These research activities are considered to meet the federal definition of human subject research and should be independently submitted to the IRB. However, when students conduct research as part of a course of study, a faculty member who serves as the PI, ultimately is responsible for the protection of the subjects, even if the student is the primary researcher and actually directs the project. Students are not routinely allowed to be PI(s). However, if appropriate and the student obtains special permission from their Department Chair and Dean of their school acknowledging their approval as a PI then consideration will be given by the IRB. Principal Investigators are routinely required to be faculty. Advisers assume the responsibility for students engaged in independent research, and instructors are responsible for research that

is conducted as part of a course.

Students may not serve as Principal Investigators. They must have a faculty sponsor who fulfills the principal investigator eligibility criteria and who will serve as Principal Investigator and faculty advisor on the study.

## 17.5 Oral History

The following is based on guidance received from OHRP.

A decision whether oral history or other activities solely consisting of open ended qualitative type interviews are subject to the policies and regulations outlined in an institution's FWA and HHS regulations for the protection of human research subjects (45 CFR 46) is based on the prospective intent of the investigator and the definition of research under HHS regulations at 45 CFR 46.102(d): "a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge."

Specifically, for the purposes of this policy, the evaluation of such activities hinges upon whether:

- The activity involves a prospective research plan which incorporates data collection, including qualitative data, and data analysis to answer a research question
- The activity is designed to draw general conclusions (i.e., knowledge gained from a study may be applied to populations outside of the specific study population), inform policy, or generalize findings.

To be subject to the Institution's human research protection policies, the activity must meet both of the above standards.

General principles for evaluating Oral History type activities:

1. Oral history activities, such as open ended interviews, that ONLY document a specific historical event or the experiences of individuals without intent to draw conclusions or generalize findings would NOT constitute "research" as defined by HHS regulations 45 CFR part 46. Example: An oral history video recording of interviews with holocaust survivors is created for viewing in the Holocaust Museum. The creation of the video tape does NOT intend to draw conclusions, inform policy, or generalize findings. The sole purpose is to create a historical record of specific personal events and experiences related to the Holocaust and provide a venue for Holocaust survivors to tell their stories.

2. Systematic investigations involving open-ended interviews that are designed to develop or contribute to generalizable knowledge (e.g., designed to draw conclusions, inform policy, or generalize findings) WOULD constitute research as defined by HHS regulations at 45 CFR part 46. Example: An open-ended interview of surviving Gulf War veterans to document their

experiences, and to draw conclusions about their experiences, inform policy, or generalize findings.

3. Oral historians and qualitative investigators may want to create archives as a resource for others to do research. Since the intent of the archive is to create a repository of information for other investigators to conduct research as defined by 45 CFR part 46, the creation of such an archive WOULD constitute research under 45 CFR part 46. Example: Open ended interviews are conducted with surviving Negro League Baseball players to create an archive for future research. The creation of such an archive would constitute research under 45 CFR part 46 since the intent is to collect data for future research.

Investigators are advised to consult with the IRB Office regarding whether their oral history project requires IRB review.

## **17.6 Repositories of Tissue or Data**

Repositories of both data and of tissue provide unique research opportunities- they allow the accumulation of research materials over time and allow new technologies to evolve. The establishment and operation of a repository requires coordinated efforts from the collectors of the information/ specimens, the operators of the repository, and the recipient investigators. Each component is required to comply with applicable regulatory requirements, accreditation standards, and Institutional policy.

Chancellor's Memorandum-33 outlines the Institutional standards for the review and approval of repositories, as well as the security and privacy standards. It is LSUHSC-S policy that repositories of human data or tissues for research will operate in accordance with applicable state and federal regulations regarding the protection of human research subjects and the privacy and security of health information, as well as relevant accreditation standards and Institutional policies.

The details of the review process and standards are found in CM-33. Each repository of either tissue from and/or data about human participants that is being implemented for research purposes must receive a prior IRB approval. The proposal submission must include appropriate consent, data/tissue submittal forms, and tissue/data usage agreements.

After the repository is established, subsequent research protocols must be approved by the IRB prior to commencement of research activities; a copy of the IRB approved consent form for the repository must be included with the application.

### **Non-Research Repositories**

- If specimens or data were originally collected for non-research purposes (clinical care)

AND were added to a non-research repository/database without any identifiable private data or information or links (codes, pathology numbers, medical record numbers) to identifiable private data or information, it is a non-research repository/database. If links are included, this policy section does not apply. Studies using specimens/data from non-research repositories or databases are generally considered Not Human Subjects Research.

## Research Repositories

- If specimens or data were collected for research purposes, it is a research repository. Collection of specimens/data, repository storage or data management and use of specimens or disclosure of data are all considered research activities and require IRB review and approval.
- Specimen/data repositories may include two kinds of specimens/data: a) those collected with the expressed purpose of distribution to other investigators, and b) those collected by individual investigators, and not originally intended to be shared with others, but which are subsequently shared as part of a repository.
- Any collection which contains specimens/data that are potentially identifiable (i.e. directly or indirectly with a code or link) and are distributed to someone other than the original named investigator(s) making the collection, regardless of the original intent, may be considered to be a repository requiring IRB oversight.
- If the original named investigator(s) wishes to use the potentially identifiable specimens or data for any future use that is not part of the original IRB approved protocol then the subsequent use will also require IRB approval and oversight.

## Collection of a Specimen/Data for a Repository

- Investigators who collect directly or indirectly identifiable specimen/data must request IRB review and approval of the activity. Under most circumstances, written informed consent and HIPAA Authorization from the subject is required and should include information about the repository, the conditions under which the specimens/data will be shared with others and if the specimen/data will be store for future use beyond the current research.

Confidentiality risks of research participation may extend beyond the duration of the subject's direct participation in research. This is common when records or samples with identifiers are retained by the investigator. These confidentiality risks and/or new disclosure concerns are important to consider. The ability to re-test samples containing extractable DNA has made it possible that retained samples may contain information that cannot be foreseen at the time of initial collection, but that may eventually be of great importance or sensitivity. Investigators should destroy identifiers to their samples/data when possible.

Regarding storing data/ specimens outside of LSUHSC-S, if the repository is located at an

external institution or organization, the investigator must submit (to the LSUHSC-S IRB) a copy of the external site's IRB approval letter for operation of the repository at that institution or organization. The IRB at the institution where the repository is located must approve and maintain oversight of a protocol that: (a) specifies the conditions under which data and specimens may be accepted and shared with other investigators or designees and (b) ensures adequate privacy and confidentiality protections for subjects contributing to the repository. Any research specimen/data repository that distributes materials/data requires IRB approval prior to the distribution.

The investigator must follow the conditions under which the specimens/data will be shared as described in the IRB initial review application. These conditions must consider the privacy of the individuals from whom the tissue came, what the informed consent permitted, and the intent of the person to whom the tissue is sent. The recipient of the tissue samples must abide by the conditions specified. A gatekeeper or repository director, established under the IRB guidelines and pursuant to the IRB approval for the repository, should evaluate each request for samples to see if the request is consistent with the IRB's conditions for sharing samples and with the original informed consent and the repository's policies.

The transfer of data to outside collaborators or to external repositories requires a Data Use Agreement or other types of agreements/contracts between the parties involved. All agreements need to be signed by an authorized agent of LSUHSC-S.

The transfer of materials to outside collaborators requires the use of Material Transfer Agreements (MTAs). The Office of Sponsored Programs and Technology Transfer (OSPTT) coordinates the completion of MTAs. MTAs need to be signed by an authorized agent of LSUHSC-S. MTAs ensure LSUHSC-S rights are protected when specimens or reagents are shared with outside investigators or institutions. An MTA protects the intellectual and other property rights of the provider and generally addresses:

- Limits on the use of the research materials, inventions, and results
- Prohibitions on the redistribution of the material
- Conditions of use, including prohibitions of use in animals or humans
- Conditions for publication, usually with provisions that the manuscript must be seen by the donor before submission for publication
- A hold-harmless clause, meaning that the donor has no liability resulting from the use of the material
- The return of unused materials

The following procedure should be followed when establishing a repository at LSUHSC-S. The investigator is to develop written policies and procedures on operating and managing the repository. The policies and procedures are to be provided to the IRB as part of the initial application. The following documents must be included with the Template Protocol (HRP-503):

- Purpose of the repository

- Specimen and data collection procedures
- Specimen and data storage/retention
- Specimen derivation and processing
- Specimen and data distribution
- Obtaining informed consent
- Procedures for protecting privacy and confidentiality (for example, anonymization of specimens/data, coding of specimens/data, encryption, limited access/secure storage)
- Confidentiality measures
- Procedures for return of research results (if and under what conditions)
- Repository oversight
- Model informed consents for subjects contributing to the repository
- Model agreements for investigators collecting tissues for the repository and for investigators receiving tissues from the repository. These agreements should address use of specimens/data, human subject protections, sharing of specimens with third parties, commercial use of specimens, biohazards, and indemnification.
- A plan for the disclosure of clinically relevant results/incidental findings including the mechanism for evaluating whether the results of research testing are clinically relevant and might warrant disclosure to the research participants. A mechanism for disclosure to participants of clinically relevant results/incidental findings to be included.
- A Certificate of Confidentiality, if needed. Certificates of Confidentiality are issued by the National Institutes of Health to protect identifiable research information from forced disclosure. Certificates of Confidentiality may be granted for studies collecting information that, if disclosed, could have adverse consequences for subjects or damage their financial standing, employability, insurability, or reputation. Additional information is available at the NIH Certificate of Confidentiality Kiosk web site.

If the experimental design allows it, all identifiers should be stripped from the stored samples or data, such that they can never be traced to the individual. If the experimental design requires that the specimens/data be referable back to an individual subject, retention creates a durable confidentiality risk that must be both controlled and disclosed. Storage with easily traceable identifiers such as patient names, initials, social security numbers, or medical record numbers is almost never appropriate. An additional safeguard for maintaining confidentiality while retaining a link is to use a code in place of identifiers and retaining a master list that provides a key to the code.

## 17.7 Genetic Studies

Genetic research studies may create special risks to human subjects and their relatives. These involve medical, psychosocial, and economic risks, such as the possible loss of privacy, insurability, and employability, change in immigration status and limits on education options, and may create a social stigma. Knowledge of one's genetic make-up may also affect one's knowledge of the disease risk status of family members.

In studies involving genetic testing, several questions need to be addressed, including:

1. Will test results be given?
2. Will disease risk be quantified, including the limits on certainty of the testing?
3. Will a change in a family relationship be disclosed, such as mistaken paternity?
4. Does the subject or family member have the option not to know the results? How will this decision be recorded?
5. Could other clinically relevant information be uncovered by the study? How will disclosure of this added information occur?
6. Do any practical limitations exist on the subject's right to withdraw from the research, withdraw data, and/or withdraw DNA?
7. Is the subject permitted to participate in the study while refusing to have genetic testing (such as in a treatment study with a genetic testing component)?

For DNA banking studies, several questions need to be addressed, including:

1. Will DNA be stored or shared? If shared, will the subject's identity be known by the new recipient investigator?
2. Will the subject be contacted in the future by the investigator to obtain updated clinical information?
3. How can the subject opt out of any distribution or subsequent use of his/her genetic material?

Investigators planning to submit large-scale human genomic data to an NIH-designated data repository must request certification of the genomic data sharing plan from the IRB prior to the submission of data or approval of funding. The IRB Director, IRB Chair or designee will verify for the Institutional Official or designee that all data meet criteria for submission to the data repository. The reviewer will use Worksheet: NIH GDS Institutional Certification (HRP-332) to evaluate and document whether the investigator's genomic data sharing plan meets the criteria for submission to an NIH-designated data repository. The reviewer will complete the NIH GDS Institutional Certification Form as a guide for the Institutional Certification letter and insert submission-specific information. [http://gds.nih.gov/Institutional\\_Certifications.html](http://gds.nih.gov/Institutional_Certifications.html). The certification letter will be signed by the Institutional Official or designee and copy filed in the IRB Office. The investigator will forward a copy of the signed GDS Institutional Certification to the NIH.

## **17.8 Research Involving Coded Private Information or Biological Specimens**

LSUHSC-S policy is based on the OHRP guidance document entitled, "Coded Private Information or Specimens Use in Research, Guidance (2008)." <https://www.hhs.gov/ohrp/regulations-and-policy/guidance/research-involving-coded-private-information/>. This document:

- Provides guidance as to when research involving coded private information or specimens is or is not research involving human subjects, as defined under HHS regulations for the protection of human research subjects (45 CFR part 46).

- Reaffirms OHRP policy that, under certain limited conditions, research involving **only** coded private information or specimens is not human subjects' research.
- Provides guidance on who should determine whether human subjects are involved in research.

For purposes of this policy, coded means that: (1) identifying information (such as name or social security number) that would enable the investigator to readily ascertain the identity of the individual to whom the private information or specimens pertain has been replaced with a number, letter, symbol, or combination thereof (i.e., the code); and (2) a key to decipher the code exists, enabling linkage of the identifying information to the private information or specimens.

Under the definition of human subject in Section 1.4 of this policy, obtaining identifiable private information or identifiable specimens for research purposes constitutes human subjects research. Obtaining means; receiving or accessing identifiable private information or identifiable specimens for research purposes. This includes an investigator's use, study, or analysis for research purposes of identifiable private information or identifiable specimens already in the possession of the investigator.

In general, private information or specimens are individually identifiable when they can be linked to specific individuals by the investigator(s) either directly or indirectly through coding systems. Private information or specimens are not considered to be individually identifiable when they cannot be linked to specific individuals by the investigator(s) either directly or indirectly through coding systems.

Research involving only coded private information or specimens do not involve human subjects if the following conditions are both met:

1. the private information or specimens were not collected specifically for the currently proposed research project through an interaction or intervention with living individuals; and
2. the investigator(s) cannot readily ascertain the identity of the individual(s) to whom the coded private information or specimens pertain because, for example:
  - a. the key to decipher the code is destroyed before the research begins
  - b. the investigators and the holder of the key enter into an agreement prohibiting the release of the key to the investigators under any circumstances, until the individuals are deceased (note that the HHS regulations do not require the IRB to review and approve this agreement); data use agreement
  - c. there are IRB-approved written policies and operating procedures for a repository or data management center that prohibit the release of the key to the investigators under any circumstances, until the individuals are deceased
  - d. there is other legal requirements prohibiting the release of the key to the

investigators, until the individuals are deceased.

In some cases an investigator who obtains coded private information or specimens about living individuals under one of the conditions cited in 2(a)-(d) above may (1) unexpectedly learn the identity of one or more living individuals, or (2) for previously unforeseen reasons now believe that it is important to identify the individual(s). If, as a result, the investigator knows, or may be able to readily ascertain, the identity of the individuals to whom the previously obtained private information or specimens pertain, then the research activity now would involve human subjects. Unless this human subject research is determined to be exempt (See Section 3.4), IRB review of the research would be required. Informed consent of the subjects also would be required unless the IRB approved a waiver of informed consent (See Section 5.8).

### **17.8.1 Research Involving Coded Private Information or Specimens**

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The investigator in consultation with the IRB Chair or Designee will determine if the research involving coded information or specimens requires IRB review. The investigator submits a written request or a formal submission. The request must include sufficient documentation of the activity to support the determination. Formal submissions will be responded to in writing and a copy of the submitted materials and determination letter/email will be kept on file.

### **17.8.2 Case Reports Requiring IRB Review**

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In general, an anecdotal report on a series of patients seen in one's own practice and a comparison of these patients to existing reports in the literature is not research and would not require IRB approval. Going beyond one's own practice to seek out and report cases seen by other clinicians creates the appearance of a systematic investigation with the intent to contribute to generalizable knowledge and therefore would be considered research and would require IRB approval.

### **17.8.3 Definitions**

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Single Case Report - The external reporting (e.g., publication or poster/verbal presentation) of an interesting clinical situation or medical condition of a single patient. Case reports normally contain detailed information about an individual patient and may include demographic information and information on diagnosis, treatment, response to treatment, follow-up after treatment, as well as a discussion of existing relevant literature. The patient information used in the report must have been originally collected solely for non-research purposes as the result of a clinical experience. A single case report does not meet the definition of a systematic investigation and may not be human subject research.

Case Series - The external reporting (e.g., publication or poster/verbal presentation) of an interesting clinical situation or medical condition in a series of patients (i.e., more than one patient). Case series usually contain detailed information about each patient and may include

demographic information and information on diagnosis, treatment, response to treatment, follow-up after treatment, as well as a discussion of existing relevant literature. The information used in the report must have been originally collected solely for non-research purposes as the result of a clinical experience. A case series of three (3) or more usually meets the definition of a systematic investigation and may be considered human subject research.

## **17.9 International Research**

The IRB will review all international research utilizing human participants to assure adequate provisions are in place to protect the rights and welfare of the participants. Approval of research is permitted if the procedures prescribed by the foreign institution afford protections that are at least equivalent to those provided in 45 CFR 46. The LSUHSC-S IRB must receive and review the foreign institution or site's IRB review and approval of each study prior to the commencement of the research at the foreign institution or site.

For Federally funded research, approval of research for foreign institutions or sites engaged in research is only permitted if the foreign institution or site holds an Assurance with OHRP and local IRB review and approval is obtained.

Approval of research for foreign institutions or sites not engaged in research is only permitted if one or more of the following circumstances exist:

- When the foreign institution or site has an established IRB/IEC, the Investigator must obtain approval to conduct the research at the "not engaged" site from the site's IRB/IEC or provide documentation that the site's IRB/IEC has determined that approval is not necessary for the Investigator to conduct the proposed research at the site.
- When the foreign institution or site does not have an established IRB, a letter of cooperation must be obtained demonstrating that the appropriate institutional or oversight officials are permitting the research to be conducted at the performance site.
- IRB approval to conduct research at the foreign institution or site is contingent upon receiving documentation of the performance site's IRB/IEC determination, or letter of cooperation, as applicable.
- It is the responsibility of the LSUHSC-S Investigator and the foreign institution or site to assure that the resources and facilities are appropriate for the nature of the research.
- It is the responsibility of the LSUHSC-S Investigator and the foreign institution or site to notify the IRB promptly if a change in research activities alters the performance site's engagement in the research (e.g., performance site "not engaged" begins consenting research participants, etc.).
- The IRB will consider local research context when reviewing international studies to assure protections are in place that are appropriate to the setting in which the

research will be conducted.

- In the case where there is no local IRB review the IRB may require an expert consultant, either from the local country where the research is conducted or from an international organization, with the expertise or knowledge required to adequately evaluate the research in light of local context.
- The informed consent documents must be in a language understandable to the proposed participants. Therefore, the IRB will review the document and a back translation of the exact content contained in the foreign language informed consent document which must be provided by the Investigator, with the credentials of the translator detailed in the IRB application or amendment form. Verification of the back translation should be made available for the IRB file.

### **17.9.1 Monitoring of Approved International Research**

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The IRB is responsible for the ongoing review of international research conducted under its jurisdiction through the continuing review process in accordance with all applicable federal regulations.

The IRB will require documentation of regular correspondence between the LSUHSC-S Investigator and the foreign institution or site and may require verification from sources other than the LSUHSC-S Investigator that there have been no substantial changes in the research since its last review.

### **17.9.2 VA Participation in Research**

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Non-veterans may be entered into VA approved research studies only when there are insufficient veterans available to complete the study and all regulations pertaining to the participation of veterans as research subjects including requirements for indemnification in case of research-related injury pertain to non-veteran subjects enrolled in VA-approved research. VA research requires that subjects' medical records (paper or electronic) be flagged to protect the subject's safety. This requirement may be waived when: (1) the subject's participation in the study involves only one encounter, only the use of a questionnaire or only involves the use of previously collected biological specimens. Additionally, flagging may be waived if the identification of the subject in a not greater than minimal risk study would place the subject at greater than minimal risk.

VA general requirements for informed consent do not apply to research ruled exempt from IRB review. In all other VA research, an investigator may not involve a human being as a subject in research unless the investigator has obtained the legally effective informed consent of the person or the person's legally authorized representative. If someone other than the investigator conducts the interview and obtains consent from a patient, the investigator needs to formally delegate this responsibility. The person so delegated must have received appropriate training to perform this activity and must be knowledgeable about the research to

be conducted and the consenting process, and must be able to answer questions about the study. A VA investigator must seek such consent only under circumstances that provide the prospective subject (or legally-authorized representative) sufficient opportunity to consider whether to participate and that minimize the possibility of coercion or undue influence. The information that is given to the subject or the subject's representative must be in language understandable to the subject or the subject's representative. Also, no informed consent, whether oral or written, may include any exculpatory language through which the subject or the subject's representative is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution, or its agents from liability for negligence. All VA research must use VA Informed Consent and all required consent elements must be present.

VA requires the basic elements for informed consent previously listed in this document with specific designation of the name of the study and the name of the PI. VA description of reasonable risks may include, for example, privacy risks that involve legal, employment or social risks. Concerning confidentiality of records, VA may include the Office for Human Research Protections and the Government Account Office in the confidentiality statement. VA specific language will be used in VA Informed Consent to word compensation available for research involving more than minimal risk. VA investigators need to note charges will not be made for medical services, including transportation, furnished as part of a VA-approved research study. If services are furnished to a person who is not eligible for services as a veteran, the medical care appropriation will be reimbursed from associated research funds.

VA consents may also include the additional elements of informed consent previously discussed in this document. VA consents will include any additional costs to the subject as is consist with the federal laws concerning veterans' eligibility for medical care and treatment.

When appropriate, VA requires one or more of the following elements of information be provided to each subject. Also, when any of these additional elements are appropriate, the VA requires them to be documented in the IRB-approved consent document, unless documentation of consent is waived:

- Commercial Product. If applicable, that the investigator believes that the human biologic specimens obtained could be part of, or lead to the development of, a commercially valuable product.
- Future Use of Specimens. If the specimens are to be retained after the end of the study for future research, where the specimens will be retained, who will have access to them, and how long they will be retained. Current applicable institutional, VA and other Federal requirements must be met for handling, use and storage of biologic specimens and data.
- Future use of data. If any of the data will be retained after the study for future research, where the data will be stored, and who will have access to the data. Organizations, VA, and other federal requirements must be met for use and storage of data.

- Re-contact. If the subject will be re-contacted for future research whether within a VA facility or outside a VA facility.
- Payment for participating in the study. If appropriate, a statement regarding any payment the subject is to receive for participating in the study and how the payment is to be made.
- Disclosure of results. If the subject will receive a report of the aggregate results or any results specific to the subject

If genetic testing is to be done, VA requirements pertaining to genetic testing must also be met. As appropriate, a statement regarding any payments the subject is to receive and how payment will be made. VA sensitive information must not be transmitted by remote access unless VA-approved protection mechanisms are used. Additional security controls are required to guard VA sensitive information stored on computers used outside VA facilities. If LSUHSC Shreveport personnel become aware of the theft, loss or compromise of any device used to transport, access or store VA information, or of the theft, loss or compromise of any VA data, the user must immediately report the incident to his or her supervisor. That supervisor must inform the Information Security Officer, at 318.210.2200 or 318.221.8411, extension 7155 or Medical Center Director, at 318.424.6037.

## **18. HRPP POLICY MAINTENANCE**

### **18.1 Policy**

This procedure outlines the process for the development, approval and maintenance of policies and procedures under the jurisdiction of the LSUHSC-S Human Research Protection Program (HRPP).

### **18.2 Review and Maintenance of HRPP and IRB Policies**

#### **18.2.1 Investigator**

- a. The Investigator should be knowledgeable of the LSUHSC-S HRPP and IRB Standard Operating Procedures as part of his/her training for conducting human research at LSUHSC-S. Current policies and procedures are located on the HRPP website.
- b. It is the responsibility of the Investigator to routinely view the HRPP website for new or revised HRPP / IRB policies and procedures.
- c. The Investigator will contact the IRB Office or the HRPP QA/QI Coordinator for clarification of policies, procedures, guidance or forms as warranted.

#### **18.2.2 HRPP and IRB Administration**

- a. The HRPP Educator, QA/QI Coordinator(s), the IRB Administrator, AVCRM and IO or designee will routinely view the OHRP and FDA websites for issuance of guidance documents, changes in regulations, and determination letters and stay current on LSUHSC-S policies that may affect the protection of research participants.
- b. The IRB Administrator and HRPP Educator, QA staff , AVCRM and IO or designee are responsible for identifying when guidance on necessary revisions of policies and procedures may be required.
- c. The HRPP/IRB and the Office of Legal Affairs & Organizational Integrity will collaborate on changes and assist with interpretation of Federal, State and Local regulations or other LSUHSC-S policies and procedures affecting HRPP/ IRB policies and procedures.
- d. The HRPP Education/QA staff will provide educational sessions to the IRB Committee members and HRPP staff regarding HRPP/ IRB policies and procedures, as well as updates or revisions, in a timely manner.
- e. The HRPP team is responsible for reviewing policies and procedures to ensure they remain current.

### **18.2.3 IRB Staff Responsibilities**

- a. The IRB Staff will use the HRPP/IRB policies and procedures posted on the HRPP website and in the IRB Handbook when processing research activities.
- b. The IRB Staff may consult with the HRPP Staff Director, IRB Chair or other knowledgeable member of the IRB or HRPP staff for guidance in applying the HRPP/IRB policies and procedures.
- c. If a staff member notices that a policy or procedure is inaccurate or out of date, the staff member should bring it to the attention of the HRPP Staff Director. It is the responsibility of the entire HRPP staff to keep the HRPP/IRB policies and procedures current and applicable to the daily processes.

### **18.3 Development or Revision of Policies and Procedures**

Institutional officials, IRB chairs, members and staff, researchers and members of other institutional departments and oversight committees responsible for the protection of LSUHSC-S research participants, are welcome to propose a new or revised policy or procedures at any time. The proposal should be submitted in writing to the AVCRM or designee, along with an explanation of the reasons supporting the proposal.

Policies and procedures will be drafted or modified when deemed necessary due to new guidance, changes in regulations or other documents published by federal agencies, or when necessary due to changes in LSUHSC-S policy, procedure or practice.

The development or modification of policy and/or procedure is overseen directly by the AVCRM when necessary, in conjunction with other departments responsible for research protection

and compliance.

Resources used to support the development of policies and procedures may include federal regulations, state law, institutional policies, other research institutions, consultants (with permission), and other references deemed appropriate.

### **18.3.1 Review and Approval of Draft IRB Policies and Procedures**

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The draft policy or procedure is initially reviewed by the AVCRM or designee to determine the appropriate approval hierarchy required given the complexity and impact of the proposal. Approval authorities may include the Institutional Official Advisory Committee, the fully convened IRB's, the IRB Chairs, the IRB Administrator/HRPP Medical Director, AVCRM, the Institutional Official or the Office of Legal Affairs & Organizational Integrity.

If the draft proposal substantively changes the way the IRB considers and evaluates research protocols, or is drafted in response to newly released guidance or law from federal agencies, the proposal will be discussed with the IRB Chairs or designee, the HRPP Medical Director, or the Office of Legal Affairs & Organizational Integrity as needed.

If the draft policy or procedure affects the regulatory or ethical review and approval of research but that does not significantly affect Institutional policy and applies only to the IRB, the draft will be reviewed and approved or disapproved by the Chair(s) and the IO or designee. The Institutional Official will be informed of such changes as they occur. If the draft policy or procedures significantly affects Institutional policy, the Institutional Official Advisory Committee shall review and approve or disapprove the draft with any necessary revisions.

### **18.3.2 Deployment of New and Revised Policies**

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Educational sessions for IRB members and HRPP staff will be conducted in a timely manner when new or newly revised policies and procedures that affect the responsibilities of the IRB or designated reviewers are being considered. The HRPP Education Coordinator is responsible for disseminating to the research community new and revised policies and procedures related to the protection of human research participants in a timely manner.

New or revised policies are retained in the electronic data system (Shields), noting the date of implementation and the office responsible for oversight. The policies are available for public reference on the HRPP web site. In addition, a broadcast email is sent to the research community announcing the release of the new policy, which includes the website location where the policy can be reviewed, and inviting comments from the research community, where appropriate.

## **18.4 Responding to Feedback**

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Suggested revisions to policies and procedures are accepted on a continuing basis. Suggestions are reviewed by the HRPP Education Coordinator and Outreach Staff and the AVCRM or designee who is responsible for assessing the recommendation.

### **18.5 Ongoing Review of Policies**

The AVCRM or designee is responsible for ensuring review and revision of policies when there are changes in regulation, law, policy or practice that affect policies. The AVCRM or designee is also responsible for ensuring the periodic comprehensive review of all policies and procedures.

### **18.6 Record Keeping**

HRPP/IRB policies and procedures contain the initial date of approval and the date(s), if any, of revisions along with the name of the responsible office.

## **APPENDIX**

### **APPENDIX A – ADDITIONAL REQUIREMENTS**

#### **A.1 Additional Requirements for DHHS-Regulated Research**

1. When a subject decides to withdraw from a clinical trial, the investigator conducting the clinical trial should ask the subject to clarify whether the subject wishes to withdraw from all components of the trial or only from the primary interventional component of the trial. If the latter, research activities involving other components of the clinical trial, such as follow-up data collection activities, for which the subject previously gave consent may continue. The investigator should explain to the subject who wishes to withdraw the importance of obtaining follow-up safety data about the subject.
2. Investigators are allowed to retain and analyze already collected data relating to any subject who chooses to withdraw from a research study or whose participation is terminated by an investigator without regard to the subject's consent, provided such analysis falls within the scope of the analysis described in the IRB-approved protocol. This is the case even if that data includes identifiable private information about the subject.
3. For research not subject to regulation and review by FDA, investigators, in consultation with the funding agency, can choose to honor a research subject's request that the

investigator destroy the subject's data or that the investigator exclude the subject's data from any analysis.

4. When seeking the informed consent of subjects, investigators should explain whether already collected data about the subjects will be retained and analyzed even if the subjects choose to withdraw from the research.

## **A.2 Additional Requirements for FDA-Regulated Research**

### **1. Financial Disclosure Reports:**

- a. The Financial Disclosure by Clinical Investigators regulation (21 CFR part 54) requires applicants who submit a marketing application for a drug, biological product or device to submit certain information concerning the compensation to, and financial interests and arrangements of, any clinical investigator conducting clinical studies covered by the regulation.
  - i. A clinical investigator must disclose to the sponsor sufficient accurate financial information to allow the applicant to submit complete and accurate certification or disclosure statements required under 21 CFR §54.
    1. For the purposes of 21 CFR 54 a "clinical investigator" means a "listed or identified investigator or sub-investigator [on Form FDA 1572] who is directly involved in the treatment or evaluation of research subjects," including the spouse and each dependent child of the investigator or sub-investigator.
  - ii. The investigator must promptly update this information if any relevant changes occur during the course of the investigation and for 1 year following completion of the study.
  - iii. The following are financial interests, arrangements, and payments that must be disclosed (see 21 CFR § 54.4(a)(3):
    1. Any compensation made to the investigator by any sponsor of the covered clinical study in which the value of compensation could be affected by study outcome.
    2. A proprietary interest in the tested product including, but not limited to, a patent, trademark, copyright or licensing agreement.
    3. Any equity interest in any sponsor of the covered clinical study, i.e., any ownership interest, stock options, or other financial interest whose value cannot be readily determined through reference to public prices. The requirement applies to interests held during the time the clinical investigator is carrying out the study and for one year following completion of the study.
    4. Any equity interest in any sponsor of the covered study if the sponsor is a publicly held company and the interest exceeds \$50,000 in value. The requirement applies to interests held during the time the clinical investigator is carrying out the study and for one year following completion of the study.

5. Significant payments of other sorts (SPOOS) are payments that have a cumulative monetary value of \$25,000 or more and are made by any sponsor of a covered study to the investigator or the investigator's institution during the time the clinical investigator is carrying out the study and for one year following completion of the study. This would include payments that support activities of the investigator (e.g., a grant to the investigator or to the institution to fund the investigator's ongoing research or compensation in the form of equipment), exclusive of the costs of conducting the clinical study or other clinical studies, or to provide other reimbursements such as retainers for ongoing consultation or honoraria.
2. When a subject withdraws from a study:<sup>1</sup>
    - b. The data collected on the subject to the point of withdrawal remains part of the study database and may not be removed.
    - c. An investigator may ask a subject who is withdrawing whether the subject wishes to provide continued follow-up and further data collection subsequent to their withdrawal from the interventional portion of the study. Under this circumstance, the discussion with the subject would distinguish between study-related interventions and continued follow-up of associated clinical outcome information, such as medical course or laboratory results obtained through non-invasive chart review, and address the maintenance of privacy and confidentiality of the subject's information.
    - d. If a subject withdraws from the interventional portion of the study, but agrees to continued follow-up of associated clinical outcome information as described in the previous bullet, the investigator must obtain the subject's informed consent for this limited participation in the study (assuming such a situation was not described in the original informed consent form). IRB approval of informed consent documents is required.
    - e. If a subject withdraws from the interventional portion of a study and does not consent to continued follow-up of associated clinical outcome information, the investigator must not access for purposes related to the study the subject's medical record or other confidential records requiring the subject's consent.
    - f. An investigator may review study data related to the subject collected prior to the subject's withdrawal from the study, and may consult public records, such as those establishing survival status.
  3. For FDA-regulated research involving investigational drugs:
    - b. Investigators must abide by FDA restrictions on promotion of investigational drugs:<sup>2</sup>
      - i. An investigator, or any person acting on behalf of an investigator, must not represent in a promotional context that an investigational new drug is safe

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<sup>1</sup> <http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM126489.pdf>

<sup>2</sup> <http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.7>

or effective for the purposes for which it is under investigation or otherwise promote the drug.

- ii.* This provision is not intended to restrict the full exchange of scientific information concerning the drug, including dissemination of scientific findings in scientific or lay media. Rather, its intent is to restrict promotional claims of safety or effectiveness of the drug for a use for which it is under investigation and to preclude commercialization of the drug before it is approved for commercial distribution.
  - iii.* An investigator must not commercially distribute or test market an investigational new drug.
- c. Follow FDA requirements for general responsibilities of investigators<sup>3</sup>
  - i.* An investigator is responsible for ensuring that an investigation is conducted according to the signed investigator statement, the investigational plan, and applicable regulations; for protecting the rights, safety, and welfare of subjects under the investigator's care; and for the control of drugs under investigation.
  - ii.* An investigator must, in accordance with the provisions of 21 CFR §50, obtain the informed consent of each human subject to whom the drug is administered, except as provided in 21 CFR §50.23 or §50.24 of this chapter.
  - iii.* Additional specific responsibilities of clinical investigators are set forth in this part and in 21 CFR §50 and 21 CFR §56.
- d. Follow FDA requirements for control of the investigational drug<sup>4</sup>
  - i.* An investigator must administer the drug only to subjects under the investigator's personal supervision or under the supervision of a sub-investigator responsible to the investigator.
  - ii.* The investigator must not supply the investigational drug to any person not authorized under this part to receive it.
- e. Follow FDA requirements for investigator recordkeeping and record retention<sup>5</sup>
  - i.* Disposition of drug:
    - 1. An investigator is required to maintain adequate records of the disposition of the drug, including dates, quantity, and use by subjects.
    - 2. If the investigation is terminated, suspended, discontinued, or completed, the investigator must return the unused supplies of the drug to the sponsor, or otherwise provide for disposition of the unused supplies of the drug under 21 CFR §312.59.
  - ii.* Case histories.
    - 1. An investigator is required to prepare and maintain adequate and accurate case histories that record all observations and

<sup>3</sup> <http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.60>

<sup>4</sup> <http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.61>

<sup>5</sup> <http://www.accessdata.fda.gov/SCRIPTS/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.62>

other data pertinent to the investigation on each individual administered the investigational drug or employed as a control in the investigation.

2. Case histories include the case report forms and supporting data including, for example, signed and dated consent forms and medical records including, for example, progress notes of the physician, the individual's hospital charts, and the nurses' notes. The case history for each individual must document that informed consent was obtained prior to participation in the study.
- iii. Record retention: An investigator must retain required records for a period of 2 years following the date a marketing application is approved for the drug for the indication for which it is being investigated; or, if no application is to be filed or if the application is not approved for such indication, until 2 years after the investigation is discontinued and FDA is notified.
- e. Follow FDA requirements for investigator reports<sup>6</sup>
  - i. Progress reports: The investigator must furnish all reports to the sponsor of the drug who is responsible for collecting and evaluating the results obtained.
  - ii. Safety reports: An investigator must promptly report to the sponsor any adverse effect that may reasonably be regarded as caused by, or probably caused by, the drug. If the adverse effect is alarming, the investigator must report the adverse effect immediately.
  - iii. Final report: An investigator must provide the sponsor with an adequate report shortly after completion of the investigator's participation in the investigation.
  - iv. Financial disclosure reports (see above).
- f. Follow FDA requirements for assurance of IRB review<sup>7</sup>
  - i. An investigator must assure that an IRB that complies with the requirements set forth in 21 CFR §56 will be responsible for the initial and continuing review and approval of the proposed clinical study.
  - ii. The investigator must also assure that he or she will promptly report to the IRB all changes in the research activity and all unanticipated problems involving risk to human subjects or others, and that he or she will not make any changes in the research without IRB approval, except where necessary to eliminate apparent immediate hazards to human subjects.
- g. Follow FDA requirements for inspection of investigator's records and reports<sup>8</sup>
  - i. An investigator must upon request from any properly authorized officer or employee of FDA, at reasonable times, permit such officer or

<sup>6</sup> <http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.64>

<sup>7</sup> <http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.66>

<sup>8</sup> <http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.68>

ii. The investigator is not required to divulge subject names unless the records of particular individuals require a more detailed study of the cases, or unless there is reason to believe that the records do not represent actual case studies, or do not represent actual results obtained.

- i. If the investigational drug is subject to the Controlled Substances Act, the investigator must take adequate precautions, including storage of the investigational drug in a securely locked, substantially constructed cabinet, or other securely locked, substantially constructed enclosure, access to which is limited, to prevent theft or diversion of the substance into illegal channels of distribution.

i. An investigator is responsible for ensuring that an investigation is conducted according to the signed agreement, the investigational plan and applicable FDA regulations, for protecting the rights, safety, and welfare of subjects under the investigator's care, and for the control of devices under investigation. An investigator also is responsible for ensuring that informed consent is obtained in accordance with 21 CFR §50.

- i. Awaiting approval: An investigator may determine whether potential subjects would be interested in participating in an investigation, but must not request the written informed consent of any subject to participate, and must not allow any subject to participate before obtaining IRB and FDA approval.

iii. Supervising device use: An investigator must permit an investigational device to be used only with subjects under the investigator's supervision. An

v. Disposing of device: Upon completion or termination of a clinical

<sup>11</sup> <http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=812.110>

investigation or the investigator's part of an investigation, or at the sponsor's request, an investigator must return to the sponsor any remaining supply of the device or otherwise dispose of the device as the sponsor directs.

- c. Maintain the following accurate, complete, and current records relating to the investigator's participation in an investigation:<sup>12</sup>
  - i. All correspondence with another investigator, an IRB, the sponsor, a monitor, or FDA, including required reports.
  - ii. Records of receipt, use or disposition of a device that relate to:
    - 1. The type and quantity of the device, the dates of its receipt, and the batch number or code mark.
    - 2. The names of all persons who received, used, or disposed of each device.
    - 3. Why and how many units of the device have been returned to the sponsor, repaired, or otherwise disposed of.
  - iii. Records of each subject's case history and exposure to the device. Case histories include the case report forms and supporting data including, for example, signed and dated consent forms and medical records including, for example, progress notes of the physician, the individual's hospital charts, and the nurses' notes. Such records must include:
    - 1. Documents evidencing informed consent and, for any use of a device by the investigator without informed consent, any written concurrence of a licensed physician and a brief description of the circumstances justifying the failure to obtain informed consent.
    - 2. Documentation that informed consent was obtained prior to participation in the study.
    - 3. All relevant observations, including records concerning adverse device effects (whether anticipated or unanticipated), information and data on the condition of each subject upon entering, and during the course of, the investigation, including information about relevant previous medical history and the results of all diagnostic tests.
    - 4. A record of the exposure of each subject to the investigational device, including the date and time of each use, and any other therapy.
  - iv. The protocol, with documents showing the dates of and reasons for each deviation from the protocol.
  - v. Any other records that FDA requires to be maintained by regulation or by specific requirement for a category of investigations or a particular investigation.

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<sup>12</sup> <http://www.accessdata.fda.gov/SCRIPTS/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=812.140>

d. Inspections<sup>13</sup>

- i. Entry and inspection: A sponsor or an investigator who has authority to grant access must permit authorized FDA employees, at reasonable times and in a reasonable manner, to enter and inspect any establishment where devices are held (including any establishment where devices are manufactured, processed, packed, installed, used, or implanted or where records of results from use of devices are kept).
- ii. Records inspection: A sponsor, IRB, or investigator, or any other person acting on behalf of such a person with respect to an investigation, must permit authorized FDA employees, at reasonable times and in a reasonable manner, to inspect and copy all records relating to an investigation.
- iii. Records identifying subjects: An investigator must permit authorized FDA employees to inspect and copy records that identify subjects, upon notice that FDA has reason to suspect that adequate informed consent was not obtained, or that reports required to be submitted by the investigator to the sponsor or IRB have not been submitted or are incomplete, inaccurate, false, or misleading.

e. Prepare and submit the following complete, accurate, and timely reports<sup>14</sup>

- i. Unanticipated adverse device effects. An investigator must submit to the sponsor and to the reviewing IRB a report of any unanticipated adverse device effect occurring during an investigation as soon as possible, but in no event later than [5] working days (in accordance with LSUHSC-S HRPP policy) after the investigator first learns of the effect.
- ii. Withdrawal of IRB approval. An investigator must report to the sponsor, within 5 working days, a withdrawal of approval by the reviewing IRB of the investigator's part of an investigation.
- iii. Progress. An investigator must submit progress reports on the investigation to the sponsor, the monitor, and the reviewing IRB at regular intervals, but in no event less often than yearly.
- iv. Deviations from the investigational plan:
  - 1. An investigator must notify the sponsor and the reviewing IRB of any deviation from the investigational plan to protect the life or physical well-being of a subject in an emergency.
  - 2. Such notice must be given as soon as possible, but in no event later than 5 working days after the emergency occurred.
  - 3. Except in such an emergency, prior approval by the sponsor is required for changes in or deviations from a plan, and if these changes or deviations may affect the scientific soundness of the plan or the rights, safety, or welfare of human subjects, FDA and

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<sup>13</sup> <http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=812.145>

<sup>14</sup> <http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=812.150>

IRB also is required.

- v. Informed consent. If an investigator uses a device without obtaining informed consent, the investigator must report such use to the sponsor and the reviewing IRB within 5 working days after the use occurs.
- vi. Final report. An investigator must, within 3 months after termination or completion of the investigation or the investigator's part of the investigation, submit a final report to the sponsor and the reviewing IRB.
- vii. Other. An investigator must, upon request by a reviewing IRB or FDA, provide accurate, complete, and current information about any aspect of the investigation.

### **A.3 Additional Requirements for Clinical Trials (ICH-GCP)**

#### **1. Investigator's Qualifications and Agreements**

- a. The clinical trial should be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with good clinical practice and the applicable regulatory requirements.
- b. The investigator should be qualified by education, training, and experience to assume responsibility for the proper conduct of the trial, should meet all the qualifications specified by the applicable regulatory requirements, and should provide evidence of such qualifications through up-to-date curriculum vitae and/or other relevant documentation requested by the sponsor, the IRB, and/or the regulatory authorities.
- c. The investigator should be thoroughly familiar with the appropriate use of the investigational product, as described in the protocol, in the current Investigator's Brochure, in the product information and in other information sources provided by the sponsor.
- d. The investigator should be aware of, and should comply with, GCP and the applicable regulatory requirements.
- e. The investigator/institution should permit monitoring and auditing by the sponsor, and inspection by the appropriate regulatory authorities.
- f. The investigator should maintain a list of appropriately qualified persons to whom the investigator has delegated significant trial-related duties.

#### **2. Adequate Resources**

- a. The investigator should be able to demonstrate (e.g., based on retrospective data) a potential for recruiting the required number of suitable subjects within the agreed recruitment period.
- b. The investigator should have sufficient time to properly conduct and complete the trial within the agreed trial period.
- c. The investigator should have available an adequate number of qualified staff and adequate facilities for the foreseen duration of the trial to conduct the trial properly and safely.
- d. The investigator should ensure that all persons assisting with the trial are adequately informed about the protocol, the investigational product, and their trial-related duties

and functions.

### 3. Medical Care of Trial Subjects

- a.* A qualified physician (or dentist, when appropriate), who is an investigator or a sub-investigator for the trial, should be responsible for all trial-related medical (or dental) decisions.
- b.* During and following a subject's participation in a trial, the investigator/institution should ensure that adequate medical care is provided to a subject for any adverse events, including clinically significant laboratory values, related to the trial. The investigator/institution should inform a subject when medical care is needed for intercurrent illnesses of which the investigator becomes aware.
- c.* It is recommended that the investigator inform the subject's primary physician about the subject's participation in the trial if the subject has a primary physician and if the subject agrees to the primary physician being informed.
- d.* Although a subject is not obliged to give his/her reasons for withdrawing prematurely from a trial, the investigator should make a reasonable effort to ascertain the reasons, while fully respecting the subject's rights.

### 4. Communication with IRB

- a.* Before initiating a trial, the investigator/institution should have written and dated approval opinion from the IRB for the trial protocol, written informed consent form, consent form updates, subject recruitment procedures (e.g., advertisements), and any other written information to be provided to subjects.
- b.* As part of the investigator's/institution's written application to the IRB, the investigator/institution should provide the IRB with a current copy of the Investigator's Brochure. If the Investigator's Brochure is updated during the trial, the investigator/institution should supply a copy of the updated Investigator's Brochure to the IRB.
- c.* During the trial the investigator/institution should provide to the IRB all documents subject to review.

### 5. Compliance with Protocol

- a.* The investigator/institution should conduct the trial in compliance with the protocol agreed to by the sponsor and, if required, by the regulatory authorities and which was given approval opinion by the IRB. The investigator/institution and the sponsor should sign the protocol, or an alternative contract, to confirm agreement.
- b.* The investigator should not implement any deviation from, or changes of the protocol without agreement by the sponsor and prior review and documented approval opinion from the IRB of an amendment, except where necessary to eliminate an immediate hazards to trial subjects, or when the changes involves only logistical or administrative aspects of the trial (e.g., change in monitors, change of telephone numbers).
- c.* The investigator, or person designated by the investigator, should document and explain any deviation from the approved protocol.
- d.* The investigator may implement a deviation from, or a change of, the protocol to eliminate an immediate hazard to trial subjects without prior IRB approval opinion. As

soon as possible, the implemented deviation or change, the reasons for it, and, if appropriate, the proposed protocol amendments should be submitted: a) to the IRB for review and approval opinion, b) to the sponsor for agreement and, if required, c) to the regulatory authorities.

#### 6. Investigational Product

- a. Responsibility for investigational product accountability at the trial site rests with the investigator/institution.
- b. Where allowed/required, the investigator/institution may/should assign some or all of the investigator's/institution's duties for investigational product accountability at the trial site to an appropriate pharmacist or another appropriate individual who is under the supervision of the investigator/institution.
- c. The investigator/institution and/or a pharmacist or other appropriate individual, who is designated by the investigator/institution, should maintain records of the product's delivery to the trial site, the inventory at the site, the use by each subject, and the return to the sponsor or alternative disposition of unused product. These records should include dates, quantities, batch/serial numbers, expiration dates (if applicable), and the unique code numbers assigned to the investigational product and trial subjects. Investigators should maintain records that document adequately that the subjects were provided the doses specified by the protocol and reconcile all investigational product received from the sponsor.
- d. The investigational product should be stored as specified by the sponsor and in accordance with applicable regulatory requirements.
- e. The investigator should ensure that the investigational product are used only in accordance with the approved protocol.
- f. The investigator, or a person designated by the investigator/institution, should explain the correct use of the investigational product to each subject and should check, at intervals appropriate for the trial, that each subject is following the instructions properly.
- g. Randomization Procedures and Unblinding: The investigator should follow the trial's randomization procedures, if any, and should ensure that the code is broken only in accordance with the protocol. If the trial is blinded, the investigator should promptly document and explain to the sponsor any premature unblinding (e.g., accidental unblinding, unblinding due to a serious adverse event) of the investigational product.

#### 7. Informed Consent of Trial Subjects

- a. In obtaining and documenting informed consent, the investigator should comply with the applicable regulatory requirements, and should adhere to GCP and to the ethical principles that have their origin in the Declaration of Helsinki. Prior to the beginning of the trial, the investigator should have the IRB's written approval opinion of the written informed consent form and any other written information to be provided to subjects.
- b. The written informed consent form and any other written information to be provided to subjects should be revised whenever important new information becomes available that may be relevant to the subject's consent. Any revised written informed consent form, and written information should receive the IRB's approval opinion in advance of

use. The subject or the subject's legally acceptable representative should be informed in a timely manner if new information becomes available that may be relevant to the subject's willingness to continue participation in the trial. The communication of this information should be documented.

- c. Neither the investigator, nor the trial staff, should coerce or unduly influence a subject to participate or to continue to participate in a trial.
- d. None of the oral and written information concerning the trial, including the written informed consent form, should contain any language that causes the subject or the subject's legally acceptable representative to waive or to appear to waive any legal rights, or that releases or appears to release the investigator, the institution, the sponsor, or their agents from liability for negligence.
- e. The investigator, or a person designated by the investigator, should fully inform the subject or, if the subject is unable to provide informed consent, the subject's legally acceptable representative, of all pertinent aspects of the trial including the written information and the approval opinion by the IRB.
- f. The language used in the oral and written information about the trial, including the written informed consent form, should be as non-technical as practical and should be understandable to the subject or the subject's legally acceptable representative and the impartial witness, where applicable.
- g. Before informed consent may be obtained, the investigator, or a person designated by the investigator, should provide the subject or the subject's legally acceptable representative ample time and opportunity to inquire about details of the trial and to decide whether or not to participate in the trial. All questions about the trial should be answered to the satisfaction of the subject or the subject's legally acceptable representative.
- h. Prior to a subject's participation in the trial, the written informed consent form should be signed and personally dated by the subject or by the subject's legally acceptable representative, and by the person who conducted the informed consent discussion.
- i. If a subject is unable to read or if a legally acceptable representative is unable to read, an impartial witness should be present during the entire informed consent discussion. After the written informed consent form and any other written information to be provided to subjects, is read and explained to the subject or the subject's legally acceptable representative, and after the subject or the subject's legally acceptable representative has orally consented to the subject's participation in the trial and, if capable of doing so, has signed and personally dated the informed consent form, the witness should sign and personally date the consent form. By signing the consent form, the witness attests that the information in the consent form and any other written information was accurately explained to, and apparently understood by, the subject or the subject's legally acceptable representative, and that informed consent was freely given by the subject or the subject's legally acceptable representative.
- j. Both the informed consent discussion and the written informed consent form and any other written information to be provided to subjects should include explanations of the following:

- i.* That the trial involves research.
- ii.* The purpose of the trial.
- iii.* The trial treatments and the probability for random assignment to each treatment.
- iv.* The trial procedures to be followed, including all invasive procedures.
- v.* The subject's responsibilities.
- vi.* Those aspects of the trial that are experimental.
- vii.* The reasonably foreseeable risks or inconveniences to the subject and, when applicable, to an embryo, fetus, or nursing infant.
- viii.* The reasonably expected benefits. When there is no intended clinical benefit to the subject, the subject should be made aware of this.
- ix.* The alternative procedures or courses of treatment that may be available to the subject, and their important potential benefits and risks.
- x.* The compensation and/or treatment available to the subject in the event of trial related injury.
- xi.* The anticipated prorated payment, if any, to the subject for participating in the trial.
- xii.* The anticipated expenses, if any, to the subject for participating in the trial.
- xiii.* That the subject's participation in the trial is voluntary and that the subject may refuse to participate or withdraw from the trial, at any time, without penalty or loss of benefits to which the subject is otherwise entitled.
- xiv.* That the monitors, the auditors, the IRB, and the regulatory authorities will be granted direct access to the subject's original medical records for verification of clinical trial procedures and/or data, without violating the confidentiality of the subject, to the extent permitted by the applicable laws and regulations and that, by signing a written informed consent form, the subject or the subject's legally acceptable representative is authorizing such access.
- xv.* That records identifying the subject will be kept confidential and, to the extent permitted by the applicable laws and/or regulations, will not be made publicly available. If the results of the trial are published, the subject's identity will remain confidential.
- xvi.* That the subject or the subject's legally acceptable representative will be informed in a timely manner if information becomes available that may be relevant to the subject's willingness to continue participation in the trial.
- xvii.* The persons to contact for further information regarding the trial and the rights of trial subjects, and whom to contact in the event of trial-related injury.
- xviii.* The foreseeable circumstances and/or reasons under which the subject's participation in the trial may be terminated.
- xix.* The expected duration of the subject's participation in the trial.
- xx.* The approximate number of subjects involved in the trial.
- k.* Prior to participation in the trial, the subject or the subject's legally acceptable representative should receive a copy of the signed and dated written informed

consent form and any other written information provided to the subjects. During a subject's participation in the trial, the subject or the subject's legally acceptable representative should receive a copy of the signed and dated consent form updates and a copy of any amendments to the written information provided to subjects.

- l.* When a clinical trial (therapeutic or non-therapeutic) includes subjects who can only be enrolled in the trial with the consent of the subject's legally acceptable representative (e.g., minors, or patients with severe dementia), the subject should be informed about the trial to the extent compatible with the subject's understanding and, if capable, the subject should sign and personally date the written informed consent.
- m.* Except as described above, a non-therapeutic trial (i.e. a trial in which there is no anticipated direct clinical benefit to the subject), should be conducted in subjects who personally give consent and who sign and date the written informed consent form.
- n.* Non-therapeutic trials may be conducted in subjects with consent of a legally acceptable representative provided the following conditions are fulfilled: a) The objectives of the trial cannot be met by means of a trial in subjects who can give informed consent personally. b) The foreseeable risks to the subjects are low. c) The negative impact on the subject's well-being is minimized and low. d) The trial is not prohibited by law. e) The approval opinion of the IRB is expressly sought on the inclusion of such subjects, and the written approval opinion covers this aspect. Such trials, unless an exception is justified, should be conducted in patients having a disease or condition for which the investigational product is intended. Subjects in these trials should be particularly closely monitored and should be withdrawn if they appear to be unduly distressed.
- o.* In emergency situations, when prior consent of the subject is not possible, the consent of the subject's legally acceptable representative, if present, should be requested. When prior consent of the subject is not possible, and the subject's legally acceptable representative is not available, enrolment of the subject should require measures described in the protocol and/or elsewhere, with documented approval opinion by the IRB, to protect the rights, safety and well-being of the subject and to ensure compliance with applicable regulatory requirements. The subject or the subject's legally acceptable representative should be informed about the trial as soon as possible and consent to continue and other consent as appropriate should be requested.

#### 8. Records and Reports

- a.* The investigator should ensure the accuracy, completeness, legibility, and timeliness of the data reported to the sponsor in the CRFs and in all required reports.
- b.* Data reported on the CRF, that are derived from source documents, should be consistent with the source documents or the discrepancies should be explained.
- c.* Any change or correction to a CRF should be dated, initialed, and explained (if necessary) and should not obscure the original entry (i.e. an audit trail should be maintained); this applies to both written and electronic changes or corrections.

Sponsors should provide guidance to investigators and/or the investigators' designated representatives on making such corrections. Sponsors should have written procedures to assure that changes or corrections in CRFs made by sponsor's designated representatives are documented, are necessary, and are endorsed by the investigator. The investigator should retain records of the changes and corrections.

- d.* The investigator/institution should maintain the trial documents as specified in Essential Documents for the Conduct of a Clinical Trial and as required by the applicable regulatory requirements. The investigator/institution should take measures to prevent accidental or premature destruction of these documents.
- e.* Essential documents should be retained until at least 2 years after the last approval of a marketing application in an ICH region and until there are no pending or contemplated marketing applications in an ICH region or at least 2 years have elapsed since the formal discontinuation of clinical development of the investigational product. These documents should be retained for a longer period however if required by the applicable regulatory requirements or by an agreement with the sponsor. It is the responsibility of the sponsor to inform the investigator/institution as to when these documents no longer need to be retained.
- f.* The financial aspects of the trial should be documented in an agreement between the sponsor and the investigator/institution.
- g.* Upon request of the monitor, auditor, IRB, or regulatory authority, the investigator/institution should make available for direct access all requested trial-related records.

#### 9. Progress Reports

- a.* The investigator should submit written summaries of the trial status to the IRB annually, or more frequently, if requested by the IRB.
- b.* The investigator should promptly provide written reports to the sponsor, the IRB and, where applicable, the institution on any changes significantly affecting the conduct of the trial, and/or increasing the risk to subjects.

#### 10. Safety Reporting

- a.* All serious adverse events (SAEs) should be reported immediately to the sponsor except for those SAEs that the protocol or other document (e.g., Investigator's Brochure) identifies as not needing immediate reporting. The immediate reports should be followed promptly by detailed, written reports. The immediate and follow-up reports should identify subjects by unique code numbers assigned to the trial subjects rather than by the subjects' names, personal identification numbers, and/or addresses. The investigator should also comply with the applicable regulatory requirements related to the reporting of unexpected serious adverse drug reactions to the regulatory authorities and the IRB.
- b.* Adverse events and/or laboratory abnormalities identified in the protocol as critical to safety evaluations should be reported to the sponsor according to the reporting requirements and within the time periods specified by the sponsor in the protocol.
- c.* For reported deaths, the investigator should supply the sponsor and the IRB with any additional requested information (e.g., autopsy reports and terminal medical

reports).

- d. **Premature Termination or Suspension of a Trial** If the trial is prematurely terminated or suspended for any reason, the investigator/institution should promptly inform the trial subjects, should assure appropriate therapy and follow-up for the subjects, and, where required by the applicable regulatory requirements, should inform the regulatory authorities. In addition:
  - i. If the investigator terminates or suspends a trial without prior agreement of the sponsor, the investigator should inform the institution where applicable, and the investigator/institution should promptly inform the sponsor and the IRB, and should provide the sponsor and the IRB a detailed written explanation of the termination or suspension.
  - ii. If the sponsor terminates or suspends a trial, the investigator should promptly inform the institution where applicable and the investigator/institution should promptly inform the IRB and provide the IRB a detailed written explanation of the termination or suspension.
  - iii. If the IRB terminates or suspends its approval opinion of a trial, the investigator should inform the institution where applicable and the investigator/institution should promptly notify the sponsor and provide the sponsor with a detailed written explanation of the termination or suspension.
11. **Final Reports by Investigator:** Upon completion of the trial, the investigator, where applicable, should inform the institution; the investigator/institution should provide the IRB with a summary of the trial's outcome, and the regulatory authorities with any reports required.

#### **A.4 Additional Requirements for Department of Defense (DOD) Research**

1. When appropriate, research protocols must be reviewed and approved by the IRB prior to the Department of Defense approval. Consult with the Department of Defense funding component to see whether this is a requirement.
2. Employees of the Department of Defense (including temporary, part-time, and intermittent appointments) may not be able to legally accept payments to participate in research and should check with their supervisor before accepting such payments. Employees of the Department of Defense cannot be paid for conducting research while on active duty.
3. Service members must follow their command policies regarding the requirement to obtain command permission to participate in research involving human subjects while on-duty or off-duty.
4. Components of the Department of Defense might have stricter requirements for research-related injury than the DHHS regulations.
5. There may be specific educational requirements or certification required.

6. When assessing whether to support or collaborate with this institution for research involving human subjects, the Department of Defense may evaluate this institution's education and training policies to ensure the personnel are qualified to perform the research.
7. When research involves U.S. military personnel, policies and procedures require limitations on dual compensation:
  - a. Prohibit an individual from receiving pay of compensation for research during duty hours.
  - b. An individual may be compensated for research if the participant is involved in the research when not on duty.
  - c. Federal employees while on duty and non-Federal persons may be compensated for blood draws for research up to \$50 for each blood draw.
  - d. Non-Federal persons may be compensated for research participating other than blood draws in a reasonable amount as approved by the IRB according to local prevailing rates and the nature of the research.
8. Other specific requirements of the Department of Defense research be found in the Additional Requirements for Department of Defense (DOD) Research section in the IRB's Worksheet: Additional Federal Criteria (HRP-318).
9. When following Department of Defense (DoD) regulations, the following shall be reported promptly (no greater than 30 days) to the DoD human research protection officer:
  - a. When significant changes to the research protocol are approved by the IRB.
  - b. The results of the IRB continuing review.
  - c. Changes of reviewing IRB.
  - d. When the organization is notified by any federal department, agency or national organization that any part of the HRPP is under investigation for cause involving a DoD supported research protocol.

#### **A.5 Additional Requirements for Department of Energy (DOE) Research**

1. Research that involves one or more of the following is considered by DOE to be human subjects research and requires IRB review:
  - a. Intentional modification of the human environment
  - b. Study of human environments that use tracer chemicals, particles or other materials to characterize airflow.
  - c. Study in occupied homes or offices that:
    - i. Manipulate the environment to achieve research aims.
    - ii. Test new materials.
    - iii. Involve collecting information on occupants' views of appliances, materials, or devices installed in their homes or their energy-saving behaviors through surveys and focus groups.
2. You must complete and submit to the IRB the DOE "Checklist for IRBs to Use in Verifying

that HS Research Protocols are In Compliance with DOE Requirements” ([http://human.subjects.energy.gov/other-resources/documents/IRB-template-for-reviewing-PII-protocols-2010\\_ac.pdf](http://human.subjects.energy.gov/other-resources/documents/IRB-template-for-reviewing-PII-protocols-2010_ac.pdf)) if your research includes Personally Identifiable Information. Please indicate with each item in the checklist where this is addressed within the protocol you have submitted to the IRB for review.

3. You must report the following within ten business days to the Department of Energy human subjects research program manager:
  - a. Any significant adverse events, unanticipated risks; and complaints about the research, with a description of any corrective actions taken or to be taken
  - b. Any suspension or termination of IRB approval of research
  - c. Any significant non-compliance with HRPP procedures or other requirements.
4. You must report the following within three business days to the Department of Energy human subject research program manager.
  - a. Any compromise of personally identifiable information must be reported immediately.
5. Research involving human participants also includes studies of the intentional modification of the human environment; generalizable includes the study of tracer chemical, particles or other materials to characterize airflow.
6. Generalizable also includes studies in occupied home or offices that:
  - a. Manipulate the environment to achieve research aim;
  - b. Test new materials;
  - c. Involve collecting information on occupants’ views of appliances, materials; or
  - d. Devices installed in their homes or their energy-saving behaviors through surveys and focus groups. Generalizable should be viewed in terms of the contribution to knowledge with the specific field of study.
7. Other specific requirements of the Department of Energy (DOE) research can be found in the Additional Requirements for Department of Energy (DOE) Research section in the IRB’s Worksheet: Additional Federal Criteria (HRP-318).

## **A.6 Additional Requirements for Department of Justice (DOJ) Research**

### **A.6.1 Additional Requirements for DOJ Research Conducted in the Federal Bureau of Prisons**

1. Implementation of Bureau programmatic or operational initiatives made through pilot projects is not considered to be research.
2. The project must not involve medical experimentation, cosmetic research, or pharmaceutical testing.
3. The research design must be compatible with both the operation of prison facilities and protection of human subjects.
4. Investigators must observe the rules of the institution or office in which the research is conducted.
5. Any investigator who is a non-employee of the Bureau of Prisoners must sign a statement in which the investigator agrees to adhere to the requirements of 28 CFR §512.

6. The research must be reviewed and approved by the Bureau Research Review Board.
7. Incentives cannot be offered to help persuade inmate subjects to participate. However, soft drinks and snacks to be consumed at the test setting may be offered. Reasonable accommodations such as nominal monetary recompense for time and effort may be offered to non-confined research subjects who are both: No longer in Bureau of Prisons custody. Participating in authorized research being conducted by Bureau employees or contractors.
8. A non-employee of the Bureau may receive records in a form not individually identifiable when advance adequate written assurance that the record will be used solely as a statistical research or reporting record is provided to the agency.
9. Except as noted in the consent statement to the subject, you must not provide research information that identifies a subject to any person without that subject's prior written consent to release the information. For example, research information identifiable to a particular individual cannot be admitted as evidence or used for any purpose in any action, suit, or other judicial, administrative, or legislative proceeding without the written consent of the individual to whom the data pertain.
10. Except for computerized data records maintained at an official Department of Justice site, records that contain non-disclosable information directly traceable to a specific person may not be stored in, or introduced into, an electronic retrieval system.
11. If you are conducting a study of special interest to the Office of Research and Evaluation but the study is not a joint project involving Office of Research and Evaluation, you may be asked to provide Office of Research and Evaluation with the computerized research data, not identifiable to individual subjects, accompanied by detailed documentation. These arrangements must be negotiated prior to the beginning of the data collection phase of the project.
12. Required elements of disclosure additionally include:
  - a. Identification of the investigators.
  - b. Anticipated uses of the results of the research.
  - c. A statement that participation is completely voluntary and that the subject may withdraw consent and end participation in the project at any time without penalty or prejudice (the inmate will be returned to regular assignment or activity by staff as soon as practicable).
  - d. A statement regarding the confidentiality of the research information and exceptions to any guarantees of confidentiality required by federal or state law. For example, an investigator may not guarantee confidentiality when the subject indicates intent to commit future criminal conduct or harm himself or herself or someone else, or, if the subject is an inmate, indicates intent to leave the facility without authorization.
  - e. A statement that participation in the research project will have no effect on the inmate subject's release date or parole eligibility.
13. You must have academic preparation or experience in the area of study of the proposed research.
14. The IRB application must include a summary statement, which includes:

- a.* Names and current affiliations of the investigators.
  - b.* Title of the study.
  - c.* Purpose of the study.
  - d.* Location of the study.
  - e.* Methods to be employed.
  - f.* Anticipated results.
  - g.* Duration of the study.
  - h.* Number of subjects (staff or inmates) required and amount of time required from each.
  - i.* Indication of risk or discomfort involved as a result of participation.
15. The IRB application must include a comprehensive statement, which includes:
- a.* Review of related literature.
  - b.* Detailed description of the research method.
  - c.* Significance of anticipated results and their contribution to the advancement of knowledge.
  - d.* Specific resources required from the Bureau of Prisons.
  - e.* Description of all possible risks, discomforts, and benefits to individual subjects or a class of subjects, and a discussion of the likelihood that the risks and discomforts will actually occur.
  - f.* Description of steps taken to minimize any risks.
  - g.* Description of physical or administrative procedures to be followed to: Ensure the security of any individually identifiable data that are being collected for the study.
  - h.* Destroy research records or remove individual identifiers from those records when the research has been completed.
  - i.* Description of any anticipated effects of the research study on Institutional programs and operations.
  - j.* Relevant research materials such as vitae, endorsements, sample consent statements, questionnaires, and interview schedules.
16. The IRB application must include a statement regarding assurances and certification required by federal regulations, if applicable.
17. You must assume responsibility for actions of any person engaged to participate in the research project as an associate, assistant, or subcontractor.
18. At least once a year, you must provide the Chief, Office of Research and Evaluation, with a report on the progress of the research.
19. At least 12 working days before any report of findings is to be released, you must distribute one copy of the report to each of the following: the chairperson of the Bureau Research Review Board, the regional director, and the warden of each institution that provided data or assistance.
20. You must include an abstract in the report of findings.
21. In any publication of results, you must acknowledge the Bureau's participation in the research project.
22. You must expressly disclaim approval or endorsement of the published material as an expression of the policies or views of the Bureau.

23. Prior to submitting for publication the results of a research project conducted under this subpart, You must provide two copies of the material, for informational purposes only, to the Chief, Office of Research and Evaluation, Central Office, Bureau of Prisons.
24. Other specific requirements of the Department of Justice (DOJ) Research Conducted within the Federal Bureau of Prisons (BOP) can be found in the Additional Requirements for Department of Justice (DOJ) Research Conducted within the Federal Bureau of Prisons (BOP) section in the IRB's Worksheet: Additional Federal Criteria (HRP-318).

#### **A.6.2 Additional Requirements for DOJ Research Funded by the National Institute of Justice**

1. The project must have a privacy certificate approved by the National Institute of Justice Human Subjects Protection Officer.
2. All investigators and research staff are required to sign employee confidentiality statements, which are maintained by the responsible investigator.
3. The confidentiality statement on the consent document must state that confidentiality can only be broken if the subject reports immediate harm to subjects or others.
4. Under a privacy certificate, investigators and research staff do not have to report child abuse unless the subject signs another consent document to allow child abuse reporting.
5. A copy of all data must be de-identified and sent to the National Archive of Criminal Justice Data, including copies of the informed consent document, data collection instruments, surveys, or other relevant research materials.
6. Other specific requirements of the Department of Justice (DOJ) Research Funded by the National Institute of Justice can be found in the Additional Requirements for Department of Justice (DOJ) Research section in the IRB's Worksheet: Additional Federal Criteria (HRP-318).

#### **A.7 Additional Requirements for Department of Education (ED) Research**

1. Each school at which the research is conducted must provide an assurance that they comply with the Family Educational Rights and Privacy Act (FERPA) and the Protection of Pupil Rights Amendment (PPRA).
2. Provide a copy of all surveys and instructional material used in the research. Upon request parents of children<sup>15</sup> involved in the research<sup>16</sup> must be able to inspect these materials.
3. The school in which the research is being conducted must have policies regarding the administration of physical examinations or screenings that the school may administer to

<sup>15</sup> Children are persons enrolled in research not above the elementary or secondary education level, who have not reached the age or majority as determined under state law.

<sup>16</sup> Research or experimentation program or project means any program or project in any research that is designed to explore or develop new or unproven teaching methods or techniques.

students.

4. Other specific requirements of the Department of Education (ED) Research can be found in the Additional Requirements for Department of Education (ED) Research section in the IRB's Worksheet: Additional Federal Criteria (HRP-318).

#### **A.8 Additional Requirements for Environmental Protection Agency (EPA) Research**

1. Research conducted, supported, or intended to be submitted to EPA is subject to Environmental Protection Agency Regulations.
2. Intentional exposure of pregnant women or children to any substance is prohibited.
3. Observational research involving pregnant women and fetuses are subject to additional DHHS requirements for research involving pregnant women (45 CFR §46 Subpart B) and additional DHHS requirements for research involving children (45 CFR §46 Subpart D.)
4. Research involving children must meet category #1 or #2.
5. Other specific requirements of the Environmental Protection Agency (EPA) Research can be found in the Additional Requirements for Environmental Protection Agency (EPA) Research and Research Intended to be Submitted to the Environmental Protection Agency section in the IRB's Worksheet: Additional Federal Criteria (HRP-318).

#### **A.9 Additional Requirements for Veterans Administration (VA) Research**

- The investigator must follow this Institution's procedures to ensure reporting in writing to the IRB within 5 business days of becoming aware of unanticipated problems involving risks to subjects or others, apparent serious or continuing non-compliance, suspension of IRB approval, termination of IRB approval, and local (i.e., occurring in the reporting individual's own VA facility) unanticipated serious adverse events in writing to the IRB within five business days of becoming aware. This requirement is in addition to other applicable reporting requirements (e.g., reporting to the sponsor under FDA requirements.) The unfounded classification of a serious adverse event as anticipated constitutes serious non-compliance.
- The investigator must give first priority to the protection of research subjects, uphold professional and ethical standards and practices, and adhere to all applicable VA and other federal requirements, including the local VA facility's policies and procedures, regarding the conduct of research and the protection of human subjects. The investigator must hold a current VA appointment to conduct VA research.
- The responsibilities of the investigator may be defined in the protocol or IRB application. Specifically, the principle investigator's and local site investigator's responsibilities include, but are not limited to
  - Qualifications to Conduct Human Subjects Research. VA investigators must have the appropriate training, education, expertise, and credentials to conduct the

research according to the research protocol.

- o PIs must ensure that all research staff are qualified (e.g., including but not limited to appropriate training, education, expertise, and credentials) to perform procedures assigned to them during the course of the study.
- o Investigators and their staff conducting human subjects research must be credentialed and privileged as required by current local and VA requirements (see VHA Handbook 1100.19 and VHA Directive 2012-030, Credentialing of Health Care Professionals, or successor policy). Investigators and their research staff may only perform those activities in a research study for which they have the relevant credentials and privileges.
- o Investigators and co-investigators must be identified on the IRB application and must provide credentials, conflict of interest statements or other documentation required by VA and local facility policies.
- o All individuals involved in conducting VA human subjects research are required to complete training in ethical principles on which human subjects research is to be conducted. Specific requirements regarding the type and frequency of training are found on ORD's Web site at: <https://www.research.va.gov/pride/training/>. All other applicable VA and VHA training requirements at the local and national level must be met (e.g., privacy and information security training).
- o Research Protocol. The investigator must develop and submit a research protocol that is scientifically valid, describes the research objectives, background and methodology, provides for fair and equitable recruitment and selection of subjects, minimizes risks to subjects and others, and describes a data and safety monitoring plan consistent with the nature of the study. The research must be relevant to the health or welfare of the Veteran population. When relevant, the protocol must include the following safety measures:
  - o The type of safety information to be collected including AEs
  - o Frequency of safety data collection
  - o Frequency or periodicity of review of cumulative safety data
  - o Statistical tests for analyzing the safety data to determine if harm is occurring
  - o Conditions that trigger an immediate suspension of the research, if applicable.
- o Approvals. The investigator must submit the protocol for initial review and obtain written approvals from the IRB, other applicable committees, and from the R&D Committee. In addition, the investigator must receive written notice from the ACOS/R&D that the research may commence before initiating the research.
  - o Once approved by the IRB, the protocol must be implemented as approved. All modifications to the approved research protocol or consent form must be approved by the IRB prior to initiating the changes except when necessary to eliminate apparent immediate hazards to the subject.
- o The investigator must also obtain continuing review and approval at a frequency established by the IRB, but not less than once every year and is expected to submit all materials required for continuing review in sufficient

time to assure approval prior to the expiration date. No research activities may be conducted at any time without a currently valid IRB approval.

- o Conflict Of Interest. The investigator must disclose to the IRB any potential, actual, apparent, or perceived conflict of interest of a financial, professional, or personal nature that may affect any aspect of the research, and comply with all applicable VA and other federal requirements regarding conflict of interest.
- o Initial Contact. During the recruitment process, members of the research team must make initial contact with potential subjects in person or by letter prior to initiating any telephone contact, unless there is written documentation that the subject is willing to be contacted by telephone about the study in question or a specific kind of research as outlined in the study. (This does not apply to situations where a Veteran calls in response to an advertisement. If a research repository from a previous study is used to identify subjects, there must be an IRB approved HIPAA waiver for this activity in the new protocol.)
  - o Any initial contact by letter or telephone must provide a telephone number or other means that the potential subject can use to verify that the study constitutes VA research.
  - o If a contractor makes the initial contact by letter, the VA investigator must sign the letter.
- o Informed Consent for Research. The investigator must obtain and document legally effective informed consent of the subject or the subject's LAR prospectively (i.e., no screening or other interaction or intervention involving a human subject can occur until after the IRB-approved informed consent requirements have been met) that is in alignment with ethical principles that govern informed consent for research. The only exceptions are if the IRB determines the research is exempt, or approves a waiver of the informed consent process, or approves a waiver of the signed informed consent document.
  - o If the investigator does not personally obtain informed consent, the investigator must delegate this responsibility in writing (e.g., by use of a delegation letter) to research staff sufficiently knowledgeable about the protocol and related concerns to answer questions from prospective subjects, and about the ethical basis of the informed consent process and protocol.
  - o If the investigator contracts with a firm, e.g., a survey research firm, to obtain consent from subjects, collect private individually identifiable information from human subjects, or are involved in activities that would institutionally engage the firm in human subjects research, the firm must have its own IRB oversight of the activity. In addition, the PO must determine that there is appropriate authority to allow the disclosure of individual names and other information to the contracted firm.
  - o The investigator must ensure that all original signed and dated informed consent documents are maintained in the investigator's research files, readily retrievable, and secure.
- o HIPAA Authorization. The investigator or designee must obtain HIPAA authorization

for the use and disclosure of the subject's PHI, or obtain an IRB-approved waiver of HIPAA authorization unless there is a limited data set and appropriate DUA.

- o Reporting. The investigator is responsible for reporting unanticipated problems involving risks to subjects or others, serious unanticipated problems involving risks to subjects or others, local unanticipated serious adverse events, apparent serious or continuing noncompliance, any termination or suspension of research; and privacy or information security incidents related to VA research, including: any inappropriate access, loss, or theft of PHI; noncompliant storage, transmission, removal, or destruction of PHI; or theft, loss, or noncompliant destruction of equipment containing PHI, in accordance with local facility or IRB SOPs and VHA Handbook 1058.01.
- o Research Records. All written information given to subjects must be in the investigator's research file along with the consent form(s). The investigator's research records should be disposed in accordance with VHA RCS 10-1. If the investigator leaves VA, all research records must be retained by the VA facility where the research was conducted.
- o VHA Health Record. A VHA health record must be created or updated, and a progress note created, for all research subjects (Veterans or Non-Veterans) who are admitted to VA medical facilities as in-patients, treated as outpatients at VA medical facilities, or when research procedures or interventions are used in or may impact the medical care of the research subject at a VA medical facility or at facilities contracted by VA to provide services to Veterans (e.g., Community-Based Outpatient Clinics or nursing homes) (see VHA Handbook 1907.01). Informed consent documents are not required to be in the health record.
- o Investigational Drugs and Devices. The investigator must conduct VA human subjects research involving investigational drugs and devices in accordance with all applicable VA policies and other federal requirements including, but not limited to: VHA Handbook 1200.05, VHA Handbook 1108.04, and applicable FDA regulations. The storage and security procedures for test articles used in research must be reviewed and approved by the IRB and follow all applicable federal rules.
- o The PI or Local Site Investigator (LSI) must provide the Pharmacy Service with the following:
  - o Written approval letter signed by the ACOS for R&D that all relevant approvals have been obtained and that the study may be initiated at the site (VHA Handbook 1200.01)
  - o An IRB approval letter
  - o A copy of the approved study protocol
  - o A copy of VA Form 10-9012, when appropriate
  - o An IB, when appropriate
  - o Any sponsor-provided documents relating to the storage, preparation, dispensing, and accountability of the investigation products
  - o Protocol revisions, amendments, and updates after IRB approval and after the IRB approved the amendment

- o Updates and changes to authorized prescribers after IRB approval;
- o Documentation of IRB continuing review approval
- o Notice if clinical investigation is suspended or terminated by the IRB, R&D Committee, FDA, or other oversight group (e.g., ORO or the study sponsor)
- o Notice of when the study is closed.
- o The PI or LSI must provide Pharmacy Service and/or the Research Service Investigational Pharmacy, investigational drug information on each patient receiving an investigational drug through the electronic medical record or other locally-approved means. This documentation is to include allergies, toxicities, or adverse drug events related to the investigational drug, or the potential for interaction with other drugs, foods, or dietary supplements (herbals, nutraceuticals).
- o The PI or LSI must place the completed VA Form 10-9012, or electronic equivalent, in the subject's medical record.
- o Initiation of Research Projects. IRB approval is for a specified time period based on the degree of risk of the study, not to exceed 1 year. The IRB determines the expiration date based upon its date of review and communicates that date to the investigator in the written approval letter. The investigator must not initiate the IRB approved research protocol until all applicable requirements in VHA Handbook 1200.01 have also been met including obtaining R&D Committee approval.
- o Expiration of IRB Approval. There is no provision for any grace period to extend the conduct of research beyond the expiration date of IRB approval. Therefore, continuing review and re-approval of research must occur on or before the date when IRB approval expires. If approval expires, the investigator must:
  - o Stop all research activities including, but not limited to, enrollment of new subjects, analyses of individually identifiable data, and research interventions or interactions with currently participating subjects, except where stopping such interventions or interactions could be harmful to those subjects; and
  - o Immediately submit to the IRB Chair a list of research subjects who could be harmed by stopping specified study interventions or interactions. The IRB Chair must determine within 2 business days whether or not such interventions or interactions may continue.
- o Documentation of Informed Consent
  - o When documentation of informed consent is not waived by IRB, the investigator or designee must ensure that the informed consent document is signed and dated by:
    - The subject or the subject's legally authorized representative
      - o The person obtaining the informed consent (unless the signature is waived by the IRB)
  - o If consent is obtained electronically, the following must be met:
    - Authentication controls on electronic consent provide reasonable assurance that such consent is rendered by the proper individual
    - The subject dates the consent as is typical or that the software provides the

current date when signed

- Other specific requirements of Veterans Administration (VA) research be found in the “Additional Requirements for Veterans Administration (VA) Research” section in the IRB’s “WORKSHEET: Additional Federal Criteria (HRP-318).”
- Vulnerable Subjects
  - The following populations are considered categorically vulnerable and have specific VA requirements for their inclusion in research:
    - Fetuses. Research in which the focus is either a fetus, or human fetal tissue, in-utero or ex-utero (or uses human fetal tissue), must not be conducted by VA investigators while on official duty, or at VA facilities, or at VA approved off-site facilities.
    - Neonates. Interventional research enrolling neonates cannot be conducted by VA investigators while on official duty, or at VA facilities, or at VA approved off-site facilities. Prospective observational and retrospective record review studies that involve neonates or neonatal outcomes are permitted.
    - Pregnant Women. The VA medical facility Director must certify that the medical facility has sufficient expertise in women’s health to conduct the proposed research.
    - Prisoners
    - Children
    - Subjects who Lack Decision-making Capacity.
- Research Involving Prisoners
  - Research involving prisoners cannot be conducted by VA investigators while on official VA duty, at VA facilities, or at VA-approved off-site facilities unless a waiver has been granted by the CRADO.
  - If such a waiver is granted, the research must comply with the requirements of 45 CFR 46.301 - 46.306.
- Research Involving Children
  - Research involving children must not be greater than minimal risk.
  - The VA medical facility Director must approve participation in the proposed research that includes children.
  - Research involving biological specimens or data obtained from children is considered to be research involving children even if de-identified. If the biological specimens or data were previously collected, they must have been collected under applicable policies and ethical guidelines.
  - The IRB must have the appropriate expertise to evaluate VA research involving children and must comply with the requirements of 45 CFR 46.401 - 46.404 and 46.408.
- Research Involving Persons Who Lack Decision-Making Capacity
  - The protocol must include a plan, that it is appropriate given the population and setting of the research, for how investigators will determine when a legally authorized representative will be required to provide informed consent. In general, the research staff must perform or obtain and document a clinical assessment of

decision-making capacity for any subject suspected of lacking decision-making capacity.

- o When the potential subject is determined to lack decision-making capacity, investigators must obtain consent from the LAR of the subject (i.e., surrogate consent). NOTE: Investigators and IRBs have a responsibility to consult with the Office of General Counsel (OGC) regarding state or local requirements for surrogate consent for research that may supersede VA requirements.
- o The following persons are authorized to consent on behalf of persons who lack decision-making capacity in the following order of priority:
  - o (1) Health care agent (i.e., an individual named by the subject in a Durable Power of Attorney for Health Care)
  - o (2) Legal guardian or special guardian
  - o (3) Next of kin: a close relative of the patient 18 years of age or older, in the following priority: spouse, child, parent, sibling, grandparent, or grandchild; or
  - o (4) Close friend.
- o If feasible, the investigator must explain the proposed research to the prospective research subject even when the legally authorized representative gives consent. Although unable to provide informed consent, some persons may resist participating in a research protocol approved by their representatives. Under no circumstances may a subject be forced or coerced to participate in a research study even if the LAR has provided consent.
- o Legally authorized representatives must be told that their obligation is to try to determine what the subjects would do if able to make an informed decision. If the potential subjects' wishes cannot be determined, the legally authorized representatives must be told they are responsible for determining what is in the subjects' best interest.
- Research Involving Certificates of Confidentiality
  - o For studies that do not involve a medical intervention (e.g., observational studies, including interview and questionnaire studies), no annotation may be made in the health record.
  - o For studies that involve a medical intervention, a progress note entry should indicate that an individual has been enrolled in a research study, any details that would affect the subject's clinical care, and the name and contact information for the investigator conducting the study. Subjects' informed consent forms and HIPAA authorization documents are not to be included in the health record.
  - o Investigators should work with the research office in their facility to assure that when Veterans are enrolled in a study protected by a Certificate of Confidentiality, they are not simultaneously enrolled in other interventional studies unless it is absolutely clear that this enrollment does not raise safety issues.
- Collaborative Research
  - o This addresses collaborations between VA and non-VA investigators. Collaboration is encouraged when VA investigators have a substantive role in the design, conduct, and/or analysis of the research. VA may also serve as a Coordinating

Center for collaborative studies. NOTE: Collaborative studies do not include studies conducted under a CRADA with pharmaceutical companies or other for-profit entities.

- o IRB of Record Approval. Each institution is responsible for safeguarding the rights and welfare of human subjects and providing oversight of the research activities conducted at that institution.
  - o Each collaborating institution engaged in human subjects research must obtain approval from its IRB of Record and hold a FWA or another assurance acceptable to VA, e.g. DoD assurance.
  - o VA investigators must submit a protocol or other documentation to their VA IRB of Record that delineates which research activities will be conducted by VA.
  - o Each institution engaged in the collaborative research must use the informed consent document and HIPAA authorization required by their respective institutional policies for subjects recruited from that institution, or procedures requiring participation of the subject at that institution. The informed consent document may contain information on the project as a whole as long as the document clearly describes which procedures will be performed at VA and which will be performed at other institutions.
    - The VA informed consent document must clearly state when procedures mentioned at other institutions are part of the VA's portion of the study.
    - The informed consent document and HIPAA authorization must be consistent and include information describing the following:
      - PHI to be collected and/or used by the VA research team
      - PHI to be disclosed to the other institutions
      - Purpose for which the PHI may be used
- o Waivers. PHI obtained in research for which the IRB of Record has waived the requirements to obtain a HIPAA authorization and a signed informed consent document may not be disclosed outside VA unless the VA facility Privacy Officer ensures and documents VA's authority to disclose the PHI to another institution. A waiver of HIPAA authorization is not sufficient to fulfill the requirements of other applicable privacy regulations such as the Privacy Act of 1974 (5 U.S.C. 552a).
- o Research Data. The protocol, addendum, and/or IRB of Record application must describe the data to be disclosed to collaborators, the entity(ies) to which the data are to be disclosed, and how the data are to be transmitted. This includes data from individual subjects as well as other data developed during the research such as the analytic data and the aggregate data.
  - o Each VA facility must retain a complete record of all data obtained during the VA portion of the research in accordance with privacy requirements, the Federal Records Act, and VHA Records Control Schedule (RCS) 10-1.
  - o All disclosures and data transmission must meet privacy and security requirements per VA Directive 6500, VHA Handbook 6500, and VHA Handbook 1605.1.
- o Written agreements. Collaborative research involving non-VA institutions may

not be undertaken without a signed written agreement (e.g., a CRADA or a Data Use Agreement (DUA)) that addresses such issues as the responsibilities of each party, the ownership of the data and the reuse of the data for other research. Any reuse must be consistent with the protocol, the informed consent document, and the HIPAA authorization.

- Photography, Video and/or Audio Recording for Research Purposes
  - The informed consent for research must include information describing any photographs, video, and/or audio recordings to be taken or obtained for research purposes, how the photographs, video, and/or audio will be used for the research, and whether the photographs, video, and/or audio will be disclosed outside the VA.
    - An informed consent to take a photograph, video, and/or audio recording cannot be waived by the IRB.
    - The consent for research does not give legal authority to disclose the photographs, video, and/or audio recordings outside VA. A HIPAA authorization is needed to make such disclosures.
- International Research:
  - VA international research is defined as any VA-approved research conducted at international sites (i.e., not within the United States (U.S.), its territories, or Commonwealths), any VA-approved research using either identifiable or de-identified human biological specimens or identifiable or de-identified human data originating from international sites, or any VA-approved research that entails sending such specimens or data out of the U.S. This definition applies regardless of the funding source (funded or unfunded) and to research conducted through any mechanism of support including MOUs, CRADAs, grants, contracts, or other agreements. NOTE: Research conducted at U.S. military bases, ships, or embassies is not considered international research.
    - Sending specimens or data to individuals with VA appointments at international sites (e.g., a WOC appointment, a VA investigator on sabbatical at an international site) is considered international research. Remote use of data that is maintained on VA computers within the U.S. or Puerto Rico and accessed via a secure connection is not considered international research.
    - International research includes multi-site trials involving non-U.S. sites where VA is the study sponsor, a VA investigator is the overall study-wide PI, VA holds the Investigational New Drug (IND), or the VA manages the data collection and the data analyses.
    - International research does not include studies in which VA is only one of multiple participating sites where the overall study-wide PI is not a VA investigator (i.e., the PI for the study as a whole is not a VA investigator).
  - Before approving international research involving human subjects research, the IRB must ensure that human subjects outside of the U.S. who participate in research projects in which VA is a collaborator receive equivalent protections as research participants inside the U.S. (see OHRP guidance at

<http://www.hhs.gov/ohrp/international/index.html>). NOTE: The VA medical facility Director must approve participation in the proposed international research.

- o All international research must also be approved explicitly in a document signed by the VA medical facility Director, except for Cooperative Studies Program activities which must be approved by the CRADO.
- Use Preparatory To Research:
  - o VA investigators may use individually-identifiable health information to prepare a research protocol prior to submission of the protocol to the IRB for approval without obtaining a HIPAA authorization or waiver of authorization.
  - o VA investigators must not arbitrarily review PHI based on their employee access to PHI until the investigator documents the following required information as Preparatory to Research in a designated file that is readily accessible for those required to audit such information (e.g., Health Information Manager or PO):
    - Access to PHI is only to prepare a protocol
    - No PHI will be removed from the covered entity (i.e., VHA)
    - Access to PHI is necessary for preparation of the research protocol.
  - o Non-VA researchers may not obtain VA information for preparatory to research activities without appropriate VA approvals (see VHA Handbook 1605.1).
  - o During the preparatory to research activities the VA investigator:
    - Must only record aggregate data. The aggregate data may only be used for background information to justify the research or to show that there are adequate numbers of potential subjects to allow the investigator to meet enrollment requirements for the research study
    - Must not record any individually identifiable health information
    - Must not use any individually identifiable information to recruit research subjects.
    - Preparatory activities can include reviewing database output (computer file or printout) containing identifiable health information generated by the database owner, if the investigator returns the database output to the database owner when finished aggregating the information.
  - o Contacting potential research subjects and conducting pilot or feasibility studies are not considered activities preparatory to research.
  - o Activities preparatory to research only encompass the time to prepare the protocol and ends when the protocol is submitted to the IRB.
- Participation of Non-Veterans As Research Subjects
  - o Non-Veterans may be entered into a VA-approved research study that involves VA outpatient or VA hospital treatment (38 CFR 17.45, 17.92), but only when there are insufficient Veteran patients suitable for the study. The investigator must justify including non-Veterans and the IRB must review the justification and provide specific approval for recruitment of non-Veterans.
  - o Outpatient Care for Research Purposes. Any person who is a bona fide volunteer may be furnished outpatient treatment when the treatment to be

rendered is part of an approved VA research study and there are insufficient Veteran patients suitable for the study (38 CFR §17.92).

- o Hospital Care for Research Purposes. Any person who is a bona fide volunteer may be admitted to a VA hospital when the treatment to be rendered is part of an approved VA research study and there are insufficient Veteran patients suitable for the study (38 CFR §17.45).
- o Non-Veterans may be recruited for studies that will generally benefit Veterans and their well-being but would not include Veterans as subjects. Examples include surveys of VA providers, studies involving Veterans' family members, or studies including active duty military personnel. Although active duty military personnel are not considered Veterans, they should be included in VA studies whenever appropriate.
- o In addition to the non-Veterans referenced above, active duty military personnel may be entered into VA research conducted jointly by VA and DoD or within DoD facilities.
- o All VA regulations and policies related to Veterans as research subjects apply to non-Veterans entered into VA research.
- o Non-Veterans may not be entered into VA studies simply because a non-Veteran population is easily accessible to the investigator.
- o Investigators must follow VHA Handbook 1605.04, Notice of Privacy Practices, to provide notice of privacy practices and acknowledgement for any non-Veteran enrolled in the approved protocol.
- Student and Other Trainee Research at Veterans Administration (VA) Facilities
  - o Trainees (e.g., students, residents, or fellows of any profession) may serve as participants, but not PIs within a VA facility, use VA human subjects data, or use human biological specimens that have been collected within VA for clinical, administrative, or research purposes only when:
    - o The study has been approved by the local VA medical facility and IRB, if appropriate
    - o Either they are:
      - Enrolled in an institution with an educational affiliation agreement with that VA facility
      - Directly appointed to a VA training program that has not external institutional sponsorship (e.g., VA Advanced Fellowship). A waiver may be obtained from the CRADO under special circumstances.
  - o A VA investigator sufficiently experienced in the area of the trainee's research interest must serve as PI and is responsible for oversight of the research and the trainee/student. The PI is responsible for ensuring the trainee/student complies with all applicable local, VA and other Federal requirements including those related to research, information security, and privacy.
  - o If the trainee does not complete all aspects of the research prior to leaving VA, the investigator must ensure the protocol is completed or terminated in an orderly fashion, and in accordance with all applicable local, VA, and other Federal

requirements.

- o When the trainee leaves VA, the VA investigator is responsible for ensuring that all research records are retained by the VA.

## **APPENDIX B – IRB MEETING CONVENED VIA TELEPHONE CONFERENCE CALL**

IRB Meetings Convened via Telephone Conference Call: OPRR Memorandum (2000)

March 28, 2000

TO: Division of Human Subject Protections, OPRR

FROM: Director, Division of Human Subject Protections, OPRR

SUBJECT: IRB Meetings Convened via Telephone Conference Call

As you know, Department of Health and Human Services (HHS) regulations at 45 CFR 46.108(b) require that Institutional Review Boards (IRBs) "review proposed research at convened meetings at which a majority of the members of the IRB are present ...."

Wherever possible, OPRR strongly recommends that such meetings take place with all participating IRB members physically present. However, OPRR recognizes that circumstances sometimes warrant conducting IRB meetings via telephone conference call.

Effective immediately, OPRR will recognize as "convened" those IRB meetings conducted via telephone conference call, provided that each participating IRB member (i) has received all pertinent material prior to the meeting, and (ii) can actively and equally participate in the discussion of all protocols. Minutes of such meetings must clearly document that these two conditions have been satisfied in addition to the usual regulatory requirements (e.g., attendance, initial and continued presence of a majority of members, including at least one non-scientist member; actions taken by the IRB; the vote on such actions; discussion and resolution of controverted issues).

Recognition by OPRR of IRB meetings convened via telephone conference call is consistent with longstanding Food and Drug Administration (FDA) policy (46 FR 8967, January 27, 1981).

/SIGNED/

J. Thomas Puglisi, Ph.D.

Attachment

cc: Dr. Gary Ellis  
Dr. Melody Lin  
Ms. Michele Russell-Einhorn

## APPENDIX C – OTHER RESOURCES

- International Conference of Harmonization- Good Clinical Practice  
<http://www.ich.org/home.html>
- 45 CFR 46 Human Subjects  
<http://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/index.html>
- Declaration of Helsinki  
<http://www.cirp.org/library/ethics/helsinki/>
- Nuremberg Code  
<https://history.nih.gov/research/downloads/nuremberg.pdf>
- The Belmont Report  
<http://www.hhs.gov/ohrp/regulations-and-policy/belmont-report/>
- Categories of Research That May Be Reviewed by the IRB Through an Expedited Review Procedure  
<http://www.hhs.gov/ohrp/regulations-and-policy/guidance/categories-of-research-expedited-review-procedure-1998/index.html>
- OHRP Home  
<http://www.hhs.gov/ohrp/>
- OHRP Compliance Oversight Procedures for Evaluating Institutions  
<http://www.hhs.gov/ohrp/compliance-and-reporting/evaluating-institutions/>
- OHRP Determination Letters  
<http://www.hhs.gov/ohrp/compliance-and-reporting/determination-letters/index.html>
- OHRP Regulations & Policy  
<http://www.hhs.gov/ohrp/regulations-and-policy/index.html>
- FDA Clinical Trial Guidance Documents  
<http://www.fda.gov/RegulatoryInformation/Guidances/ucm122046.htm>
- ClinicalTrials.gov  
<https://clinicaltrials.gov/>
- NIH Research & Training  
<https://www.nih.gov/research-training>
- HIPAA Privacy Rule  
<http://www.hhs.gov/hipaa/for-professionals/privacy/>

## APPENDIX D – OHRP HUMAN SUBJECT REGULATIONS DECISION CHARTS

February 16, 2016

The Office for Human Research Protections (OHRP) provides the following graphic aids as a guide for institutional review boards (IRBs), investigators, and others who decide if an activity is research involving human subjects that must be reviewed by an IRB under the requirements of the U.S. Department of Health and Human Services (HHS) regulations at 45 CFR part 46. OHRP welcomes comment on these decision charts. The charts address decisions on the following:

- whether an activity **is research** that must be reviewed by an IRB
- whether the review may be performed by **expedited procedures**, and
- whether **informed consent** or its documentation may be waived.

### Considerations

The charts are intended to assist IRBs, institutions, and investigators in their decision-making process and should not be used as substitutes for consulting the regulations. OHRP cautions that the full text of applicable regulatory provisions should be considered in making final decisions.

These charts are necessarily generalizations and may not be specific enough for particular situations. Other guidance documents are available related to specific topics, at [OHRP Policy Guidance by Topic](#). OHRP invites inquiries for additional information.

The charts do not address requirements that may be imposed by other organizations, such as the Food and Drug Administration, National Institutes of Health, other sponsors, or state or local governments.

[Chart 1](#): Is an Activity Research Involving Human Subjects?

[Chart 2](#): Is the Human Subjects Research Eligible for Exemption?

[Chart 3](#): Does Exemption 45 CFR 46.101(b)(1) (for Educational Settings) Apply?

[Chart 4](#): Does exemption 45 CFR 46.101(b)(2) or (b)(3) (for Tests, Surveys, Interviews, Public Behavior Observation) Apply?

[Chart 5](#): Does Exemption 45 CFR 46.101(b)(4) (for Existing Data, Documents, Records and Specimens) Apply?

[Chart 6](#): Does Exemption 45 CFR 46.101(b)(5) (for Public Benefit or Service Programs) Apply?

[Chart 7](#): Does Exemption 45 CFR 46.101(b)(6) (for Food Taste and Acceptance Studies) Apply?

[Chart 8](#): May the IRB Review Be Done by Expedited Procedures?

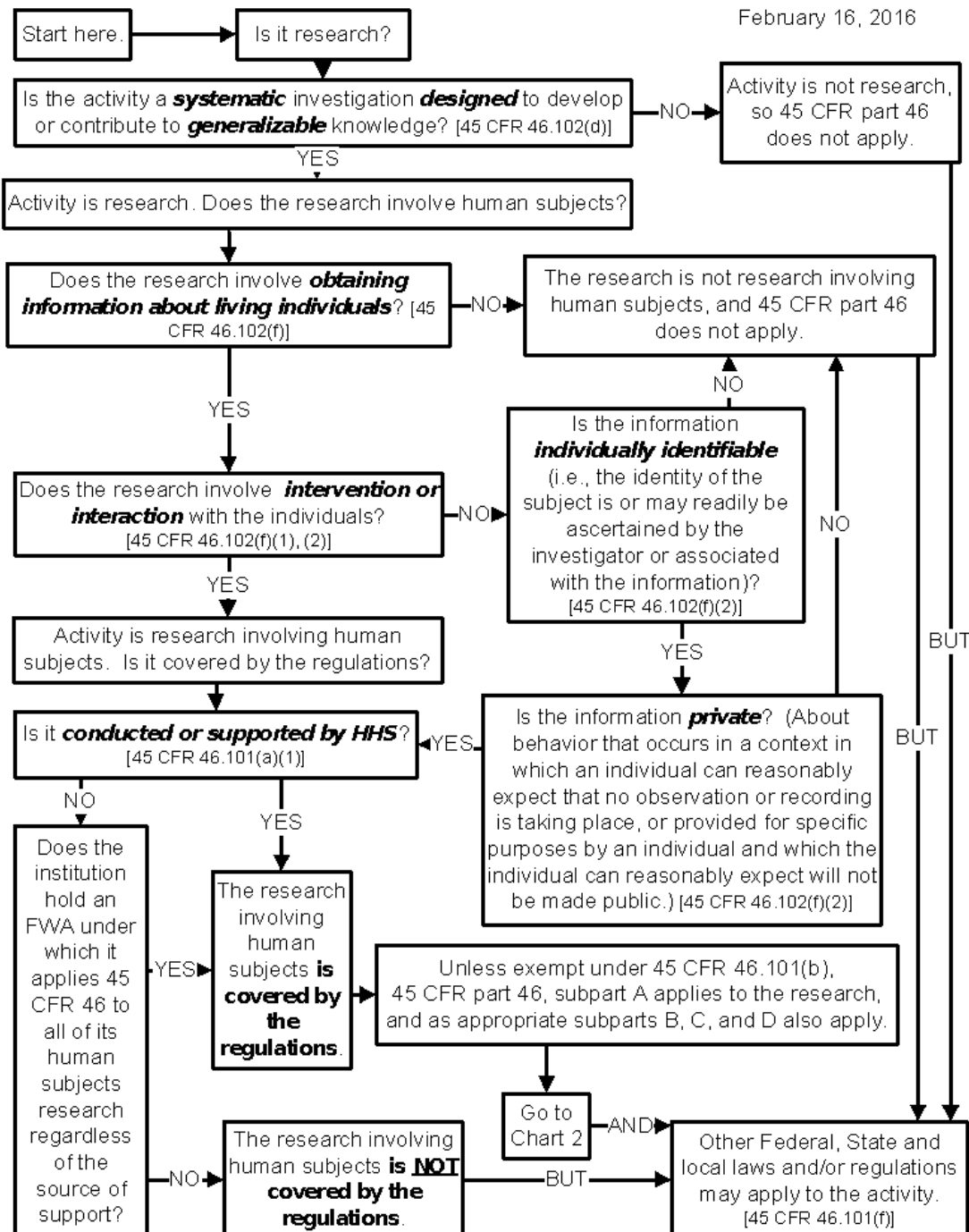
[Chart 9](#): May the IRB Continuing Review Be Done by Expedited Procedures?

[Chart 10](#): May Informed Consent Be Waived or Consent Elements Be Altered under 45 CFR 46.116(d)?

[Chart 11](#): May Documentation of Informed Consent Be Waived Under 45 CFR 46.117(c)?

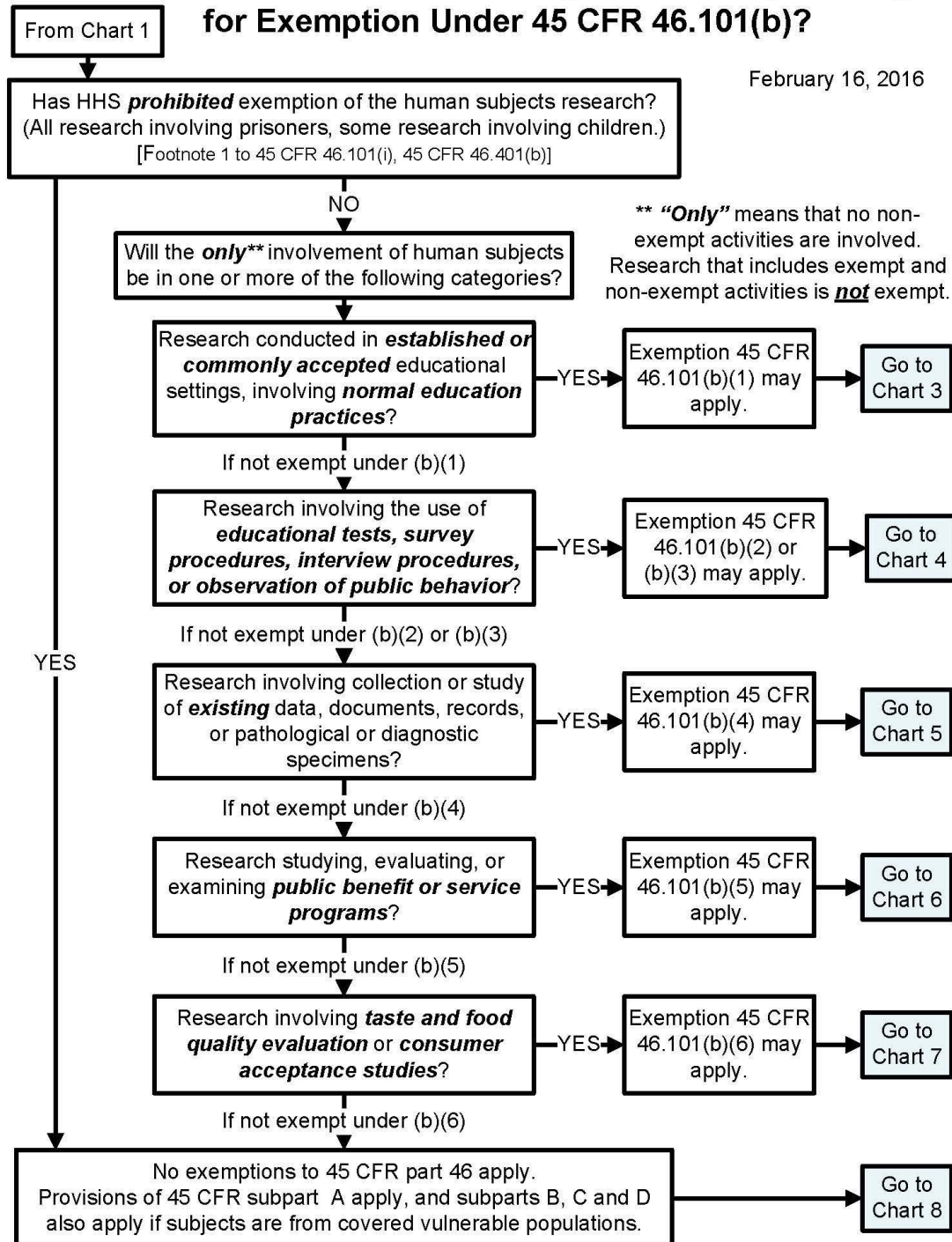
## Chart 1: Is an Activity Research Involving Human Subjects Covered by 45 CFR part 46?

February 16, 2016

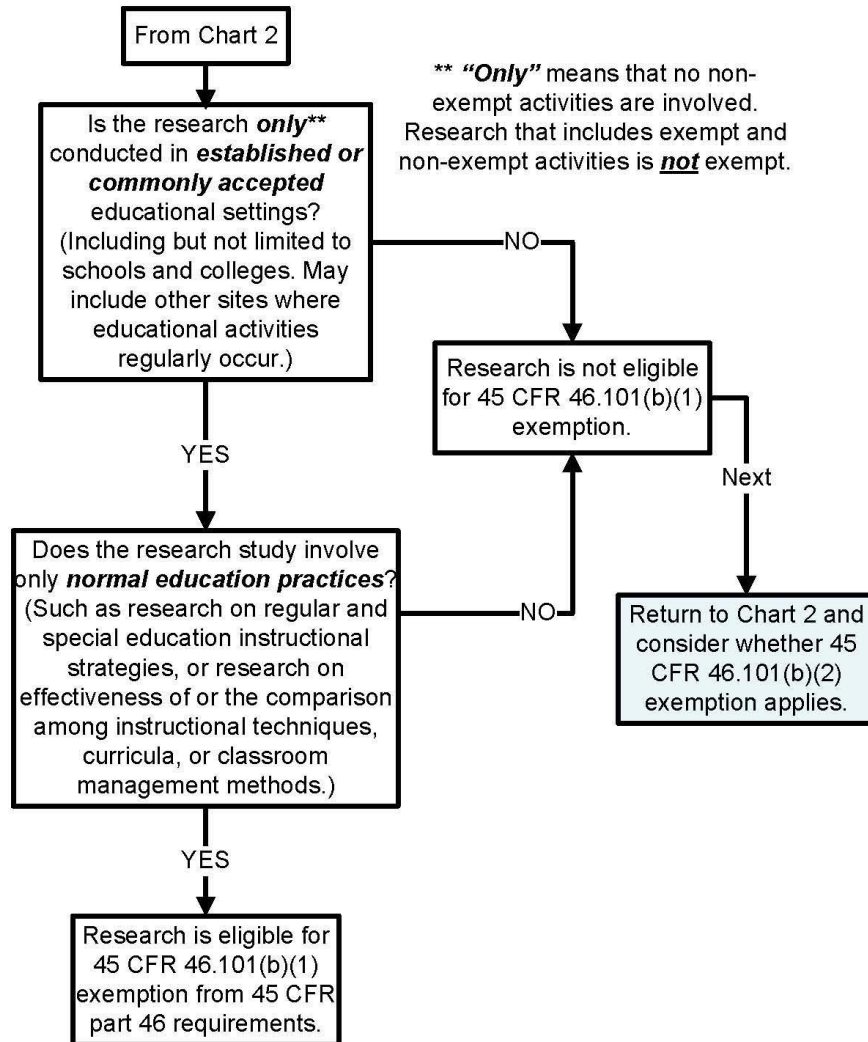


## Chart 2: Is the Research Involving Human Subjects Eligible for Exemption Under 45 CFR 46.101(b)?

February 16, 2016



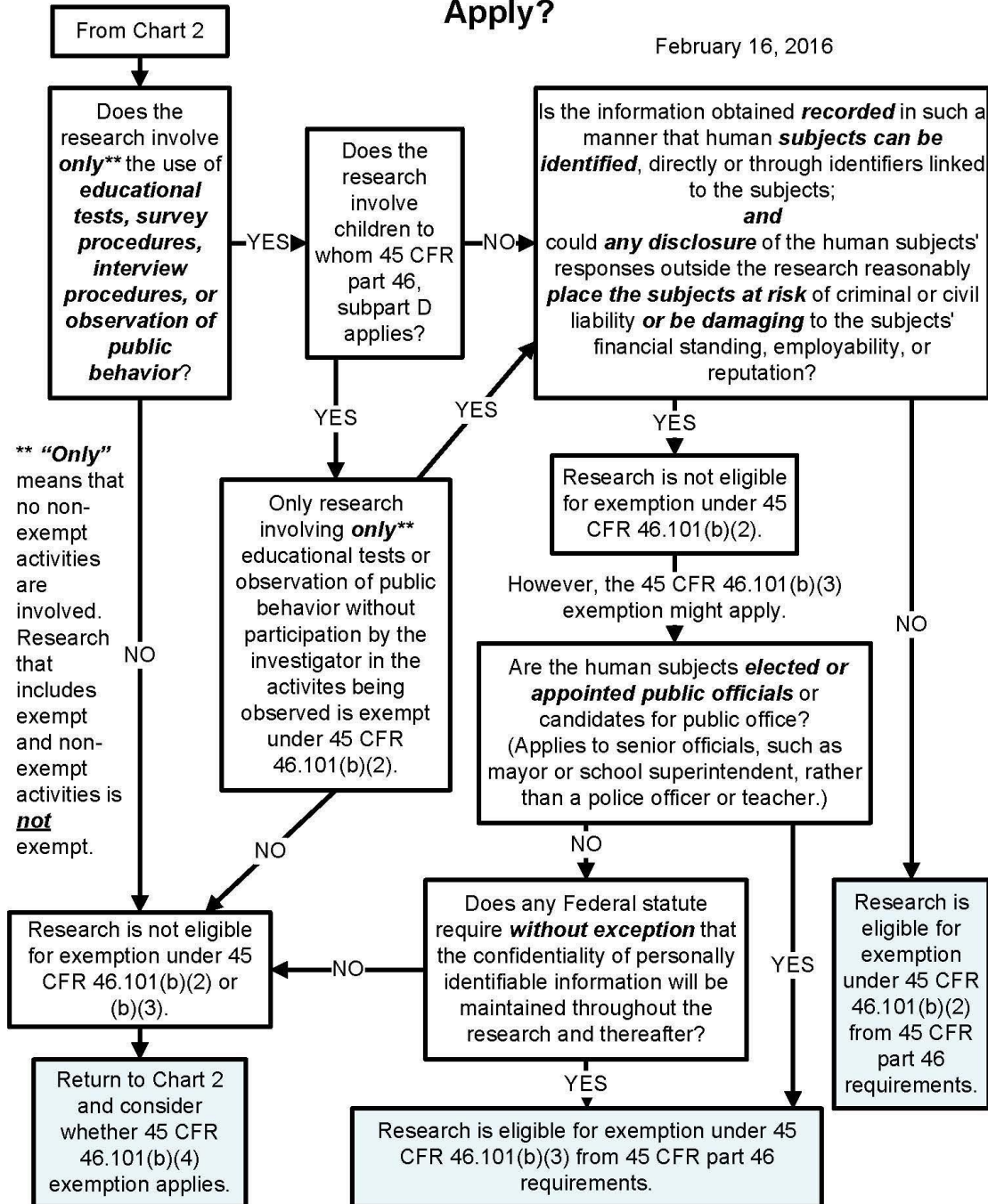
**Chart 3: Does Exemption 45 CFR 46.101(b)(1)  
(for Educational Settings) Apply?**



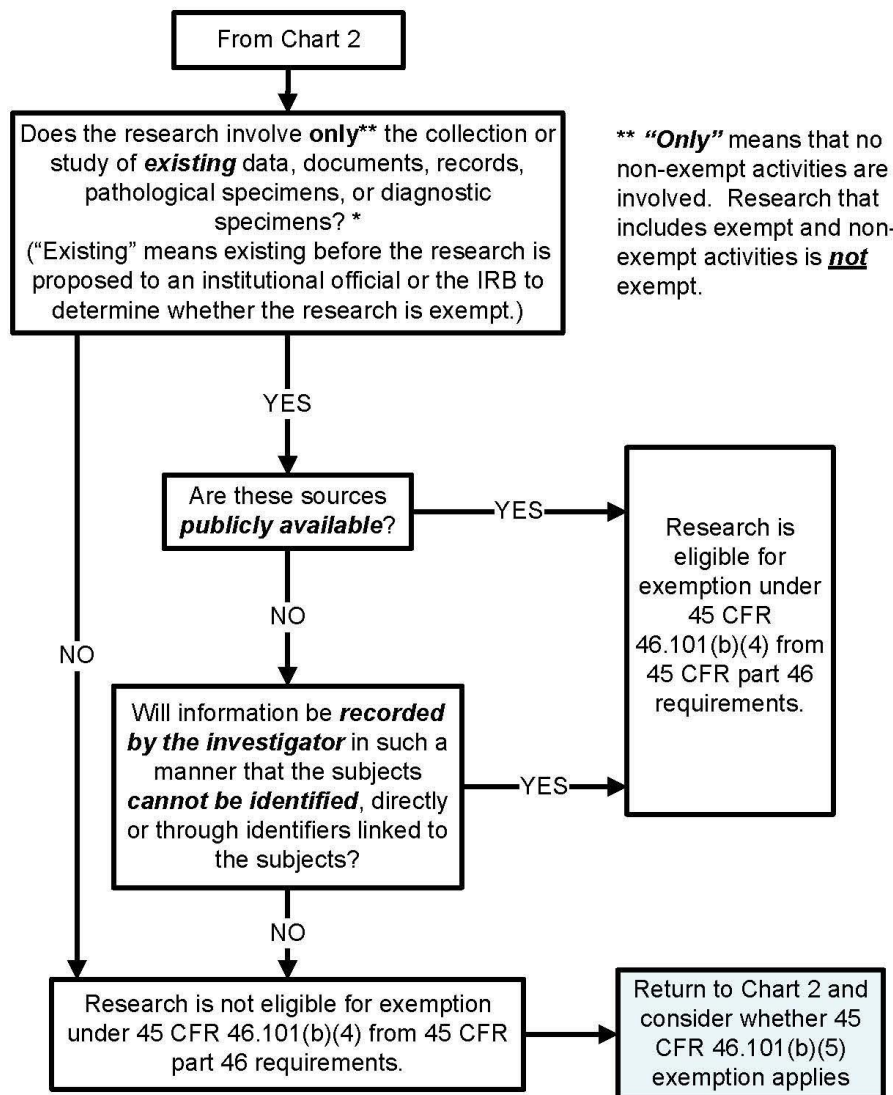
February 16, 20126

**Chart 4: Does Exemption 45 CFR 46.101(b)(2) or (b)(3)  
(for Tests, Surveys, Interviews, Public Behavior Observation)  
Apply?**

February 16, 2016



## Chart 5: Does Exemption 45 CFR 46.101(b)(4) (for Existing Data Documents and Specimens) Apply?

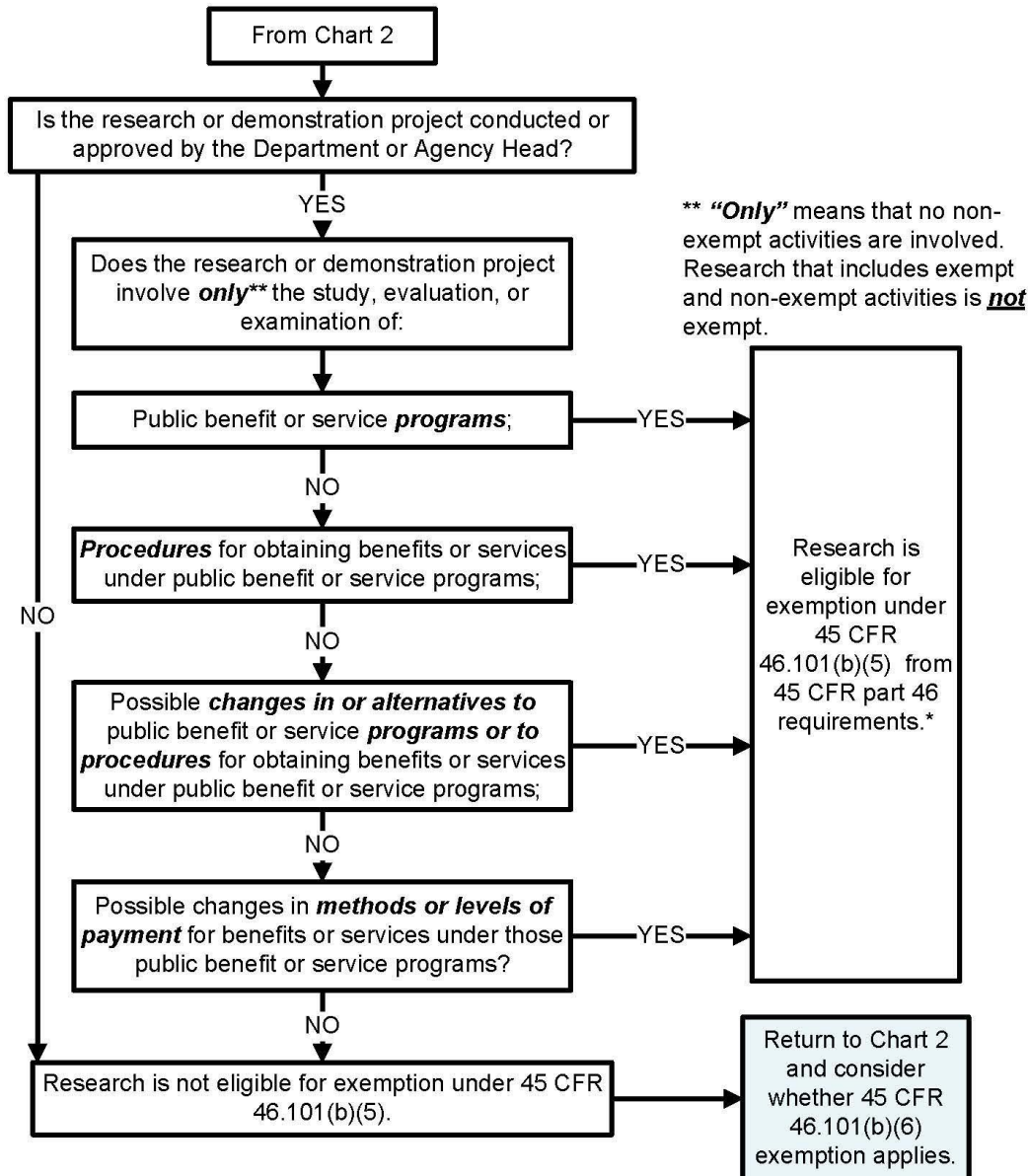


\*\* "**Only**" means that no non-exempt activities are involved. Research that includes exempt and non-exempt activities is **not** exempt.

\* Note: See **OHRP** guidance on research use of stored data or tissues and on stem cells at <http://www.hhs.gov/ohrp/regulations-and-policy/guidance/guidance-on-research-involving-stem-cells/index.html>, and on coded data or specimens at <http://www.hhs.gov/ohrp/regulations-and-policy/guidance/research-involving-coded-private-information/index.html> for further information on those topics.

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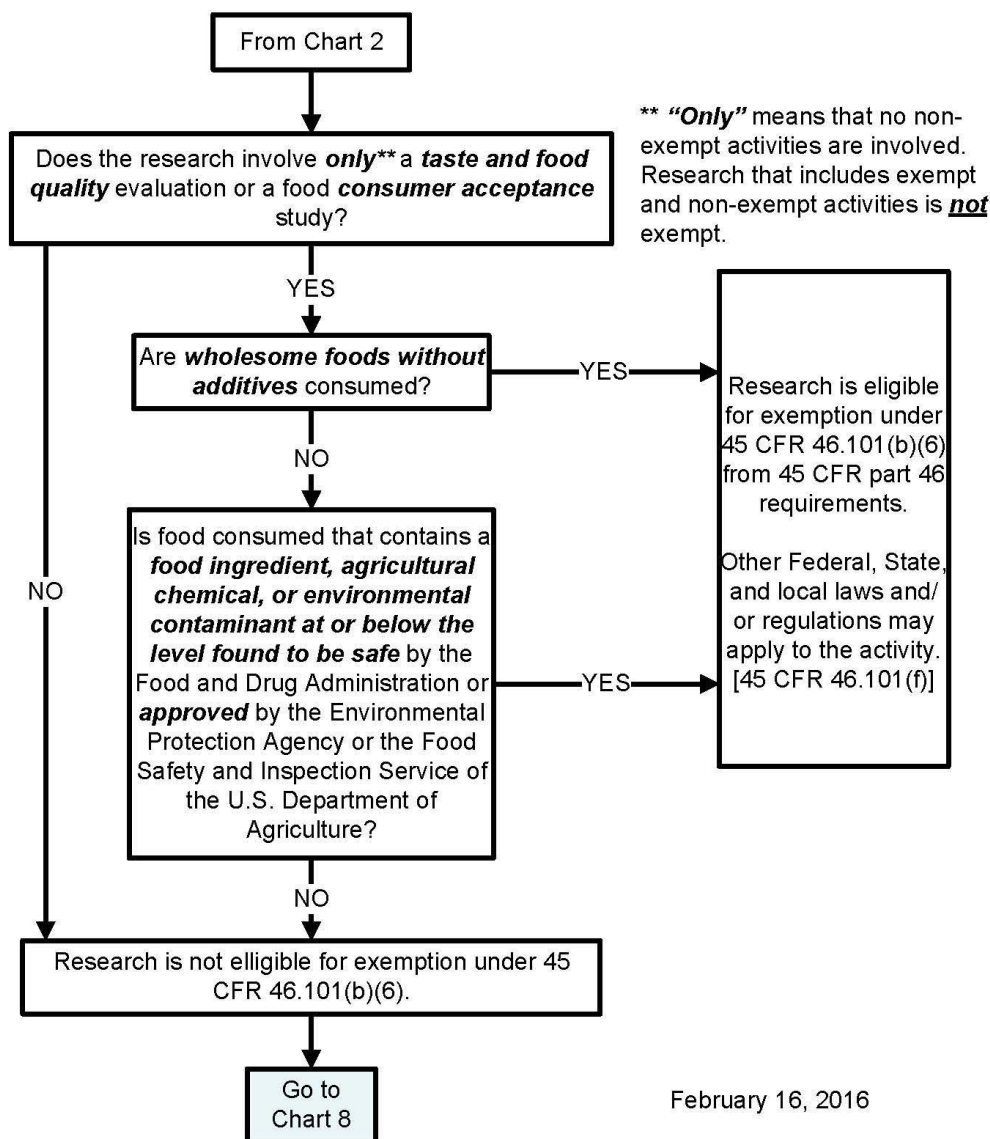
## Chart 6: Does Exemption 45 CFR 46.101(b)(5) (for Public Benefit or Service Programs) Apply?



\* Note: See **OHRP** guidance on exemptions at <http://www.hhs.gov/ohrp/regulations-and-policy/guidance/exemptions-for-public-benefit-and-service-programs/index.html> for further description of requirements for this exemption.

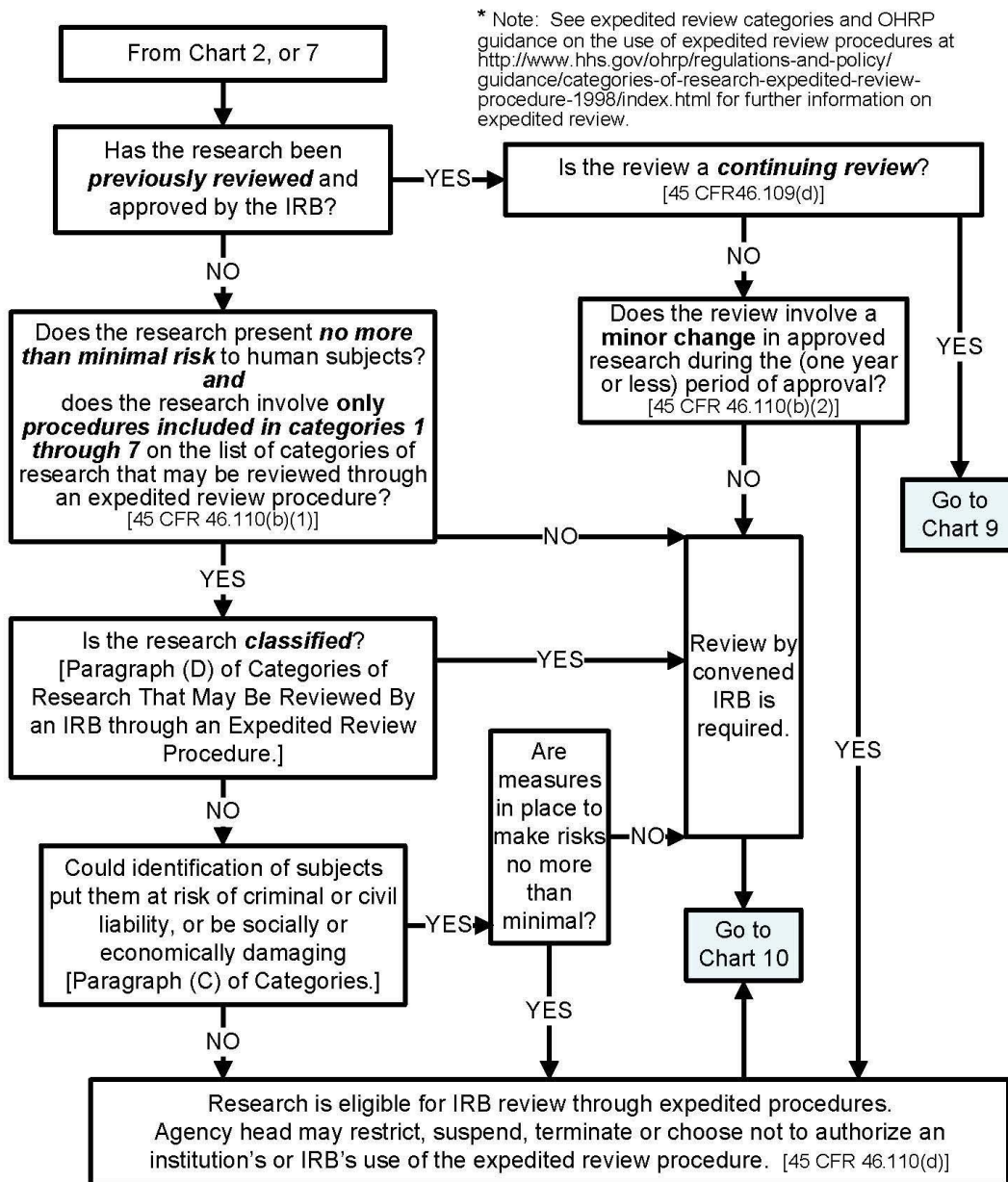
February 16, 2016

**Chart 7: Does Exemption 45 CFR 46.101(b)(6)  
(for Food Taste and Acceptance Studies) Apply?**



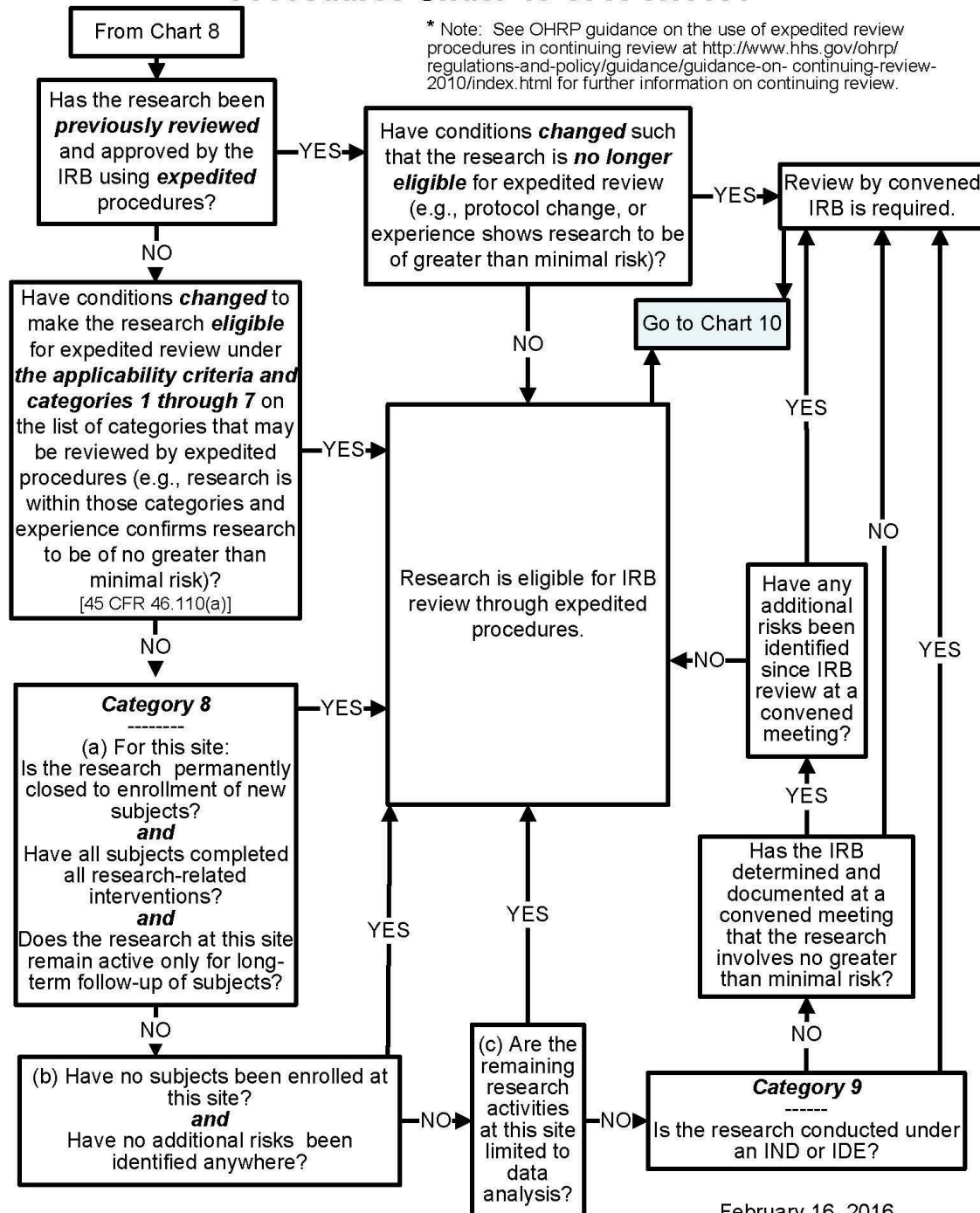
February 16, 2016

**Chart 8: May the IRB Review Be Done by Expedited Procedures Under 45 CFR 46.110?\***



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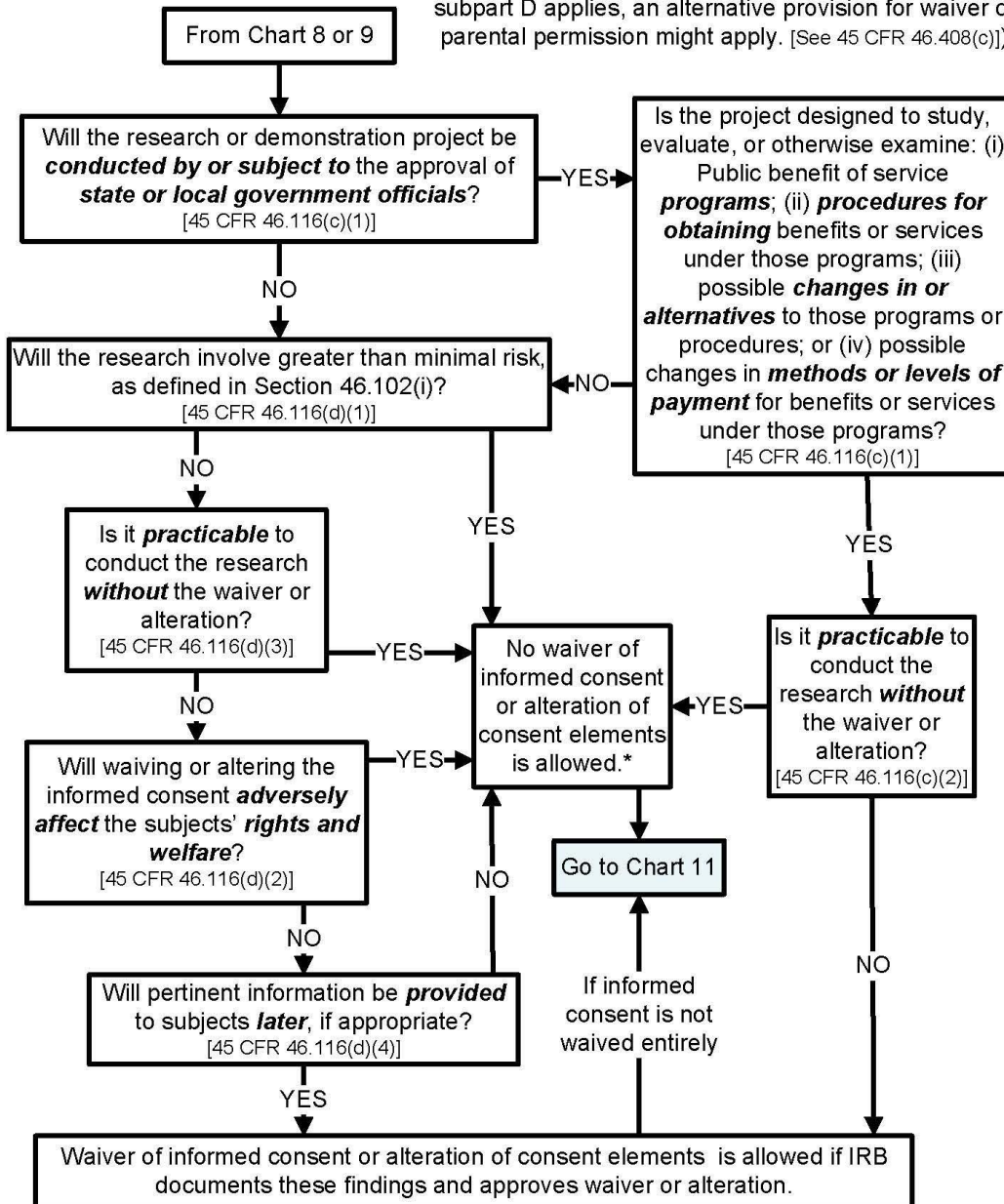
**Chart 9: Can Continuing Review be Done by Expedited Procedures Under 45 CFR 46.110?**



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## Chart 10: Can Informed Consent Be Waived or Consent Elements Be Altered Under 45 CFR 46.116(c) or (d)?\*\*

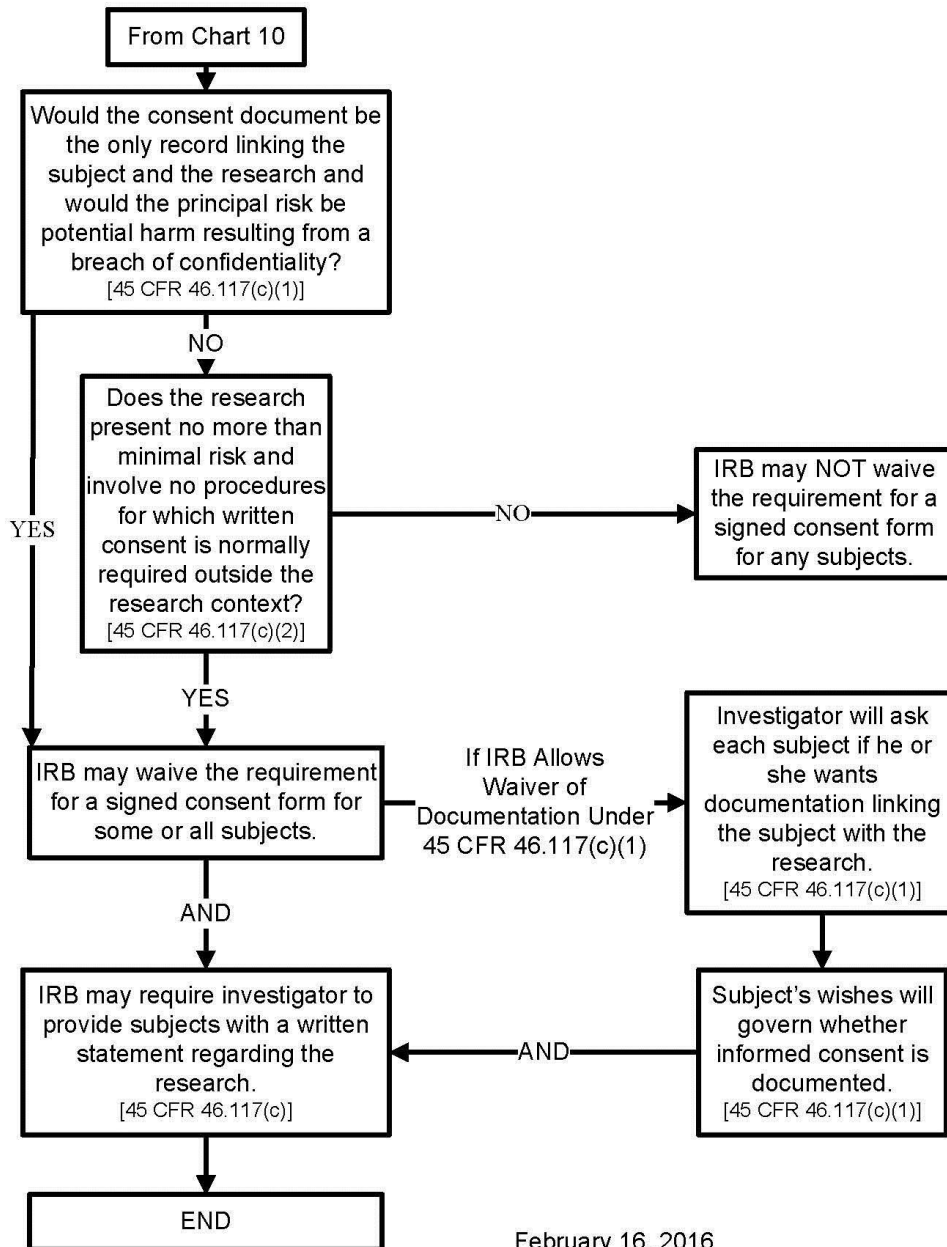
\*\* (Note: If subjects include children to whom 45 CFR part 46, subpart D applies, an alternative provision for waiver of parental permission might apply. [See 45 CFR 46.408(c)])



\* Note: See OHRP guidance on informed consent requirements in emergency research at <http://www.hhs.gov/ohrp/regulations-and-policy/guidance/emergency-research-informed-consent-requirements/index.html> for further information on emergency research informed consent waiver.

February 16, 2016

**Chart 11: May Documentation of Informed Consent Be Waived Under 45 CFR 46.117(c)?**



February 16, 2016

## **APPENDIX E – FDA INSPECTION**

### **E.1 FDA Arrival**

1. Identify who is to be notified at the time inspection commences.
2. Identify who is authorized to receive and accompany FDA inspector.
3. Develop a plan for managing oral inquiries and requests for documents.
4. Greet the FDA inspector and request identification and FDA Form 482.
5. Confirm the purpose of FDA inspection.
6. Provide the inspector with a work area that affords privacy.
7. Ensure phone/internet/power is available.
8. Keep conversation polite and professional.
9. Extend common courtesy.

### **E.2 During Inspection**

1. Accompany FDA inspector (s) at all times other than when they are in the designated room reviewing documents. FDA inspectors should not be allowed to enter patient care areas or research staff work areas unescorted at any point during the inspection.
2. Keep an accurate written record of the following:
  - b. Areas of the site visited and to whom FDA inspector spoke.
  - c. Accurate and complete record of all comments and suggestions made by inspector, unanswered questions, and site commitments.
  - d. Any commitments made to the FDA by the investigator or designee.
3. Schedule a daily summation with FDA, and separately with site staff.
4. If additional inspection days are required, prepare an agenda for next day(s) with FDA.
5. Prepare daily report to management, if applicable.
6. Maintain a list of the study subjects reviewed by the inspector and their corresponding study numbers.
7. If the FDA inspector asks for the identities and demographics of the study subjects because of some concern, comply with the request.
8. Be concise; Only answer the question that was asked.
9. Answer as honestly and openly as you can.
10. Do not volunteer additional information.
11. Do not argue with the inspector.

### **E.3 Document Marking and Duplication**

1. Do not permit marking of documents by FDA inspector.
2. When an inspector requests a copy of a document, retain a second copy for the site's records.
3. Mark as "confidential" documents containing trade secret or confidential information before providing to the FDA inspector.

4. If confidential information is conveyed orally, establish these facts to FDA.

#### **E.4 What the FDA inspector/s will be reviewing during the inspection**

##### **E.4.1 Subject Records**

1. Did the principal investigator maintain records that are supportive of each entry in CRFs for each subject?
2. Were all CRFs completed in a timely fashion?
3. Reporting of Study Progress
  - Did principal investigator terminate or discontinue the study before completion?
  - Were reports of Serious Adverse Events to Sponsor and IRB handled properly?
  - Did principal investigator maintain copies of all reports submitted to sponsor and IRB?
  - Did the site enroll subjects who did not meet the inclusion/exclusion criteria (screen failure of subjects)?
  - Did the site make any changes in the protocol in dosage, frequency, time of dosing, or method of dosing of the 'test article'?
  - Did the site fail to report serious adverse events promptly to the SHC IRB and the sponsor?
  - Did the site fail to document illnesses, hospitalizations, and other significant problems concurrent with the study?
  - Did the site fail to perform critical tests, examinations, or assessments at the protocol-specific time or visit?
  - Was there any administration of concomitant therapy that could compromise the study results?
  - Did the site fail to record or report all concomitant therapy?
  - Did the site enroll more subjects into the study than originally approved by the SHC IRB or the sponsor?
4. Did the sponsor maintain accounting procedures for the test article?
5. Were all unused supplies returned to sponsor or disposed of properly?
6. Did the investigator, pharmacist/s, or designees limit test article access and distribution?
7. Was the route of administration and proper use of the investigational product maintained?
8. Medical/Clinical Laboratory Facilities
  - Are the facilities adequate and proper diagnostic equipment available to fulfill protocol requirements?
  - Is the equipment in good working order?
  - Does the equipment require calibration and are there records documenting the required equipment calibration?
  - Is the laboratory accreditation/license documentation current?
9. Is there proper documentation and storage of trial samples?
10. Safety Information on Serious Adverse Events
  - How does the sponsor ensure that the principal investigator notifies the sponsor and the LSUHSC-S IRB promptly of Unanticipated Problems (UAPs)?

- Is the monitor involved in reporting?
- Is the timeframe for reporting UAPs and SAEs consistent with regulations?
- Do source data support the SAEs?
- Were there any deaths or dropouts due to SAEs?

#### 11. IRB Communication

- Did the site obtain proper IRB approval and documentation for protocol and informed consent?
- Does the site have documentation of the IRB qualifications?
- Has the site maintained all communication/correspondence between principal investigator and the IRB?
- Have all required continuing reviews been submitted and approved within the timeline required by the IRB?

### E.4.2 Suggested ways to organize documents

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The following is provided to assist investigators and their staff to organize the numerous documents, making them easily retrievable when needed. (In funded studies, sponsors may require such files, maintained in a specific fashion.) Although the information provided below is weighted toward clinical studies, best practices suggest it is advisable to include a variation of it in most research studies with human subjects.

- All files should be kept in one designated area (e.g., the Principal Investigator's office, lab, etc.)
- All documents should be maintained in chronological order. A sturdy three ring binder, containing dividers with some or all of the following headings (depending on the study), is recommended; however, investigators may also consider maintaining their records electronically:
  - Sponsor Correspondence if the study is funded or sponsored (e.g., NIH, NSF; drug/device company).
  - Investigator's Assurance and other forms, such as the HHS form 596 and/or FDA 1572, 1573, 1574 forms.
  - IRB Approvals\*
- \*IRB Approvals can be subdivided, as follows:
- Initial Approval
  - Retain a copy of the original IRB application and documents that were included in the initial application.
  - The original IRB approval letter.
  - A copy of the final, IRB approved, dated protocol along with any amendments.
- \*\* (If there is a "master" protocol, it, along with revised sections, might also be filed separately under the heading "Master Protocol" toward the back of the file, or in a separate binder.)
- Modification Forms - Requests/Approvals
  - Include a copy of the Shields modification form submitted electronically.

- Continuing Review - Applications/Approvals
  - Include a copy of the continuing review application submitted electronically the current IRB approval letter covering the next approval period as well as any revised stamped consent form.
- Adverse Event Reports
  - Include a copy of each, noting the dates that each report was sent to the IRB as required (unanticipated problem), sponsor, FDA, etc. If any change to the protocol or consent form is made as a result of adverse experiences, maintain a copy of the changes with the pertinent AE reports.
- Approved Consent form(s)
  - Include a copy of each (if there are more than one) approved consent form (with the IRB's stamp affixed thereon). \*\*The most currently approved consent form is the one from which copies are to be made when enrolling new subjects.
  - To avoid the possibility of using an obsolete version, retain the most currently approved version on top, and draw a diagonal line through each page of the obsolete version when the newly approved one is received or print out the latest IRB approved version of the consent in Shields.
  - Subdividers can be used to separate years (e.g. 2001 approval, 2002 approval, 2003 approval, etc.) for studies which will continue over several years.
- Approved Advertising (when applicable)
  - Maintain a copy of each advertisement (including flyers, posters, "scripts," etc.) approved for use by the IRB (and containing the 3 required IRB elements ).
  - Notes can be made on each advertisement showing when it was placed and where. Any correspondence relating to advertising can be maintained in this section as well.
- Study Closure/Completion
  - Complete the Continuing Review/closure forms (check first four milestones) and submit it to the IRB electronically to close a study. Print a copy of the electronic closure form.
- In studies sponsored by a drug or device company, the following, additional sections will likely be required:
  - Subject Enrollment/Assignment Log
  - Drug Dispense/Return Log and Drug Receipt/Ship Log
    - These will be the originals received from the sponsor for drug receipt, dispensing date, drug count, and final return.
  - Shipment Receipts/Lab Supplies
    - If the study requires that samples be sent to a central lab, or if the sponsor provides lab supplies (special catheters, test kits, etc.) the accompanying invoices, shipment logs, or UPS/Fed Ex receipts will need to be retained.
  - Monitor Visit Log (as applicable)
  - Master Protocol
    - As mentioned previously, a large, bulky master protocol may be maintained in a separate section.

- When revisions/amendments to protocols are made by a sponsor, most sponsors will provide investigators dated replacement pages. Unless the sponsor specifically requires the old pages be discarded, it is suggested that a horizontal line be drawn through the page(s) or section(s) being revised and the new information inserted.
- Sponsor Agreement(s)/Contract(s)
  - This material should include the final fully executed copy signed by the appropriate authorities, and any revisions or other documents pertaining to agreements between the institution and the sponsor relative to performance of the study.
- Miscellaneous

### **E.5 Exit Interview**

1. The FDA inspector will discuss their findings with the designated site management and principal investigator.
2. This is an opportunity for the site to correct any misunderstandings; identify incorrect deficiencies.
3. The FDA may also prepare an affidavit about the inspection/audit findings. A signature on this affidavit constitutes an acknowledgment of the contents. LSUHSC-S does not authorize LSU research personnel to sign FDA Inspection/Audit Affidavits. If the FDA inspector requires signature on the affidavit, forward to the Assistant Vice-Chancellor for Research Management for review. The Assistant Vice-Chancellor for Research Management will review with LSUHSC-S Legal Affairs Office and if appropriate will have the LSUHSC-S Institutional Official sign. A copy of the FDA affidavit is to be sent to the LSUHSC-S IRB.
4. If a FDA Form 483 is issued, each observation should be reviewed with the inspector and understood.
5. Begin plan to correct deficiencies; however, it is best to document those plans in the response to the Form FDA 483 (see below) and not during the exit interview.
6. Provide the inspector with a timetable for future actions to correct the identified deficiencies (answer will be recorded by FDA).

### **E.6 What to Do If You Receive an FDA Form 483**

1. The principal investigator should consult with the Assistant Vice-Chancellor for Research Management and/or LSUHSC-S Legal Affairs Office and sponsor for guidance on how to respond.
2. A copy of the FDA Form 483 is to be forwarded to the Assistant Vice-Chancellor for Research Management and the LSUHSC-S IRB.
4. The principal investigator is to discuss the findings with the Assistant Vice-Chancellor for Research Management and other organizational offices as necessary as determined by the findings.
5. The principal investigator will prepare a written response to the FDA Form 483. LSUHSC-

S internal research sites will seek guidance and input from the Assistant Vice-Chancellor for Research Management, the LSUHSC-S Legal Office and any other appropriate persons to any observations noted in the FDA Form 483 and send the response to the FDA within the time specified by FDA, typically within 15 days. The written response is to:

- Address each observation and explain what steps have been implemented or will be implemented to remedy the observation and prevent future occurrences of similar observations, and
  - Be factual and the tone should be respectful, professional, and cooperative.
6. The principal investigator or designee may attempt to obtain a copy of the official FDA investigator's field audit report (i.e., Establishment Inspection Report [EIR]) under the Freedom of Information Act.) This request can be made at the conclusion of the FDA Form 483 response. The principal investigator can make this request separately and the LSUHSC-S Legal Affairs Office may assist. Typically, FDA will not respond to an EIR request until the matter is formally closed.

## APPENDIX F – INVESTIGATOR KNOWLEDGE BASE

### F.1 How do I Add CV's and Training Certificates to My Research Profile?

Each investigator is required to keep a current CV on file with the IRB. SHieLDS doesn't currently allow investigators to upload their own CVs or other items to their profiles. However, IRB staff will add investigator CV's, training certificates and any other research experience documentation to your profile.

### F.2 How do I Submit a New Human Research to the IRB?

All projects that require a determination by the IRB must be submitted through Shields, the IRB electronic submission system. Shields may be accessed

at: <https://shieldsirb.lsuhealthsystem.org/IRB>

Submission requirements may vary for different types of research. Reference the following worksheets to determine submission requirements:

- HRP-340 Documents Required for Research on Devices
- HRP-339 Documents Required for Research on Drug or Biologics
- HRP-338 Documents Required for Investigator Initiated – Minimal Risk Research
- HRP-337 Documents Required for Research on Existing Data, Records or Specimens
- HRP-335 External IRB Review of Onsite Research (for NIH NCI Studies)

Complete the appropriate protocol template and upload all requested supplements and have applicable forms signed by the individuals listed in the form. Maintain electronic copies of all information submitted to the IRB in case revisions are required. Before submitting the research for initial review, you must:

- Obtain the financial interest status ("yes" or "no") of each research staff.
- Obtain the agreement of each research staff to his/her role in the research.
- Verify that each member of the research staff has completed their human subjects educational requirements and COI disclosure.

The Principal Investigator must ensure that any individual that is assigned a role or task is qualified by education, training, and experience to perform the function and assume the responsibility for the delegated function.

<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM187772.pdf>

### F.3 How do I Write An Investigator Protocol?

As a starting point for drafting a new research protocol use the Template Protocol: HRP-503, HRP-503.1 or equivalent and reference the instructions in italic text for the information the IRB looks for when reviewing research. All italicized comments are meant to be guides. They are to be deleted prior to submission. Depending upon the nature of the research, certain sections of the template protocol may not be applicable to the research study. Indicate this as appropriate. You may also seek further information regarding the Criteria for Approval used by the IRB to approve research at <http://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/index.html#46.111>.

The template protocols, HRP-503 and HRP-503.10, are designed to provide the IRB with information to analyze risks and the measures used to minimize such risks including that the risks to participants are reasonable in relation to the potential benefits.

Here are some key points to remember when developing an Investigator Protocol:

- Use sound scientific design and ethical procedures that are consistent with your discipline.
- The italicized bullet points in the Template Protocol: HRP-503 serve as guidance to investigators when developing an Investigator Protocol for submission to the IRB. All italicized comments are meant to be deleted prior to submission.
- For any items described in the sponsor's protocol or other documents submitted with the application, investigators may simply reference the page numbers of these documents within the Investigator Protocol rather than repeat information.
- When writing an Investigator Protocol, always keep an electronic copy. You will need to modify this copy when making changes to the Investigator Protocol. You will need to assign a Version date to the original protocol and revise for tracking as changes are made to the document.
- If you believe your activity may not be Human Research, please provide this information to the IRB Staff in the 'brief description' found on the Basic Information page in Shields.
- Note that, depending on the nature of your research, certain sections of the template may not be applicable to your Investigator Protocol. Indicate this as appropriate by noting N/A.
- All research involving greater than minimal risk must include an adequate data and safety monitoring plan for the protection of participants.
- You may not involve any individuals who are members of the following populations as subjects in your research unless you indicate this in your inclusion criteria as the inclusion of subjects in these populations has regulatory implications. Additional protections for these populations must be addressed in the vulnerable populations section of the protocol.

- Adults unable to provide legally effective consent
  - Individuals who are not yet adults (infants, children, teenagers)
  - Pregnant women
  - Prisoners
- If you are conducting community-based participatory research, you may contact the IRB Office for information about:
  - Research studies using a community-based participatory research design
  - Use of community advisory boards
  - Use of participant advocates
  - Partnerships with community-based Institutions
- Describe how you have adequate resources, facilities, time and qualified staff to carry out the research.
- Describe any plans for addressing incidental findings or other consequences of the research.
- Adequately describe your recruitment plan.

#### F.4 How do I Create a Consent Document?

Use the Template Consent Document: HRP-502 to create a consent document.

If you are conducting sponsored research and the sponsor has provided a model consent, please insert that necessary language from the model consent into the Template Consent: HRP-502.

Regardless of the template used to create your document, all long form consents must contain all of the required and all additional appropriate elements of informed consent disclosure. Always review the “Long Form of Consent Documentation” section in the IRB’s Worksheet: Criteria for Approval: HRP-314, to ensure that these elements are addressed before submitting the document to the IRB.

The consent document should provide the participants with information on how to address concerns, complaints, or questions about the research with the investigator and the HRPP. The consent document should be written at the 8<sup>th</sup> grade reading level.

Short form consent documents are to be used for non-English speaking subjects, only. Note that summaries for short form consent documents must contain all of the required and all additional appropriate elements of informed consent disclosure. When using the short form of consent documentation the appropriate signature block from Template Consent: HRP-502 should be used on the short form.

The IRB requires that you insert a version letter (A, B, C, etc.) to the left side of the footer for each new version of the consent or assent document submitted for review. The IRB will stamp the document approval date on the right side of the footer. These measures are to ensure that you use the most recent version approved by the IRB.

### **F.5 How do I Conduct and Document Informed Consent?**

Informed Consent is a voluntary agreement to participate in research. It is not merely a form that is signed but is an ongoing process, in which the subject understands the research and its risks. Informed consent is essential before enrolling a participant and ongoing once enrolled. Informed Consent must be obtained for all types of human subjects research including; diagnostic, therapeutic, interventional, social and behavioral studies.

Obtaining consent involves informing the subject about his or her rights, the purpose of the study, the procedures to be undergone, alternatives to the research and the potential risks and benefits of participation. Subjects in the study must participate willingly. Vulnerable populations (i.e. prisoners, children, pregnant women, etc.) must receive extra protections. The legal rights of subjects may not be waived and subjects may not be asked to release or appear to release the investigator, the sponsor, the institution or its agents from liability for negligence.

The goal of the informed consent process is to provide sufficient information so that a participant can make an informed decision about whether or not to enroll in a study or to continue participation. The informed consent document must be written in language easily understood by the participant, it must minimize the possibility of coercion or undue influence, and the subject must be given sufficient time to consider participation. The policy of LSUHSC-S is that the informed consent document be written at an 8<sup>th</sup> grade reading level.

Use the signature page approved by the IRB. Complete all items on the signature page, including dates and times. The following are the requirements for long form consent documents:

- The subject or representative signs and dates the consent document.
- The individual obtaining consent signs and dates the consent document.
- LSUHSC-S requires a witness to the signature to sign and date the consent document.
- For subjects who cannot read and whenever required by the IRB or the sponsor, a witness to the oral presentation is to sign and date the consent document.
- A copy of the signed and dated consent document is to be provided to the subject.
- Place a copy of the signed and dated consent document along with the HIPAA Authorization with the subjects medical record also for drug studies, place a copy of the IDIR in the subjects medical record and for device studies place a copy of the label and instructions for use in the subjects medical record.

The following are the requirements for short form consent documents. Remember the short form is approved only for subjects that do not speak English:

- The subject or representative signs and dates the short form consent document and the summary.
- The individual obtaining consent signs and dates the short form consent document and the summary.
- The witness to the oral presentation signs and dates the short form consent document and the summary.
- Copies of the signed and dated consent document and summary are provided to the subject or representative.

### **F.6 How do I Submit A Modification?**

Modification requests are processed through the electronic system, Shields.

- Open the main study page and choose the activity 'Create Modification/CR'.
- Choose the purpose of the submission
- Choose the 'Modification Scope'
  - Make sure you choose both 'Modification Scope' options if making personnel changes that include an updated delegation log.
- Update the study electronic forms as needed.
- Be sure to upload any new or revised protocols, consents or other documents.
- After all changes are made remember to 'Submit' the modification. If you do not hit the submit button the research is never sent to the IRB and remains on the Investigators' side.

Please note that you cannot carry out any changes to the research until IRB approval is received except when necessary to eliminate apparent immediate hazards to the subjects.

### **F.7 How do I Submit Continuing Review?**

Continuing reviews are processed through the electronic IRB system, Shields.

- Open the main study page and choose the activity 'Create Modification/CR'.
- Choose 'Continuing Review' as the purpose of the submission or 'Modification and Continuing Review' if also making changes to the research.
- Determine whether any member of the research staff has a financial interest related to

the research. Input a “yes” or “no” answer.

Input enrollment information, check the appropriate research milestones and check the items that are true since the last review period.

Upload a written summary of the study activity since the last approval period. Include number of active subjects, relevant safety information and any other information that is pertinent to the study.

If the continuing review application is not received by the study expiration date you will be restricted from submitting new Human Research until the completed application has been received.

If the approval of Human Research expires all Human Research procedures related to the protocol under review must cease, including recruitment, advertisement, screening, enrollment, consent, interventions, interactions, and collection or analysis of private identifiable information.

Continuing Human Research procedures is a violation of Institutional and federal policy. If current subjects will be harmed by stopping Human Research procedures that are available outside the Human Research context, provide these on a clinical basis as needed to protect current subjects and notify the IRB.

If current subjects will be harmed by stopping Human Research procedures that are not available outside the Human Research context, immediately contact the IRB chair and provide a written list of the currently enrolled subjects and why they will be harmed by stopping Human Research procedures.

#### **F.8 How do I Determine if an Adverse Event (AE) is an Unanticipated Problem that Needs to be Reported to the IRB?**

To aid you in determining whether an adverse event is an unanticipated problem that needs to be reported to the LSUHSC-S IRB, the following is excerpted from Guidance for Clinical Investigators, Sponsor, and IRBs – Adverse Event Reporting to IRBs – Improving Human Subject Protection. U.S. Department of Health and Human Services January 2009. (<https://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM126572.pdf>)

“An adverse event observed during the conduct of a study should be considered an unanticipated problem involving risk to human subjects and reported to the IRB, **only** if it was unexpected, serious, and would have implications for the conduct of the study (e.g., requiring a significant, and usually safety-related, change in the protocol such as revising inclusion/exclusion criteria or including a new monitoring requirement, informed consent revision or change to the investigator’s brochure). An individual AE occurrence **ordinarily** does not meet the criteria because, as an isolated event, its implications for the study cannot be

understood.

Many types of AEs generally require an evaluation of their relevance and significance to the study, including an aggregate analysis of other occurrences of the same (or similar) event, before they can be determined to be an unanticipated problem involving risk to human subjects. For example, an aggregate analysis of a series of AEs that are commonly associated with the underlying disease process that the study intervention is intended to treat (e.g., deaths in a cancer trial), or that are otherwise common in the study population independent of drug exposure (e.g., cardiovascular events in an elderly population), may reveal that the event rate is higher in the drug treatment group compared to the control arm. In this case, the AE would be considered an unanticipated problem. In the absence of such a finding, the event is uninterpretable.

Because they have been previously observed with a drug, the AEs listed in the investigator's brochure would, by definition, not be considered unexpected and thus would not be unanticipated problems. Possible exceptions would include situations in which the specificity or severity of the event is not consistent with the description in the investigator's brochure, or it can be determined that the observed rate of occurrence for a serious, expected AE in the clinical trial represents a clinically important increase in the expected rate of occurrence.

Therefore, the FDA recommends that there be careful consideration of whether an AE is an unanticipated problem that must be reported to IRBs. In summary, the FDA believes that only the following AEs should be considered as unanticipated problems that must be reported to the IRB.

- A single occurrence of a serious, unexpected event that is uncommon and strongly associated with drug exposure (such as angioedema, agranulocytosis, hepatic injury or Stevens-Johnson syndrome).
- A single occurrence, or more often a small number of occurrences, of a serious, unexpected event that is not commonly associated with drug exposure, but uncommon in the study population (e.g. tendon rupture, progressive multifocal leukoencephalopathy).
- Multiple occurrences of an AE that, based on an aggregate analysis, is determined to be an unanticipated problem. There should be a determination that the series of AEs represents a signal that the AEs were not just isolated occurrences and involve risk to human subjects (e.g., a comparison of rates across treatment groups reveals higher rate in the drug treatment arm versus a control).
- An AE that is described or addressed in the investigator's brochure, protocol, or informed consent documents, but occurs at a specificity or severity that is inconsistent with prior observations. For example, if transaminase elevation is listed in the

investigator's brochure and hepatic necrosis is observed in study subjects, hepatic necrosis would be considered an unanticipated problem involving risk to subjects.

- A serious AE that is described or addressed in the investigator's brochure, protocol, or informed consent documents, but for which the rate of occurrence (ordinarily, reporting would only be triggered if there were a credible baseline rate for comparison).
- Any other AE or safety finding (e.g., based on animal or epidemiologic data) that would cause the sponsor to modify the investigator's brochure, study protocol, or informed consent documents, or would prompt other action by the IRB to ensure the protection of human subjects."

## **F.9 How do I Close Out a Study?**

Closing out a study involves the same procedures described in the section above 'How do I submit a Continuing Review'. The only difference is selecting the appropriate research milestones.

A study cannot be closed out if you are interacting or intervening with living individuals or their identifiable private information or identifiable specimens. When all these activities are complete you will be able to select the first four research milestones. Selecting the first four milestones on the electronic continuing review form automatically closes out your study.

If you fail to submit a continuing review form to close out Human Research, you will be restricted from submitting new Human Research until the completed closure has been received.

## **F.10 Types of Study Activities**

### **F.10.1 Prescreening**

Once the IRB has granted approval, you may begin to pre-screen/screen for prospective participants to assess for clinical trial inclusion/exclusion.

### **F.10.2 Screening**

1. Informed Consent: The investigator, CRC, or designee will conduct the consenting process or verify prior completion of the informed consent document including correct version, correct date, and signatures, witness signature, date and signature of the person obtaining consent prior to performing any screening procedures, including holding or stopping therapy ("washout") for the purposes of participating in the clinical trial. Regardless of which written form of the consent or assent, a written narrative of the informed consent process should be included in the participant's source document. A copy of the informed

consent document is to be provided to the participant or responsible party. A copy of the informed consent document is to be placed in the Medical Record. The original document should remain in the subject's source document.

2. Clinical Evaluations: The investigator, CRC, or designee (in accordance with the IRB approved Delegation of Authority Log) will perform the protocol-required clinical evaluations for the assigned protocol including but not limited to, physical assessment; medical history and medication history review, and laboratory tests and/or procedures coordination.
3. Medications: The investigator, CRC or designee will obtain a medication history as directed by the protocol, and for inclusion/exclusion eligibility for all prospective subjects. Medications may be documented on the visit-specific flowsheet or on a subject-specific medication log. If the protocol requires documentation of concomitant medications, the medication start dates, stop dates, dosage, route, and frequency must be documented. If the date is unknown, all attempts should be made to identify the year and estimate the start date as DD MM YYYY. The principal investigator and research team will verify that no study exclusionary medications are being used by the research subject.
4. Procedures and Laboratory Analysis: The investigator, CRC or designee will ensure that all necessary research procedures and laboratory analyses are obtained as outlined in the protocol after the subject has provided written informed consent. The investigator, CRC or designee will coordinate with the receiving laboratories to ensure that the correct protocol procedures are used, the specimens are labeled and collected, and that either the local or central laboratory is available to receive and process the specimens. All clinical trial test results and procedures will be reviewed, signed and dated by the investigator promptly. Abnormal results will be evaluated and if clinically significant must be documented, including action taken. Refer to the protocol for recording of abnormal lab inclusion/exclusion.
5. Eligibility Criteria Checklist: The investigator, CRC or designee will use an eligibility checklist to verify that all inclusion criteria are met and that no exclusion criteria exist. An eligibility criteria checklist may be provided by the study sponsor or created by the research site. Supportive documentation of all inclusion/exclusion criteria must be contained within the research record. The investigator and CRC, or designee will confirm each subject's eligibility prior to the research subject's randomization and study entry. The PI should confirm subject eligibility.
6. Scheduling Return Visits: The investigator, CRC or designee will schedule next visits and verify that visits occur within the protocol specified timeframe. The investigator, CRC or designee is responsible for notifying the study subject and research team, including data management, receiving laboratories, and investigational pharmacy (if applicable) of the anticipated randomization (study entry) date. The investigator, CRC or designee will keep a

schedule of anticipated study visits. Missed visits must be followed up and documented. A protocol specific visit log should be maintained.

7. Source Documentation: The CRC or designee will complete a protocol-specific flowsheet or other source documentation for the study visit. Source documents may be provided by the study sponsor or created by the research site investigator, CRC or designee. If required by protocol and/or sponsor, the principal investigator will review source documentation and sign.
8. Case Report Forms (CRF): The investigator, CRC or designee will complete CRFs as required by the protocol or sponsor CTA.
9. Investigational Pharmacy: The investigator, CRC or designee will verify communication with the investigational pharmacist when a randomization visit is scheduled for protocols that include investigational drugs as applicable.

### **L.10.3 Randomization/Entry Visit**

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After eligibility has been confirmed by the principal investigator, CRC will schedule and implement the randomization (entry) visit within the protocol specific timeline and conduct the randomization visit as directed in the protocol.

1. Randomization: The investigator, CRC, or designee ensure that protocol specifications are followed. See protocol for timeline/restrictions.
2. Clinical Evaluation: The investigator, CRC, or designee in accordance with the LSUHSC-S IRB approved Delegation log will perform the required randomization/entry evaluations for the assigned protocol including, but not limited to, physical assessment, signs/symptoms, diagnoses, medical and medication history review, and laboratory tests and/or procedures coordination.
3. Medications: The investigator, CRC or designee will record all study and concomitant medications in the flowsheet or medication log as required by the protocol at the randomization/entry visit. If the investigator or CRC chooses to use a medication log, the visit flowsheet should document that a medication log is being used, and that it was reviewed and updated at this visit (e.g., "Medication log reviewed. No changes noted at today's visit." or "Medication log reviewed. Changes noted and documented on the medication log.").
4. Research Procedures and Laboratory Analysis: The investigator, CRC or designee will coordinate with the receiving laboratories to ensure that the correct procedures and specimens are collected and laboratory staff are available to receive and process research specimens. All research tests and procedures will be reviewed, signed, and dated by the principal investigator. Abnormal results will be evaluated and, if clinically significant must be documented, including action taken. The research team will verify protocol required action and ensure compliance.
5. Pharmacy: The investigator, CRC or designee will coordinate randomization requirements

with the investigational pharmacist. The agent, route, dose, and frequency of all investigational medications (or changes) must be recorded in the source documents, flowsheet, record, drug accountability log, or study medication log.

6. Return Visits: The investigator, CRC or designee is responsible for notifying the study subject of the return date and keeping a schedule of anticipated study visit returns. Missed visits must be followed up and documented.
7. Source Documentation: The CRC or designee will complete a protocol-specific flowsheet or other source documentation (patient record) for the appropriate study visit, containing all protocol specified events during that visit. The CRC or designee will submit the source documentation/flow-sheet to the principal investigator for signature. All signed source documents must be filed in the research site record. Source documents to include a section for investigational medication where adherence, side effects, and dosing are reviewed and documented. Hard copy lab or test results are also to be filed in the subject source binder.
8. Case Report Forms: The investigator, CRC or designee will complete CRFs as required by the protocol or sponsor CTA.

#### **F.10.4 Study Visits during Treatment Phase of Protocol/ Device Guidance**

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The investigator, CRC, or designee in accordance with the LSUHSC-S IRB approved Delegation log will implement the evaluations during the treatment phase as directed by the assigned protocol.

1. Clinical Evaluation: The investigator, CRC, or designee will perform the required follow-up evaluations for the assigned protocol including, but not limited to physical assessment (i.e., signs/symptoms, new diagnoses, hospitalizations); medication changes review; and investigational medications, laboratory tests and/or procedures adherence.
2. Medications: The investigator, CRC or designee will record all study and concomitant medications in the flowsheet or medication log as required by the protocol at the randomization/entry visit. If the investigator or CRC chooses to use a medication log, the visit flowsheet should document that a medication log is being used, reviewed, and updated at this visit (e.g., "Medication log reviewed. No changes noted at today's visit." or "Medication log review. Changes noted and documented on the medication log.").
3. Research Procedures and Laboratory Analysis: The investigator, CRC or designee will coordinate with the receiving laboratories to ensure that the correct procedures and specimens are collected and laboratory staff are available to receive and process research specimens. All research tests and procedures will be reviewed, signed, and dated by the principal investigator. Abnormal results will be evaluated, and if clinically significant must be documented, including action taken. The research team will verify protocol required action and ensure compliance.
4. Pharmacy: The investigator, CRC or designee will coordinate investigational medication dispensing requirements with the investigational pharmacist. The agent, route, dose, and frequency of all investigational medications (or changes) must be recorded in the source documents, flowsheet, record, drug accountability log, or study medication log.
5. Return Visits: The investigator, CRC or designee is responsible for notifying the study subject

of the return date and keeping a schedule of anticipated study visit returns. Missed visits must be followed up and documented.

6. Source Documentation: The CRC or designee will complete a protocol-specific flowsheet or other source documentation for the appropriate study visit, containing all protocol specified events during that visit. The CRC or designee will submit the source documentation/flowsheet to the principal investigator for signature. All signed source documents must be filed in the research site record/source documents. Source documents are to include a section for investigational medication where adherence, side effects, and dosing are reviewed and documented. Hard copy lab or test results are also to be filed in the subject source binder.
7. Case Report Forms: The investigator, CRC or designee will complete CRFs as required by the protocol or CTA with sponsor.

#### **F.10.5 On-Study/Off-Treatment or other Long-Term Follow-Up**

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For protocols using study medications, the protocol may require subjects who have stopped the investigational medication or completed the treatment phase of the protocol to be followed. Treatment evaluation must be followed as directed by the assigned protocol.

1. Clinical Evaluation: The investigator, CRC, or designee will perform the required follow-up evaluations for the assigned protocol including, but not limited to physical assessment (i.e., signs/symptoms, new diagnoses, hospitalizations); medication changes review; and investigational medications, laboratory tests and/or procedures adherence.
2. Medications: The investigator, CRC or designee will record all study and concomitant medications in the flow-sheet or medication log as required by the protocol at the randomization/entry visit. If the investigator or CRC chooses to use a medication log, the visit flowsheet should document that a medication log is being used, and that it was reviewed and updated at this visit (e.g., "Medication log reviewed. No changes noted at today's visit." or "Medication log review. Changes noted and documented on the medication log.").
3. Research Procedures and Laboratory Analysis: The investigator, CRC or designee will coordinate with the receiving laboratories to ensure that the correct procedures and specimens are collected and laboratory staff are available to receive and process research specimens. All research tests and procedures will be reviewed, signed, and dated by the principal investigator. Abnormal results will be graded, and if clinically significant must be documented, including action taken. The research team will verify protocol required action and ensure compliance.
4. Pharmacy: The investigator, CRC or designee will notify the investigational pharmacy of the subject's status as off-treatment.
5. Return Visits: The investigator, CRC or designee is responsible for notifying the study subject of the return date and keeping a schedule of anticipated study visit returns. Missed visits must be followed up and documented.
6. Source Documentation: The CRC or designee will complete a protocol-specific flow-sheet or other source documentation for the appropriate study visit, containing all protocol specified

events during that visit. The CRC or designee will submit the source documentation/flowsheet to the principal investigator for signature. All signed source documents must be filed in the research site record/source documents. Source documents to include a section for investigational medication where adherence, side effects, and dosing are reviewed and documented. Hard copy lab or test results are also to be filed in the subject source binder.

7. Case Report Forms: The investigator, CRC or designee will complete CRFs as required by the protocol sponsor CTA.

#### **F.10.6 Study Discontinuation Visit**

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In anticipation of study discontinuation, the investigator, CRC or designee will notify the team of upcoming study discontinuation to aid in the transition to health management follow-up and marketed medication (if applicable). The investigator, CRC or designee will implement the study discontinuation evaluation as directed by the assigned protocol.

1. Clinical Evaluation: The investigator, CRC, or designee will perform the required follow-up evaluations for the assigned protocol including, but not limited to physical assessment; signs/symptoms, new diagnoses, hospitalizations, medication changes review; and investigational medications and laboratory tests and/or procedures adherence.
2. Medications: For protocols requiring follow-up on concomitant medications, the investigator, CRC or designee must record all study and concomitant medications in the source document flow-sheet, study/clinic note, or appropriate medication log.
3. Research Procedures and Laboratory Analysis: The investigator, CRC or designee will coordinate with the receiving laboratories to ensure that the correct procedures and specimens are collected and laboratory staff are available to receive and process research specimens. All research tests and procedures will be reviewed, signed, and dated by the principal investigator. Abnormal results will be evaluated and, if clinically significant must be documented, including action taken. The research team will verify protocol required action and ensure compliance.
4. Discontinuation of Investigational Medication and Communication with PCP: The investigator, CRC or designee will communicate with the investigational pharmacist regarding the discontinuation of investigational drug and collaborate with the subject's primary care provider if applicable for continued health care management.
5. Investigational Drug Return: For protocols using investigational agents (drugs or devices), the investigational pharmacist, investigator, CRC, or designee must record the return or destruction of all investigational study medications in the source document flowsheet, clinic/study visit note, or appropriate drug accountability log at the discontinuation visit in accordance with sponsor direction.

#### **F.10.7 Follow-Up Visit(s)**

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Protocols using investigational drugs may require a follow-up visit weeks after the investigational drug is discontinued. Additionally, subjects with ongoing adverse events (AE) with suspected study participation causality at study discontinuation will need to be followed

under study until the event has resolved. The study protocol may allow for some of these follow-up visits to occur through telephone contact as long as no additional study or laboratory evaluations are required.

1. Clinical Evaluation: The investigator, CRC, or designee will perform and document the required follow-up evaluations for the assigned protocol, including, but not limited to physical assessments; signs and symptoms, new diagnoses, hospitalizations, serious adverse events, medication changes, and status of ongoing AEs review, and laboratory tests and/or procedures adherence.
2. Research Procedures and Laboratory Analysis: The investigator, CRC or designee will ensure that all necessary research procedures and laboratory analysis are obtained as outlined in the protocol. The CRC or designee will coordinate with the receiving laboratories to ensure that the correct procedures and specimens are collected and laboratory staff are available to receive and process research specimens. All research test results and procedures will be reviewed, signed, and dated by the principal investigator. Abnormal results will be evaluated and, if clinically significant must be documented, including action taken. The research team will verify protocol required action and ensure compliance.
3. Medications: The investigator, CRC or designee will query and document any changes in the completion of the study medications.
4. Source Documentation: The CRC or designee will complete a source clinic note or protocol-specific flowsheet for the follow-up visit or telephone call.
5. Case Report Forms: If the protocol includes a follow-up CRF, the investigator, CRC or designee will complete the CRF as required by the assigned protocol.

#### **F.10.8 Missed Study Visits**

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Study visits that are missed or out of the protocol-specified timeframe must be documented as missed study visits. The investigator, CRC or designee, together with the research team, will attempt to contact/locate the study participant and bring the study subject back into care. All attempts and action to locate and bring the study participant back into care or for study discontinuation must be documented and filed as source documentation.

If the study participant chooses to discontinue the study prematurely, then a discontinuation visit will be scheduled (see Study Discontinuation Visit section for details). Additionally, the study team, including investigational pharmacy and the sponsor, must be notified of the premature discontinuation visit. Subjects that choose to discontinue should be referred for primary health care management.

If the study participant missed two consecutive study visits and all attempts to locate the subject are unsuccessful, the study participant may be prematurely discontinued as lost to follow-up (refer to protocol for specifics on premature discontinuation). Subjects should not be discontinued as lost to follow-up until all efforts to locate and bring the subject back into care have been exhausted.

#### **F.11 When a Subject Withdraws Consent**

Although a participant is not obliged to give his or her reasons for withdrawing from a study prematurely, the investigator, CRC, or designee will make a reasonable effort to ascertain the reason, while fully respecting the participant's rights to withdraw from participation.

The data collected on the subject to the point of withdrawal remains part of the study database and may not be removed. However, an investigator may ask a subject who is withdrawing whether the subject wishes to provide continued follow-up and further data collection after their withdrawal from the interventional portion of the study. Under this circumstance, the discussion with the subject is to clearly distinguish between study-related interventions and continued follow-up of associated clinical outcome information, such as medical course or laboratory results obtained through non-invasive chart review, and address the maintenance of privacy and confidentiality of the subject's information.

- If a subject withdraws from the interventional portion of the study, but agrees to continued follow-up of associated clinical outcome information, the investigator is to obtain the subject's informed consent for this limited participation in the study (assuming such a situation was not described in the original informed consent form). IRB approval of all informed consent documents is required.
- If a subject withdraws from the interventional portion of a study and does not consent to continued follow-up of associated clinical outcome information, the investigator may not access, for purposes related to the study, the subject's medical record or other confidential records requiring the subject's consent.

An investigator may review study data related to the subject collected prior to the subject's withdrawal from the study and may consult public records, such as those establishing survival status.

## **F.12 Adverse Events Including Serious Adverse Events, Unexpected Adverse Drug Experiences, and Unanticipated Adverse Device Effects**

### **F.12.1 Adverse Event Assessment and Recording**

An Adverse Event (AE) may be a symptom (e.g., pruritis), a sign (e.g., rash), a lab result (e.g., ANC of 450), or a diagnosis (e.g., PCP). Each protocol or sponsor will specify requirements for recording AEs. The investigator, CRC, or designee will continuously screen study participants for AEs on an ongoing basis using patient reported histories, physical assessment/exam, laboratory reports, chart review, and any other available data. When an AE is identified, the investigator, CRC or designee will document the AE on a study flowsheet or an AE log sheet specific to the study participant. The principal investigator will review all subject AEs and assess causality and required course of action in accordance with the protocol and clinical trial's requirements. The investigator should follow all AE's to resolution. The patient's primary caregiver is to be kept informed of any adverse events requiring treatment interruption or changes, as well as any

results that may confuse the clinical picture or complicate care.

### **F.12.2 Serious Adverse Event Assessment and Recording**

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The investigator, CRC, or designee will continuously screen for a Serious Adverse Events (SAE) on an ongoing basis using patient or family-reported events, home-base care reports, in-patient census, obituaries, or any other available data. The CRC or designee will immediately communicate SAE reports with the principal investigator (if not already aware). As soon as the site receives information of an SAE, an initial report must be made to the sponsor within 24 hours of notification. For deaths, the investigator, CRC, or designees will supply the sponsor with any additional requested information (e.g., autopsy reports and terminal medical reports). SAEs that meet the definition of an unanticipated problem are to be submitted to the LSUHSC-S IRB. See section above: How Do I Determine if an Adverse Event (AE) is an Unanticipated Problem that Needs to be Reported to the IRB?

## **F.13 Protocol Deviations, Protocol Violations or Protocol Exceptions**

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### **F.13.1 Protocol Deviation/Violation**

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If the reported deviation/violation involves an event that requires prompt reporting to the IRB or if it involves a failure to follow federal regulations, institutional policies governing human subject research, requirements or determinations of the IRB, follow SOP section: Reportable New Information Items.

### **F.13.2 Protocol Exceptions**

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An exception to the currently approved protocol is a planned temporary variance that has received IRB approval prior to its initiation (e.g., enrollment of subject who does not meet eligibility criteria or accommodation of a subject who moves out of the area for the remainder of his/her participation in research). To submit a request for review of a protocol exception, use the Modification option in SHleLDS.

## **F.14 What is HIPAA?**

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The Health Insurance Portability and Accountability Act of 1996 (HIPAA) is a federal law that was intended to improve the efficiency and effectiveness of the health care system. HIPAA has three main parts. The first, the "Administrative Simplification" provisions, include national standards for transactions of electronic patient health, administrative and financial data between health care providers and health plans. The second and third parts concern security and privacy, and protect the confidentiality and integrity of health information. This website focuses on the Privacy Rule, which has special regulations that particularly affect clinical

research. LSUHSC-S is a covered entity under the Privacy Rule. (University Health is a separate covered entity under the privacy rule).

#### **F.14.1 What is the Privacy Rule?**

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The HIPAA Privacy Rule establishes the conditions under which health information may be used or disclosed for research purposes. Research is defined in the Privacy Rule as "a systematic investigation, including research development, testing, and evaluation, designed to contribute to generalizable knowledge." The Privacy Rule strives to protect the privacy of health information, while at the same time ensuring that investigators will continue to have access to medical information necessary to conduct vital research.

Privacy is a concern among research subjects. Therefore the Privacy Rule also defines the means by which individuals participating in human studies research are informed of uses and disclosures of their medical information for research purposes, and their rights to access information about them held by covered entities.

The Privacy Rule does not directly regulate the conduct of research. Rather, the Privacy Rule regulates the handling of individually identifiable health information that is created or received in the course of a research study. The Privacy Rule thus works in conjunction with the other applicable federal regulations (i.e. Title 45, part 46, subpart A of the Code of Federal Regulations, also known as "The Common Rule;" and the FDA human subject protection regulations) to further strengthen the rights and protections of individuals who participate in human studies research.

The HIPAA Privacy Rule became final on August 14, 2002. The date by which all covered entities had to be in compliance was April 14, 2003. The Privacy Rule is located at 45 CFR Part 160 and Subparts A and E of Part 164.

The Office of Civil Rights (OCR) within the Department of Health and Human Services is the federal enforcement agency of the Privacy Rule. At LSUHSC-S, the Institutional Review Board will serve as the Privacy Board.

The Office of Civil Rights mandates that the Privacy Board be responsible for determining whether or not a research study is subject to HIPAA privacy regulations. This means that investigators themselves may not decide whether their human research study is subject to HIPAA. OCR also authorizes the Privacy Board to approve waivers to Privacy Rule regulations on research studies.

#### **F.14.2 What kinds of health information does the Privacy Rule protect?**

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The Privacy Rule protects health information, including demographic information, that:

- Is created or received by a covered entity
- Relates to the past, present, or future physical or mental health, condition or treatment

of an individual, and that

- Identifies the individual or may be reasonably used to identify the individual. Information that the Department of Health and Human Services (DHHS) feels can be used to identify individuals is listed in Table 1:

**Table 1: Direct Identifiers (PHI)**

1. Names
2. Geographic subdivisions smaller than a state including street address, city, county, precinct, ZIP Code, and their equivalent geographical codes, except for the initial three digits of a ZIP Code if, according to the current publicly available data from the Bureau of the Census:
  1. The geographic unit formed by combining all ZIP Codes with the same three initial digits contains more than 20,000 people.
  2. The initial three digits of a ZIP Code for all such geographic units containing 20,000 or fewer people are changed to 000.
3. All elements of dates (except year) for dates that are directly related to an individual. These include dates of admission, discharge, birth, death, and ages over 89 and all elements of dates (including year) indicative of such age, except that such ages and elements may be aggregated into a single category of age 90 or older.
4. Telephone numbers
5. Fax numbers
6. Electronic mail address
7. Social security numbers
8. Medical record numbers
9. Health plan beneficiary numbers
10. Account numbers
11. Certificate/license numbers
12. Vehicle identification and serial numbers, including license plate numbers
13. Device identifiers and serial numbers
14. Web URLs
15. Internet protocol (IP) addresses
16. Biometric identifiers, including fingerprints and voice recordings
17. Full-face photos and comparable images
18. Any other unique number, characteristic, code that could reasonably be used to identify an individual.

Information that includes any one of the above criteria is classified as Individually Identifiable Health Information (IIHI). When IIHI is transmitted or stored in any medium by a LSUHSC-S (and/or University Health) it becomes Protected Health Information (PHI) that is protected by the Privacy Rule.

Generally, PHI is transmitted/stored by an institution as part of a Designated Record Set that includes medical records, billing records, and any other record that is used to make decisions about the health care of an individual.

### **F.14.3 What types of Research are Subject to the Privacy Rule?**

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As a general rule, if your research uses PHI that is created or received by LSUHSC-S (and/ or University Health) (e.g. medical or billing records), then it is subject to the Privacy Rule.

This may include, for example:

- Research that accesses PHI from a medical record, or creates PHI that will go back into a medical record, or
- Research that includes billable services to research subjects, such as clinical trials.

Research that may not be subject to the Privacy Rule is discussed below. For other types of research, the IRB/Privacy Board may waive some Privacy Rule requirements if specific criteria are met, as discussed below.

### **F.14.4 How does the Privacy Rule affect Research?**

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The Privacy Rule is extremely complex and required LSUHSC-S to put into place a number of policies and procedures. The major requirements for investigators are:

1. Application materials for research protocols that are submitted to the IRB/Privacy Board contain questions relating to the privacy of study subjects. Investigators must explain what measures will be taken to protect the subjects' privacy and how protected health information is received and stored.
2. If an investigator wishes to review currently existing medical records or records maintained in other databases at LSUHSC-S and/or University Health for research purposes, IRB/Privacy Board approval is required. A copy of the approval notice should be attached to a Data Request Form and submitted by the investigator to the appropriate report writer.
3. Authorization Forms are to be signed by the study subject, which gives the investigator permission to use and share the subject's protected health information. This is done at the same time Informed Consent is obtained.
4. Rigorous criteria are used by the IRB/Privacy Board to waive the requirement for informed consent and privacy authorization. Most research that is subject to the Privacy Rule will not qualify for a waiver.

If the authorization requirement is waived in a research study, the Privacy Rule requires that the investigator adhere to the Minimum Necessary Standard, which means that all reasonable efforts must be made to limit the use and disclosure of protected health information to the minimum amount necessary to accomplish the research.

The Privacy Rule also requires that all disclosures be tracked in research studies where

authorization is not obtained. The purpose of this tracking requirement is to provide research subjects, upon their request, with a list of how protected health information was released to external entities without their knowledge. A Disclosure refers to the release of protected health information to anyone or any entity outside of the organization that created or received the PHI as well as to external research collaborators and sponsors.

Tracking is not required when PHI is shared with researchers within their own organization. The Privacy Rule refers to this as 'Use'.

5. In some cases, a Business Associate Agreement is needed between investigators and outside entities who are providing research-related services like consulting, statistical analysis, and subject screening, prior to those entities obtaining access to protected health information.

#### **F.14.5 Does the Study Involve Protected Health Information?**

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The IRB/Privacy Board, not the investigator, is responsible for determining whether or not a research study is subject to the Privacy Rule. The IRB/Privacy Board will make this determination based on information provided by the investigator on the IRB application for a research protocol. As discussed above, a research study is subject to the Privacy Rule if it uses protected health information that is created or received by the institution. This includes most research that involves:

- Access to patient medical records,
- Creation of new data that is put into patient medical records, or
- Billable services that may be recorded in billing records (e.g. clinical trials).

If a research study is subject to the Privacy Rule, then it is the investigator's responsibility to choose the appropriate mechanism for accessing PHI in compliance with the Privacy Rule. In most cases, investigators will be required to obtain written authorization from subjects in human studies in order to use/disclose the subjects' PHI. This requirement will be waived only if the study meets stringent criteria. Alternatively, investigators may use health information in which identifiers have been reduced or eliminated.

#### **F.14.6 How do investigators access Protected Health Information in compliance with the Privacy Rule?**

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There are SIX (6) METHODS to obtain PHI access for research.

1. Authorization for Research Uses and Disclosure
2. De-identifying Protected Health Information
3. Limited Data Set and Data Use Agreement
4. Waiver or Alteration of the Authorization Requirements

5. Activities Preparatory to Research
6. Research on Decedents Protected Health Information

## 1. When Authorization is obtained for Research Uses and Disclosure

The Privacy Rule establishes the right of a research subject to authorize a covered entity to use and disclose his/her PHI for research purposes by signing an Authorization form. This requirement is in addition to the informed consent to participate in research required by federal regulations and LSUHSC-S policy. The Privacy Rule imposes more specific requirements for authorization to use/disclose PHI.

- See also: What do I need to know about a subject's ability to revoke authorization?
- Minimum Necessary Standard does not apply: When written authorization for use/disclosure of PHI is obtained from research subjects, the Minimum Necessary standard does not apply. However, investigators are encouraged to limit PHI uses/disclosures to the minimum necessary to accomplish the research goals.

Tracking of Disclosures is not required: When written authorization for use/disclosure of PHI is obtained from research study subjects, the tracking of disclosures is not required.

You are required to place a copy of the signed HIPAA Authorization along with the signed and dated consent document in the subjects medical record also for drug studies, place a copy of the IDIR in the subjects medical record and for device studies place a copy of the label and instructions for use in the subjects medical record.

## 2. De-Identified Protected Health Information

If no direct identifiers are needed to accomplish a research study, investigators are encouraged to use De-Identified Information.

The Privacy Rule provides allows two methods of de-identification: 1) a formal determination by a qualified expert; or 2) the removal of all of the 18 elements listed in Table 1 that relate to an individual, or the individual's relatives or employer as well as absence of actual knowledge by the covered entity that the remaining information could be used alone or in combination with other information to identify the individual (e.g. a rare diagnosis, condition, treatment or procedure which would allow the individual to be identified).

- Minimum Necessary Standard does not apply if only de-identified data is used in the research.
- Tracking of Disclosures is not required if only de-identified data is used to conduct the research.

De-Identified information can usually be obtained from data repositories, registries or publically available databases.

Coded Data: Coded data is linked to direct identifiers using a code. The Privacy Rule permits covered entities under the Rule to determine that health information is de-identified even if the health information has been assigned, and retains, a code or other means of record identification, provided that:

1. the code is not derived from or related to the information about the individual;
2. the code could not be translated to identify the individual; and
3. the covered entity does not use or disclose the code for other purposes or disclose the mechanism for re-identification (see HHS guidance entitled, Institutional Review Boards and the HIPAA Privacy Rule, page 6, Q and A #3, at [http://privacyruleandresearch.nih.gov/pdf/IRB\\_Factsheet.pdf](http://privacyruleandresearch.nih.gov/pdf/IRB_Factsheet.pdf)).

However, OHRP under 45 CFR 46 would ordinarily consider such private information to be individually identifiable to the investigator if that private information retains a link to the subject's records. However, OHRP does not ordinarily consider such information to be individually identifiable to the investigator if (1) the investigator and the holder of the individually identifying information sign an agreement prohibiting the release of individually identifying information to the investigator under any circumstances, or (2) there are other legal requirements prohibiting the release of the link to the investigator.

### 3. Limited Data Set Provisions

If only a limited number of specific direct identifiers are needed for a research study, investigators may use a Limited Data Set. This "middle" option between de-identified and fully identifiable information allows investigators to retain the following data elements in a data set:

- o Town, city, state, and the 5-digit zip code (but not street address);
- o Dates such as birth date, admission date, discharge date, and date of death; and
- o Unique numbers, characteristics, and codes.

All other identifiers listed in Table 1 are to be excluded to qualify as a Limited Data Set.

Recipients who receives protected health information under the limited data set provisions are required to sign a Data Use Agreement. The data use agreement generally describes the permitted uses and disclosures of the information and prohibits re-identifying or using the information to contact individuals. The required elements of a data use agreement are:

- The recipient will use the PHI contained in the data set only as permitted by the Privacy Rule;
- Limits will be placed on who can use or receive the data;
- The recipient agrees not to re-identify the data or to contact the research subjects;
- Appropriate safeguards will be used to prevent use/disclosure of the limited data set other than as permitted by the data use agreement and the Privacy Rule or as required by law.

Minimum Necessary Standard applies: Limited Data Sets are subject to the Minimum Necessary standard. Investigators are to obtain only the identifying data elements that are necessary to accomplish the research goal if using a limited data set to conduct their research. This will be monitored by the IRB/Privacy Board and enforced through the provisions of the Data Use Agreement.

Tracking of Disclosures is not required: Disclosures of Limited Data Sets are subject to provisions of the Data Use agreement.

#### 4. Waiver of Authorization

Many research projects and protocols cannot be undertaken using health information that has been de-identified. Also, it may not be feasible or practicable for a researcher to obtain a signed Authorization for all PHI the researcher needs to obtain for the research study. To address these and other situations that may arise in the course of a research project or protocol, the Privacy Rule contains criteria for waiver or alterations of Authorizations by an IRB or a Privacy Board.

For research uses and disclosures of PHI an IRB or Privacy Board may approve a waiver or an alteration of the Authorization requirement in whole or in part. A complete waiver occurs when the IRB or Privacy Board determines that no Authorization will be required for a covered entity to use and disclose PHI for a particular research project.

A partial waiver of Authorization occurs when an IRB or Privacy Board determines that a covered entity does not need Authorization for all PHI uses and disclosures for research purposes, such as disclosing PHI for research recruitment purposes (See Activities Preparatory to Research).

The IRB/Privacy Board may waive authorization to use/disclose PHI of research subjects only if the investigator provides documentation that ALL of the following conditions have been satisfied:

1. The use/disclosure of the PHI involves no more than minimal risk to the privacy of the research subjects, based on the presence of at least the following elements:
  - i. An adequate plan to protect the identifiers from improper use and disclosure;
  - ii. An adequate plan to destroy the identifiers at the earliest opportunity consistent with the conduct of the research, unless there is a health or research justification for retaining the identifiers or such retention is otherwise required by law; and
  - iii. Adequate written assurances that the PHI will not be reused or disclosed to any other person or entity, except as required by law or for authorized oversight of the research project;
2. The research could not be practicably conducted without the waiver; and
3. The research could not be practicably conducted without access to and use of the PHI.

Minimum Necessary Standard applies: The use/disclosure of PHI subject to a waiver must be held to the minimum necessary to achieve the research purpose.

Tracking of Disclosures is not required: Tracking will be required when the authorization of the subject has been waived by the IRB/Privacy Board and the information is being disclosed outside the covered entity.

## 5. Activities Preparatory to Research

Under the preparatory to research provision, a covered entity may permit a researcher who works for that covered entity to use PHI for purposes preparatory to research as long as the investigator agrees to the following: (1) the use or disclosure is requested solely to review PHI as necessary to prepare a research protocol or for similar purposes preparatory to research, (2) the PHI will not be removed from the covered entity in the course of review, and (3) the PHI for which use or access is requested is necessary for the research.

However, an investigator who is not a part of the covered entity may not use the preparatory to research provision to receive PHI or contact prospective research subjects unless the IRB or Privacy Board approves a Waiver of Authorization in whole or in part as permitted at 45 CFR 164.512(i)(1)(i).

The preparatory to research provision of the HIPAA Privacy Rule at 45 CFR 164.512(i)(1)(ii) allows an investigator who is not a part of the covered entity to obtain contact information through a Partial Waiver of Authorization. This allows an investigator to obtain protected health information (PHI) as necessary to recruit potential research subjects.

For example, even if an IRB does not waive informed consent and individual authorization for participation in the study itself, it may waive authorization to permit the disclosure of protected health information as necessary for the investigator to be able to contact and recruit individuals into the study (Partial Waiver of Authorization).

The investigator must submit the research protocol and include the recruitment plan for IRB review and approval to obtain approval of the Partial Waiver of Authorization. The Privacy Rule requirements and conditions for a waiver for apply.

See HRP-502.3- Partial Waiver of Authorization for Recruitment to request a partial Waiver of Authorization for recruitment purposes.

## 6. Research on Decedents Protected Health Information

If a researcher is seeking access to decedents' PHI the researcher must present in writing to the covered entity's HIPAA compliance officer: (1) that the use and disclosure is sought solely for research on the PHI of decedents, (2) the PHI for which use or disclosure is sought is necessary

for the research purposes, and (3) documentation, at the request of the covered entity, of the death of the individuals whose PHI is sought by the researchers.

#### **F.14.7 What do I need to know about a subject's ability to revoke an authorization to use his or her protected information?**

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An individual always has the right to revoke consent to participate in the research. The Privacy Rule now requires that a research subject has the ability to revoke a previously signed authorization for investigators to use or disclose his/her protected health information for research. Investigators must honor this request, except to the extent they have already "relied on" the permission.

As an example, if investigators have already included a subject's protected information in the analysis of the data, the analysis can be maintained. In addition, investigators may continue using and disclosing protected health information that was obtained prior to the time the subject revoked his/her authorization, as necessary to maintain the integrity of the research study.

However, investigators may not use or disclose additional information that they have not yet accessed at the time the authorization is being withdrawn, except for purposes such as accounting for the subject's withdrawal, reporting adverse events, or complying with investigations.