



Human Research Protection Program Institutional Review Board Policies and Procedures Guidebook

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1.0 FEDERAL, STATE, AND UNIVERSITY REGULATIONS RELATED TO THE IRB

The LSUHSC-NO Human Research Protection Program (HRPP) is guided by ethical principles established by the World Medical Association, and its adoption of the Declaration of Helsinki, and the Belmont Report. These principles are implemented in consonance with applicable university, state and federal laws and regulations. Review by the LSUHSC-NO IRB is required for all research and related activities involving human beings and/or information and tissue from human beings conducted by investigators with an appointment (hereafter referred to as employee) at LSUHSC-NO.

As appropriate, LSUHSC-NO conducts its research and Institutional Review Board (IRB) oversight in compliance with the following federal regulations:

- The Code of Federal Regulations related to the Office for Human Research Protections (OHRP) authority (45 CFR 46, Subparts A-D) <http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html>
- The Federalwide Assurance with OHRP that LSUHSC-NO has adopted can be viewed at the OHRP website at <http://www.hhs.gov/ohrp/>. Note that while LSUHSC-NO has chosen not to formally extend the Common Rule to all of its human subjects research through its Federalwide Assurance (FWA), LSUHSC-NO adheres to the ethical principles established by the Belmont Report and their application as expounded in the Common Rule. This approach applies to all human subjects research conducted by this institution independent of the sponsorship of the project.
- Other federal agency Code of Federal Regulations (CFRs) incorporating the Common Rule or in addition to the Common Rule.
- The Code of Federal Regulations related to the Food and Drug Administration (FDA) <http://www.fda.gov> authority (Title 21 CFR Parts 50, 56, 312, 600 and 812.66) <http://www.gpoaccess.gov/cfr/index.html>.

As applicable, the Institution and IRB comply with the International Conference on Harmonization (ICH) "Guidance for Industry—E6 Good Clinical Practice: Consolidated Guideline." Generally this applies to FDA-regulated studies where data are submitted to the regulatory agency. When following ICH-GCP (E6), clinical trials are conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and are consistent with good clinical practice and the applicable regulatory requirements.

Approval of any submission to the IRB is contingent upon meeting all of the requirements of LSUHSC-NO's Human Research Protection Program (HRPP) policies detailed in this Guide, of 45 CFR 46 (Subparts A-D) for all federally-funded research, and 21 CFR 50, 56, 312, 600 and 812, including all operative Subparts, for FDA-regulated research. All other human subjects studies not OHRP- or FDA-regulated must adhere to the policies set forth in the current document. Submissions must also comply with all state and local requirements and laws. The HRPP looks to the LSUHSC-NO Senior Staff Attorney for advice on legal issues and to help resolve any conflicts between federal, state, and local laws.

It is the policy of LSUHSC-NO that all projects involving human beings and/or information or tissue collected from human beings must be presented to the IRB for a determination whether:

1. The project is human subjects research,
2. The human subjects research project can be given Exempt status under the regulations, or
3. The human subjects research project must have IRB review, approval, and continued oversight.

These determinations are made, as described in the following sections, by the Chair or his/her designee. As part of these considerations and based upon guidance provided by OHRP at (<http://www.hhs.gov/ohrp/policy/engage08.html>) and the definition of human subjects research provided in the next section, the Chair and/or designee makes a determination whether the investigator and institution are engaged in human subjects research. Requests for a determination should be made through an email to the IRB.

Policies and procedures of the LSUHSC-NO IRB are described in the following chapters. All regulatory documents and these policies must be understood and adhered to by all investigators. Questions regarding human subjects protection and related issues should be directed to the HRPP staff and/or Chair of the IRB.

1.1 Definition of Human Subjects Research

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.

A "*systematic investigation*" is an activity designed to test an hypothesis, permit conclusions to be drawn, and thereby to develop or contribute to generalizable knowledge.

"*Generalizable knowledge*" is expressed, for example, in theories, principles, and statements of relationships. This is information that will potentially be useful to society in general as opposed to information that is specific to the operation of a unit or entity usually within an organization.

Human subject means 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.

A "*human subject*" includes an individual on whose specimen a device is used. This means that for medical device studies involving *in vitro* diagnostics and unidentified

tissue specimens, the FDA defines the unidentified tissue specimens as human subjects.

Specifically when following FDA regulations, *human subject* means an individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject might be either a healthy individual or a patient. For research involving medical devices a human subject is also an individual on whose specimen an investigational device is used.

Additionally under FDA regulations, *research* means that 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, or need not meet the requirements for prior submission to the Food and Drug Administration under these sections of the Federal Food, Drug and Cosmetic 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 terms research, clinical research, clinical study, study, and clinical investigation are synonymous for purposes of FDA regulations. (21 CFR 50.3(c), 21 CFR 56.102(c).

As described in the previous section of this Guide, human subjects research must have approval from the IRB before initiation of the project. Some activities involving human beings are not necessarily research and IRB approval and oversight may not be required. Examples of such activities are quality improvement projects or single patient case reports. However, as presented earlier, determinations of whether a project is human subjects research requiring IRB approval can only be made by the IRB Chair or the Chair's designees.

If you require additional assistance call the IRB office at (504) 568-4970.

2.0 RESPONSIBILITIES AND FUNCTIONS OF THE HEALTH SCIENCES CENTER ADMINISTRATION

2.1 Administration of the IRB by the IO

The administration of the LSUHSC-NO has delegated to the IRB the full authority of the Chancellor's Office for the conduct of the program. The Chancellor has designated the Vice-Chancellor for Academic Affairs as the Institutional Official for the IRB. The IO provides oversight and guidance to the HRPP and IRB Chair and exercises functions that require official action. The day-to-day conduct of the program will be the responsibility of the Chair or Vice-Chair of the IRB. While the Chair answers directly to the Vice-Chancellor for Academic Affairs, the Chair has the authority to interact directly with the Chancellor (Chief Executive Officer of LSUHSC-NO) if needed. Specifically, the IO for the administration shall:

- A. Maintain active files for all investigators submitting protocols to the IRB for approval
- B. Ascertain that all proposals are screened relative to the need for IRB evaluation

- C. Allocate resources to provide necessary support services for the IRB and financial and personnel support to assure the HRPP can adequately protect the rights and welfare of study participants
- D. As appropriate, transmit to the US Department of Health and Human Services (DHHS) all actions on DHHS-supported activities, and transmit to other federal agencies actions taken on activities supported by those agencies
- E. The IO is designated as the Signatory Official on the Federalwide Assurance with OHRP. The Chair completes FWA submissions, updates, and renewals to maintain that institutional policies are in compliance with the U.S. federal regulations for the protection of human subjects in research.
- F. Make certain that all recommended actions are initiated pursuant to IRB decisions
- G. Present appropriate and ongoing educational opportunities for IRB staff, Board members, investigators and others, concerning human subjects protection, related federal regulations and IRB policies and procedures
- H. The IO will evaluate the Chair, and the Chair will evaluate the staff annually to make certain that the professional staff is informed as to the responsibilities of the institution for protection of human subjects, for meeting attendance and minute notes, and accuracy and quality of their IRB work, among other things. Feedback is provided individually regarding any areas for improvement.
- I. Develop necessary arrangements with affiliated and other institutions for mutual assurance of protection of human subjects
- J. Implement FDA regulations and transmit reports regarding investigational new drugs, devices, and biologics
- K. Provide the liaison and channeling of appropriate information among staff, IRB, the administration, and governmental agencies
- L. Exercise a continuous surveillance of the IRB program by:
 - 1. Reviewing all grant applications and clinical trials and research agreements to determine that IRB review has been instituted where required. The functions of the HRPP are separate from Post-award Sponsored Research functions. Those persons who are responsible for business development are not allowed to serve on the IRB or carry out day-to-day operations of review process
 - 2. Maintaining files on IRB actions
 - 3. Reviewing IRB activities to make certain that the guidelines are being implemented to adequately protect subjects
 - 4. Reviewing HRPP activities for Quality Improvement with the goal of assessing compliance with organizational policies and procedures and applicable laws, regulations, codes, and guidance, to ensure compliance with all federal, state, and organizational laws, regulations, policies and professional standards. To measure compliance, the HRPP annually

plans to assess a certain percentage of research sites and IRB reviews for compliance with regulatory requirements. For example, the program might decide, in a given year, to evaluate 100% of clinical sites conducting FDA-regulated research; a 10% sample of non-clinical studies, or 100% of meeting minutes.

The HRPP uses site visits and HRPP records to assess compliance and make improvements, as described in Section 4.6 of this Guidebook, under *Post-Approval Monitoring*. The HRPP monitors research based on the complexity of the research, degree of risk, and the qualifications and experience of the research site staff. Periodic site visits enable the HRPP to assess compliance with applicable laws, regulations and policies, and verify that research is conducted in accordance with the IRB-approved protocols. Periodic review of IRB records enables the HRPP to determine compliance with regulations, laws, and policies.

The HRPP conducts a not-for-cause site visit at selected facilities where clinical research is being conducted at least once per year; the HRPP conducts site visits when the IRB directs an audit to assess compliance (for-cause audits); The HRPP audits a sample of studies on a quarterly basis to monitor the IRB's compliance with regulations. Sample audit activities include auditing meeting minutes for quorum and required regulatory determinations, or consent documents for required disclosures. Results are reported to the IRB.

5. Continually monitoring IRB processes and practices for improvement in the protection of subjects
6. Carrying out an HRPP Quality Improvement plan which periodically assesses the quality, efficiency or effectiveness of the program. Goals of the plan are, for example,
 - to increase the level of quality of research submissions received,
 - to generate fewer requests for changes to applications,
 - to lower the incidence of compliance issues, among other things.

On an annual basis the HRPP uses the following types of measures to assess whether program performance meets targets (these are examples; actual measures may vary depending on the need to evaluate performance of different aspects of the program, and new measures may be added as required):

- Time required for review of new FB applications (target= ≤ 3 hours)
- Time required for Board deliberation of new FB applications (target $\leq \frac{1}{2}$ hour)
- Time required to compose PI memo with Board-mandated changes to new FB study (target ≤ 1 hour)
- Individual investigators needing to be educated re: submission of new protocols (target $< 15\%$)

- Incidence of compliance issues occurring in a quarter (target <2)
- Individual investigators needing to be educated re: compliance (target <5%)

Results are reported to leadership. The program uses the information to design and implement improvement plans.

The program will review national benchmarks annually (such as AAHRPP's published data) and review to determine whether LSUHSC-NO HRPP meets these benchmarks and to help determine whether changes are indicated in HRPP processes and procedures.

In addition, satisfaction surveys are sent to investigators and the study team with each study approval packet, to be returned, if desired, with signed Assurance letters. The results are tabulated periodically and adjustments to the program made as warranted.

7. On an annual basis, a formal evaluation meeting of the Institutional Official, IRB Chair, IRB Vice-Chair, selected members of the IRB, HRPP/IRB staff, and selected PIs and research coordinators is conducted to determine whether resources for the HRPP/IRB are adequate to properly protect the rights and welfare of research participants. The evaluation includes, but is not limited to, the following areas: space, personnel, HRPP education program, legal counsel, Conflict of Interest, quality improvement plan, community outreach and functioning of the IRB. If needs or deficiencies are identified by this group, action is taken to enhance processes, augment resources and rectify deficiencies to enhance participant protection.
8. Evaluation by the Chair, designee or staff, on an annual basis, of the effectiveness of outreach activities with regard to participant recruitment of minority and medically-underserved populations, and educational initiatives in the community. Results are assessed in light of these items and outreach activities are altered appropriately according to the results of the evaluation.

2.2 IRB Disapproval

IRB disapproval and other decisions of the IRB cannot be overruled by the Health Sciences Center administration. However, approvals may be overruled by the Chancellor's office if in the best interest of the institution.

Project directors or principal investigators (PI) may appeal IRB disapprovals or restrictions on approvals to the IRB. If the PI wishes to further challenge any decisions made by the IRB, the PI must initiate the process through the Institutional Official, the Vice-Chancellor for Academic Affairs. Such appeals must be filed by the PI within 30 days of action by the IRB.

2.3 Research Funding

Funds for any research project may be withheld at the discretion of the administration.

3.0 THE INSTITUTIONAL REVIEW BOARD

3.1 IRB Authority

The Board is designated as the Institutional Review Board (IRB) and is responsible for reviewing all research projects involving the use of human subjects to determine that (a) the risks to the subject are so outweighed by the sum of the benefits to the subject and the importance of the knowledge to be gained, as to warrant a decision to allow the subject to accept those risks; (b) the rights and welfare of the subject are adequately protected; and, (c) legally effective informed consent is obtained by adequate and appropriate methods. As defined by federal regulations, IRB authority extends to any study using live human subjects, or data, or tissue collected from live humans. It is also an institutional policy that IRB approval must be obtained to collect and use in a study any tissue collected from a cadaver when that individual had been identified before death as a person from whom tissue is needed for a research study.

LSUHSC-NO grants the IRB the authority to approve, require modifications to secure approval, and disapprove all research activities overseen and conducted by the organization; to suspend or terminate IRB approval of research not being conducted in accordance with the IRB's requirements or that had been associated with unexpected serious harm to participants; to observe, or have a third party observe, the consent process and the conduct of the research.

The Health Sciences Center administration may not approve research which has not been reviewed and approved by the IRB.

The IRB interacts directly with the departmental heads and center directors of the schools within the Health Sciences Center. Principal investigators must contact their departmental head before submitting an application to the IRB. The IRB accepts applications from the principal investigator only after signature of the departmental head or center director is obtained. The departmental head or center director's signatures verifies that: (a) the principal investigator has permission to conduct the study if approved, (b) the IRB application, protocol, and related documents have been reviewed and are recommended for submission to the IRB, (c) the principal investigator has the expertise to conduct the study, and d) the principal investigator is an employee in good standing at LSUHSC-NO.

The Board reviews all human research activities conducted by employees of LSUHSC-NO only. Student-conducted (student, fellow, resident, and others in training without a faculty appointment) research must be supervised by an LSUHSC-NO faculty mentor. The IRB application must be submitted by that mentor, who will assume the role and responsibilities of principal investigator. The approval is given to the principal investigator (faculty mentor).

Any research that involves human subjects, conducted by LSUHSC-NO employees (both full and part-time) regardless of the location of the study must be evaluated and approved by the LSUHSC-NO IRB before initiation of the project. For example, if studies are to be performed at other institutions, all LSUHSC-NO employees must apply to the LSUHSC-NO IRB even if their participation is limited to that of co-investigator or other roles. Approval by the LSUHSC-NO IRB for its employees does not extend to individuals on the project who are not LSUHSC-NO employees. Those individuals must seek IRB review from their IRB of record. LSUHSC-NO IRB is the IRB of record for all of its employees (both full and part-time). Prior to initiation, any human subjects research conducted by Gratis faculty in LSUHSC-NO facilities or through an award made to or contract with the Institution must also be evaluated and approved by the LSUHSC-NO IRB.

Categories listed as exempt by the federal regulations must also be submitted for review and approval by the IRB. Exempt research must be evaluated by the IRB as to its fulfillment of the ethical standards to which this Institution adheres: the research must hold out no more than minimal risk to participants; selection of participants must be equitable; if there is recording of identifiable information, there are adequate provisions to maintain the confidentiality of the data; and there are adequate provisions to maintain the privacy interests of participants. If there are interactions with participants, the IRB will determine whether there should be a consent process that will disclose information such as: the activity involves research; a description of the procedures; participation is voluntary and may be discontinued at any time; whether participation is anonymous; the name and contact information for the researcher.

The Board has the authority to require progress reports from the investigators, which it does in the form of an Annual Report from the investigator on the study's status, and may take any other action it deems appropriate to oversee the conduct of any study. Although studies classified as Exempt under these policies, do not require re-approval and continuing oversight by the IRB, they must meet the ethical principles of the Belmont Report. Therefore, the IRB may require that subjects give informed consent prior to participation. Such decisions are predicated on the nature of the study and factors related to risk and confidentiality.

The LSUHSC-NO HRPP does not review new research applications involving prisoners using the exempt procedure. Any such new applications received by the LSUHSC-NO IRB are reviewed at a convened meeting of the IRB. This includes research involving interaction with prisoners, as well as research that does not involve interaction with prisoners.

While approval of an IRB application is given in the principal investigator's name, it should be understood that all investigators of the study have a responsibility to ensure that all IRB policies and procedures are adhered to during the conduct of the study.

Except as described in [Section 4.11](#) of this “Guidebook” for Cooperative Group Studies and [Section 5.29](#) for PETAL network studies, LSUHSC-NO is unable to accept IRB review by other institutions in lieu of the LSUHSC-NO IRB’s review. Reciprocity of IRB review is not permitted by this institution.

To assure compliance with all policies and regulations, the Board has been granted the authority by the institution to conduct audits of all study-related documents. In addition, the IRB, following a thorough investigation, may impose a corrective action plan that must be completed by all study team members. The Board may also take actions against any or all study team members including warning, reprimand, censure, or suspension and prohibition from conducting human subjects research at LSUHSC-NO and its facilities.

Any policies and procedures governing the IRB may be changed at a convened meeting. These changes require a vote by a majority of the Board members present, based on quorum.

The IRB interacts with all governmental agencies through the Vice-Chancellor for Academic Affairs.

3.2 Responsibilities of the Board

The IRB is charged with the duty of making certain that all activities involving human subjects conform to the following guidelines:

- A. The activity is based upon established and accepted procedures.
- B. The activity is conducted or supervised by a properly qualified individual.
- C. The activity is planned to include a critical evaluation of the possibility of risk or harm (physical, physiological, sociological or others, including invasion of privacy) as the consequence of this activity. The rights and welfare of the subject must be adequately protected, based on the above evaluation.
- D. The activity must have an objective whereby risks to the subject are so outweighed by the sum of the benefits to the subject and the importance of the knowledge to be gained as to warrant a decision to allow the subject to accept those risks.
- E. The activity can be initiated only after informed consent is obtained from the subject(s), documented by adequate and appropriate methods. These are delineated in the application form instructions.
- F. Any activity that does not conform to all state and federal guidelines or IRB-required procedures is subject to termination by the Board. The IRB can suspend or terminate approval of research that is not being conducted in accordance with the IRB’s requirements or has been associated with unexpected serious harm to participants.
- G. The activity must have sufficient scientific merit in the field of research to allow subjects to participate. For DoD applications, the IRB may rely on outside experts to provide an evaluation of the scientific merit.

3.3 The Composition of the IRB and Quorum

In order to promote complete and adequate review of research and research-related activities the IRB is comprised of 11 Primary, voting members with diverse backgrounds and experiences. IRB members represent a variety of professions and disciplines to assure appropriate expertise is available to evaluate applications. Alternate members may substitute for a Primary member for whom they are designated if a Primary member is not present or is recused. In this case, the Alternate member may vote; otherwise an Alternate may attend the meeting but may not vote on any action.

All members are appointed by the Chancellor of LSUHSC-NO. The Board is comprised of both males and females and at least one member whose primary expertise is in a non-scientific area. There is at least one member whose primary concerns are in scientific areas. At least one member represents the perspective of research participants. At least one member is not an employee or an immediate family member of a person affiliated with the institution. Membership is reviewed at the end of each academic year, although continual monitoring of membership is conducted to maintain needed diversity. Members are apprised of the membership reviews, changes in membership of the Board, and of other issues, such as individual requests for augmented meeting attendance or other suggestions during the next convened meeting.

A quorum of the Board is defined as a majority of the membership. Alternate members attending the meeting in a non-voting capacity do not count toward the quorum. No member may participate in the initial or continuing review of any project in which the member has a conflicting interest except to provide information requested by the Board. Members with conflicting interests will leave the meeting room during the deliberations and voting on said project and may not be counted towards the quorum for that vote. These recusals are documented in the minutes of each convened meeting, as is the attendance. The Chair, or presiding designee, determines establishment of quorum; this is recorded in the meeting minutes. At least one member whose primary concerns are in scientific areas must be present. At least one physician member must be present when considering FDA-regulated articles. When considering research that involves prisoners as subjects, the prisoner representative must be present. When research involves categories of participants vulnerable to coercion or undue influence, at least one member who is knowledgeable about or experienced in working with such participants must be present.

Minutes will indicate attendance at least 10 of 12 meetings of at least one unaffiliated member. At least one member who represents the general perspective of participants must be present. At least one member whose primary interest is in a non-scientific area must be present. Members must be present to vote, or may be present through teleconference, as all of the meeting materials are provided to the membership on the secure server. A majority of the membership present must vote in the affirmative for a motion to be accepted. If the quorum is lost during a meeting, the IRB cannot take action (vote) on any item until the quorum is restored. If required members (e.g., non-scientific) leave the meeting room, votes cannot be taken until required

members are present, even if half of the members are still present.

Information about the Board membership is available from the IRB office, 568-4970.

3.4 IRB Member Duties

The members are required to familiarize themselves with and to evaluate all applications (new and re-approval), amendments, and adverse events provided in the agenda book which is supplied to them prior to the IRB meeting and posted on a secure server available to all members. All materials related to a study are available for Board members' review at any time.

Members acting as primary reviewers are required to evaluate all applications, amendments and adverse events assigned to them by the Chair. Evaluation Forms are distributed to assist the members in performing their assessments. The forms must be completed prior to the meeting. During the meeting, the IRB member assigned as primary reviewer for an action item is expected to present their assessment and to lead a discussion of the Board concerning the item under consideration. All members are expected to contribute to a thorough discussion of all items. The primary reviewer presents a motion for consideration.

Members may also be needed for their expertise to evaluate special concerns that may arise on any study or to provide advice to the Chair concerning expedited review decisions, issues related to potential non-compliance, or necessary actions required to protect the safety and welfare of subjects.

Committees of the Board are utilized for special concerns, e.g. consideration of new policies, issues of non-compliance, etc. Committee members are appointed by the Chair based on the required expertise for the issue at hand. Committee reports are presented for consideration by the fully-convened Board.

No member of the IRB may participate in an initial or continuing review or other action of any project in which the member has a conflict of interest, except to provide information to the IRB. Should a conflict of interest exist, the member is responsible for notifying the IRB office one week prior to review. Members with a conflict of interest must recuse themselves from the meeting during deliberation and voting on the item.

Members are expected to familiarize themselves through educational opportunities provided by the Institution with regulations and policies and procedures related to IRB function and with issues surrounding human subjects protection.

The institution also supports the members of the IRB through the following:

1. Liability coverage for all IRB members is provided by the Institution.
2. Reference materials are available in the IRB office for members or principal investigators to assist in the review and/or preparation of applications.

3. Educational opportunities and materials related to IRB function and human subjects protection.

The IRB does invite individuals who are not members to serve as expert consultants for review of selected applications. These consultants serve in a non-voting, advisory-only capacity.

Members are also required to report any undue influence placed upon them by any person or office of the institution, or any other person or facility/institution related or unrelated to the institution. Members must report such attempts to the Chair of the IRB, Vice-Chancellor for Academic Affairs, Chancellor, or the Office of Compliance Programs. Action taken in response to such attempts will be dealt with in various ways depending upon the nature and source of the attempted undue influence. Should the report of undue influence be considered credible by the administration following an investigation by the Vice-Chancellor for Academic Affairs, actions taken may include, but are not limited to: a report and follow-up by the Committee on Professional Conduct, or other administrative action if the undue influence is created by any member or unit of LSUHSC-NO; or termination of any contract or agreement with an agency outside the institution.

3.5 The IRB Chair

The daily responsibility for the management and operation of the Board and the IRB Office is vested in the Chair. The Chair is selected and appointed by the Chancellor of the LSUHSC-NO. This selection is based upon the knowledge of the individual concerning human subjects protections and policies, regulations and processes related to the IRB. The Chancellor retains the sole authority to remove the Chair. The Board has designated one member to serve as Vice-Chair. The Vice-Chair has the full authority to act for the Chair in his/her absence. The persons serving in these capacities are evaluated by the Vice-Chancellor for Academic Affairs annually for their performance in these roles. Feedback is given directly to the Chair and Vice-Chair, such as level of attendance at meetings or the pace of the meetings.

A. Authority

1. Calls emergency sessions as needed
2. May require study modifications which can include suspension of enrollment when risks/complications arise that significantly endanger the subjects, pending discussion by the full Board
3. Requests files, reports, and additional data from principal investigators when the need arises
4. May require principal investigators to appear before the IRB when questions arise about any study
5. Votes as a member of the IRB
6. May approve responses to applications submitted to the Board that resulted in a vote of Modifications Required to Secure Approval. Consultation with another Board member(s) may be necessary

7. May approve minor modifications to ongoing protocols with possible agreement by another Board member(s). These are modifications that do not significantly affect the risk to the subject
8. May conduct an expedited review procedure as defined in federal regulations and exercise all of the authority of the IRB except disapproval
9. Presides at all meetings when present
10. Signs all official notifications from the Board

B. Responsibilities

1. Schedules monthly meetings
2. Sets the agenda for monthly or called emergency meetings
3. Provides for the distribution of the meeting agenda and meeting book that includes a permanent copy of the .111 criteria for approval of research proposals, all of the study materials to be considered at the meeting and notifications of expedited review activities conducted during the prior month
4. Provides for the taking of minutes, duplication of minutes, and distribution of minutes to IRB members in a timely fashion. All actions of the Board are documented in the minutes of each convened meeting as required by Federal regulations at 45CFR46.115(a)(2) and 21CFR56.115(a)(2), and the current policies detailed in this Guidebook.
5. Distributes literature to IRB members regarding human subjects protection and IRB concerns
6. Keeps an updated file on all studies submitted to the IRB
7. Maintains a file of curriculum vitae for all members of the Board
8. For the Institution, maintains active IRB registration with OHRP and FDA
9. For the Institution, through the Institutional Official, maintains an active Assurance with OHRP
10. Develops and manages educational opportunities for the HRPP
11. Helps arrange for audits of individual studies. These include "for cause - directed" and "non-directed" audits conducted as necessary in conjunction with the Office of Compliance Programs
12. Meets regularly with HRPP staff and IRB to review HRPP policies and procedures to help improve the program

4.0 OPERATING PROCEDURES OF THE IRB

The functions of the IRB include conducting initial and continuing review of all human research activities conducted at LSUHSC-NO. The Board also conducts evaluation of all amendments, revisions, changes, advertisement for subjects, adverse events and special situations brought to the attention of the Board or the Chair or Vice-Chair, or

any member. For all of these actions, the communication to the IRB office must be signed by the principal investigator.

4.1 Criteria for IRB approval of research (based on 45CFR46.111 and 21CFR56.111)

In order to approve research covered by this policy the IRB shall determine that all of the following requirements are satisfied. This includes all initial approvals (full-board review or expedited review), considerations for amendments to ongoing studies, and re-approval applications:

- A. Risks to subjects are minimized
 - 1. By using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and
 - 2. Whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes
- B. 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) as among those research risks that fall within the purview of its responsibility.
- C. Selection of subjects is equitable. In making this assessment the IRB should take into account the purposes of the research and the setting in which the research will be conducted and should be particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, handicapped, mentally disabled persons, or economically or educationally disadvantaged persons.
- D. 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 45CFR46.116 and/or 21CFR50.
- E. Informed consent will be appropriately documented, in accordance with, and to the extent required by 45CFR46.117 and/or 21CFR27.
- F. Where appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.
- G. Where appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

- H. When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, handicapped, 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.

Data Monitoring

The IRB must determine that the research plan is appropriate in making adequate provisions for monitoring data to ensure the safety of participants. The IRB might consider provisions such as:

Safety information to be collected, including serious adverse events; how it will be collected (e.g., with case report forms, at study visits, by telephone calls with participants); the frequency of data collection, including when collection starts; the frequency or periodicity of review of cumulative safety data. The plan might include establishing a data monitoring committee and a plan for reporting data monitoring committee findings to the IRB and the sponsor, including the frequency of reporting. For studies that do not have or are not required to have a data monitoring committee and are blinded, have multiple sites, enter vulnerable populations, or employ high-risk interventions, the IRB will carefully review the data and safety monitoring plan and determine whether a data monitoring committee is needed. If the study is not using a data monitoring committee, and if applicable, statistical tests will be employed for analyzing the safety data to determine whether harm is occurring. The IRB will determine provisions for the oversight of safety data (e.g., by a data monitoring committee) and conditions that trigger an immediate suspension of the research, if applicable.

Expedited versus Full-Board Review

Expedited review is a procedure through which certain kinds of research may be reviewed and approved without convening a meeting of the IRB. The FDA's IRB regulations [21CFR56.110] and OHRP regulations [45CFR56.110] permit, but do not require, an IRB to review certain categories of research through an expedited procedure if the research involves no more than minimal risk. A list of categories was last published in the Federal Register on November 9, 1998 [63 FR 60364-60367]. The list may be found at <http://www.hhs.gov/ohrp/policy/expedited98.html>. LSUHSC-NO adopts the expedited review procedures as its own.

The IRB may also use the expedited review procedure to review minor changes in previously-approved research during the period covered by the current approval.

Under an expedited review procedure, review of research may be carried out by the IRB chairperson or by one or more experienced members of the IRB designated by the chairperson. The Chair appoints experienced IRB members to conduct reviews of new studies, changes to approved studies, unanticipated problems, and re-approval applications using the expedited procedure. "Experienced" in this context refers to

IRB members who have served for a number of years and have reviewed diverse types of research, addressing issues which require extensive knowledge of regulations and policies. The reviewer(s) may exercise all the authorities of the IRB, except disapproval. Research may only be disapproved following review by the full committee. Approval criteria for expedited review are the same as those for full-board review.

The LSUHSC-NO HRPP does not review new research applications involving prisoners by the expedited procedure. Any such new applications received by the LSUHSC-NO IRB are reviewed at a convened meeting of the IRB. This includes research involving interaction with prisoners, as well as research that does not involve interaction with prisoners. For DHHS-funded research, the IRB Chair certifies to OHRP that the duties of the IRB have been fulfilled regarding Subpart C determinations.

Minor modifications to research involving prisoners may be reviewed using the expedited procedure, by either of the two procedures described as follows, based on the type of research.

- Minor modifications to research involving interaction with prisoners may be reviewed by the expedited procedure, if a determination is made that the research involves no greater than minimal risk for the prison population being studied. The prisoner representative must concur with the determination that the research involves no greater than minimal risk, and must review the research as a reviewer, designated by the chair, or consultant. This may be as the sole reviewer or in addition to another reviewer, as appropriate.
- Minor modifications to research that does not involve interaction with prisoners may be reviewed by the expedited procedure, if a determination is made that the research involves no greater than minimal risk for the prison population being studied. Review by a prisoner representative is not required, but the prisoner representative may review the research as a reviewer or consultant if designated by the IRB chair.

All members are advised of research studies or other action items that have been approved by expedited review during the preceding month through the Monthly Report of Expedited activities, which is made available to Board members before and during the IRB meeting and at any time thereafter.

4.2 Conducting Review of New Applications

Preparation instructions for submitting applications are contained in the Application Instructions. Information regarding investigational new drug (IND) and investigational device exemption (IDE) submission requirements are also included in the instructions.

New applications are accepted throughout the month. However, the DEADLINE for submission of any new application that requires Full-Board review is the last working WEDNESDAY of the month to be eligible for the next month's meeting.

Limits on the number of items scheduled on the agenda may be made at the discretion of the Chair or Chair's designee.

Upon receipt of a new application, the IRB office date-stamps and assesses the application for completeness. If the application involves a test article, it will be confirmed that the documentation includes a copy of an approved IND, IDE, or clinical trial certificate, where required. The FDA website will be queried to confirm this documentation. Waiver of the consent form may be granted at the investigator's request if all federal regulations apply (see [Section 5.8](#)). It is recommended that the investigator contact the IRB office prior to submission to discuss these regulations. The PI will be contacted for additional information and/or incomplete data. It must be understood that if the application is incomplete and is received immediately prior to the deadline the application may be ineligible for that review cycle. Consequently, it is very important for the PI to make certain that the application and all required material are complete before submission.

Also, upon receipt of a new application, an IRB Tracking Number is assigned for that protocol. A paper file is created as well as an electronic file in the IRB management software. These two files, paper and electronic, comprise the official record for the study. All future correspondence with the IRB must reference that tracking number. Correspondence that does not identify the IRB number will be returned without further action.

All new applications are evaluated by the Chair or designee to determine if they are eligible for expedited review according to 45 CFR 46.110 and 21 CFR 56.110, and policies outlined in the present document. Applications qualifying for expedited review procedures must have an appropriately-formulated consent form depending upon the degree of risk, unless a waiver is requested. The consent form is evaluated, and corrections may be required by the Chair or designee prior to approval. Applications for exemption are evaluated by the Chair or designee to determine if they are eligible for consideration under 45CFR46.101(b) and/or 21CFR56.104, and/or policies outlined in the present document. Approval for initiation of the study and the start of the approval period are set as the signing date of the Assurance by the Chair or the Chair's designee. The process of notification and receipt of investigator assurance is identical to Full-Board considered projects.

All new applications are slated for a specific agenda. Each new application requiring Full-Board review is evaluated by the Chair or Vice-Chair who assigns a primary reviewer. If there is not at least one person on the IRB with appropriate scientific or scholarly expertise or other expertise or knowledge to conduct an in-depth review of the protocol, the Chair invites an individual who has the appropriate scientific or scholarly expertise or other expertise or knowledge to conduct an in-depth review of the protocol to serve as an expert consultant on this protocol. The consultant will serve as the primary reviewer in the IRB meeting and will perform a review under

the same criteria as an IRB member; however, the consultant will not have voting privileges. The use of a consultant is documented in the minutes.

In addition to the application and consent form, the primary reviewer receives the expanded protocol and all other related materials, including: the investigator's brochure, DHHS-approved sample consent document, the complete DHHS-approved protocol, any relevant DHHS grant applications (when they exist); and the investigator's current curriculum vitae or other documentation evidencing qualifications. These materials are provided to the primary reviewer at least one week prior to the meeting. For initial review of research by a convened IRB, when they are scheduled to attend an IRB meeting, all members (including attending alternate members) are provided and review: the application which includes a protocol summary containing the relevant information to determine whether the proposed research fulfills the criteria for approval; the proposed consent document; recruitment materials.

All other material including the full protocol is available to all members, both before and during the meeting at which the application is reviewed. Agenda materials are provided to Board members approximately 1-2 weeks prior to the scheduled meeting at which they will be discussed. An electronic version of the agenda materials is posted on a secure website available only to IRB members and staff.

The application is reviewed at the next scheduled meeting. The Board evaluates each proposal with a full discussion on the merits of the full protocol. These include, but are not limited to, scientific merit, risk/benefit ratio to subjects, expertise of the investigator, etc. Particular emphasis is placed on the risks to subjects that may be encountered as a result of enrollment in the protocol. These risks may include, but are not limited to, medical, psychological, financial and social risks. To properly prepare the protocol for the review, the investigator must consult the Information Sheet.

If the research involves a device, a determination of Significant Risk (SR)/Non-Significant Risk (SR/NSR) must be documented by the IRB. Sponsors are responsible for making the initial risk determination and presenting it to the IRB unless one has already been made by the FDA. The following elements are considered by the IRB in a determination of SR/NSR for the device:

- *What is the basis for the risk determination?* The risk determination is based on the proposed use of a device in an investigation, and not on the device alone.
- *What is the nature of harm that may result from use of the device?* SR studies are those that present a potential for serious risk to the health, safety, or welfare of a subject.
- *Will the subject need to undergo an additional procedure as part of the investigational study, for example, a surgical procedure?* IRBs should consider the potential harm the procedure could cause as well as the potential harm caused by the device.

Nonsignificant Risk Device Studies

An NSR device study is one that does not meet the definition for an SR device study. If the sponsor identifies a study as NSR, the sponsor must provide the reviewing IRB an explanation of its determination (21 CFR 812.2(b)(1)(ii)) and should provide any other information that may help the IRB in evaluating the risk of the study.

Significant Risk Device Studies

Under 21 CFR 812.3(m), an SR device means an investigational device that:

- Is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject;
- Is purported or represented to be for use supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a subject;
- Is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety, or welfare of a subject; or
- Otherwise presents a potential for serious risk to the health, safety, or welfare of a subject

Once these criteria have been reviewed by the IRB, the determination is incorporated into the motion concerning action on the application.

During the meeting, the primary reviewer, which may be a consultant, presents a summary and leads a discussion of the study. The reviewer checklist provides a framework for the reviewer to present appropriate information related to the .111 criteria. Fulfillment of the .111 criteria is monitored by the Chair. The primary reviewer then makes a recommendation based on the review of the full protocol, application, consent forms, investigator brochure, related federal grant application, and any other related material. A motion is made and seconded, members are asked for comment, and the Chair calls for a vote. The vote is recorded on the Chair's vote sheet. Notification of the Board's decision is made to the principal investigator following the meeting.

Potential recommendations of the Board are:

Approval: No further changes needed; an assurance notice is prepared to finalize the approval process.

Modifications Required to Secure Approval (MRSA): Moderate revisions are necessary. Such modifications are generally administrative in nature, e.g., misspellings, missing header and footer information on informed consent documents, queries from the board to which a "yes" or "no" answer may be given by the PI, or the requirement by the Board that certain specific language as dictated by the Board be included in the informed consent document. Modifications in the study or answers provided in response to Board concerns will be reviewed in the IRB office by the Chair or Vice-Chair to assess that changes have been incorporated. The Chair may seek assistance of any member of the Board in this process. In most cases, these

modifications will not have to be re-assessed by the Full Board. However, if the Chair or any other Board member is not satisfied with the quality of the response, it will be re-assessed by the Full Board at an officially-convened meeting. When the modifications are approved by the Chair or Vice-Chair, an assurance notice is prepared to finalize the approval process.

Withheld: Extensive revisions needed. Such modifications are generally clarifications to allow the Board to better understand the protocol and informed consent document requirements. Examples are clarifications concerning study design, clarifications of protocol procedures, substantive changes to the informed consent document. Modifications must be re-submitted for Full Board review. In order to be assessed at the next meeting, changes must be received in the IRB office by the last working Wednesday of the month. The time-frame for return of the response will be short if the investigator wishes to have the application re-evaluated at the next scheduled meeting. The investigator should be prepared to attend the meeting to discuss his/her application if so requested by the Board.

Disapproval: The scientific or ethical problems posed by the study are of grave concern to the Board. The proposal cannot be re-submitted; a new proposal must be submitted to the Board. Modifications or clarifications would not be appropriate to resolve these issues.

4.3 Notification of Investigators Following Review

The IRB office notifies each investigator in written memo form of the review of their submission. The memo will outline the necessary actions, and upon receipt of that memo the PI makes the required corrections and modifications, or re-submits a new application. If a response is not received within the time-frame noted on the letter, the application will be rescinded. This would require that a complete new application package be submitted for consideration by the Board at a future meeting if the PI wishes to pursue the study.

4.4 Investigator Assurance and Notice to the Institutional Official

Upon IRB initial approval or approval after MRSA, the IRB office generates an assurance notice, which is addressed to the Vice-Chancellor for Academic Affairs (the Institutional Official). Two copies of this notice are prepared and sent to the PI, who must sign both and return them to the IRB office. The Chair or Vice-Chair signs both copies of the notice; this signature date is the approval date of the protocol.

The approval period is also stated on the assurance and is determined by the IRB based on the merit of the study and the level of risk to the subject. The approval period will not exceed one year. The initial approval period will begin on the date of the meeting at which the application was approved or determined MRSA. If the determination that a period of less than one year is required, the IRB may set any time-period as the appropriate interval and may change that interval at any time. The IRB may require progress reports from the principal investigator. The IRB has the authority to suspend, terminate or require changes at any time. If the Board requires any restrictions in the protocol, e.g., a limitation on the initial number of

subjects allowed before a report is provided to the IRB, this information is included in the written documentation. The duration of the approval period is tracked through a computer database to generate protocol continuing review notices.

One original of the signed assurance is returned to the investigator for their files, and the other is kept in the protocol file for that project. A copy is forwarded to the Vice-Chancellor for Academic Affairs. The IRB office also forwards to the investigator a signed, stamped copy of the first page of the approved consent form and any other approved study documents. No research activities can commence until the assurance is signed by the Chair.

4.5 Changes to an Approved Protocol

All changes to protocols must be reviewed and approved by the IRB prior to implementation. Principal investigators are required to request approval of any proposed changes in writing. The IRB requires that investigators sign a document prior to final approval stating that "The investigator agrees to report to the Committee any emergent problems, serious adverse reactions, or procedural changes that may affect the status of the investigation, and that no such changes will be made without Board approval, except where necessary to eliminate apparent immediate hazards to the subject." Changes in approved research that are initiated without IRB approval to eliminate apparent immediate hazards to the subject must be promptly reported within 30 days to the IRB, and are reviewed by the IRB to determine whether each change was consistent with ensuring participants' continued welfare.

The investigator must submit a cover memo with every change that outlines the addition, deletion, or revision with an assessment of the expected impact on the conduct of the study and the consent form. Investigators must also report to the IRB new information that might affect adversely the safety of the participants or the conduct of the clinical trial, and any changes significantly affecting the conduct of the clinical trial or increasing the risk to participants. A statement must also be submitted that the PI certifies that no other changes have been made to the protocol and the consent form. The Chair and/or Vice-Chair and staff review the proposed change to determine if the change is appropriate for expedited approval as defined by federal regulations and the policies detailed in the present document. Examples of such changes are the addition of a performance site, changes in the number of subjects, the addition or deletion of a co-investigator. These are minor modifications, defined as changes considered to be minimal risk that do not change the risk/benefit ratio as determined at initial review.

Significant changes, such as the addition of a risk to the informed consent document, change in drugs used in the protocol, changes in study design, or change in PI of a greater-than-minimal-risk study, do not meet the criteria for expedited review. Generally, these changes would potentially affect the risk/benefit ratio as determined at initial review. Such changes will be reviewed only at an officially convened Full-Board meeting. In that case, the amendment is assigned to a primary reviewer who evaluates the amendment and presents a summary to the Board. All Board members receive in their meeting book and review a description of the amendment along with

all modified documents. The IRB uses the criteria to approve modifications to previously approved research when the modifications affect one or more criteria. The Board discusses issues related to the amendment, including potential impact on the risk/benefit ratio of the study, and takes a vote as to whether to approve the amendment.

A copy of the new consent form with all changes "highlighted" must be submitted and a "non-highlighted" copy of the revised consent form must also be submitted.

The IRB cannot consider changes in investigator, sites, amendments, revisions, addendums, investigator brochures, advertisements for subjects, etc. without a memo from the PI that details the impact of those items on the consent form and the conduct of the study.

Regarding research involving prisoners, if a participant becomes a prisoner while enrolled in a research study that was not reviewed according to Subpart C criteria, the IRB applies Subpart C criteria to the research. The IRB will confirm that the participant meets the definition of a prisoner, terminate enrollment or review the research study under Subpart C criteria to determine if it is feasible for the participant to remain in the study. Before terminating the enrollment of the incarcerated participant the IRB will consider the risks associated with terminating participation in the study. If the participant cannot be terminated for health or safety reasons the investigator will a) keep the participant enrolled in the study and the IRB will review the research under Subpart C criteria; if some of the requirements of Subpart C criteria cannot be met, but it is in the best interests of the participant to remain in the study, the investigator will keep the participant enrolled and the IRB will inform OHRP (if appropriate) of the decision, along with the justification; or b) remove the participant from the study and keep the participant on the study intervention under an alternate mechanism such as compassionate use, off label use, etc. If a participant is incarcerated temporarily while enrolled in a study, and the temporary incarceration has no effect on the study, the investigator will keep the participant enrolled. If the temporary incarceration has an effect on the study, it will be handled according to the above.

It is the responsibility of the principal investigator to notify the Board of any changes to a study initially classified as exempt. At that time, the Chair or designee will re-evaluate the exempt status of the study and will notify the investigator if the IRB changes the study's status.

Upon final approval, the IRB office will forward to the investigator stamped, signed, and dated copies of the face page of any revisions or amendments, and a stamped, signed, and dated first page of the consent form.

All changes to a protocol must be approved by the IRB. Implementation of any changes to a protocol without IRB approval will be considered to be non-compliance with these policies. To assure that investigators do request modifications, the Board will monitor all submitted documents for any suggestion of changes. An additional method of insuring that protocol modifications are requested prior to initiation will be

follow-up of any reports of such incidences from patients, board members, other investigators, etc. The IRB may require additional reports at any time during any investigation and may review the project in order to ascertain whether the rights and welfare of the subjects are appropriately protected or whether the risk/benefit ratio of the study has changed. When necessary the IRB conducts selected evaluation of investigator records to assure compliance with all federal and state regulations.

4.6 Continuing Review

IRB review of approved protocols is on-going. Approval is granted for a set period of time as determined by the Board. This period of approval is granted for up to one year depending upon the nature of the study and the degree of risk to the subject. The expiration date is calculated as one year from the approval date minus one day. If the approval period is for less than one year, then it is always the number of months less one day. The purpose of IRB continuing review is to assure that (a) the risk/benefit of the research remains acceptable, (b) the informed consent process and documents are still appropriate and (c) the enrollment of subjects has been appropriate. The IRB may require information from outside sources to verify that no material changes have occurred since the previous IRB review. Investigators should notify the IRB of any premature closure or completion of a study.

Studies that are considered exempt at initial review do not require continuing re-approval. However, the investigator must notify the IRB if they wish to continue the study after one year and each subsequent year from the time of initial exempt determination. Further, investigators must notify the IRB of any changes to the protocol so that an evaluation may be made to determine whether the study remains exempt from IRB oversight.

As a courtesy, a notification reminder requiring an application for continuation is forwarded by e-mail to the principal investigator two months prior to the expiration of the current approval period. This form must be returned prior to the deadline listed. This continuation application must be completed in its entirety and, if initially required, accompanied by copies of the most recently-approved consent form and HIPAA Authorization document. Copies of the three most recently-completed informed consent documents, HIPAA authorization documents and Notice of Privacy Practices acknowledgement forms signed by subjects during the current approval period, with all identifiers redacted, must also be submitted with the re-approval application. Incomplete or late re-approval applications may result in suspension of all activities for that protocol. Investigators cannot enroll new subjects, continue participation of currently-enrolled subjects (unless medically indicated for safety), or continue data collection, etc. during any period not approved by the IRB. If the investigator does not receive a signed and approved Re-approval application form back from the IRB for any reason before the study's approval period expiration date, the study is considered to be administratively de-activated on the expiration date. The expiration date is the last date of the current protocol approval period. Investigators must refrain from enrolling any subjects until formal notice of continuation is received. It should be noted that under all circumstances the investigator is ultimately responsible for assuring that an application for continuation

and all renewal materials are supplied to the Board in a timely manner. All materials must be received in the IRB offices prior to the deadline listed in the e-mailed notification to assure review at the pertinent meeting.

All applications for continuation of an on-going protocol are date-stamped when received in the IRB office. Applications are matched to study folders and the packet is provided to the Chair for consideration.

All continuing review applications are evaluated by the Chair or designee to determine if they are eligible for expedited review and re-approval as defined at 45CFR46.110, 21CFR56.110 and the policies detailed in the present document. For studies receiving expedited re-approval, the continuation period will start on the day the Chair grants approval, but in no case will that period be for longer than one year. Under most circumstances, protocols that were originally given expedited review would receive expedited re-approval review by the Chair or designee. If changes are requested in the re-approval application the study must be re-evaluated to determine if it remains eligible for approval. If not eligible for expedited review or if the status has changed, the application is forwarded to the Full Board for review.

Applications which are complete and require Full-Board review for continuation are placed on the agenda for the pertinent Full Board meeting.

If it is determined that the study must receive Full Board consideration for re-approval, the Chair assigns a primary reviewer for the evaluation of the continuation of the protocol in the same manner used for new applications. A comment checklist is provided for the reviewer's summary and recommendation.

For continuing review of research by a convened IRB, when they are scheduled to attend an IRB meeting, all members (including attending alternate members) are provided and review: the application (which represents the status report on the progress of the research) including a protocol summary containing the relevant information necessary to determine whether the proposed research continues to fulfill the criteria for approval; the currently-approved consent document; any newly-proposed consent document. These are provided in each Board member's meeting book. During the meeting, the primary reviewer presents a summary and recommendation based on the review of the full protocol file kept in the IRB office. This material is available to all members prior to and during the meeting. Members are asked for comments, a motion is made and the Chair calls for a vote. The vote is recorded on the Chair's vote sheet. The IRB determines that the current consent document is still accurate and complete, and that any significant new findings that arise from the review process and that might relate to participants' willingness to continue participation will be provided to participants. Notification of the Board's decision is made to the principal investigator following the meeting. The approved re-approval application form indicates the new approval period. That approval period starts on the date of the meeting at which the application for continuation was considered and approved. In some cases, continuing approval will not be granted at the meeting and the application may be returned to the Full Board for review. If the IRB approves the research with conditions, the date of approval is the date the

conditions are determined to be met. If the protocol approval period expires before the conditions are reviewed and approved, all research activities must stop until approval is obtained. The period of approval in all cases will be for no more than one year. In some cases, the approval period will be for less than one year.

The principal investigator receives the document indicating the new approval period. Any restrictions or additional requirements imposed by the Board are also communicated to the principal investigator in writing.

The IRB computer file record is updated to indicate the start date of the new approval period.

In order to further assure that projects are being conducted per the IRB-approved protocol, the IRB management staff in conjunction with the LSUHSC-NO Office of Compliance Programs may conduct random “non-directed” audits of selected protocols. The HIPAA Privacy Officer examines study records for compliance with HIPAA Authorization requirements and an IRB Coordinator examines study records for compliance with all aspects of protocol and informed consent requirements. Any deficiencies are reported to the IRB Chair and procedures for handling issues of non-compliance are initiated.

Post-Approval Monitoring

In addition to continual review of projects when items for action are submitted for review by the IRB; e.g., SAEs, Unanticipated Problems, amendments, etc., and at the time of re-approval, the IRB and Office of Compliance Programs conduct a formal post-approval monitoring program to assure compliance with all aspects of the research study.

Study Self-Assessment

The IRB randomly selects studies each yearly quarter for which the study team must complete the LSUHSC-NO IRB Post-Approval Self-Assessment form. Based on the results of this process, studies may be selected for “non-directed” or “directed” (based on suspected non-compliance issues) audit by the IRB. These audits may be conducted in conjunction with the Office of Compliance Programs HIPAA. All study-related materials including, but not limited to, Case Report Forms, regulatory documents, communications with the Sponsor, signed informed consent documents, and source documents must be made available to the IRB for these on-site audits.

Audits conducted by the Office of Compliance Programs and HRPP

As time and resources permit, the Office of Compliance Programs and Privacy Officer conducts randomly-selected, non-directed audits of studies selected as described in the previous section that come under the aegis of the HIPAA Privacy Rule. Authorizations and acknowledgements of distribution of Notices of Privacy Practices are examined.

As described previously, during these same audits, staff of the HRPP examine the

general conduct of studies, regulatory documents, and informed consent documents.

Directed For-Cause Audits

Based on any information received by the IRB that might suggest an issue of non-compliance, the IRB and/or Office of Compliance Programs may conduct audits of the conduct of a study including all related study documents. Such information may come from document review, reports from study subjects, reports from study team members, or anyone having knowledge of potential non-compliance. Procedures for dealing with issues of non-compliance are initiated upon receipt of any allegation of non-compliance.

4.7 Unanticipated Problems Involving Risks to Subjects or Others Reporting *(Previously referred to as Adverse Event Reporting)*

Regulatory guidance providing the basis of this policy can be viewed at the following websites:

OHRP:

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

FDA:

<http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM126572.pdf>

The IRB must assess all Unanticipated Problems Involving Risks to Subjects or Others associated with any protocol conducted by LSUHSC-NO employees. For the purposes of this policy the term *unanticipated problems* will refer to Unanticipated Problems Involving Risks to Subjects or Others. The following definitions should be considered for such reporting:

DEFINITIONS

Adverse Event

Any untoward or unfavorable medical occurrence in a human subject, including any abnormal sign (for example, abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the subject's participation in the research, whether or not considered related to the subject's participation in the research. Adverse events encompass both physical and psychological harms. They occur most commonly in the context of biomedical research, although on occasion they can occur in the context of social and behavioral research.

Serious (in the context of an adverse event - SAE)

A serious adverse event (SAE) is defined as any adverse event that results in any of the following outcomes:

1. Death,
2. A life-threatening situation,

3. Inpatient hospitalization or prolongation of hospitalization,
4. A persistent or significant disability/incapacity,
5. A congenital anomaly/birth defect, or
6. 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 (examples of such events include allergic bronchospasm requiring intensive treatment in the emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse)

Unexpected

An incident, experience, or outcome (in terms of nature, severity, or frequency) given it is (a) not described in the research procedures as presented in protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) not characteristic of the subject population being studied.

Possibly Related

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.

Related

Related means that the incident, experience, or outcome was caused by the procedures involved in the research.

Unanticipated Problem Involving Risks to Subjects or Others

Unanticipated problems in general include any incident, experience, or outcome that meets all of 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; and
3. 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.

What Must Be Reported to the IRB

Adverse events:

OHRP considers adverse events that are unexpected, related or possibly related to

participation in research, and *serious*, to be the most important subset of adverse events representing unanticipated problems because such events always suggest that the research places subjects or others at a greater risk of physical or psychological harm than was previously known or recognized, and routinely 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.

However, other adverse events which are unexpected and related, or possibly related to participation in the research, but *not* serious, would also be unanticipated problems if they suggest that the research places subjects or others at a greater risk of physical or psychological harm than was previously known or recognized.

The list of problems that need reporting includes:

1. Internal adverse events that are unexpected, involve new or increased risks, and are related to the research.
2. External adverse events that are unanticipated problems involving risks to participants or others.
3. Changes made to the research without prior IRB approval in order to eliminate apparent immediate harm.
4. Other unanticipated information that is related to the research and indicates that participants or others might be at increased risk of harm.
5. New information that may affect adversely the safety of the participants or the conduct of the clinical trial.
6. Any changes significantly affecting the conduct of the clinical trial or increasing the risk to participants.

Again, such events routinely 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.

FDA believes that only the following AEs should be considered as unanticipated problems that must be reported to the IRB:

1. 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).
2. 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).
3. Multiple occurrences of an AE that, based on 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 a

higher rate in the drug treatment arm than in controls). A summary and analyses supporting the determination must accompany the report.

4. 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 human subjects. A discussion of the divergence from the expected specificity or severity must accompany the report.

5. 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 in the study represents a clinically-significant increase in the expected rate of occurrence (ordinarily, reporting would only be triggered if there were a credible baseline rate for comparison). A discussion of the divergence from the expected rate must accompany the report.

6. 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.

As suggested by OHRP and the FDA, SAEs meeting the previous descriptions must be reported to the IRB on the LSUHSC-NO Unanticipated Problem/SAE reporting form.

Incidents that are unanticipated problems that are not adverse events:

Only a small subset of adverse events occurring in human subjects participating in research will meet the three criteria for an unanticipated problem. However, there are other types of incidents, experiences, and outcomes which occur during the conduct of human subjects research that represent unanticipated problems but are not considered adverse events. For example, some unanticipated problems involve social or economic harm instead of the physical or psychological harm associated with adverse events. In other cases, unanticipated problems place subjects or others at increased risk of harm, but no harm occurs; e.g., the loss of a laptop computer containing health records.

What information must be included when reporting to the IRB?

The following information should be included when reporting **an adverse event that is unexpected, serious, and possibly related or related, or any other incident, experience, or outcome, as an unanticipated problem** to the IRB (Note that this information is captured in the LSUHSC-NO IRB Unanticipated Problem/SAE Reporting Form and should be promptly reported):

1. Appropriate identifying information for the research protocol, such as the title,

investigators name, and the IRB project number;

2. A detailed description of the adverse event, incident, experience, or outcome;
3. An explanation of the basis for determining that the adverse event, incident, experience, or outcome represents an unanticipated problem; and
4. A description of any changes to the protocol or other corrective actions that have been taken or are proposed in response to the unanticipated problem.

For subjects enrolled by LSUHSC-NO investigators (local or internal)

Note that this group of subjects may be enrolled in either multi-center trials where LSUHSC-NO is one of a number of participating sites, or a single-site study where LSUHSC-NO is the single site. These studies may be sponsored by commercial sponsors, the federal government, other organizations or institutions, or LSUHSC-NO.

The maximum time allowed between the recognition of a reportable event and fulfilling reporting requirements is as follows: all SAEs or unanticipated problems must be submitted in writing on the LSUHSC-NO Unanticipated Problem/SAE Reporting Form within 5 working days. Fatal and life-threatening local events must be reported within 48 hours.

For subjects enrolled by non-LSUHSC-NO investigators conducting multi-center studies where the PI is an LSUHSC-NO employee

In this case, SAEs and unanticipated problems are reported to the LSUHSC-NO principal investigator on the LSUHSC-NO Unanticipated Problem/SAE Reporting Form. The PI is then responsible for following reporting requirements as described for local subjects in the previous section of this policy.

For subjects enrolled by non-LSUHSC-NO investigators (non-local or external) where the PI of a multi-center trial is a non-LSUHSC-NO investigator

For non-local/external subjects, investigators should send to the IRB only the following reports of unanticipated problems:

1. Summary safety information or analyses of adverse events provided by the sponsor that describe significant changes in a product's safety profile.
2. Reports of individual adverse events only if they have significant implications for human subject safety (e.g., a report of acute hepatic necrosis) and are determined by the sponsor or are considered in the local PI's opinion to be an unanticipated problem.
3. Reports of aggregate data (e.g., analyses and line-listings of adverse events)

identifying serious unexpected adverse events.

4. Reports from a data monitoring committee (DMC), whether these describe concerns or identify no problem.

When received, these reports are reviewed by the Chair or designee to determine whether immediate action must be taken to protect the safety and welfare of participating subjects. If action is required, the investigator and institution are notified.

Note: Individual reports related to subjects enrolled by non-LSUHSC-NO investigators (non-local/external subjects) in a multi-center trial where a non-LSUHSC-NO investigator is the PI of the overall trial **will not be accepted by the LSUHSC-NO IRB unless they have been determined by the sponsor or are considered in the opinion of the local PI to be an unanticipated problem.** Such undetermined reports will be returned to the investigator/sponsor unless specific arrangements are made between the sponsor and the LSUHSC-NO IRB. This type of arrangement will only be considered in unusual circumstances. Only reports as described in this section of the unanticipated problem reporting policy will be accepted and reviewed by the IRB.

Review by the IRB

Upon receipt of the LSUHSC-NO Unanticipated Problem/SAE Reporting Form the IRB administrative office and the IRB Chair or designee will determine if immediate action must be taken to protect the safety and welfare of past and current subjects. Usually, input from other Board members is solicited to aid in this decision. If immediate action is needed, the Chair or designee may suspend enrollment or take other action until the report can be evaluated by the Full Board. This may require an emergency meeting of the Board.

The IRB Chair or designee will use this information to make a determination as to whether the investigator has correctly identified this event as an unanticipated problem involving risks to subjects or others. All SAEs occurring with subjects enrolled by LSUHSC-NO investigators will be discussed at a Full Board meeting if considered by the principal investigator and/or the IRB Chair or designee to be an unanticipated problem.

The Chair assigns the SAE or unanticipated problem to a primary reviewer who presents a summary to the Board. All Board members receive the SAE Reporting Form in their meeting book. Following a discussion of the event, the Board will make a final determination as to whether the event is an unanticipated problem involving risks to subjects or others, and then the Board determines whether any additional corrective action not taken by the sponsor is to be recommended, and whether corrective action or substantive changes must be made in the study. The investigator is responsible for informing the sponsor of the Board's decision.

Examples of corrective actions or substantive changes that might need to be considered by the IRB in response to an unanticipated problem include:

1. Changes to the research protocol which may have been initiated by the investigator prior to obtaining IRB approval to eliminate apparent immediate hazards to subjects;
2. Modification of inclusion or exclusion criteria to mitigate the newly-identified risks;
3. Modification of informed consent documents to include a description of newly-recognized risks
4. Provision of additional information about newly-recognized risks to previously-enrolled and past subjects;
5. Modification of the information disclosed during the consent process;
6. Notification of current participants when such information may relate to participants' willingness to continue to take part in the research;
7. Requiring current participants to re-consent to participation;
8. Implementation of additional procedures for monitoring subjects and the research, and the consent process;
9. Suspension of enrollment of new subjects;
10. Suspension of research procedures in currently-enrolled subjects;
11. Modification of the continuing review schedule;
12. Termination of the research; and
13. Referral to other organizational entities.

The IRB will then make a determination as to the course of action that must be taken as a result of the unanticipated problem and will report the unanticipated problem to institutional officials and as appropriate to the FDA, OHRP, and sponsor or funding agency. For OHRP and FDA, reporting will be within thirty days after the event is defined as an unanticipated problem.

For Studies Involving Devices

For clinical investigations of devices under FDA, Investigational Device Exemption (IDE) regulations, investigators are required to submit to the IRB and the sponsor a report of any unanticipated adverse device effect (UADE) occurring during an investigation as soon as possible, but in no event later than 10 working days after

the investigator first learns of the effect. These should be reported to the IRB on the LSUHSC-NO IRB Unanticipated Problem/SAE Reporting Form.

The investigational device exemption (IDE) regulations define an unanticipated adverse device effect (UADE) as “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”.

Sponsors must immediately conduct an evaluation of a UADE, and must report the results of the evaluation to FDA, all reviewing IRBs, and participating investigators within 10 working days after the sponsor first receives notice of the effect.

All local UADEs and sponsor evaluations of UADEs will be reviewed by the LSUHSC-NO IRB through the same processes as previously described in this section.

Other SAE/U.P. Reporting Responsibilities

Note that LSUHSC-NO investigators may have other reporting responsibilities to the FDA, DoD, sponsors and performance sites.

Medical Care Provided as a Result of AEs or participation in the study

During and following a participant’s participation in a clinical trial, and consistent with any contract between sponsor and the institution, the researcher ensures that adequate medical care is provided to a participant for any adverse events, including clinically-significant laboratory values, related to the clinical trial. 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. Researchers inform participants when medical care is needed for other illnesses of which the researchers become aware.

4.8 Non-compliance by investigators

Non-compliance is defined as any deviation from approved protocol specifications or violations of federal policies or the policies outlined in the present document by an investigator or study team member. Serious non-compliance consists of deviations that place study subjects at increased risk, whether physical, emotional, or to their protected health information. Continuing non-compliance occurs whenever such practices are not corrected by the investigators but are perpetuated.

Non-compliance that is neither serious nor continuing is dealt with administratively by the IRB. The investigators are made aware of the problem and agree to correct it. The IRB confirms this through review of revised practices and documentation.

The most common lapses in investigator compliance include unreported changes in protocols, misuse or non-use of the informed consent document, and failure to submit revised protocols, modifications to a protocol, and applications for continuing approval of studies to the IRB in a timely fashion. Problems such as these are often caused by communication difficulties. With the full cooperation of the investigator, these cases can be resolved by the IRB without jeopardizing the welfare of research subjects.

Occasionally, an investigator will either avoid or ignore an IRB request. Such cases present a more serious challenge to the IRB and to the institution. Regardless of investigator intent, unapproved research involving human subjects places those subjects at an unacceptable risk. When unapproved research is discovered, the IRB and the institution will act promptly to halt the research, assure remedial action regarding any breach of regulatory or institutional human subjects protection requirements, and address the question of the investigator's fitness to conduct human subjects research.

Any protocol deviation or violation is required to be reported by the study team to the IRB via the Protocol Deviation form. Any employee who suspects an issue of non-compliance has a duty to report either directly to the Compliance Office or to the IRB, and can do so anonymously. Due consideration will be given to any information provided, and either resolved administratively or investigated for further corrective action. Issues of non-compliance may be discovered during the study Self-evaluation audit process or a Compliance Office program audit. These are provided to the IRB.

When the IRB learns of an issue of alleged non-compliance with IRB policies and regulations, the Chair will contact the PI and/or other study team members to evaluate whether the occurrence may actually involve non-compliance. If, in the estimation of the Chair that is a case of serious or ongoing non-compliance, the Chair will send a "Letter of Inquiry" to all investigators listed as participating in the study. If the study in question is still open, the Chair will also make an immediate, initial determination as to whether subjects are being placed at risk as a result of the alleged non-compliance. In most circumstances, the Chair will confer with other Board members before making this determination. If the Chair determines that this is a case of serious and/or continuing non-compliance and subjects are being placed at risk, then the study will be administratively suspended. When study approval is suspended or terminated, the Chair considers actions to protect the rights and welfare of currently-enrolled participants. The Chair considers whether procedures for withdrawal of enrolled participants take into account their rights and welfare (e.g., making arrangements for medical care outside of a research study, transfer to another researcher, and continuation in the research under independent monitoring), and considers informing current participants of the termination or suspension. The Chair will also have any adverse events or outcomes reported to the IRB. All study-related activity, including new accrual, must be halted until completion of further investigation. If it is determined that subject safety may be compromised by termination of research activities, then intervention may continue per the approved protocol after consultation with the IRB.

The principal investigator must respond to a "Letter of Inquiry" within the time period specified in the "Letter". The "Letter" will open an inquiry, and based on the response from the principal investigator the matter will either be concluded and the "Letter" revoked or a full investigation will be conducted by the IRB. Usually a committee of the Board will be appointed by the Chair to assist in conducting an investigation. During this investigation, all study team members will be questioned by the IRB and documents related to the study will be reviewed.

Management by the convened IRB is initiated at the conclusion of the investigation; the results of the interviews and the audit are presented to the Board by the committee of the Board at a convened meeting of the IRB. IRB members receive a copy of the "Letter of Inquiry" if sent by the Chair along with any response from the investigators. The IRB may then conclude the investigation and develop a corrective action plan that must be completed by all study team members as required by the IRB. If appropriate, the IRB may require modifications to the protocol or to the information disclosed during consenting, additional information to be provided to past participants, current subjects to be re-consented, modifications to the continuing review schedule, monitoring of the research or the consent process, or referral to other organizational entities. The IRB may terminate approval for the study and/or take action against any or all of the investigators on the study. These actions may include, but are not limited to, warning, reprimand, censure, or suspension, or prohibition from conducting further human subjects research at LSUHSC-NO. Current participants are notified when such information might relate to their willingness to continue to take part in the research. Additional action may be taken by the Institution at the discretion of the Chancellor. All actions of the Board are communicated to the investigators involved and to the Vice-Chancellor for Academic Affairs. All actions of the Board may be appealed by contacting the Vice-Chancellor for Academic Affairs in writing within two weeks of receipt of the Board's decisions. As part of the appeal, investigators may request an appearance before the Board.

Likewise, suspensions and terminations by someone other than the convened IRB must be reported to and reviewed by the convened IRB.

Per federal policy, any serious or on-going non-compliance with DHHS human subjects regulations or the determinations of the IRB, including termination of IRB approval, must be reported to the sponsor of the study, institutional officials, OHRP, and, if applicable, the FDA. The maximum time allowed between the recognition of a reportable event and fulfilling reporting requirements is less than 30 days.

Anyone may report (and everyone is encouraged and expected to do so) any suspected non-compliance of researchers and study team members. This includes reporting by investigators, study team members, research participants, or other observers of human subjects research conducted by this institution and its ethical review process and oversight of these activities. Any allegations must be reported upon discovery. Reports may be made anonymously to the Chancellor's office, the Vice-Chancellor for Academic Affairs, the Office of Compliance Programs or the Chair of the IRB.

A thorough investigation will be initiated by the Chair of the IRB when the Chair receives notification of concerns directly, or via the Chancellor, Vice-Chancellor for Academic Affairs or Office of Compliance Programs. If the concern is expressed by a research subject, that participant will be contacted directly by the Chair to discuss the situation. The procedure for handling the investigation follows the steps detailed earlier in this section. At the conclusion of the investigation and deliberation by the IRB and Vice-Chancellor for Academic Affairs, if appropriate, any conclusions and/or actions taken by the IRB and/or institution will be communicated to the participant.

4.9 Schedule of Meetings

The IRB meets on the third Wednesday of each month. The deadline for applications to the IRB requiring full-board consideration is the last working Wednesday of the month prior to the next month's meeting, with no exceptions. Should the IRB receive more applications than can be safely considered and thoroughly discussed at an upcoming meeting, the Chair has the authority to delay review of some studies until the next available meeting. These decisions may be made, for example, upon time of receipt of the applications or number of applications received from an investigator or unit of the institution. Studies eligible for expedited review will be received throughout the month and given consideration as soon as possible.

The IRB office prepares an agenda and an official notification of the time and place of the meeting under the direction of the Chair. The agenda, previous month's minutes, new applications, continuing review applications, adverse event packets, and significant amendments to on-going protocols are distributed at least one week in advance of the meeting to all members of the Board. This book also contains a listing of new and re-approved studies reviewed and approved through expedited procedures by the IRB Chair or the Chair's designee. All other approvals made by the Chair through expedited procedures; e.g., minor amendments and SAEs not requiring Full-Board review are presented to the Board at the Full-Board meeting.

4.10 IRB Records

The written procedures and guidelines of the IRB are maintained in the "LSU Health Sciences Center-New Orleans Human Research Protection Program Institutional Review Board Policies and Procedures Guidebook" at <http://www.lsuhscc.edu/administration/academic/ors/irb.aspx>.

The IRB maintains an electronic and a written file for each pending and approved protocol. Combined materials contained in these files comprise the official Protocol File for a study. Written documentation of communication between the investigator and the IRB are maintained in this Protocol File. All correspondence, regardless of the source, including all correspondence between the investigator and the IRB, is maintained in the Protocol File. In order to allow a reconstruction of a complete history of IRB actions related to the review and approval of the protocol, the IRB records include copies of the Investigator brochure, if any; scientific evaluations, when provided by an entity other than the IRB; recruitment materials; consent documents; progress reports submitted by researchers; reports of injuries to

participants; records of continuing review activities; data and safety monitoring reports, if any; modifications to previously-approved research; unanticipated problems involving risks to participants or others; documentation of non-compliance; significant new findings; records for initial and continuing review of research by the expedited procedure, which include the justification for using the expedited procedure, actions taken by the reviewer, and any findings required by laws, regulations, codes, and guidance to be documented; the justification for exempt determinations.

These documents create a complete record of a protocol and its activity. Note that all correspondence between the investigator and the FDA and/or OHRP must be copied to the IRB and will be maintained in the IRB protocol files.

IRB records are accessible for inspection and copying by authorized representatives of federal agencies or departments at reasonable times and in a reasonable manner.

In compliance with Louisiana State Law, protocol files are maintained for ten years following closure of the study, at which time the files are destroyed. If a protocol is cancelled without participant enrollment, IRB records are maintained for at least three years after cancellation

Any pending study is administratively rescinded and destroyed if communications are not received from the principal investigator within a two-month period following a request for information. A new application must then be submitted if further consideration is desired of the Board.

All actions of the Board are documented in the minutes of each convened meeting as required by the current policies and Federal regulations at 45CFR46.115(a)(2) and 21CFR56.115(a)(2). IRB minutes document actions taken by the IRB; separate deliberations for each action; votes for each protocol as numbers for, against, or abstaining; attendance at the meeting; when an alternate member replaces a primary member; the basis for requiring changes in research; the basis for disapproving research; a written summary of the discussion of controverted issues and their resolution; for initial and continuing review, the approval period; the names of IRB or EC members who leave the meeting because of a conflict of interest along with the fact that a conflict of interest is the reason for the absence; required determinations and protocol-specific findings justifying determinations for a waiver or alteration of the consent process, research involving pregnant women, fetuses, and neonates, prisoners, children, or participants with diminished capacity.

Minutes are prepared by the staff and reviewed by the Chair or designee for completeness prior to presentation to the Board for review and approval. Board-approved versions of the minutes are maintained in the office of the HRPP, and electronically on the server. Documentation of actions taken by the Chair through expedited procedures are attached to and made a part of the minutes.

4.11 National Cancer Institute - Central IRB (Local Management Process)

A. Overview

Louisiana State University Health Sciences Center–New Orleans (LSUHSC–NO also referred to as the Institution) and the National Cancer Institute (NCI) have initiated an authorization agreement whereby LSUHSC–NO will defer to the Adult and Pediatric CIRBs on certain CIRB-approved national multi-center cancer treatment trials. Studies reviewed by the Adult CIRB include all Phase III Adult Cooperative Group treatment trials approved by CTEP (ACOSOG, CALGB, ECOG, GOG, NCCTG, NCIC CTG, NSABP, RTOG and SWOG). The Adult CIRB may review other CTEP-approved Phase III clinical trials that are approved by CTEP, even if the sponsor is not a Cooperative Group. The Board may also review Phase II studies for rare tumors that appear on the CTSU menu. Studies reviewed by the Pediatric (Ped) CIRB include all Pilot, Phase II, and Phase III Children’s Oncology Group (COG) treatment trials approved by CTEP and/or DCP. The Ped CIRB may review other trials approved by DCP, and also other federally-funded trials (i.e., via R01 grants). The Board may review other CTEP-approved clinical trials as directed by CTEP, even if the sponsor is not a Cooperative Group.

The CIRBs will conduct reviews of the following: initial and continuing reviews, amendments, non-local serious adverse events, local serious adverse events that are not listed in the protocol or that meet the criteria of unanticipated problems, all unanticipated problems, and all instances of noncompliance. The CIRBs will also address local context issues via the Annual Institution Worksheet About Local Context, the Annual Principal Investigator Worksheet About Local Context, and the Study-Specific Worksheet About Local Context.

As the Signatory Institution, LSUHSC-NO will monitor the conduct of the research locally. This monitoring will be accomplished by the LSUHSC-NO IRB staff, the Clinical Trials Review Committee (CTRC) stationed in the Stanley S. Scott Cancer Center (SSSCC), and the Pediatric Review Committee (PRC) stationed in Children’s Hospital on behalf of the Institution. The CTRC will be utilized by the Institution for studies that will be opened under the Adult CIRB. The PRC will be utilized by the Institution for studies that will be opened under the Pediatric CIRB. LSUHSC-NO will decide on a study-by-study basis whether to open a study through the CIRB – making the CIRB the sole IRB of Record for that study – or to conduct its own local, Full Board (LSUHSC-NO IRB) review. See the “Review Process for CIRB-Approved Protocols” section below for a detailed description of this process. The principal investigator will also inform the Institution through the LSUHSC-NO IRB staff and either the CTRC or PRC of all local SAEs, all local unanticipated problems, and all local protocol deviations/violations/instances of noncompliance. In addition, the principal investigator will inform the Institution of all CIRB activity regarding the study, including initial and continuing reviews, amendment reviews, and all other study-related activity or decisions. If LSUHSC-NO determines at any point that it is no longer appropriate for the CIRB to be the IRB of record for a given study, the Institution reserves the right to require the principal investigator to submit to the

CIRB the appropriate documents to transfer IRB review responsibility from the CIRB to the LSUHSC-NO IRB. Once this transfer of responsibility is complete, the LSUHSC-NO IRB would be the IRB of record for that study.

B. Establishing Local Context

The CIRB will address local context issues via the Annual Institution Worksheet About Local Context, the Annual Principal Investigator Worksheet About Local Context, and the Study-Specific Worksheet About Local Context. The LSUHSC-NO IRB staff will complete the Annual Signatory Institution Worksheet About Local Context on behalf of LSUHSC-NO and will submit this worksheet to the CIRB. The principal investigator will complete the Annual Principal Investigator Worksheet About Local Context, and will submit this completed worksheet to both the CIRB and the LSUHSC-NO IRB staff. The principal investigator will complete the Study-Specific Worksheet About Local Context – once permission has been granted by the Institution – and will submit this completed worksheet to both the CIRB and the LSUHSC-NO IRB staff.

If at any time throughout the duration of the study the Institution determines that the CIRB-approved protocol does not satisfactorily address local context issues, the Institution reserves the right to require the principal investigator to submit to the CIRB the appropriate documents to transfer IRB review responsibility from the CIRB to the LSUHSC-NO IRB. Once this transfer of responsibility is complete, the LSUHSC-NO IRB would become the IRB of record for that study.

C. Review Process for CIRB-Approved Protocols

As part of the Signatory Institution's responsibility to monitor the conduct of the research, LSUHSC-NO will review CIRB-approved protocols to ensure that the research is appropriate for LSUHSC-NO. The CTRC, PRC, and LSUHSC-NO IRB staff will work on behalf of the Institution to fulfill this duty.

Reviews of CIRB-approved protocols will be performed as follows:

1. The principal investigator (with assistance from the SSSCC or Children's Hospital staff) who wishes to enroll subjects in a CIRB-approved protocol will download all relevant documents from the Participant's Area of the CIRB website (www.ncicirb.org) and submit these documents to either the CTRC (for studies that will utilize the Adult CIRB) or to the PRC (for studies that will utilize the Pediatric CIRB).
2. The principal investigator must also submit to the CTRC or PRC a version of the informed consent document which includes incorporation of CIRB-approved institutional boilerplate language. No changes to the CIRB-approved informed consent document may be made by the Institution, the CTRC, or the PRC. Only the CIRB-approved boilerplate language may be added to the informed consent document. This boilerplate language is submitted by the LSUHSC-NO IRB staff on behalf of LSUHSC-NO to the CIRB for approval in the Annual Institution Worksheet About Local Context. Any changes to the boilerplate language must be CIRB-approved prior to implementation. It is the

responsibility of the principal investigator to incorporate the CIRB approved institutional boilerplate language into the informed consent document. No CIRB-approved information may be deleted from the informed consent document. Revisions/changes to the local informed consent document other than those described above require Full Board review at the local level by the LSUHSC-NO IRB, and the CIRB cannot serve as the IRB of record for that protocol at LSUHSC-NO.

3. The CTRC or PRC will examine all study-related materials and decide whether a particular protocol and informed consent document are acceptable and whether they are appropriate in their local context.
4. The CTRC or PRC will notify the LSUHSC-NO IRB staff as to whether or not they believe the study is acceptable and appropriate using the Local Management Process Checklist, and will send the LSUHSC-NO IRB staff all study related documents that were used for the review.
5. The LSUHSC-NO IRB staff will notify the principal investigator of the determination with regard to each protocol submitted.
 - If the CIRB review was determined by the CTRC or PRC to be acceptable and appropriate, the Institution will inform the principal investigator that s/he may now complete the Study-Specific Worksheet About Local Context and open the study under the CIRB.
 - If the CIRB review was not determined by the CTRC or PRC to be acceptable and appropriate, the Institution will inform the principal investigator that s/he cannot complete the Study-Specific Worksheet About Local Context and cannot open the study with the CIRB. If the principal investigator intends to continue with the review process, s/he will be required to submit the necessary documents to the LSUHSC-NO IRB for local, Full Board review.
6. If permission was granted by the Institution to complete the Study-Specific Worksheet About Local Context, the principal investigator will submit this completed worksheet to the CIRB for review. The principal investigator must also submit a copy of this worksheet to the LSUHSC-NO IRB staff for their records and must notify the LSUHSC-NO IRB staff if/when the CIRB approves this worksheet.

D. Further Review Procedures

The Institution will perform reviews of further documentation as follows:

1. For amendments that were approved by the full board CIRB, the principal investigator (with assistance from the SSSCC or Children's Hospital staff) will submit to the CTRC or PRC copies of the amendments along with the CIRB approval documentation.
2. For continuing reviews that were approved by the full board CIRB, the principal investigator (with assistance from the SSSCC or Children's Hospital staff) will submit to the CTRC or PRC copies of the continuing review application, the CIRB's continuing review approval documentation, and any other materials relevant to the re-approval application. The CIRB renewal date becomes the re-approval date of record.

3. The SSSCC or Children’s Hospital staff will send the LSUHSC-NO IRB staff copies of any such items that were reviewed by the full board CIRB and subsequently received by the CTRC or PRC, along with a statement of approval indicating that the CTRC or PRC accepts (or does not accept) the results of the CIRB review.
4. The principal investigator (with assistance from the SSSCC or Children’s Hospital staff) will submit to the LSUHSC-NO IRB staff copies of any expedited CIRB activity.
5. LSUHSC-NO retains the option not to accept the CIRB review and can choose to request a local Full Board review, in which case, the principal investigator would submit the appropriate documents to the CIRB to transfer IRB review responsibility from the CIRB to the LSUHSC-NO IRB. Once this transfer is complete, the LSUHSC-NO IRB would be the IRB of record for that study.
6. The principal investigator must report local serious adverse events, local unanticipated problems, and local instances of noncompliance to the CIRB as required by the CIRB Standard Operating Procedures, and must simultaneously report to the Institution and either the CTRC or PRC all such events. The principal investigator must inform the LSUHSC-NO IRB staff and either the CTRC or PRC of any actions taken by the CIRB as a result of problems identified in these areas. LSUHSC-NO retains the option to request a local Full Board review of such events, in which case the principal investigator would submit to the CIRB the appropriate documents to transfer IRB review responsibility from the CIRB to the LSUHSC-NO IRB. Once this transfer is complete, the LSUHSC-NO IRB would be the IRB of record for that study.

E. Further Responsibilities of LSUHSC–NO

LSUHSC-NO will:

1. Comply with the CIRB’s requirements and directives
2. Report to the CIRB the names of any Component or Affiliate Institutions that rely on LSUHSC-NO IRB
3. Maintain a Federalwide Assurance (FWA) and designate the NCI CIRBs under its FWA
4. Maintain compliance with any additional state, local, or institutional requirements related to the protection of human subjects
5. Ensure that local investigators receive proper initial and continuing education on the requirements related to human subjects protections
6. Perform oversight of the local conduct of the study, monitoring study compliance, thereby ensuring the safe and appropriate performance of the research at this institution. There will also be the provision of a mechanism by which complaints about the research can be made by local study participants or others
7. The Institution will review all local SAEs, unanticipated problems and issues of non-compliance as submitted to the CIRB and evaluate whether Institutional actions in addition to those taken by the CIRB may be required
8. Provide updates to the CIRB whenever a principal investigator is no longer the responsible party for a study under the purview of the CIRB

9. Provide to the CIRB and keep current the names and addresses of local contact persons who have authority to communicate for the Institution, such as the local IRB administrator
10. Notify the CIRB when a regulatory deficiency has been cited on an audit that occurred during the time that the CIRB was responsible for study review
11. Maintain a regulatory file for each study under CIRB purview as per local institution and Cooperative Group policy

5.0 ITEMS OF SPECIAL INTEREST

5.1 Human Subject Protection Educational Policies and Resources

A. Investigator(s)

It is the policy of the LSUHSC-NO IRB that all LSUHSC-NO investigators desiring to engage in research using human subjects must familiarize themselves with all IRB policies and procedures and related federal regulations. Policies and Procedures are posted on the IRB website at <http://www.lsuhs.edu/administration/academic/ors/irb.aspx>. Any changes to these policies are distributed by e-mail to all employees. Investigators new to the Institution must meet with the IRB Chair, Vice-Chair or a staff member prior to submission of an IRB application. Investigators should maintain an on-going relationship with the IRB office staff to gain assistance in the preparation of applications and in following all IRB policies and procedures during the conduct of their studies. This will help assure that both investigators and the Institution remain in compliance with all state and federal regulations regarding research involving human subjects.

All employees involved in human subjects research must take advantage of the educational opportunities listed below.

- All investigators and their research team members submitting an initial or continuation application to the IRB must read the LSUHSC IRB "[Guidebook](#)" and the "[Belmont Report](#)".
- In addition, they must complete appropriate (Biomedical or Social/Behavioral learner groups) Collaborative Institutional Training Initiative (CITI) <https://www.citiprogram.org/default.asp?language=english> modules as described in the Instructions for completing CITI training at http://www.lsuhs.edu/administration/academic/ors/docs/CITI_Instructions.pdf.
- In addition to training in human subjects protection, any investigative team conducting FDA-regulated research must complete the appropriate learner group for Good Clinical Practice (GCP) also available at <https://www.citiprogram.org/default.asp?language=english>.
- Continuing education of all investigators and their team members is required every three years. Appropriate refresher learner groups on the LSUHSC-NO CITI page are available for this purpose. Studies cannot be approved, amended or re-approved until all training requirements are met by all study team members.

B. Members

Members of the IRB have the important responsibility of protecting the many individuals in our community who volunteer to participate in this Institution's human subjects research programs. New Board members are expected to familiarize themselves completely with the IRB process in the manner described above for investigators. New members are asked to attend a number of scheduled IRB meetings to observe, and to contribute to, the discussion at the meeting prior to being assigned primary reviewer responsibility. New members should interact with the IRB Chair, Vice-Chair and IRB office staff regarding the requirements of, and for assistance with, reviews.

For the purposes of continuing education at each IRB meeting, an Educational Component is included in which issues of current interest related to human subjects protection are discussed. Related written materials are distributed as part of the Educational Component and a copy of the *Human Research Report* is provided to each member at each meeting. Additional items of interest are distributed by email to all members.

All members are required to read the LSUHSC-NO Guidebook and the Belmont Report. They must complete the IRB Members learner group in the CITI program <https://www.citiprogram.org/default.asp?language=english> and maintain continuing education requirements of CITI courses every three years. Compliance is monitored by the IRB staff. Failure to comply with the requirements will result in termination of IRB membership.

C. IRB Staff

All IRB staff are required to read the LSUHSC-NO HRPP Guidebook, the OHRP Guidebook and the Belmont Report. They must complete all CITI learner modules at <https://www.citiprogram.org/default.asp?language=english>. They are carefully trained to understand all federal regulations related to human subjects protection and drug and device development. Continuing education occurs during attendance at all IRB meetings, by participating in the IRB Forum list-serve, by attending regional and national IRB conferences and workshops and completing continuing education modules offered by CITI. Compliance is monitored by the IRB Chair. Failure to comply with the requirements may result in personnel action taken by the Institution which can result in reassignment or include termination of employment.

D. Other Educational Opportunities

1. Lectures

Presentations by the IRB Chair, Vice-Chair and staff concerning IRB issues are made at departmental faculty meetings, business manager meetings, workshops, courses, and other academic settings to familiarize investigators and staff with the IRB process, human subjects protection, and with IRB policies and procedures. In addition, a number of IRB members lecture on IRB issues in ethics classes taught on campus.

2. Educational Meetings

On an unscheduled basis, the Institution sponsors, with other institutions and national organizations such as OHRP, locally-held meetings concerning IRB issues and human subjects protection, and invites consultants to present such issues to our employees. OHRP, PRIM&R, NCURA and AAMC have numerous national and regional meetings dealing with IRB issues, and announcements of these meetings are widely distributed. Our investigators and IRB members are encouraged to attend such meetings. The IRB Chair, Vice-Chair and staff regularly attend such meetings.

3. Resources

The educational materials mentioned are available from the IRB office to assist all investigators in familiarizing themselves with the history of human subjects protection, factors which necessitated the development of the IRB process, and regulations underlying IRB policies and procedures. Materials are also available in LSUHSC-NO libraries. The IRB library, housed in the IRB office, contains numerous videos and written materials on the history and operation of IRBs and human subjects protection. This includes Cynthia Dunn and Gary Chadwick's book entitled *Protecting Study Volunteers in Research* (Center Watch, Inc. Boston, MA 1999). Copies may also be purchased in the LSUHSC-NO campus bookstore. OHRP, FDA and other organizations and institutions have educational materials concerning human subjects protection and IRB function available on their websites. Such information is electronically distributed to all employees.

5.2 Assessment of Risks to Subjects

No subject in a scientific investigation may be exposed to unreasonable risks to health or well-being. An individual is at risk if exposed to the possibility of any harm (e.g. physical, psychological, sociological, or legal). Determination of risk is a matter of the application of common sense and sound professional judgment. The LSUHSC-NO IRB is the final authority regarding the determination of risk to subjects participating in research at this institution.

- A. "No risk" refers to investigations in which the subject is not placed in jeopardy of any kind. Examples are use of educational tests, observation of public behavior or interview procedures, each under certain conditions. This type of investigation may qualify for exempt status verification by the IRB.
- B. "Minimal risk" means that the risks of harm anticipated in the proposed research are no greater, considering the probability of and magnitude of harm, than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. Examples are voice recordings made for research purposes, moderate exercise by healthy volunteers, veni-puncture under certain conditions, or collection of urine specimens. Some "minimal risk" protocols may qualify as involving "vulnerable populations." Definitions of minimal risk are as follows:

Definition of 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 (45CFR46.102.(i))

Definition of Minimal Risk for 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 (45CFR46.303(d))

- C. Psychological injury might involve subjection of subjects to deceit or withholding of information, public exposure, humiliation, invasion of privacy, or coercion. Social injury can occur if there is risk of loss of personal reputation or professional status, defamation of character, personal degradation in the eyes of others, or revelation of information related to sensitive social issues.

Examples of projects which may involve "greater than minimal risk" are surgical procedures, including removal of organs or tissues for biopsy, transplantation, or banking; administration of drugs, chemicals, biological agents, or radiation; use of indwelling catheters or electrodes; or the requirement of strenuous physical exertion. Greater than minimal risk may also include studies in which extremely sensitive information is collected through surveys, for example, studies asking about the use of illegal drugs or unusual sex-practices, or other questions that might place the subject's reputation at risk or that may reveal illegal activities. All projects involving greater than minimal risk and/or vulnerable populations must be reviewed at a regularly-scheduled meeting of the IRB.

5.3 Subject Population

It is the responsibility of the principal investigator to identify the sources of potential subjects; describe the characteristics of the subject population, such as their anticipated number, age, sex, ethnic background, and state of health; identify the criteria for inclusion and exclusion; explain the rationale for the use of special classes of subjects, such as fetuses, pregnant women, children, institutionalized individuals (mentally disabled, prisoners or others) especially those whose ability to give voluntary informed consent may be in question. In addition, the rationale for involvement of disproportionate numbers of racial or ethnic minorities, the aged, or persons of low socioeconomic status must be stated. Likewise, the lack of inclusion of these groups, including children, must be explained.

Community-based participatory research also requires additional considerations in reviewing the protocol. Research which involves community members in the research process must be fully described in the application. Review by the Board will include the design and implementation of research and the dissemination of results. IRB members are educated in this type of research, and members or outside consultants with expertise in this area are called upon for their input.

Vulnerable Populations

Subjects from vulnerable populations are those whose ability to give voluntary informed consent may be in question. Examples of vulnerable populations are children, pregnant women, fetuses, terminally-ill patients, prisoners, institutionalized persons (mentally ill), wards, and individuals who might be under psychological pressure to volunteer. If vulnerable populations are to be used, investigators must deal thoroughly with the potential for risk. It should be understood that the definition of “minimal risk” for vulnerable populations is different than for non-vulnerable populations. Consultation with the IRB Office on this issue is strongly urged if vulnerable populations are being asked to participate as research subjects. Federal regulations require additional IRB considerations if vulnerable populations of subjects are used.

Children as Research Subjects

Any proposed research in which children (individuals less than 18 years of age) are enrolled must meet the standards of 45CFR46, Subpart D and 21CFR50, Subpart D.

45CFR46, Subpart D

§46.404 Research not involving greater than minimal risk.

HHS will conduct or fund research in which the IRB finds that no greater than minimal risk to children is presented, only if the IRB finds that adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians, as set forth in [§46.408](#).

§46.405 Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects.

HHS will conduct or fund research in which the IRB finds that more than minimal risk to children is presented by an intervention or procedure that holds out the prospect of direct benefit for the individual subject, or by a monitoring procedure that is likely to contribute to the subject's well-being, only if the IRB finds that:

- (a) The risk is justified by the anticipated benefit to the subjects;
- (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 the children and permission of their parents or guardians, as set forth in [§46.408](#).

§46.406 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.

HHS will conduct or fund research in which the IRB finds that more than minimal risk to children is presented by an intervention or procedure that does not hold out the prospect of direct benefit for the individual subject, or by a monitoring procedure which is not likely to contribute to the well-being of the subject, only if the IRB finds that:

- (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;
- (c) The intervention or procedure is likely to yield generalizable knowledge about the subjects' disorder or condition which is of vital importance for the understanding or amelioration of the subjects' disorder or condition; and
- (d) Adequate provisions are made for soliciting assent of the children and permission of their parents or guardians, as set forth in [§46.408](#).

§46.407 Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children.

HHS will conduct or fund research that the IRB does not believe meets the requirements of [§46.404](#), [§46.405](#), or [§46.406](#) only if:

- (a) 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 children; and
- (b) the Secretary, after consultation with a panel of experts in pertinent disciplines (for example: science, medicine, education, ethics, law) and following opportunity for public review and comment, has determined either:
 - (1) that the research in fact satisfies the conditions of [§46.404](#), [§46.405](#), or [§46.406](#), as applicable, or (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 accordance with sound ethical principles;
 - (iii) adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians, as set forth in [§46.408](#).

§46.408 Requirements for permission by parents or guardians and for assent by children.

(a) In addition to the determinations required under other applicable sections of this subpart, the IRB shall determine that adequate provisions are made for soliciting the assent of the children, when in the judgment of the IRB the children are capable of providing assent. In determining whether children are capable of assenting, the IRB shall take into account the ages, maturity, and psychological state of the children involved. This judgment may be made for all children to be involved in research under a particular protocol, or for each child, as the IRB deems appropriate. If the IRB determines that the capability of some or all of 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 where the IRB determines that the subjects are capable of assenting, the IRB may still waive the assent requirement under circumstances in which consent may be waived in accord with [§46.116](#) of [Subpart A](#).

(b) In addition to the determinations required under other applicable sections of this subpart, the IRB shall determine, in accordance with and to the extent that consent is required by [§46.116](#) of [Subpart A](#), that adequate provisions are made for soliciting the permission of each child's parents or guardian. Where parental permission is to be obtained, the IRB may find that the permission of one parent is sufficient for research to be conducted under [§46.404](#) or [§46.405](#). Where research is covered by [§§46.406](#) and [46.407](#) and permission is to be obtained from parents, both parents must give their permission unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.

(c) In addition to the provisions for waiver contained in [§46.116](#) of [subpart A](#), if the IRB determines that a research protocol is designed for conditions or for a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects (for example, neglected or abused children), it may waive the consent requirements in [Subpart A](#) of [this part](#) and [paragraph \(b\)](#) of this section, provided an appropriate mechanism for protecting the children who will participate as subjects in the research is substituted, and provided further 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.

(d) Permission by parents or guardians shall be documented in accordance with and to the extent required by [§46.117](#) of [subpart A](#).

(e) When the IRB determines that assent is required, it shall also determine whether and how assent must be documented.

§46.409 Wards.

(a) Children who are wards of the state or any other agency, institution, or entity can be included in research approved under [§46.406](#) or [§46.407](#) only if such research is:

(1) Related to their status as wards; or

(2) Conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards.

(b) If the research is approved under [paragraph \(a\)](#) of this section, the IRB shall require appointment of an advocate for each child who is a ward, in addition to any other individual acting on behalf of the child as guardian or in loco parentis. One individual may serve as advocate for more than one child. The advocate shall 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 and who is not associated in any way (except in the role as advocate or member of the IRB) with the research, the investigator(s), or the guardian organization.

21CFR50, Subpart D

§50.51 Clinical investigations not involving greater than minimal risk.

Any clinical investigation within the scope described in §§50.1 and 56.101 of this chapter in which no greater than minimal risk to children is presented may involve children as subjects only if the IRB finds that:

(a) No greater than minimal risk to children is presented; and

(b) Adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians as set forth in §50.55.

§50.52 Clinical investigations involving greater than minimal risk but presenting the prospect of direct benefit to individual subjects.

Any clinical investigation within the scope described in §§50.1 and 56.101 of this chapter in which more than minimal risk to children is presented by an intervention or procedure that holds out the prospect of direct benefit for the individual subject, or by a monitoring procedure that is likely to contribute to the subject's well-being, may involve children as subjects only if the IRB finds that:

(a) The risk is justified by the anticipated benefit to the subjects;

(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 the children and permission of their parents or guardians as set forth in §50.55.

§50.53 Clinical investigations involving greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subjects' disorder or condition.

Any clinical investigation within the scope described in §§50.1 and 56.101 of this chapter in which more than minimal risk to children is presented by an intervention or procedure that does not hold out the prospect of direct benefit for the individual subject, or by a monitoring procedure that is not likely to contribute to the well-being of the subject, may involve children as subjects only if the IRB finds that:

- (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;
- (c) The intervention or procedure is likely to yield generalizable knowledge about the subjects' disorder or condition that is of vital importance for the understanding or amelioration of the subjects' disorder or condition; and
- (d) Adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians as set forth in §50.55.

§50.54 Clinical investigations not otherwise approvable that present an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children.

If an IRB does not believe that a clinical investigation within the scope described in §§50.1 and 56.101 of this chapter and involving children as subjects meets the requirements of §50.51, §50.52, or §50.53, the clinical investigation may proceed only if:

- (a) The IRB finds that the clinical investigation presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children; and
- (b) The Commissioner of Food and Drugs, after consultation with a panel of experts in pertinent disciplines (for example: science, medicine, education, ethics, law) and following opportunity for public review and comment, determines either:
 - (1) That the clinical investigation in fact satisfies the conditions of §50.51, §50.52, or §50.53, as applicable, or
 - (2) That the following conditions are met:

(i) The clinical investigation presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children;

(ii) The clinical investigation will be conducted in accordance with sound ethical principles; and

(iii) Adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians as set forth in §50.55.

§50.55 Requirements for permission by parents or guardians and for assent by children.

(a) In addition to the determinations required under other applicable sections of this subpart D, the IRB must determine that adequate provisions are made for soliciting the assent of the children when in the judgment of the IRB the children are capable of providing assent.

(b) In determining whether children are capable of providing assent, the IRB must take into account the ages, maturity, and psychological state of the children involved. This judgment may be made for all children to be involved in clinical investigations under a particular protocol, or for each child, as the IRB deems appropriate.

(c) The assent of the children is not a necessary condition for proceeding with the clinical investigation if the IRB determines:

(1) That the capability of some or all of the children is so limited that they cannot reasonably be consulted, or

(2) That the intervention or procedure involved in the clinical investigation 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 clinical investigation.

(d) Even where the IRB determines that the subjects are capable of assenting, the IRB may still waive the assent requirement if it finds and documents that:

(1) The clinical investigation involves no more than minimal risk to the subjects;

(2) The waiver will not adversely affect the rights and welfare of the subjects;

(3) The clinical investigation could not practicably be carried out without the waiver; and

(4) Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

(e) In addition to the determinations required under other applicable sections of this subpart D, the IRB must determine, in accordance with and to the extent that consent is required under part 50, that the permission of each child's parents or guardian is granted.

(1) Where parental permission is to be obtained, the IRB may find that the permission of one parent is sufficient for clinical investigations to be conducted under §50.51 or §50.52.

(2) Where clinical investigations are covered by §50.53 or §50.54 and permission is to be obtained from parents, both parents must give their permission unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.

(f) Permission by parents or guardians must be documented in accordance with and to the extent required by §50.27.

(g) When the IRB determines that assent is required, it must also determine whether and how assent must be documented.

§50.56 Wards.

(a) Children who are wards of the State or any other agency, institution, or entity can be included in clinical investigations approved under §50.53 or §50.54 only if such clinical investigations are:

(1) Related to their status as wards; or

(2) Conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards.

(b) If the clinical investigation is approved under paragraph (a) of this section, the IRB must require appointment of an advocate for each child who is a ward.

(1) The advocate will serve in addition to any other individual acting on behalf of the child as guardian or in loco parentis.

(2) One individual may serve as advocate for more than one child.

(3) The advocate must be an individual who has the background and experience to act in, and agrees to act in, the best interest of the child for the duration of the child's participation in the clinical investigation.

(4) The advocate must not be associated in any way (except in the role as advocate or member of the IRB) with the clinical investigation, the investigator(s), or the guardian organization.

LSUHSC-NO adopts the standards of these regulations and protections as its own.

Prisoners as Research Subjects

Any research proposed in which prisoners (individuals whose freedom is limited through governmental edict) must meet the standards of 45CFR46 Subpart C. LSUHSC-NO adopts the standards of these regulations and protections as its own.

Fetuses and Pregnant Women

Pregnant women are recognized as a vulnerable population because of the additional health concerns during pregnancy. There is also a need to avoid unnecessary risk to the fetus. Any research proposed in which fetuses and pregnant women are the subject of or are participants in the research must meet the standards of 45CFR46 Subpart B. LSUHSC-NO adopts the standards of these regulations and protections as its own.

Students

Any research proposed that will incorporate students as research subjects must follow federal regulations protecting those students and their families as explained in the "Family Educational Rights and Privacy Act Regulations (FERPA)" at 34CFR Part 99: (see <http://www2.ed.gov/policy/gen/reg/ferpa/index.html>) and under Protection of Pupil Rights Amendment (PPRA) (20 U.S.C. § 1232h; 34 CFR Part 98) (see <http://www2.ed.gov/policy/gen/guid/fpco/ppra/index.html>). The process to comply with FERPA will be implemented at the time of Departmental Review. As part of this process the IRB consults with the LSUHSC-NO Registrar, the office at LSUHSC-NO responsible for FERPA interpretation as related to LSUHSC-NO students.

There is in place a process to grant exceptions to parental or student consent to release student records for research. This responsibility is delegated to the IRB Chair or Vice-Chair. An educational agency or institution may disclose personally-identifiable information from an education record of a student without consent if the disclosure is part of an agreement between organizations or researchers conducting studies for, or on behalf of, educational agencies or institutions to: develop, validate, or administer predictive tests; administer student aid programs; or improve instruction.

A school district or postsecondary institution that uses this exception is required to enter into a written agreement with the Organization or Researcher conducting the research that specifies: the determination of the exception; the purpose, scope, and duration of the study; the information to be disclosed; that information from education records may only be used to meet the purposes of the study stated in the written agreement and must contain the current requirements in Department of Education regulations on re-disclosure and destruction of information; that the study will be conducted in a manner that does not permit personal identification of parents and students by anyone other than representatives of the Organization with legitimate interests; that the Organization is required to destroy or return all personally-identifiable information when no longer needed for the purposes of the study; and the time period during which the Organization must either destroy or

return the information.

Education records may be released without consent under FERPA if all personally-identifiable information has been removed including: student's name and other direct personal identifiers, such as the student's social security number or student number; indirect identifiers, such as the name of the student's parent or other family members, the student's or family's address, and personal characteristics or other information that would make the student's identity easily traceable, and date and place of birth and mother's maiden name; biometric records, including one or more measurable biological or behavioral characteristics that can be used for automated recognition of an individual, including fingerprints, retina and iris patterns, voiceprints, DNA sequence, facial characteristics, and handwriting; other information that, alone or in combination, is linked or linkable to a specific student that would allow a reasonable person in the school community, who does not have personal knowledge of the relevant circumstances, to identify the student with reasonable certainty.

The IRB has in place a process to comply with the Protection of Pupil Rights Amendment.

For research funded by the U.S. Department of Education, no student shall be required, as part of any research project, to submit without prior consent to surveys, psychiatric examination, testing, or treatment, or psychological examination, testing, or treatment, in which the primary purpose is to reveal information concerning one or more of the following: political affiliations; mental and psychological problems potentially embarrassing to the student or his or her family; sex behavior and attitudes; illegal, anti-social, self-incriminating and demeaning behavior; critical appraisals of other individuals with whom the student has close family relationships; legally-recognized privileged and analogous relationships, such as those of lawyers, physicians, and ministers; religious practices, affiliations, or beliefs of the student or student's parent; income, other than that required by law to determine eligibility for participation in a program or for receiving financial assistance under a program.

Prior consent means prior consent of the student, if the student is an adult or emancipated minor; or prior written consent of the parent or guardian, if the student is an un-emancipated minor. Schools and contractors obtain prior written parental consent before minor students are required to participate in any ED-funded survey, analysis, or evaluation.

For research not funded by the US Department of Education, the IRB must verify compliance with U.S. Department of Education regulations that schools are required to develop and adopt policies in conjunction with parents regarding the following:

- the right of a parent of a student to inspect, upon the request of the parent, a survey created by a third party before the survey is administered or distributed by a school to a student;
- any applicable procedures for granting a request by a parent for reasonable access to such survey within a reasonable period of time after the request is received;

- arrangements to protect student privacy that are provided by the agency in the event of the administration or distribution of a survey to a student containing one or more of the following items (including the right of a parent of a student to inspect, upon the request of the parent, any survey containing one or more of such items): political affiliations or beliefs of the student or the student's parent; mental or psychological problems of the student or the student's family; sex behavior or attitudes; illegal, anti-social, self-incriminating, or demeaning behavior; critical appraisals of other individuals with whom respondents have close family relationships; legally-recognized privileged and analogous relationships, such as those of lawyers, physicians, and ministers; religious practices, affiliations, or beliefs of the student or student's parent; income, other than that required by law to determine eligibility for participation in a program or for receiving financial assistance under a program.
- The right of a parent of a student to inspect, upon the request of the parent, any instructional material used as part of the educational curriculum for the student.
- Any applicable procedures for granting a request by a parent for reasonable access to instructional material received.
- The administration of physical examinations or screenings that the school or agency may administer to a student.
- The collection, disclosure, or use of personal information collected from students for the purpose of marketing or for selling that information (or otherwise providing that information to others for that purpose), including arrangements to protect student privacy that are provided by the agency in the event of such collection, disclosure, or use.
- The right of a parent of a student to inspect, upon the request of the parent, any instrument used in the collection of personal information before the instrument is administered or distributed to a student.
- Any applicable procedures for granting a request by a parent for reasonable access to such instrument within a reasonable period of time after the request is received.

For research funded by the National Institute on Disability and Rehabilitation Research, when an IRB reviews research that purposefully requires inclusion of children with disabilities or individuals with mental disabilities as research participants, the IRB must include at least one person primarily concerned with the welfare of these research participants.

Employees/students of LSUHSC-NO

Under most circumstances, employees/students at LSUHSC-NO may not participate in projects where the investigators, in their roles of faculty members or supervisors, are involved in grading the academic or clinical performance of, or otherwise evaluating, the subjects. Research involving students/employees as subjects is reviewed on a case-by-case basis. The single most important factor in considering exceptions to the above rule is the complete absence of either coercion or the perception of coercion by the students/employees who are asked to participate. Other factors affecting this decision of exception include: having a mechanism to assure anonymity; having a method to assure that no penalties can be imposed on

students/employees who refuse to participate, etc. It is unusual for the IRB to approve projects utilizing students/employees that are considered greater than minimal risk. The request to include LSUHSC-NO students/employees must be included in the application project summary.

5.4 Subject Entry Site Approval

Since most institutions have committees that assess the impact of the proposed research at their facility, it is the responsibility of the investigator to assure that approval has been obtained from the appropriate officials of the non-LSUHSC-NO sites listed on the application form. Except for LSU facilities, e.g., Health Care Services Division hospitals and clinics or LSUHSC-NO Health Care Network clinics, this documentation must be provided to the IRB prior to approval and implementation of that location as a performance site for the study.

5.5 Subject Payment

Compensation to subjects must never constitute undue influence or coercion to participate, and should be limited to nominal payment for time and the inconvenience of participation and/or travel expenses. Such compensation should not be construed nor described as a benefit of the research. Any payment(s) made must be prorated, based on time actually spent on the study, regardless of whether the subject completes the study. Payments must be made in equal amounts for each visit throughout the course of the study.

5.6 Advertisements for Subjects

If notices are posted or other advertising is used for recruitment of volunteers to participate in the research, the specific advertisement and methods of recruitment must be approved by the IRB prior to use. Any type of advertising for research subjects that is intended to be seen or heard by prospective subjects is considered as part of the informed consent and subject selection process. Since this may be the initial contact by the investigator with the subject, the IRB must ensure that the information is not misleading to subjects. This is especially important when a study may involve subjects who are likely to be vulnerable to undue influence, for example, financially-impaired subjects.

When advertising is to be used, the IRB must review both the information contained in the advertisement and the mode of its communication in order to determine that the procedure for recruiting subjects is not coercive and that the recruitment material does not state or imply a certainty of favorable outcome or other benefits beyond what is outlined in the consent document and the protocol.

Advertising for recruitment of participation into investigational drug, biologic or device studies should not use terms such as "new treatment" or "new medication" without explaining that the test article is investigational.

A phrase such as "you will receive new treatments" incorrectly implies that all study subjects will be receiving newly-approved products of proven worth. Advertisements

should not promise "free medical treatment" when the reality is only that subjects will not be charged for taking part in the investigation.

If an investigator decides to begin advertising for subjects after the study has received IRB approval, the advertising is considered as an amendment to the ongoing study and must be reviewed by the IRB. When such advertisements are easily compared to the consent, the IRB will review and approve the advertisement using expedited procedures. When the comparison is not obvious or other complicating issues are involved, the advertisement will be reviewed at a convened meeting.

Generally, advertisements should be limited to the information the prospective subjects need in order to determine their eligibility and interest. The following items must be addressed in order for the advertisement to qualify for review:

1. The name of the investigator, the name and phone number of the contact person for the study and the name of the institution (e.g., LSU Health Sciences Center in New Orleans)
2. The purpose of the research (e.g., the condition under study or the goal of the project)
3. The eligibility criteria (which may be in summary form, or listed as bullets or points)
4. The time-frame required for participation
5. A short list of benefits (Note that payments to subjects for participation are not benefits. The payment may be mentioned; however, it cannot be emphasized.)

Investigators who require assistance with advertisement formatting or composition should contact the LSUHSC-NO Director of Information Services at 504-568-4806. This office must be contacted if the recruitment material will appear in print media, be presented on television or radio, or placed on the internet.

Regarding acceptable and unacceptable payment arrangements for the sponsor, organization, researcher, and those referring research participants, all financial issues related to research projects supported by a sponsor must be detailed in the payment schedule associated with the clinical trial agreement. Such payments may include all costs associated with the research including time and effort for the principal investigator and study team members. However, note that so called "finder's fees" or "referral fees" in exchange for referrals or recruitment of research participants are not allowed. Similarly, payments to individuals designed to accelerate recruitment are not allowed and any such arrangement for the institution will be examined very closely for potential influence on subject selection at the time of clinical trial agreement negotiation.

5.7 Educational Materials for Subjects

Education materials related to the consent process or which will be used as part of the study; e.g., videos, brochures, etc., must be reviewed and approved by the IRB

before use. If available at the time, these items must be submitted with any new application for IRB approval.

5.8 Informed Consent

Basic elements of informed consent.

In seeking informed consent the following information shall 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 risks or discomforts to the subject;
- (3) A description of any benefits to the subject or to others which may reasonably be expected of 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 and notes 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, or 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 and research subjects' rights, and whom to contact in the event of a research-related injury to the subject; contact information for the research team for questions, concerns, or complaints, and for someone independent of the research team for problems, concerns, questions, information, or input; and
- (8) A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

Additional elements of informed consent.

When appropriate, one or more of the following elements of information shall also be provided to each subject:

- (1) A statement that the particular 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) A statement that the results of the research will be posted on clinicaltrials.gov;
- (3) Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent;
- (4) Any additional costs to the subject that may result from participation in the research; and the amount and schedule of all payments to subjects;
- (5) The consequences of a subject's decision to withdraw from the research and

procedures for orderly termination of participation;

(6) 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; and

(7) The approximate number of subjects involved in the study.

As required by U.S. law, a description of qualifying clinical trials must be available on the clinical trial registry <http://www.ClinicalTrials.gov>. Criteria for required inclusion on this website are available at <http://www.ClinicalTrials.gov>. If required, then a statement that this information is available to subjects (including the National Clinical Trials number for the study) must be included in the informed consent document for the study. Please refer to the LSUHSC-NO informed consent template for this appropriate language.

When following ICH-GCP(E6) guidelines, the consent document contains:

- The approval/favorable opinion of the IRB.
- The probability for random assignment to each treatment.
- The participant's responsibilities.
- When applicable, the reasonably-foreseeable risks or inconveniences to an embryo, fetus, or nursing infant.
 - The important potential benefits and risks of the alternative procedures or courses of treatment that may be available to the participant.
 - When there is no intended clinical benefit to the participant, the participant is made aware of this.
 - A statement that the monitors, the auditors, the IRB, and the regulatory authorities will be granted direct access to the participant's original medical records for verification of clinical trial procedures and data, without violating the confidentiality of the participant, to the extent permitted by the applicable laws and regulations and that, by signing a written informed consent form, the participant or the participant's legally authorized representative is authorizing such access.
 - If the results of the trial are published, the participant's identity will remain confidential.

Researchers and research staff provide all the disclosures and follow the requirements pertaining to consent covered by ICH-GCP (E6).

Waiver or Alteration of Informed Consent

Federal regulations at 45CFR46.116(c) & (d) and LSUHSC-NO policies allow for waiver of informed consent when the following conditions are met. The IRB may waive parental permission by determining that the criteria for waivers or alterations are met. The IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth above, or waive the requirement to obtain informed consent provided the IRB finds and documents that:

(1) 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: (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; or (iv) possible changes in methods or levels of payment for benefits or services under those programs; and

(2) The research could not practicably be carried out without the waiver or alteration.

The IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth in this section, or waive the requirement to obtain informed consent provided the IRB finds and documents that:

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

The issue of the test of practicability can be met, for example, by:

1. The need for a large numbers of subjects
2. A presumed or demonstrated inability to contact subjects for whom contact information may not be accurate
3. The fact that many of the subjects may have died, or
4. The fact that a lack of data from a few subjects may make the number of subjects available for the study too few to make the study valid

To request a waiver of informed consent, each of the above questions must be addressed in the request.

(e) The informed consent requirements in this policy are not intended to preempt any applicable federal, state, or local laws which require additional information to be disclosed in order for informed consent to be legally effective.

(f) Nothing in this policy is intended to limit the authority of a physician to provide emergency medical care, to the extent the physician is permitted to do so under applicable federal, state, or local law.

Documentation of Informed Consent

Except as provided in the following section on Waiver of Documentation of Informed Consent, informed consent shall be documented by the use of a written consent form approved by the IRB and signed by the subject or the subject's legally authorized representative. A copy shall be given to the person signing the form.

The consent form may be either of the following:

- (1) A written consent document that embodies the elements of informed consent

required by §46.116. This form may be read to the subject or the subject's legally authorized representative, but in any event the investigator shall give either the subject or the representative adequate opportunity to read it before it is signed; or

(2) A short-form written consent document in the language of the subject stating that the elements of informed consent required by §46.116 have been presented orally to the subject or the subject's legally authorized representative. When this method is used, there shall be a witness to the oral presentation. Also, the IRB shall approve a written summary of what is to be said to the subject or the representative. Only the short form itself is to be signed by the subject or the representative. However, the witness shall sign both the short form and a copy of the summary, and the person actually obtaining consent shall sign a copy of the summary. A copy of the summary shall be given to the subject or the representative, in addition to a copy of the short form.

Waiver of Documentation of Informed Consent

Federal regulations at 45CFR46.117(c) and LSUHSC-NO policies allow for a waiver of documentation of informed consent when the following conditions are met.

An IRB may waive the requirement for the investigator to obtain a signed consent form for some or all subjects if it finds either:

(1) That the only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern; or

(2) That the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.

In cases in which the documentation requirement is waived, the IRB may require the investigator to provide subjects with a written statement regarding the research.

For studies regulated by the FDA, regulations at 21CFR56.109(c)(1) also allow for a waiver of documentation of informed consent if the research presents no more than minimum risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context. When following FDA regulations and guidance, the IRB is prohibited from waiving or altering the consent process.

For studies involving randomization, the researcher must follow the clinical trial's randomization procedures, if any, and ensure that the code is broken only in accordance with the protocol. If the clinical trial is blinded, the researcher must promptly document and explain to the Sponsor any premature unblinding.

The researcher must inform the participant's primary physician about the participant's participation in the clinical trial if the participant has a primary physician and if the participant agrees to the primary physician being informed.

Although a participant is not obliged to give his or her reasons for withdrawing prematurely from a clinical trial, the researcher must make a reasonable effort to ascertain the reason, while fully respecting the participant's rights.

Genetic studies

Informed consent must be obtained for all studies conducting genetic analysis of tissue. This requirement must be followed even if no personal identifiers related to the tissue are collected or maintained.

5.9 Child Assent Policy

Assent is a child's affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent. In any research project in which children are subjects, adequate provisions for soliciting assent must be described in the IRB application and included in the consent form. Following an explanation of the study in language appropriate for the age group, assent should be obtained unless it is determined by the investigator that the child is not capable of providing assent. In most circumstances, written assent (unless documentation is waived by the IRB) should be obtained from any child seven years of age or older. However, in making this determination, the child's age, maturity, and psychological state must be taken into consideration. For children from the ages of 7 to 13 years of age, a separate assent form should be developed using language appropriate for this age-group. For children from 14 to 17 years of age an assent line may be used on the informed consent document of the study. If assent is not obtained as required by the IRB, then the reasons for not obtaining assent must be fully documented. This documentation must be particularly thorough in the case of research that is non-therapeutic in nature and/or does not hold out the prospect of direct benefit to the child.

The IRB may determine that as a group the children asked to participate in a research project are incapable of providing assent, and this requirement may be waived by the IRB. If the capability of some or all of 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 IRB may determine that the assent of the children is not a necessary condition for proceeding with the research.

5.10 Pregnant Partners

In many studies sponsors wish to collect information concerning the health status of a research subject's partner when that partner becomes pregnant. Even though pregnancy may be an exclusion criterion for subjects, or the protocol requires the use of birth control measures, pregnancy may occur. In this case the collection of information about the pregnant partner (before and/or after parturition) or child (following delivery) may only be obtained pursuant to documentation of informed

consent and HIPAA authorization from the pregnant partner. This procedure does not imply that consent of the pregnant partner and documentation of permission to collect health information makes the pregnant partner an enrolled subject in the main part of the research study. Rather, this procedure provides ethical protection for the privacy and welfare of the pregnant partner.

5.11 Confidentiality of Data and HIPAA Privacy Rule

When the research involves collection of data which might be harmful to subjects if disclosed to third parties in an individually-identifiable form, the investigator must be attentive to the adequacy of provisions to protect the confidentiality of data. The investigator must limit the collection of personal information to that which is essential for the research. Depending upon the degree of sensitivity of the data, the methods for protecting the confidentiality of data may include coding or removal of identifiers as soon as possible, limitation of access to data to the investigator and authorized staff, the use of locked file cabinets, the use of password-protected computers and computer servers, encryption of data on computers, and plans for the ultimate disposition of data.

The investigator should be aware of the extensive vulnerability of research data to subpoena, particularly in studies that collect data that would put subjects in legal jeopardy if disclosed. The subject names should be recorded only when necessary and subjects must be informed that their identity can be protected only to the extent allowed by law. When and where possible Certificates of Confidentiality should be requested for investigator-initiated studies including projects establishing data and tissue repositories where personal identifiers or codes to identifiers are maintained. See OHRP guidance on Certificates of Confidentiality at <http://www.hhs.gov/ohrp/policy/certconf.html> and the Certificate of Confidentiality Kiosk on the National Institutes of Health website <http://grants.nih.gov/grants/policy/coc/index.htm>.

Where appropriate, all studies must adhere to regulations concerning privacy at 45CFR Parts 160 and 164 (Standards for Privacy of Individually-Identifiable Health Information or **HIPAA Privacy Rule**.) If HIPAA Authorization is required of subjects, the signed authorization document must be maintained with the signed informed consent document for the study (attach these two documents together). In addition, the LSU Notice of Privacy Practices must be provided to all subjects enrolled into a study in which HIPAA Authorization is required. Acknowledgement procedures must be followed and documented as described at the Office of Research Services webpage "HIPAA and Research".

Investigators are directed to <http://www.lsuhs.edu/administration/academic/ors/hipaa.aspx> for additional information related to these regulations.

5.12 Record-Keeping by Investigators

Copies of all signed consent forms and associated HIPAA Authorization documents must be kept by the principal investigator and made accessible for review by the IRB. Files of all signed consent forms and associated HIPAA Authorization documents from research must be retained for a period of ten years following closure of the study.

For FDA-regulated studies, Case Report Forms and other related study documents must be retained for two years following when the termination or discontinuation of the investigational study (not merely an investigator's portion of a study) occurs or the records are no longer required for pursuit of marketing approval from the FDA.

Projects involving the intraocular lens have the following additional requirements: Files must be maintained for A.) A period of two years after the date on which the Food and Drug Administration approves the marketing of the intraocular lens for the purposes that were the subject of the study, and B.) A period of five years after the date on which the results of the study are submitted to the Food and Drug Administration in support of the marketing of the intraocular lens for the purpose that was the subject of the study. However, if any period is shorter than ten years from the close of the study, Louisiana state law requires that human research records be maintained for ten years following closure of the study. Furthermore, Louisiana state law requires that all patient records be maintained for 10 years after discharge unless related to a research project. In this case, the ten year rule following study closure applies.

5.13 Essential HRPP Functions Conducted by the ORS

A. Grant Applications

For all IRB applications related to a federal grant proposal a complete copy of the full grant proposal must be provided for review by the IRB for congruency. The Office of Research Services (ORS) reviews all grants and contracts received by LSUHSC-NO investigators that will be awarded to the LSUHSC. The investigator's department and the LSUHSC-NO Office of Sponsored Programs are responsible for post-award financial management. The ORS Coordinator of Grants and Development shares information concerning clinical trial agreements with IRB Coordinators, department managers and the Office of Sponsor Projects as required.

B. HIPAA Activities Related to Research

Under the Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule, the Institution's Privacy Officer is located in the LSUHSC-NO Office of Compliance Programs (OCP) and manages the Institution's HIPAA Program. HIPAA activities related to research that is reviewed by the IRB are managed by the ORS Coordinator of CoI on a daily basis with oversight by the OCP.

5.14 Essential HRPP Functions Conducted by the IBC and Radiation Safety

The Institutional Biosafety Committee (IBC) and Institutional Radiation Safety Committee (IRSC) review projects for compliance with biosafety and radiation safety guidelines. All research projects conducted at LSUHSC-NO must receive IBC approval and where applicable, obtain a radiation registration. These approvals are not given until all compliance issues have been satisfactorily addressed. This information is shared with IRB coordinators. IBC approval must be provided to the IRB office before IRB approval will be granted. The IBC application is available at <http://www.lsuhs.edu/administration/academic/ors/ibc.aspx>.

5.15 Conflicts of Interest (CoI)

As defined in the LSUHSC-NO Conflict of Interest policy (CM-35), "Conflict of Interest" means any "Financial Conflict of Interest" and/or any "Non-Financial Conflict of Interest". A potential or actual Conflict of Interest occurs in the context of Sponsored Projects if:

- there is a chance that an Interest could reasonably appear to affect the project; or
- if there is a chance that research or other LSUHSC-NO activities could reasonably appear to affect the interests of an external entity in which the Investigator (or Immediate Family Member) or the Institution has an Interest.

"Financial Conflict of Interest" means a Significant Financial Interest that could directly and significantly affect the design, conduct, or reporting of research and occurs when an Investigator's or Immediate Family Member(s)' Financial Interests compromise or have the appearance of compromising, an Investigator's professional judgment in proposing, conducting, supervising, or reporting research.

"Non-Financial Conflict of Interest" occurs when an Investigator's or Immediate Family Member's role in the University or other outside activities compromise or have the appearance of compromising an Investigator's professional judgment in proposing, conducting, supervising, or reporting research or come into conflict with an Investigator's primary commitment to maintain scientific objectivity.

"Immediate Family Member" means the spouse of the Investigator, dependent children of the Investigator, and any other individual that the Investigator knows or should know maintains an Interest that may be impacted by research or project the Investigator is proposing or conducting. Additionally, any other relationship that a reasonably prudent person might consider as an appearance of a conflict of interest is also included in the definition of "Immediate Family" and should be disclosed as well.

A full description of the LSUHSC-NO's Conflict of Interest policy is described in Chancellor's Memorandum 35 (CM35) which is available at the following URL: <http://www.lsuhs.edu/administration/cm/>.

A. Investigators and Study Team Members

The LSUHSC-NO Human Subjects Protection Program and IRB expands on this policy as follows and in Section C.:

All study team members are required to submit a CoI Attestation form at the time of submission of the initial IRB application and at the time of continuing re-approval. This submission is independent of the source of funding for the human subjects research project. Should any potential CoI be identified by the study team member through this document, they must engage the following process and provide a full disclosure to the Office of Research Services.

B. IRB Members

CoIs for IRB Members can occur due to financial interests: anything of monetary value, including, but not limited to, salary or other payments for services (e.g., consulting fees or honoraria); equity interests (e.g., stocks, stock options or other ownership interests); or intellectual property rights (e.g., patents, copyrights and royalties from such rights) that would reasonably appear to be affected by or to affect their consideration or review of the research.

1. As defined earlier, no member with a CoI may participate in the discussion of or vote on any item under consideration by the Board.
2. A notice to this effect is made at the beginning of each meeting and is documented in the minutes of the meeting.
3. Members with a CoI financial, commitment or otherwise related to any item under consideration by the Board may not act as a reviewer for that item.
4. Such members may provide information at the request of the Board but must be otherwise recused.
5. Any member with a potential CoI must disclose such interest through the process described for investigators and study team members in the previous section of this Guidebook.

If a consultant is utilized, the consultant is bound by the CoI requirements and restrictions pertaining to IRB members.

C. Individual CoI

Introduction

It is the objective of the Louisiana State University Health Sciences Center-New Orleans (LSUHSC-NO) to enact policies and procedures that ensure the highest quality patient care possible, an excellent teaching environment for training future

health care professionals, and an environment that supports transparent medical and scientific research. LSUHSC-NO must ensure that patient care, education, and research are performed under the highest standards of ethical conduct, with integrity and openness, and the rights of human beings are protected.

In addition, these policies and procedures are to protect the credibility and integrity of the LSUHSC-NO's faculty and staff so that public trust and confidence in the LSUHSC-NO's sponsored activities are ensured. LSUHSC-NO understands the increasing complexity of relationships between universities, members of their faculty and staff, federal and state governments, private industry, and the non-profit sector.

LSUHSC-NO encourages faculty, staff, students, house officers and other employees to participate in meaningful professional relationships with industry, government and private entities. These relationships are established for mutually-beneficial reasons and many times produce knowledge and intellectual property that will help the community at large. However, these relationships may create non-financial interests as well as financial interests that may create a bias in decisions related to a sponsored project, such as payments for services, equity interests, or intellectual property rights. The value of the results of funded research to the advancement of health care must not be compromised by any investigator's financial and/or non-financial interest that could bias the design, conduct or reporting of the research.

This policy seeks to maintain a reasonable balance between these competing interests, give LSUHSC-NO the ability to identify and manage financial and non-financial interests that may bias the research, and minimize reporting and other burdens on the investigators.

Scope

This policy applies to all LSUHSC-NO faculty members (including part-time, gratis, and visiting faculty), staff and other employees, house officers, and students (including post-doctoral fellows) who propose, conduct or report research on behalf of LSUHSC-NO, regardless of funding source.

This policy only addresses Conflicts of Interest in Research Projects. There are other areas in which Financial and Non-financial conflicts may arise and other types of conflicts, e.g. conflicts of commitment or other outside activities, which may conflict with LSUHSC-NO obligations.

Policy

An Investigator shall not be permitted to begin any research activity (e.g. design, conduct or reporting of research, educational, or service activities) when there is an actual or potential Conflict of Interest, until a written review of the disclosure has been conducted and a Conflict of Interest Resolution Plan has been developed, if necessary, and has been received by the Investigator from the Vice-Chancellor of Academic Affairs.

Each Investigator is responsible for determining whether he/she or his/her

Immediate Family Member has a potential Conflict of Interest.

Investigators and/or Immediate Family Members should evaluate potential Conflicts of Interest not only at the outset of their research and continually throughout the period of the award, but also when a change occurs in their relationship with an outside entity. This may occur at the time a new proposal is submitted, when a new relationship is established with an outside entity, or when a prior relationship with an outside entity changes.

The Director of Research Services and the Conflict of Interest Review Committee (CIRC) are the institutional official(s) to solicit and review disclosures of Significant Financial Interests from each Investigator planning to participate or participating in research.

Requirements for Disclosure

Investigators shall disclose 1) those Conflicts of Interest that would reasonably appear to be affected by or to affect their research or educational activities; and 2) any Conflict of Interest in entities whose interest would reasonably appear to be affected by or to affect the Investigator's performance of his or her LSUHSC-NO duties, activities and responsibilities. In other words, if an Investigator has a Conflict of Interest, then disclosure shall be necessary if 1) there is a chance that this interest could reasonably appear to affect his or her research, teaching, or other LSUHSC-NO activities; or 2) if there is a chance that his or her research, teaching, or other LSUHSC-NO activities could reasonably appear to affect the interests of the external entity in which the Investigator or Immediate Family Member has a Conflict of Interest. In addition, Investigators are encouraged to disclose any other Conflicts of Interest that could present an actual Conflict of Interest, or might be perceived to present a Conflict of Interest.

Each Principal Investigator or Co-Principal Investigator shall be responsible for ensuring that Investigators under his or her supervision who are involved in proposing, conducting or reporting research on the Principal or Co-Principal Investigator's project shall comply with this policy in identifying and disclosing any potential Conflicts of Interest.

Procedures for Disclosure of Conflicts of Interest

Investigators must disclose any Conflicts of Interest of the Investigator and his/her Immediate Family Members, prior to submitting the research proposal, and the disclosure must be updated annually.

This disclosure must be submitted to the Office of Research Services through completion of the Conflict of Interest Disclosure Form, and the appropriate attachments, including but not limited to PM-11 and/or PM-67 disclosure forms. Conflict of Interest Disclosure Forms must be updated to reflect any new or previously undisclosed Conflicts of Interest within thirty (30) days of discovering or acquiring a new Significant Financial Interest.

All Conflict of Interest disclosures shall first receive an administrative pre-review to assess the circumstances of a potential Conflict of Interest and whether significant financial interest is related to the proposed research by the Director of Research Services or designee.

Investigators may be required to provide additional information for this initial assessment. If the Director determines that a potential Conflict of Interest may exist, the Director shall forward his or her pre-review to the LSUHSC-NO's Conflict of Interest Review Committee (CIRC), which is responsible for reviewing Conflict of Interest disclosures and providing recommendations to reduce, manage or eliminate Conflicts of Interest, as appropriate.

Within sixty (60) days of an Investigator new to participating in an ongoing research project disclosing a Significant Financial Interest; an Investigator who previously did not timely disclose a Significant Financial Interest; or a Significant Financial Interest which was not previously reviewed by LSUHSC-NO, the Director of Research Services shall review the disclosure and determine whether the disclosure must be submitted to the CIRC.

Depending on the nature of the Significant Financial Interest, the Director of Research Services may determine that interim measures are necessary, and impose interim measures with regard to the Investigator's participation before the CIRC concludes its review.

The CIRC, within sixty (60) days, will review the disclosure of Significant Financial Interest to determine:

- whether it is related to the proposed research
- whether a conflict of interest exists

If a Conflict of Interest exists, the CIRC will consider management of the interest. The CIRC Committee shall include, but is not limited to the following factors in its evaluation of the potential Conflict of Interest:

- Length or nature of the involvement with the Sponsor
- Type of Sponsor, how the Research Project is supported or financed
- Estimated degree of separation between the Research Project's and Investigator's activities
- The nature of the Conflict of Interest and when and where the relationship commenced
- Whether the conditions of the relationship have changed
- Whether the results of the Research Project are likely to be affected by the Conflict of Interest
- The mechanisms to ensure the integrity of the Research Project, such as peer review, other independent research monitors, or controls
- The availability of alternatives to avoid the Conflict of Interest
- Risks to the rights and safety of human subjects research
- Risks to the rights and obligations of students, including fellows, participating in the research
- By whom the study is designed

- Whether LSUHSC-NO is the appropriate site for the Research
- Transparency of relationships

If the CIRC determines that an actual or potential Conflict of Interest exists, then the Committee shall develop a Conflict of Interest Resolution Management Plan which may impose, singularly or in combination, any of the following:

- Public disclosure of Conflicts of Interest
- Disclosure to subjects through the consent process
- Review of the Research protocol by independent reviewers
- Monitoring of the Research project by independent parties
- Reduction of equity holdings
- Clear separation of Research from paid activities
- Modification or disapproval of the Research plan
- Divestiture of Conflicts of Interest, complete or partial
- Appointment of a non-conflicted Principal Investigator
- Severance of relationships that create actual or potential Conflicts of Interest
- Disqualification of the Investigator with the Conflicts of Interest from participating in all or a portion of the Research
- As the regulations require, a retrospective review and a mitigation report for PHS-funded projects

The Plan may also impose other restrictions which the CIRC deems necessary, to reduce, manage or eliminate actual or potential Conflicts of Interest.

In certain circumstances, the CIRC may determine that the Investigator has presented compelling circumstances to justify allowing research to proceed despite the presence of a Conflict of Interest. Whether the circumstances are deemed compelling shall depend upon the following:

- the nature of the science,
- the nature of the Conflict of Interest
- the amount of the Financial Interest
- how closely the Conflict of Interest is related to the Research
- the degree to which the Conflict of Interest may be affected by the Research, and
- the degree to which the Conflict of Interest can be effectively managed

No “compelling circumstances” will be approved which may violate federal regulations or result in actions detrimental to the LSUHSC-NO and the goals of this policy.

If the CIRC determines that there are compelling circumstances that the Research should go forward despite the Conflict of Interest, then the CIRC may allow the research to go forward, and shall include in the Conflict of Interest Resolution Plan:

- The compelling circumstances which support including the conflicted Investigator in the project
- The stages of the research and the specific activities for which there are compelling reasons for the Investigator’s involvement
- The activities the Investigator will be allowed to perform
- Any restriction plan imposed to prevent the conflict from influencing or appearing to influence the outcome of the project, and strategy to restrict the time of

involvement to a minimum

Conflict of Interest Resolution Plans involving human subject research studies shall be submitted to the LSUHSC-NO Institutional Review Board for approval. If the IRB determines that the Plan does not satisfactorily protect human subjects, then the Plan may be returned to the CIRC for further consideration, modification, and re-submitted to the IRB for approval. No Conflict of Interest Resolution Plan involving human subjects research studies shall be implemented without IRB approval.

Conflict of Interest Resolution Plans must be signed by the Principal and/or Co-Principal Investigator, the Investigator with the Conflict of Interest, the Chairperson of the CIRC, Dean of the School of the Investigator with the Conflict of Interest, and the Vice-Chancellor for Academic Affairs.

Monitoring

Whenever a Conflict of Interest Resolution Management Plan is instituted by the CIRC, the Director of Research Services or designee shall monitor compliance with the management plan. Upon activation of the management plan approved by the IRB, a monthly report must be submitted by the PI to the IRB as confirmation of adherence to the plan. These reports will be reviewed by the Chair and administratively approved if appropriate. If any questions arise, the PI will be asked to provide clarification. If this is considered to be inadequate, the research may be halted or suspended until the issues are satisfactorily resolved. If resolution is not forthcoming, employee sanctions may be invoked. These could include warning, reprimand, censure, or suspension, or prohibition from conducting further human subjects research at LSUHSC-NO. Additional action may be taken by the Institution at the discretion of the Chancellor.

Retrospective Reviews--for PHS-funded research only

In cases where a Conflict of Interest is not identified or managed in a timely manner, including failure by the Investigator to disclose a Significant Financial Interest that is determine by the Institution to constitute a Financial Conflict of Interest, failure by the Institution to review or manage such a Financial Conflict of Interest, or failure by the Investigator to comply with a Conflict of Interest Resolution Management Plan, LSUHSC-NO shall within one-hundred and twenty (120) days from the determination of non-compliance, conduct a retrospective review of the Investigator's activities and any PHS-funded research project conducted during the time-period of noncompliance for bias in the design, conduct, or reporting of such research.

LSUHSC-NO shall document the review; the documentation shall include, but is not limited to:

- Project number
- Project Title
- PD/PI or contact PD/PI if multiple PD/PI model is used;
- Name of the Investigator with the Financial Conflict of Interest
- Name of the entity with which the Investigator has a Financial Conflict of Interest

- Reason(s) for the retrospective review
- Detailed methodology used for the retrospective review
 - Methodology of the review process, composition of the review panel, documents reviewed
- Findings of the review
- Conclusions of the review

If appropriate, based upon the results of the review, LSUHSC-NO shall update the previously-submitted FCoI report, specifying the actions that will be taken to manage the Financial Conflict of Interest going forward.

If bias is found as a result of the review, LSUHSC-NO shall promptly notify and submit a mitigation report to the PHS Awarding component.

The mitigation report shall include, but is not limited to:

- The key elements documented in the retrospective review noted above
- A description of the impact of the bias on the research project
- LSUHSC-NO's plan of action taken to eliminate or mitigate the effect of bias on the research project
- Extent of harm done, including any qualitative or quantitative data to support any actual or future harm
- Analysis of whether the research project is salvageable

Reporting Requirements—PHS-funded research only

Prior to LSUHSC-NO expenditure of any funds under a PHS-funded research project, LSUHSC-NO shall provide to the PHS Awarding Component a FCoI report regarding any Investigator's Significant Financial Interest found by LSUHSC-NO to be conflicting, and ensure that a Conflict of Interest Resolution Management Plan has been implemented.

For any Significant Financial Interest that LSUHSC-NO identifies as conflicting subsequent to the initial FCoI report, LSUHSC-NO shall provide to the PHS Awarding Component, within sixty (60) days, a FCoI report regarding the Financial Conflict of Interest, and ensure that a Conflict of Interest Resolution Management Plan has been implemented.

Where a FCoI report involves a Significant Financial Interest that was not disclosed timely by an Investigator or was not previously reviewed by LSUHSC-NO, a retrospective review shall be conducted to determine whether any PHS-funded research conducted prior to the identification and management of the Financial Conflict of Interest was biased in the design, conduct or reporting. If bias is found, a mitigation report shall be submitted to the PHS Awarding Component.

A FCoI report shall include, but not be limited to:

- Project number
- PD/PI or Contact PD/PI if a multiple PD/PI model is used
- Name of the Investigator with the Financial Conflict of Interest
- Name of the entity with which Investigator has the Financial Conflict of Interest

- Nature of the Significant Financial Interest (e.g. equity, consulting fee, travel reimbursement, honorarium)
- Value of the Significant Financial Interest or a statement that the interest is one whose value cannot be readily determined through reference to public prices or other reasonable measures of fair market value
- A description of how the Significant Financial Interest relates to the PHS-funded research and the basis for the determination that the interest conflicts with the research; and
- A description of the key elements of the Conflict of Interest Resolution Management Plan, including:
 - Role and principal duties of the conflicted Investigator in the research project
 - Conditions of the management plan
 - How the management plan is designed to safeguard objectivity in the research project
 - Confirmation of the Investigator's agreement to the management plan
 - How the management plan will be monitored to ensure Investigator compliance;

Annual Report:

LSUHSC-NO shall provide the PHS Awarding Component an annual FCoI report that addresses the status of the Financial Conflicts of Interest, any changes to the management plan for the duration of the project, whether the Financial Conflict of Interest is still being managed or why the interest no longer exists.

In accordance with the regulations, when LSUHSC-NO identifies a Financial Conflict of Interest and eliminates it prior to the expenditure of PHS-awarded funds, LSUHSC-NO shall not submit a FCoI report to the PHS Awarding Component.

Training

Investigators shall complete training regarding the Conflict of Interest in Research policy at least every four years and immediately when any of the following circumstances apply:

- LSUHSC-NO revises the Conflict of Interest in Research policy or procedures in any way that affects the requirements of Investigators
- An Investigator is new to LSUHSC-NO
- An investigator is in non-compliance with the LSUHSC-NO Conflicts of Interest policy or in non-compliance with a Conflict of Interest Resolution Management Plan

Sub-Contracts

If federally-funded research is conducted through collaborators, sub-grantees, or subcontractors, the Principal Investigator and/or Co-Principal Investigator shall ensure that such entities comply with this policy or provide written certification that their entities comply with federal regulations.

If LSUHSC-NO carries out PHS-funded research through a sub-recipient, LSUHSC-NO

must take reasonable steps to ensure that any sub-recipient Investigator complies with PHS Conflict of Interest requirements. Any PHS sub-recipient of LSUHSC-NO shall certify as part of the agreement that its Conflict of Interest policy complies with the PHS requirements. Any agreement for PHS sub-recipients shall specify time period(s) for the sub-recipient to report all identified Financial Conflicts of Interest to LSUHSC-NO.

Confidentiality

Appropriate steps shall be taken by LSUHSC-NO to protect the confidentiality of the information provided; however, LSUHSC-NO shall make certain Conflicts of Interest information available when required by law, mandated by sponsoring entities, or determined to carry out the purpose and administration of this Policy.

Records

Records relating to disclosures of actual or potential Conflicts of Interest and determinations, management plans, or retrospective reviews of the CIRC shall be maintained by the Vice-Chancellor for Academic Affairs for at least three (3) years after the date of the final expenditures report, termination or completion of the Research project, or the resolution of any government action or litigation, whichever is later.

The existence of any Conflict of Interest Resolution Plan must be reported as required by law.

Violations and Sanctions

Violations of this Policy and implementing procedures including, but not limited to, the failure to file timely disclosures, filing incomplete, erroneous or inaccurate disclosures, or failure to comply with prescribed procedures for managing or resolving Conflicts of Interest, will be handled in accordance with applicable LSUHSC-NO policies and procedures and may result in civil or criminal liability.

If the failure of the Investigator to comply with LSUHSC-NO's policy has biased the Research, LSUHSC-NO must promptly notify the funding agency and any other application agencies of the corrective action taken. If the awarding agency is PHS, LSUHSC-NO agrees to make information on conflicting interests available, and how those interests have been managed, reduced, or eliminated.

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 which was not disclosed or managed, LSUHSC-NO must require the Investigator to disclose the conflicting interest in each public presentation of the results of the Research.

Public Accessibility—PHS funded research only

LSUHSC-NO will provide information concerning any Significant Financial Interest disclosed to LSUHSC-NO within five (5) days of written request if the following criteria are met:

1. The Significant Financial Interest was disclosed and is still held by the Investigator
2. LSUHSC-NO has determined that the Significant Financial Interest is related to the PHS-funded research
3. LSUHSC-NO determined that there is a Financial Conflict of Interest

The information provided to the requestor shall include, at a minimum, the following:

- The Investigator's name
- The Investigator's title and role with respect to the research project
- The name of the entity in which the Significant Financial Interest is held
- The nature of the Significant Financial Interest
- The approximate dollar value of the Significant Financial Interest, or a statement that the interest is one whose value cannot be readily determined through reference to public prices or other reasonable measures of fair market value.

Definitions

"Financial Conflict of Interest" means a Significant Financial Interest that could directly and significantly affect the design, conduct, or reporting of research, and occurs when an Investigator's or Immediate Family Members' financial interests compromise, or have the appearance of compromising, an Investigator's professional judgment in proposing, conducting, supervising, or reporting research. A Financial Conflict of Interest depends on the situation and not on the character of the individual.

"Significant Financial Interest" means one or more of the following interests of the Investigator and those of the Investigator's Immediate Family Members 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 one or more of the following interests of the Investigator and those of the Investigator's Immediate Family Members reasonably appears to be related to the Investigator's institutional responsibilities:
 - any remuneration is received from the entity in the twelve (12) months proceeding the disclosure, and the value of any equity interest in the entity as of the date of disclosure. 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 any remuneration is received from the entity in the past twelve (12) months preceding the disclosure, or when the Investigator or the Investigator's Immediate Family Members hold any equity interest (e.g. stock, stock options, or other ownership interest); or Intellectual property rights and interests (e.g. patents, copyrights) upon receipt of income related to such rights and interests.
- Investigators must also disclose the occurrence of any reimbursed or sponsored travel (i.e., that which is paid on behalf of the Investigator so that the exact monetary value may not be readily available), related to their institutional responsibilities; provided that this disclosure requirement does not apply to travel that is reimbursed or sponsored by a Federal, state or local government agency, an Institution of higher education as defined at 20 U.S.C 1001(a), an academic teaching hospital, a medical center, or a research institute that is affiliated with an Institution of higher education.

The term "Significant Financial Interest" does not include the following types of financial interests:

- salary, royalties, or other remuneration paid by the Institution to the Investigator if the Investigator is currently employed or otherwise appointed by the Institution, including intellectual property rights assigned to the Institution and agreements to share in royalties related to such rights, any ownership interest in the Institution held by the Investigator
- income from investment vehicles, such as mutual funds and retirement accounts, as long as the Investigator does not directly control the investment decisions made in these vehicles
- income from seminars, lectures, or teaching engagements sponsored by a Federal, state, or local government agency, an Institution of higher education as defined at 20 U.S.C 1001(a), an academic teaching hospital, a medical center or a research institute that is affiliated with an Institution of higher education, or
- income from service on advisory committees or review panels for a Federal, state or local government agency, an Institution of higher education as defined at 20 U.S.C 1001(a), an academic teaching hospital, a medical center or a research institute that is affiliated with an Institution of higher education

Please note that the above-mentioned exclusions shall not apply if the compensations or transfer of equity interest is conditioned upon a particular outcome in a research project.

"Non-Financial Conflict of Interest" occurs when an Investigator's or Immediate Family Member's role in the University or other outside activities compromise or have the appearance of compromising an Investigator's professional judgment in proposing, conducting, supervising, or reporting research, or come into conflict with an Investigator's primary commitment to maintain scientific objectivity.

Non-Financial Interest includes, but is not limited to:

Conflicts of Commitment regarding Time and Effort

Using a student to perform services for a company in which the Investigator or

Immediate Family Member has an ownership or management role when 1) the student is currently enrolled in the Investigator's or Immediate Family Member's class or 2) the Investigator or Immediate Family Member currently supervise(s) the student in an academic capacity; or 3) the Investigator or Immediate Family Member otherwise has the ability to influence the academic progress of the student.

"Conflict of Interest" means any "Financial Conflict of Interest" and/or any "Non-Financial Conflict of Interest".

"Conflict of Interest Resolution Management Plan" is a written plan developed by the Conflict of Interest Review Committee and approved by the Vice-Chancellor of Academic Affairs, designed to eliminate, reduce or manage a specific Conflict of Interest of an Investigator.

"Conflict of Interest Review Committee (CIRC)" is a committee appointed by the Vice-Chancellor of Academic Affairs, charged with determining whether potential Conflicts of Interest exist, and if so, developing a Conflict of Interest Resolution Plan for Investigators who have reported Conflicts of Interest to the Office of Research Services.

"FCoI report" is a report of a Financial Conflict of Interest to a PHS Awarding Component.

"Investigator" means any LSUHSC-NO Principal Investigators, Co-Principal Investigators, Project Directors, and any other research personnel, including but not limited to, any other LSUHSC-NO employee, (whether faculty or staff), student, or house officer who is responsible for the design, conduct or reporting of the research activity, regardless of funding, and/or status (e.g., faculty key personnel, research associates, technicians, nurse coordinators, administrators, and students).

"Immediate Family Member" means the spouse of the Investigator, dependent children of the Investigator, and any other individual that the Investigator knows or should know maintains Conflicts of Interest that may be impacted by research the Investigator is proposing or conducting. Additionally, any other relationship that a reasonably-prudent person might consider as an appearance of a Conflict of Interest is also included in the definition of "Immediate Family" and should be disclosed as well.

"Institutional Responsibilities" means an Investigator's professional responsibilities on behalf of LSUHSC-NO.

"Research Project": means a systematic investigation, study or experiment designed to develop or contribute to generalizable knowledge relating broadly to public health, including basic and applied research, behavioral, and social research, biomedical research, product development and other scholarly activity.

"Related To" refers to the situation where the Director of Research Services and/or the CIRC reasonably determines that the research could directly and significantly affect the design, conduct, or reporting of the project.

D. Institutional CoI

1. Institutional Conflict of Interest (Institutional CoI)

An institutional Conflict of Interest describes a situation in which the financial interests of an institution or an institutional official, acting within his or her authority on behalf of the institution, may affect or appear to affect the research, education, clinical care, business transactions, or other activities of the institution. Institutional CoIs are of significant concern when financial interests create the potential for inappropriate influence over the institution's activities. The risks are particularly acute in the context of human subjects research, when the protection of human subjects and the integrity of the institution's research may be threatened. The policy is intended to protect against exposure from these risks as they may affect research performed at or under the auspices of the institution.

An institution, including its officials, must balance many competing pressures. It engages in relationships with a variety of sponsors that may lead to financial benefit for the institution in many forms, including major gifts, royalty payments and equity from licensing intellectual property, as well as sponsored educational and research agreements. In addition, university-industry relationships are essential to advancing scientific frontiers and enabling the commercial development of academic discoveries to the benefit of the public. Nonetheless, while generally part of legitimate educational, research, and business activities, relationships with commercial entities cannot be allowed to compromise, or appear to compromise, the integrity of the institution's primary missions, including the safety and integrity of its research, education, and clinical care. The protection of human research subjects and integrity of the institution must remain of the highest priority.

2. Definition of Institutional Conflict of Interest

An institution may have a Conflict of Interest ("institutional CoI") in human subjects research whenever the financial interests of the institution, or of an institutional official acting within his or her authority on behalf of the institution, might affect—or reasonably appear to affect—institutional processes for the design, conduct, reporting, review, or oversight of human subjects research.

3. Identification of Potential Institutional Conflicts of Interest

The following significant financial and fiduciary interests of the institution (greater than \$100,000) warrant formal review of potential institutional CoI with respect to human subjects research, as provided in this policy: 1.) Royalty payments received from the licensing of intellectual property (IP) related to human subjects research and owned by the institution, 2.) Non-publically traded equity in a company sponsoring human subjects research such as a start-up company, 3.) Publically traded equity in a company sponsoring human subjects research, 4.) Investment revenue from any of these sources, 5.) Equity interest senior administration may hold in sponsors of human subjects research, or 6.) Donations made to the LSUHSC-NO Foundation or directly to LSUHSC-NO for human subjects research.

When a human subjects research application is submitted to the IRB, the Chair of the IRB requests that the Director of the Office of Research Services make inquiries as to whether any potential institutional CoI exists as follows: 1) The Director contacts the LSUHSC-NO Office of Technology Management to determine if the Institution holds any patents or licenses related to the research project. (Note that any royalties being received by an investigator for such IP must be disclosed through the LSUHSC-NO CM35 individual Conflict of Interest policy as described earlier), 2) The Director contacts the Vice-Chancellor for Administration and Finance to determine whether the Institution holds any equity interest in the sponsoring company (either publically or non-publically traded) or whether the Institution is receiving any investment revenue related to any of these holdings, and 3) The Director contacts the LSUHSC-NO Office of Sponsored Projects to ascertain whether the Institution has received any donations related to the research of the proposed project and contacts the LSUHSC-NO Foundation for similar information.

For any study where no institutional CoI is determined to exist, the Director of the Office of Research Services will make an annual inquiry as described previously to determine that no new institutional CoI has developed.

4. Review and Management of Institutional Conflict of Interest

Note that many policies of the LA State Ethics Code, LSU Board of Supervisors as denoted in the LSU Bylaws and Regulations, and by LSU System Permanent Memoranda preclude institutional CoI. For example, any state employee holding significant financial interest in a company is prohibited from executing any contractual relationship with that company. Further, senior institutional officials must provide a yearly financial disclosure to Legislative Auditors and must recuse themselves when they hold equity in any company wanting to contract with the Institution.

Any donations made to the Institution or to the LSUHSC-NO Foundation are only accepted absent any *quid pro quo* and are not accepted if directed to a specific human subject research project.

Also, any royalty payments, income from investments, or revenues from equity holdings are managed by the Chancellor's office and do not flow down to specific investigator activities.

Since LSUHSC-NO has adopted AAUP policies on CoI and academic freedom as expressed in the LSUHSC-NO Faculty Handbook investigators cannot be pressured with regard to the conduct of their specific research activities by senior administration or others. Such attempts to influence human subjects research must be reported to the office of Compliance Programs for evaluation.

When a potential institutional CoI that involves a human research project is identified, the Director of the Office of Research Services notifies the CoI committee for an evaluation of the potential CoI and a determination as to whether a conflict resolution plan must be developed. The Director does not notify the full IRB during IRB deliberations of the protocol and must recuse himself/herself for the deliberations

and vote on that project if serving in a voting capacity on the IRB.

If the CoI committee determines that the conflict creates a real institutional CoI, then the committee must develop a CoI resolution plan that either eliminates, reduces or manages the conflict. The conflict resolution plan may include one or more of the following, or other approaches, depending on the circumstance:

- a. Disclosure of the institutional CoI in the informed consent process;
- b. Where the institutional CoI involves a senior official, formal recusal of the conflicted official from the chain of authority over the project and possibly also from authority over salary, promotion, and space allocation decisions affecting the investigator, as well as communication of the recusal arrangements to the official's superior and colleagues.
- c. Where the institutional CoI involves a senior official, designation of a "safe haven" (e.g., a non-conflicted senior individual) with whom the investigator can address institutional CoI-related concerns;
- d. External monitoring of the study, particularly endpoint assessments;
- e. Use of an external DSMB or similar review board to evaluate the design, analytical protocols, and primary and secondary endpoint assessments, and to provide ongoing evaluation of the study for safety, performance issues and the reporting of results;
- f. Disclosure of the institutional CoI in public presentations and publications;
- g. Disclosure of the institutional CoI to other centers in a multi-center trial.

Following deliberations of the IRB concerning the protocol, the CoI resolution plan is presented to the IRB for a determination as to whether the plan adequately addresses the safety and welfare of study participants.

The conflict resolution plan as developed by the CoI committee and approved by the IRB must be reviewed and approved by either the Vice-Chancellor for Academic Affairs or the Chancellor if one or the other is a subject of the CoI.

5. Implementation and Monitoring of the Resolution Plan

The Director of the Office of Research Services is responsible for implementing the conflict resolution plan and monitoring adherence to the plan. On a quarterly basis the Director will make inquiries as previously described to determine if additional elements of conflict have developed, such as new equity interest obtained by the Institution in a sponsoring company. Such circumstances may require an enhancement of the conflict resolution plan through reconsideration by the CoI committee.

References:

State Code of Ethics
LSU Board of Supervisors Bylaws and Regulations
LSUHSC-NO Faculty Handbook
AAUP Policies on CoI and Academic Freedom
LSUHSC-NO Foundation Policies

PM 9
PM 64
PM67

5.16 Protocol Deviations

All protocol deviations must be reported to the IRB on the [Notification of Protocol Deviations/Violations Form](#).

5.17 Notification of Termination of the Study

Termination of a research protocol must be reported in writing to the IRB on the LSUHSC-NO [IRB Re-Approval or Closure Form](#) by the principal investigator. The report must provide the number of subjects enrolled, the number withdrawn, and any results that are known at the time of closure.

5.18 Emergency Use Notification and Reporting Procedures

The FDA has recognized circumstances where a test article (an investigational drug, biologic or device) may be used in patients with life-threatening or other serious diseases, for which no alternative treatment exists.

Under certain circumstances, a test drug or device may need to be administered to a human subject in a life-threatening situation, where there is no standard acceptable treatment available, or the standard treatments have failed. Such emergency use exemption is allowed under 21CFR56.104(c).

Under FDA regulations, the emergency use of a test article, other than a medical device, is a clinical investigation, the patient is a participant, and the FDA may require data from an emergency use to be reported in a marketing application.

DHHS regulations do not permit data obtained from patients to be classified as human participants research, nor permit the outcome of such care to be included in any report of a research activity subject to DHHS regulations.

If the research involves an investigational drug, the FDA has issued an IND.

Requirements

Each of the following conditions must exist to justify the emergency use of an unapproved investigational drug, biologic or device:

- The patient must have a life-threatening condition that requires immediate treatment
- There must be no generally-acceptable or available alternative for treating the patient

- Because of the immediate need to use the drug or device, there is not sufficient time to obtain IRB (i.e., Full Board) approval

All LSUHSC-NO employees must report any usage allowed under 21CFR56.104(c). This report must be received in writing by the LSUHSC IRB within five working days. This exemption allows for one (1) emergency use of a test article by the institution (LSUHSC-NO) without prospective IRB review. The IRB requires that any subsequent use of the investigational product by any LSUHSC-NO employee must have prospective IRB review and approval.

Informed Consent Requirements

Even for emergency use, informed consent must be obtained from the subject or the subject's legally authorized representative (LAR). Informed consent is sought from each prospective participant or the participant's legally authorized representative, in accordance with and to the extent required by 21 CFR 50 and informed consent is appropriately documented, in accordance with and to the extent required by 21 CFR 50.27. Informed consent may be waived if all the following conditions are met, and if the investigator and a physician not otherwise participating in the investigation certify in writing before the use of the test article that all of these conditions are met:

- The subject is confronted with a life-threatening situation necessitating the use of the test article.
- Informed consent cannot be obtained because of an inability to communicate with, or obtain legally effective consent from, the subject.
- Time is not sufficient to obtain consent from the subject's legal representative.
- No alternative method of approved or generally-recognized therapy is available that provides an equal or greater likelihood of saving the subject's life.

When there is not time to obtain certification of another physician prior to the emergency use of the test article informed consent is not required because all of the following are true:

- Immediate use of the test article is, in the investigator's opinion, required to preserve the life of the participant.
- Time is not sufficient to obtain the independent determination of a physician who is not otherwise participating in the clinical investigation.

If time does not allow for such certification prior to use of the investigational product then the investigator should obtain such certification in writing from an independent physician and forward it to the IRB within five days of use of the article.

The Chair of the IRB or the Chair's designee will review reports submitted by

investigators that are related to Emergency Use.

Planned Emergency Use

LSUHSC-NO HRPP does not participate in exception from informed consent for planned emergency research as noted in 21CFR50.

5.19 Humanitarian Use Devices (HUD)

FDA regulations (21CFR814.3(n)) allow for treatment of diseases or disorders affecting fewer than 4,000 individuals per year in the United States under a Humanitarian Device Exemption (HDE). The use of HUDs is not considered to be research under the FDA regulations since they are considered to be legally-marketed devices being used for clinical purposes, and there is no requirement for documentation of informed consent or authorization under the HIPAA Privacy Rule. However, IRB approval is required for the use of a HUD and in some cases informed consent may be required by the IRB. In most cases a well-prepared informational brochure describing the device and related procedures approved by the IRB may be used. Re-approval by the IRB is required at a minimum of a one-year duration, although other requirements such as a shorter approval period or certain reporting requirements may be imposed by the IRB. All information requested in the LSUHSC-NO re-approval application must be provided for consideration of re-approval for the use of a HUD.

Off-Label use of a HUD

Use of a HUD for a condition other than the approved indication may be subject to Investigational Device Exemption (IDE) requirements. However, in an emergency, or if the physician determines that there is no alternative device for the patient's condition a HUD may be used. If a physician wants to use a HUD outside its approved indication(s), FDA recommends that the physician obtain informed consent from the patient and ensure that reasonable patient protection measures are followed, such as devising schedules to monitor the patient, taking into consideration the patient's specific needs and the limited information available about the risks and benefits of the device. FDA further recommends that the physician submit a follow-up report on the patient's condition to the HDE holder and first check with the IRB before such use to review any institutional policy.

Emergency use of a HUD

If a physician in an emergency situation determines that IRB approval for the use of the HUD at the facility cannot be obtained in time to prevent serious harm or death to a patient, a HUD may be used without prior IRB approval. The physician must report the emergency use within five days, provide written notification of the use to the IRB chair including identification of the patient involved, the date of the use, and the reason for the use (21 CFR 814.124).

5.20 Quality Assurance/Improvement Studies

Since QA/QI studies do not meet the definition of research, IRB approval and oversight of such projects is not required. However, making the determination as to whether a project is QA/QI or research can often be difficult. It must be kept in mind that projects can be both QA/QI and research requiring IRB approval and oversight. Therefore, a determination of this QA/QI status must be requested from the LSUHSC-NO IRB before any QA/QI project to be conducted by LSUHSC-NO personnel is initiated. Note that this requirement does not apply to QA/QI projects conducted by LSUHSC-NO employees for HCSD or other hospital operations.

5.21 Use of Radioactive Isotopes

If radioactive isotopes are to be used in vivo, a radioisotope approval must be submitted to the IRB. Call The Office of Radiation Safety (568-6585) for further information and an application form (see the LSUHSC-NO website at <http://www.lsuhs.edu/admin/pfm/ehs/rad.aspx>). Radiation Safety approval should be submitted to the IRB. This approval must be received prior to IRB approval.

5.22 Use of Discarded Human Tissue

In studies where discarded human tissue (including blood, excretions, and teeth) that has not been collected for research purposes is received by the investigator with none of the 18 HIPAA identifiers, and there is no code linking the tissue to the person from whom the tissue is obtained, the investigation does not qualify as human subjects research. This includes protocols involving the collection, use and/or banking of de-identified discarded tissue. As for all work involving interaction with humans, information from humans, or in this case tissue from humans, investigators must request a determination from the IRB Chair as to whether the project meets the definition of human subjects research requiring IRB approval and oversight.

5.23 Unspecified Future Research

One of the underlying principles of the Belmont Report is "Respect for Person". It is the interpretation of the LSUHSC-NO Human Research Protection Program that this principle provides the right of an individual subject to determine whether they want to allow their tissue or health information to be used for unspecified future research. It is the policy of this program that subjects must be provided the right to choose whether they will allow the use of their tissue or health information for such purposes. Participation in the main study under consideration by the subject cannot be conditioned on a subject's affirmative agreement to the use of their tissue or health information in any unspecified future research. Following a complete description of such a request in the informed consent document, a check box can be used, for substudies related to the parent study to provide documentation of the subject's preference. This check box should be initialed or signed and dated by the subject. This policy does not prevent the development of "stand-alone" tissue banks or research data repositories from which tissue or data will be extracted for future research projects. Such repositories and banks must be developed pursuant to IRB

approval as do any studies for which tissue or information from these repositories will be utilized. For all tissue banks and data repositories whether associated with collection from a parent study or not, informed consent must be obtained and informed consent documents should describe the general nature of the research for which the material may be used, e.g., oncology studies. If the intent is to develop a “stand alone” tissue repository for unspecified future research by collecting tissue during a parent study, a separate consent form and HIPAA authorization document must be used.

5.24 International Research

Research conducted outside of the United States by LSUHSC-NO investigators must offer research subjects the same or equivalent levels of participant protection as offered subjects of research conducted domestically at LSUHSC-NO. Investigators must ensure that the research complies with the policies set forth by the LSUHSC-NO Human Research Protection Program, with the relevant HHS and FDA regulations, and when appropriate with ICH Good Clinical Practice guidelines. Research conducted outside of the United States must also respect the customs and comply with the laws of the foreign setting where the research will take place. All aspects of the research must take into account the cultural context of the foreign setting. See the Office of Human Research Protections (OHRP) International Compilation of Research Standards for a listing of key organizations, laws, regulations, and guidelines governing human subjects research in various countries (<http://www.hhs.gov/ohrp/international/intlcompilation/intlcomp2013.pdf.pdf>).

A. LSUHSC-NO IRB Review

Research conducted outside of the United States by employees or agents of LSUHSC-NO must be approved by the LSUHSC-NO IRB before the research can be initiated. The LSUHSC-NO IRB is responsible for monitoring the conduct of the research, including continuing reviews, amendment reviews, and additional post-approval monitoring. In order to ensure pertinent information will be provided to the LSUHSC-NO IRB in a timely fashion, the LSUHSC-NO investigator must submit to the LSUHSC-NO IRB information regarding how communication will be maintained between the investigator, study team, and the LSUHSC-NO IRB.

B. Foreign Review and Engagement

The LSUHSC-NO investigator must provide the LSUHSC-NO IRB with information regarding whether or not foreign IRB, ethics committee (EC), or any other form of review and approval is available and required in the foreign setting. If additional approval is required, the investigator must provide the LSUHSC-NO IRB with documentation that the approval was granted. The investigator may not initiate the study until both LSUHSC-NO IRB approval and all required foreign approvals have been granted. Foreign approval does not guarantee approval by the LSUHSC-NO IRB. When applicable, the LSUHSC-NO IRB will enter into a written agreement with the foreign IRB detailing respective responsibilities as deemed appropriate for the specific

study, and will maintain communication with the foreign IRB/EC to the extent appropriate for the given study.

LSUHSC-NO will consider an institution outside of the United States to be engaged in a non-exempt 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. See the OHRP Guidance on Engagement of Institutions in Human Subjects Research for more detailed scenarios of institutional engagement and non-engagement (<http://www.hhs.gov/ohrp/policy/engage08.html>).

According to HHS regulations [45 CFR 46.103(a); 45 CFR 46.103(b)], if an institution will be engaged in a non-exempt research project and the research project is conducted or supported by a U.S. federal department or agency, that institution must: 1) provide written assurance satisfactory to the department or agency head that it will comply with the requirements set forth in the regulations; and 2) certify to the department or agency head that the research has been reviewed and approved by an IRB provided for in the assurance, and will be subject to continuing review by the IRB.

If an institution outside of the United States will be engaged in the research study, the LSUHSC-NO investigator must provide the LSUHSC-NO IRB with the following: 1) documentation of the foreign institution's OHRP-approved FWA, 2) a copy of the policies and procedures of the IRB provided for in the assurance, and 3) any other information the LSUHSC-NO IRB deems necessary to understand the policies, procedures, and practices of the institution, its IRB, and its employees or agents that will be involved in the research.

The investigator must also provide to the LSUHSC-NO IRB evidence that all non-LSUHSC-NO investigators and study team members possess the qualifications to offer subjects the appropriate human subjects research protections and adhere to the applicable standards set forth for conducting human subjects research in the country (see the OHRP International Compilation of Human Research Standards for a listing of such standards, <http://www.hhs.gov/ohrp/international/intlcompilation/intlcomp2013.pdf.pdf>).

C. Exempt Research

The LSUHSC-NO IRB Chair or his/her designee will determine if a study can be given Exempt status or if the study requires continued oversight by the IRB. Emphasis will be placed on the foreign setting's local context when considering the study's risk-benefit ratio and all other aspects of the research project. Due to variations in local context, a study that would qualify for exempt status when conducted domestically at LSUHSC-NO might not necessarily qualify for exempt status when conducted outside of the United States. If the study is determined to qualify for Exempt status by the LSUHSC-NO IRB, the study team must uphold all ethical principles expected

of Exempt research conducted domestically at LSUHSC-NO while taking into consideration the local context of the foreign setting. If any factors or relevant events alter the risk-benefit ratio of the research project, the LSUHSC-NO investigator must notify the LSUHSC-NO IRB immediately.

D. Local Context

In order to conduct thorough and appropriate reviews, the LSUHSC-NO IRB must possess the appropriate knowledge and expertise regarding the country, culture, and subject population that will be involved in the research project. In cases where the LSUHSC-NO IRB does not possess sufficient expertise regarding the local context of the foreign setting, an expert consultant may be invited to advise members of the LSUHSC-NO IRB about the culture and context, to review experimental protocols and materials, and to provide any other relevant information as deemed necessary. If an expert consultant is invited to a Full Board meeting, the consultant may serve in a non-voting, advisory-only capacity.

The research study must be conceptually and methodologically appropriate in the given local context of the foreign setting. Additionally, the research team must be qualified to perform the research in that setting. Therefore the LSUHSC-NO investigator must demonstrate to the LSUHSC-NO IRB that: (1) the research is appropriate given the local context of the foreign setting, and (2) the investigator and the other members of the research team possess sufficient experience and expertise regarding the country, culture, and subject population that will be involved in the research project.

The LSUHSC-NO investigator must also provide the LSUHSC-NO IRB with information regarding each of the following topics:

- The country and region/community where the research will take place (including current social, economic, and political conditions)
- Whether or not participating in the research poses any additional risks for subjects due to the local context of the foreign setting (and if so, how those risks will be minimized)
- The performance sites where the research will be conducted
- The country's organizations that provide oversight for human subjects research
- Legislation, regulations, and guidelines in place regarding the conduct of human subjects research in the foreign setting
- Country and other approvals that are needed to conduct human subjects research in the foreign setting
- Any form of compensation that will be provided to subjects for participation (including an explanation of the significance of the compensation in terms of relative local context)
- The contact person that will be available in the foreign setting to address subjects' questions or concerns (and how that person can be contacted by subjects)

- The age of majority in the country
- Languages spoken by potential subjects and which members of the research team are fluent in those languages
- Whether or not translators will be needed, qualifications of translators, and relationship of translators to research subjects

If translated consent forms or other translated experimental materials are needed, the LSUHSC-NO investigator will provide the LSUHSC-NO IRB with copies of both the translated and English documents. The investigator must also provide documentation of verification of the translations.

E. Informed Consent

Investigators conducting research outside of the United States must obtain informed consent from every subject or their legally authorized representative in a manner that offers equivalent protections as would be offered subjects consented domestically, while respecting the customs and laws of the foreign setting. Additionally, the informed consent information must be given to the subject or representative in a language understandable to the subject or representative (45 CFR 46.116; 21 CFR 50.20). The LSUHSC-NO investigator must provide the LSUHSC-NO IRB with a detailed description of the informed consent process, including all of the following information:

- Where the consenting process will take place
- What language will be used during the consenting process
- Who will be administering consent
- Whether or not any individuals other than the subject will be providing consent for the subject to participate
- Any other relevant factors (e.g. subject illiteracy, potential unwillingness of subjects to document consent due to local culture, etc.)

Documentation of consent will be expected unless the investigator shows that the study meets the criteria for a waiver of consent [45 CFR 46.116(c) and (d)] or the criteria for a waiver of documentation of consent [45 CFR 46.117(c); 21 CFR 56.109(c)(1)]. These criteria must be fulfilled in light of the cultural context of the foreign setting. If the LSUHSC-NO IRB determines that a waiver of documentation of consent is appropriate for a particular study, the investigator must submit to the LSUHSC-NO IRB an explanation of how subjects will be provided information regarding the research. This includes submitting both English and translated copies of any language that will be used during the (undocumented) consenting process.

F. HIPAA Authorization

LSUHSC-NO will consider any individually identifiable health information collected in the context of international research and transmitted to LSUHSC-NO (a covered entity) to be protected health information (PHI) as defined by 45 CFR 160.103. Therefore, investigators conducting international research which utilizes such

information must abide by the regulations of the HIPAA Privacy Rule (45 CFR Parts 160 and 164) when appropriate.

In cases where language and cultural barriers may impede the population of subjects in the foreign setting from fully understanding the concepts presented in the standard HIPAA Authorization form, the investigator may submit a request for alteration of Authorization to the LSUHSC-NO IRB. Such an alteration would consist of a simplified version of the elements of authorization. The investigator must provide a satisfactory rationale for requesting the alteration.

When appropriate, the investigator may choose to request a waiver of HIPAA Authorization from the LSUHSC-NO IRB. As part of this request, the investigator must provide a satisfactory rationale for requesting the waiver.

The use of an alteration or waiver of HIPAA Authorization must be appropriate in the context of the foreign setting. Additionally, the following criteria set forth by 45 CFR 164.512 (i)(2)(ii) must be fulfilled in order for a request of alteration or waiver of HIPAA Authorization to be approved: (1) the use or disclosure of protected health information involves no more than a minimal risk to the privacy of individuals; (2) the research could not practicably be conducted without the waiver or alteration; and (3) the research could not practicably be conducted without access to and use of the protected health information.

The investigator must submit to the LSUHSC-NO IRB both English and translated copies of any HIPAA forms that will be presented to subjects, along with documentation of verification of translations.

G. Research Involving Children

If research conducted outside of the United States will involve children as subjects, investigators must demonstrate that the research meets standards of such research conducted domestically [see 45 CFR 46 Subpart D; 21 CFR 50 Subpart D], while respecting the customs and laws of the foreign setting. The LSUHSC-NO investigator must provide the LSUHSC-NO IRB with information regarding children in the context of the foreign setting. Specifically, the investigator must provide the LSUHSC-NO IRB with information regarding the following topics:

- The relationship between parents and their children in the country
- An acceptable and effective parental permission process in the foreign setting
- An acceptable and effective child assent process in the foreign setting
- Laws of the foreign setting pertaining to children as research subjects
- Laws of the foreign setting pertaining to orphans/wards as research subjects, if applicable

H. Application

LSUHSC-NO investigators who wish to conduct research outside of the United

States must submit the Supplementary Application for International Research along with a standard research application. The Supplementary Application for International Research and the standard research applications are posted on the LSUHSC-NO IRB website at <http://www.lsuhs.edu/administration/academic/ors/irb.aspx>

5.25 Further Investigator Responsibilities

The researcher provides 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.

The researcher is familiar with the appropriate use of the investigational product, as described in the protocol, in the current investigator brochure, in the product information, and in other information sources provided by the sponsor.

The researcher ensures the accuracy, completeness, legibility, and timeliness of the data reported to the sponsor.

Description of Researcher Responsibilities when following Department of Education regulations:

1. All instructional material--including teachers' manuals, films, tapes, or other supplementary instructional material--which will be used in connection with any research or experimentation program or project, must be available for inspection by the parents or guardians of the children engaged in such research.
2. 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.
3. 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.

Reporting to the Sponsor, Regulatory Authority and the IRB:

The researcher reports all serious adverse events (SAEs) 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 researcher follows regulatory requirements related to the reporting of unexpected serious adverse drug reactions to the regulatory authority and the IRB.

The researcher reports adverse events or laboratory abnormalities 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.

For reported deaths, the researcher supplies the sponsor and the IRB with any additional requested information (e.g., autopsy reports and terminal medical reports).

The researcher provides written reports to the sponsor, the IRB, and, where applicable, the organization on any changes significantly affecting the conduct of the clinical trial or increasing the risk to participants.

If the researcher terminates or suspends a clinical trial without prior agreement of the sponsor, the researcher informs the organization, sponsor, and the IRB.

If the IRB terminates or suspends approval of the clinical trial, the researcher promptly notifies the sponsor.

Upon completion of the clinical trial, the researcher informs the organization, the IRB with a summary of the trial's outcome, and the regulatory authority with any reports required.

5.26 IRBChoice Initiative (previously IRBShare)

LSUHSC-NO has signed an agreement to participate in the IRBChoice initiative. This agreement is signed by institutions around the country in which they agree to accept the IRB review of one of the participating institutions. LSUHSC-NO participation in this program, however, is restricted to consortium institutions of the Louisiana Clinical and Translational Science (LaCaTS) Center NIH award to prime awardee, Pennington Biomedical Research Center. These institutions have agreed to the reciprocal review of the various IRBs of the consortium institutions. Vanderbilt University's IRBChoice website is used for this purpose.

The LaCaTS consortium institutions (LSUHSC-New Orleans, LSUHSC-Shreveport, Tulane University, Pennington Biomedical Research Center, LSU A&M and Xavier University) have agreed to IRB reciprocity of review through an IRBChoice Master Agreement. For example, if an LSUHSC-NO investigator presents a study to the LSUHSC-NO IRB for review, and the project is approved by the LSUHSC-NO IRB then that information can be posted by the IRB on the IRBChoice website. In this instance, this information is only visible to consortium institutions, i.e., no other IRBChoice institutions can view the information.

Each of the consortium institutions can then engage an administrative review of the information provided on the IRBChoice website by the LSUHSC-NO IRB. If the consortium institution decides to participate in that study, then they can accept the LSUHSC-NO IRB review for their approval of the study. Similarly, a study posted by another LaCaTS consortium institution can be administratively reviewed by the LSUHSC-NO IRB for approval should a LSUHSC-NO investigator be asked to participate in the study.

The IRBChoice initiative has received approval from OHRP as a legal mechanism for IRB reciprocity of review. Both minimal risk and greater than minimal risk studies can be approved through this mechanism. Studies eligible for Exempt status are not eligible for inclusion in the IRBChoice mechanism.

Note that due to the effort involved in managing and posting material on the

IRBChoice website, existing studies approved by the LSUHSC-NO IRB cannot be transferred to the IRBChoice mechanism.

5.27 Additional Requirements for Department of Defense (DoD) Research

DoD Directive 3216.02 is the DoD Instruction (DoDI) in accordance with the authority in DoDD 5134.01 to establish policy and assign responsibilities for the protection of human subjects in DoD-supported programs to implement part 219 of title 32, Code of Federal Regulations (CFR) (also known as "the Common Rule". The DoD Issuances website is <http://www.dtic.mil/whs/directives/corres/ins1.html>.

In addition to the IRB policies and procedures, the following specific requirements contained in DoD regulations and requirements are adopted. Additional information of these requirements can to be found in the "Protection of Human Subjects and Adherence to Ethical Standards in DoD-Supported Research", DoDI 3216.02 at <http://www.dtic.mil/whs/directives/corres/pdf/321602p.pdf>.

1. Non-exempt classified research must be conducted following the requirements of listed in DoDI 3216.02 13. The IRB will consider the scientific merit of the research and may rely on outside experts to provide an evaluation of the scientific merit.
2. Initial and continuing research ethics education for all personnel who conduct, review, approve, oversee, support, or manage human participants research includes any specific DoD educational requirements or certification required to ensure the personnel are qualified to perform the research, based on the complexity and risk of the research. IRB staff, chair, and members and Researchers and Research Staff participating in DoD Research are required to review DoDI 3216.02 and any other regulations and requirements specific to the project.
3. 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.
4. Any determinations of serious or continuing noncompliance of DoD-supported research will be promptly (no longer than within 30 days) reported to the DoD human research protection officer.
5. For DoD-supported research reviewed by a convened IRB or reviewed by an expedited procedure, the following will be promptly (no longer than within 30 days) reported to the DoD human research protection officer:
 - When significant changes to the research protocol are approved by the IRB.
 - The results of the IRB continuing review.
 - Change of reviewing IRB.

- When the organization is notified by any federal department, agency or national organization that any part of an HRPP is under investigation for cause involving a DoD supported research protocol.
6. Surveys performed on DoD personnel will be submitted, reviewed, and approved by the DoD after the research protocol is reviewed and approved by the IRB.
 - When significant changes to the research protocol are approved by the IRB.
 - The results of the IRB continuing review.
 - Change of reviewing IRB.
 - When the organization is notified by any federal department, agency or national organization that any part of an HRPP is under investigation for cause involving a DoD supported research protocol.
 7. Any unanticipated problems involving risks to participants or others for any DoD-supported research will be promptly (no longer than within 30 days) reported to the DoD human research protection officer.
 8. Any suspension or termination of DoD supported research will be promptly (no longer than within 30 days) reported to the DoD human research protection officer.
 9. When conducting multi-site research, a formal agreement between organizations will be required to specify the roles and responsibilities of each party.
 10. The definition of the minimal risk based on the phrase “ordinarily encountered in daily life or during the performance of routine physical or physiological examinations or tests” must not be interpreted to include the inherent risks certain categories of human subjects face in their everyday life. For example, the risks imposed in research involving human subjects 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).
 11. A research monitor will be appointed under the following circumstances:
 - Required for research involve greater than minimal risk, although the IRB or organizational official can require this for a portion of the research or studies involving no more than minimal risk, if appropriate.
 - The research monitor is appointed by name and must be independent of the team conducting the research.
 - There may be more than one research monitor (e.g. if different skills or experience are needed).

- The monitor may be an ombudsman or a member of the data safety monitoring board. The IRB must approve a written summary of the monitors' duties, authorities, and responsibilities.
 - The IRB or HRPP official must communicate with research monitors to confirm their duties, authorities, and responsibilities.
 - The duties of the research monitor are determined on the basis of specific risks or concerns about the research.
 - May perform oversight functions (e.g. observe recruitment, enrollment procedures, and the consent process, oversee study interventions and interactions, review monitoring plans and unanticipated problems involving risks to participants or others, oversee data matching, data collection and analysis).
 - May discuss the research protocol with researchers, interview human subjects, and consult with others outside of the study.
 - Report observations and findings to the IRB or a designated official.
 - The research monitor has the authority to:
 - Stop a research study in progress.
 - Remove individuals from study.
 - Take any steps to protect the safety and wellbeing of participants until the IRB can assess.
12. When research involves U.S. military personnel, research protocols will include the following guidelines for additional protections for military research participants to minimize undue influence:
- Officers are not permitted to influence the decision of their subordinates.
 - Officers and senior non-commissioned officers may not be present at the time of recruitment.
 - Officers and senior non-commissioned officers have a separate opportunity to participate.
 - When recruitment involves a percentage of a unit, an independent ombudsman is present.
 - When research involves U.S. military personnel, policies and procedures require limitations on dual compensation:
 - Prohibit an individual from receiving pay of compensation for research during duty hours.
 - An individual may be compensated for research if the participant is involved in the research when not on duty.
 - Federal employees while on duty and nonfederal persons may be compensated for blood draws for research up to \$50 for each blood draw.

- 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.
13. IRB policy and procedure for the disclosure for research-related injury follow the requirements of the DoD component listed in DoDI 3216.02 5.3.4.
14. If the research participant meets the IRB definition of “experimental subject,” a waiver of the consent process is prohibited unless a waiver is obtained from the Assistant Secretary of Defense for Research and Engineering.
- The Assistant Secretary for Defense for Research and Engineering may waive the requirements for consent when all of the following are met:
 - The research is necessary to advance the development of a medical product for the Military Services.
 - The research may directly benefit the individual experimental subject.
 - The research is conducted in compliance with all other applicable laws and regulations.
 - For classified research, waivers of consent are prohibited.
 - If the research participant does not meet the definition of “experimental subject,” policies and procedures allow the IRB or EC to waive the consent process.
15. Research involving pregnant women, prisoners, and children are subject to the DHHS Subparts B, C, and D with the following conditions:
- For purposes of applying Subpart B, the phrase “biomedical knowledge” must be replaced with “generalizable knowledge.”
 - The applicability of Subpart B is limited to research involving pregnant women as participants in research that is more than minimal risk and included interventions or invasive procedures to the woman or the fetus or involving fetuses or neonates as participants.
 - Fetal research must comply with the US Code Title 42, Chapter 6A, Subchapter III, Part H, 289g.
 - Research involving prisoners cannot be reviewed by the expedited procedure.
 - When the IRB reviews research involving prisoners, at least one prisoner representative must be present for quorum.
 - In addition to allowable categories of research on prisoners in Subpart C, epidemiological research is also allowable when:
 - The research describes the prevalence or incidence of a disease by identifying all cases or studies potential risk factor association for a disease.
 - The research presents no more than minimal risk.
 - The research presents no more than an inconvenience to the participant.

- When a participant becomes a prisoner, if the researcher asserts to the IRB that it is in the best interest of the prisoner-participant to continue to participate in the research while a prisoner, the IRB chair may determine that the prisoner participant may continue to participate until the convened IRB can review this request to approve a change in the research protocol and until the organizational official and DoD Component office review the IRB's approval to change the research protocol. Otherwise, the IRB chair must require that all research interactions and interventions with the prisoner-subject (including obtaining identifiable private information) cease until the convened IRB can review this request to approve a change in the research protocol. The convened IRB, upon receipt of notification that a previously enrolled human participant has become a prisoner, must promptly re-review the research protocol to ensure that the rights and wellbeing of the human subject, now a prisoner, are not in jeopardy. The IRB should consult with a subject matter expert having the expertise of a prisoner representative if the IRB reviewing the research protocol does not have a prisoner representative. If the prisoner participant can continue to consent to participate and is capable of meeting the research protocol requirements, the terms of the prisoner participant's confinement does not inhibit the ethical conduct of the research, and there are no other significant issues preventing the research involving human participants from continuing as approved, the convened IRB may approve a change in the study to allow this prisoner participant to continue to participate in the research. This approval is limited to the individual prisoner-participant and does not allow recruitment of prisoners as participants.
 - Research involving a detainee as a human participants is prohibited.
 - This prohibition does not apply to research involving investigational drugs and devices when the same products would be offered to US military personnel in the same location for the same condition.
 - The exemption for research involving survey or interview procedures or observation of public behavior, does not apply to research with children, except for research involving observations of public behavior when the investigator(s) do not participate in the activities being observed.
 - Policies and procedures prohibit research involving prisoners of war.
 - The IRB is aware of the definition of "prisoner of war" for the DoD component granting the addendum.
16. If consent is to be obtained from the experimental subjects' legal representative, the research must intend to benefit the individual participant. The determination that research is intended to be beneficial to the individual experimental subject will be made by the IRB.
17. In addition to IRB policy for keeping records of a research protocol well organized to allow a reconstruction of a complete history of IRB actions related to the review and approval of the research protocol or plan and to store the

records in a way that maintains confidentiality, the following apply to records of DoD research:

- Records will include documentation of compliance or non-compliance with DoD regulations.
- Records will 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.
- Records are retained for the maximum required period of time required by IRB policy or by the DoD.

5.28 Research conducted outside the jurisdiction of the State of Louisiana

In cases of human subjects research under the authority of the LSUHSC-NO IRB but conducted outside of the state of Louisiana, the LSUHSC-NO IRB confers with the LSUHSC-NO Senior Staff Counsel regarding the applicability of other state, national, or international laws to the particular project. These cases are identified in the pre-review process of an application to the IRB and the advice of counsel may be sought prior to the approval of the study. In general, if the study is conducted in the USA, the LSUHSC-NO IRB will apply the law of the state in which the research is being conducted.

Except in the case of children where NIH defines a child as being less than 21 years of age, the FDA and other DHHS agencies follow state law as to the definition of "child", "legally authorized representative", and "guardian". Counsel assists in determining these definitions for jurisdictions outside the State of Louisiana.

Within Louisiana laws and codes, these terms are defined as follows:

Child is defined as a person not attaining the age of 18 years of age (adult) as described in LaRS 15:1503, 46:2132, and other sections of the LA Revised Statutes.

Legally authorized representative is not defined for research, *per se*, in Louisiana law but rather the Louisiana Medical Consent Law (LaRS 40:1299.53) is followed as to persons who may consent to surgical or medical treatment:

In addition to such other persons as may be authorized and empowered, any one of the following persons in the following order of priority, if there is no person in a prior class who is reasonably available, willing, and competent to act, is authorized and empowered to consent, either orally or otherwise, to any surgical or medical treatment or procedures including autopsy not prohibited by law which may be suggested, recommended, prescribed, or directed by a duly licensed physician:

- 1) Any adult, for himself.

- 2) The judicially appointed tutor or curator of the patient, if one has been appointed.
- 3) An agent acting pursuant to a valid mandate, specifically authorizing the agent to make health care decisions.
- 4) The patient's spouse not judicially separated.
- 5) An adult child of the patient.
- 6) Any parent, whether adult or minor, for his child.
- 7) The patient's sibling.
- 8) The patient's other ascendants or descendants.
- 9) Upon the inability of any adult to consent for himself and in the absence of any person listed in Paragraphs (2) through (8) of this Subsection, an adult friend of the patient. For purposes of this Subsection to consent, "adult friend" means an adult who has exhibited special care and concern for the patient, who is generally familiar with the patient's health care views and desires, and who is willing and able to become involved in the patient's health care decisions and to act in the patient's best interest. The adult friend shall sign and date an acknowledgment form provided by the hospital or other health care facility in which the patient is located for placement in the patient's records certifying that he or she meets such criteria.
- 10) Any person temporarily standing in loco parentis, whether formally serving or not, for the minor under his care and any guardian for his ward.

Guardianship of children:

Art. 7 Childrens Code Article 720. Motion for guardianship

After a child has been adjudicated to be in need of care, a motion for guardianship may be filed by the department, parent, or counsel for the child; or the department may submit a case plan along with the case review report to the court and all counsel of record recommending guardianship in accordance with Children's Code Articles 674, 688, and 689.

Art. 6 Childrens Code Article 681. Dispositional alternatives

In a case in which a child has been adjudicated to be in need of care, the child's health and safety shall be the paramount concern, and the court may do any of the following:

- 1) Place the child in the custody of a parent or such other suitable person on such terms and conditions as deemed in the best interest of the child including but not limited to the issuance of a protective order pursuant to Article 618.
- 2) Place the child in the custody of a private or public institution or agency.
- 3) Commit a child found to have a mental illness to a public or private institution for persons with mental illness.
- 4) Grant guardianship of the child to a nonparent.
- 5) Make such other disposition or combination of the above dispositions as the court deems to be in the best interest of the child.

5.29 Prevention and Early Treatment of Acute Lung Injury (PETAL) – Central IRB (Local Management Process)

Louisiana State University Health Sciences Center–New Orleans (LSUHSC–NO also referred to as the Institution) and the Vanderbilt University IRB have initiated an authorization agreement whereby LSUHSC–NO will defer to the Vanderbilt University IRB, acting as the central IRB (CIRB) for PETAL Network clinical trials. The PETAL Network conducts cooperative group trials funded by the National Heart, Lung, and Blood Institute of the National Institutes of Health.

The CIRB will conduct reviews of the following: initial and continuing reviews, amendments, non-local serious adverse events, local serious adverse events that are not listed in the protocol or that meet the criteria of unanticipated problems, all unanticipated problems, and all instances of noncompliance. The CIRB will also address local context issues via the PETAL Network, Site Local Context information document.

Review Process for CIRB-Approved Protocols:

As the Signatory Institution, LSUHSC-NO will monitor the conduct of the research locally. Monitoring will be accomplished by the LSUHSC-NO IRB staff with the cooperation of the local PETAL Network, LSUHSC-NO Principal Investigator (PI) and study teams.

Reviews of CIRB-approved protocols will be performed as follows:

A PI who wishes to enroll subjects in a CIRB-approved protocol must submit a request to the Institution using the LSUHSC-NO IRB PETAL Abbreviated Application. In addition, the PI must submit the approved CIRB informed consent form (ICF) modified for local site use and the LSUHSC-NO HIPAA Authorization document. All study related documents must be made available to the LSUHSC-NO IRB through the PETAL Clinical Coordinating Center website or supplied to the LSUHSC-NO IRB as electronic versions of the documents.

The PI must submit to the LSUHSC-NO IRB the CIRB approval of the study in question.

Further Review Procedures:

The Institution will perform reviews of further documentation as follows:

1. The local PETAL PI must provide the LSUHSC-NO IRB a brief summary of all significant amendments reviewed by the full Board CIRB along with notification of CIRB approval. If amendments resulted in changes to the ICF, a copy of the newly approved ICF, that includes local context issues, must be submitted to the LSUHSC-NO IRB.

2. For continuing reviews that were approved by the full board CIRB, the local PETAL PI will submit copies of the continuing review application and the CIRB's continuing review approval documentation to the LSUHSC-NO IRB staff.
3. The local PETAL PI must provide any approved advertisements that will appear locally for enrollment into the study the LSUHSC-NO IRB staff.
4. The local PETAL PI will submit notification of any expedited CIRB activity related to the study to the LSUHSC-NO IRB staff.
5. The local PETAL PI must report local serious adverse events (SAEs), local unanticipated problems, protocol deviations and local instances of noncompliance to the CIRB as required by the CIRB Standard Operating Procedures, and must simultaneously report to the LSUHSC-NO IRB all such events. The principal investigator must inform the LSUHSC-NO IRB staff of any actions taken by the CIRB that result from problems identified in these areas.
6. Note that the Institution retains the right to expand on or to create its own corrective action plan related to issues of non-compliance with CIRB or LSUHSC-NO IRB policies, or pertinent federal regulations. Further actions by the Institution's administration may vary depending on the significance of issues involved but may include withholding of permission to conduct further human subjects research at LSUHSC-NO or termination of employment at LSUHSC-NO.
7. LSUHSC-NO retains the right to not accept determinations of the CIRB. In such a case, the study must be closed at the Institution with due consideration of the safety and welfare of enrolled subjects.

Further Responsibilities of Institution:

LSUHSC-NO will:

1. Comply with the CIRB's requirements and directives
2. Report to the CIRB the names of any Component or Affiliate Institutions that rely on LSUHSC-NO IRB
3. Maintain a Federal Wide Assurance (FWA) and designate the Vanderbilt IRB under its FWA
4. Maintain compliance with any additional state, local, or institutional requirements related to the protection of human subjects
5. Ensure that local investigators receive proper initial and continuing education on the requirements related to human subjects protections

6. Perform oversight of the local conduct of the study, monitoring study compliance, thereby ensuring the safe and appropriate performance of the research at this institution. There will also be the provision of a mechanism by which complaints about the research can be made by local study participants or others
7. Review all local SAEs, unanticipated problems, and issues of non-compliance as submitted to the CIRB and evaluate whether Institutional actions in addition to those taken by the CIRB may be required
8. Provide updates to the CIRB whenever a PI is no longer the responsible party for a study under the purview of the CIRB
9. Provide to the CIRB and keep current the names and addresses of local contact persons who have authority to communicate for the Institution, such as the local IRB administrator
10. Notify the CIRB when a regulatory deficiency has been cited on an audit that occurred during the time that the CIRB was responsible for study review
11. Maintain a regulatory file for each study under CIRB purview as per local institution and Cooperative Group policy

5.30 Research Data Protection Plan

All human subject's research submitted for consideration by the LSUHSC-NO IRB must include a department approved research data protection plan. In addition, Department Heads and/or Center Directors will be required to provide signature confirmed approvals that the proposed plan is in compliance with federal regulation, institutional information technology guidelines, and LSUHSC-NO IRB policy. The purpose of the plan is ensure research data are appropriately protected from loss or unauthorized disclosure. It should also assure research data can be recovered in the event of a disaster, equipment failure, loss of encryption keys, and theft or loss of research equipment.

The LSUHSC-NO IRB Chair or designee will review and evaluate all research data protection plans. This evaluation will be completed during the initial review consideration of the research and periodically throughout the study approval period. It will also be the LSUHSC-NO Chair's discretion to audit individual approved plan for routine review of for-cause.

The plan proposed by a Principal Investigator to the LSUHSC-NO IRB must address the following components related to the research and working environment of the research team:

1. List and describe all locations where the original and any copies of the data will be kept (and provide building name, street address, and room numbers).
2. Describe the computing environment in which the data will be used, including:

- Computing platform (e.g., personal computer, workstation, mobile or portable device) and operating systems
- Number of computers on which data will be stored or analyzed
- Whether devices used in the research project will be on a network or will be stand-alone.
- Physical environment in which computer is kept (e.g., in room with public access, in room locked when not in use by research staff)
- A list and description of all devices on which data will be stored (e.g., network server, One Drive for Business, storage device, PC hard drive, removable storage device such as USB hard drives, USB flash drives, SD cards and other memory cards, CDs, DVDs, etc.)
- Methods of data storage when data are not being used
- Methods of sanitation of equipment used in the study when no longer needed
- Methods of transmitting the data between research team members (if applicable)
- Methods of storage of computer output both in electronic form and in hard copy (on paper or other media)
- Recovery plan to be implemented in the event of loss of data due to natural disaster, equipment failure, loss of encryption keys, loss or theft of a device, etc. and
- Instruction in data protection policies that will be provided to each staff member and student before they receive access to the data as well as recurrent instruction that will be conducted at least annually.

Although LSUHSC-NO Principal Investigators are encouraged to suggest a variety of components for their research data protection plan, all plans approved by the LSUHSC-IRB must include some or all of the following features:

- Password-protected access to all devices storing the data
- Automatic activation of password-protection after five minutes of inactivity on the computer
- Encryption of all files containing Protected data stored on devices other than LSUHSC-NO servers or One Drive for Business (identify encryption software to be used e.g. Bitlocker, PGP, Veracrypt, etc.)
- No storage of the data on laptop computers, unsecured network servers, etc. without encryption
- Secure storage of any and all removable devices holding the data (e.g., USB hard drives, USB flash drives, SD cards and other memory cards, CDs, DVDs, etc.), through encryption and storage in a locked compartment or room when not in use
- Storage of detailed printouts derived from data analysis in a locked compartment or room when not in use
- Shred all detailed listings and printouts that are no longer needed
- Prepare and maintain a log of all data files acquired. Record dates that data and paperwork are received and returned or destroyed

- Protect all files containing Protected and/or Restricted Data in accordance with the Data Protection Plan and destroy or otherwise render the Protected and/or Restricted data unrecoverable once it is no longer needed by the research team
- Report any and all violations of the Data Protection Plan to the IRB and the Compliance Officer
- No transmittal of data or detailed tabulations via email or email attachment over the Internet without ensuring that the recipient supports encrypted transmission. Data can also be transmitted by LSU Health Files.
- Brief all research staff that have access to Protected Data about the Data Protection Plan, appropriate safeguards, and penalties for inappropriate use.