



Human Research Protection Program

Institutional Review Board - Policies and Procedures Guidebook

TABLE OF CONTENTS

Federal, State and University Regulations Related to the IRB	Section 1.0
Responsibilities and Functions of the Health Sciences Center Administration	Section 2.0
Administration	Section 2.1
IRB Disapproval	Section 2.2
Research Funding.....	Section 2.3
The Institutional Review Board (IRB)	Section 3.0
IRB Authority	Section 3.1
Responsibilities of the Board	Section 3.2
Composition of the IRB and Quorum	Section 3.3
Member Duties	Section 3.4
IRB Chair - Authority and Responsibilities	Section 3.5
Operating Procedures of the IRB	Section 4.0
Criteria for IRB approval of research (45CFR46.111 and 21CFR56.111)	Section 4.1
Conducting Review of New Applications	Section 4.2
Notification of Investigators Following Review	Section 4.3
Investigator Assurance and Notice to the Institutional Official.....	Section 4.4
Changes to an Approved Protocol.....	Section 4.5
Continuing Review	Section 4.6
Unanticipated Problems Involving Risks to Subjects and Others	Section 4.7
Non-compliance by Investigators	Section 4.8

Schedule of Meetings	Section 4.9
IRB Records	Section 4.10
NIH-NCI CIRB.....	Section 4.11
Items of Special Interest	Section 5.0
Emergency Use Notification and Reporting Procedures.....	Section 5.1
Assessment of Risks to Subjects	Section 5.2
Subject Population	Section 5.3
Use of Radioactive Isotopes.....	Section 5.4
Subject Entry Site Approval.....	Section 5.5
Subject Payment.....	Section 5.6
Advertisements for Subjects.....	Section 5.7
Educational Material for Subjects	Section 5.8
Confidentiality of Data and HIPAA Privacy Rule	Section 5.9
Record Keeping by Investigators.....	Section 5.10
Human Subject Protection Educational Policies and Resources	Section 5.11
Child Assent	Section 5.12
Protocol Deviations.....	Section 5.13
Notification of Termination of the Study	Section 5.14
Institutional Bio-safety Committee Review	Section 5.15
Quality Assurance/Quality Improvement Projects	Section 5.16
Conflicts of Interest.....	Section 5.17
Grant Applications.....	Section 5.18
Informed Consent	Section 5.19
Use of Discarded Human Tissue	Section 5.20
Pregnant Partners	Section 5.21
Humanitarian Use Devices (HUD)	Section 5.22

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.

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.

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.

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

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 Vice-Chancellor for Academic Affairs is the Institutional Official for the HRPP 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 or Academic Affairs, the Chair has the authority to interact directly with the Chancellor (Chief Executive Officer of LSUHSC-NO) if needed. Specifically 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. 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. Make certain that all recommended actions are initiated pursuant to IRB decisions
- F. 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
- G. Make certain that the professional staff is informed as to the responsibilities of the institution for protection of human subjects
- H. Develop necessary arrangements with affiliated and other institutions for mutual assurance of protection of human subjects
- I. Implement FDA regulations and transmit reports regarding investigational new drugs, devices, and biologics
- J. Provide the liaison and channeling of appropriate information among staff, IRB, the administration, and governmental agencies
- K. 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. Continually monitoring IRB processes and practices for improvement in the protection of subjects

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.

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. 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.

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 be sure 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, 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.
- G. The activity must have sufficient scientific merit in the field of research to allow subjects to participate.

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. 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.

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. At least one physician member must be present when considering FDA-regulated articles. When considering research that involves prisoners as subjects, the prisoner representative is 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.

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. 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 an 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.

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 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 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.

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 reviewer(s) may exercise all the authorities of the IRB, except disapproval. Approval criteria for expedited review are the same as those for full-

board review. Research may only be disapproved following review by the full committee. 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. Waiver of the consent form may be granted at the investigator's request if all federal regulations apply (see [Section 5.19](#)). 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. 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. The process of notification and receipt of investigator assurance is identical to Full-Board considered projects.

Each application requiring Full-Board review is assigned a primary reviewer by the Chair or Vice-Chair. New applications are slated for a specific agenda. In addition to

the application and consent form, the primary reviewer receives the expanded protocol and all other related materials. These materials are provided to the primary reviewer at least one week prior to the meeting. The remainder of the Board receives the application that includes the project summary, and the proposed consent form. 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.

A determination of Significant Risk/Non-Significant Risk for devices being used under an IDE is made by the IRB at this time. This determination is incorporated into the motion concerning action on the application.

During the meeting, the primary reviewer 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

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.

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

When the protocol receives final approval, the IRB office generates an approval 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; 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.

The period of approval is determined by the Board based on the merit of the study and the level of risk to the subject. The duration of the approval period is tracked through a computer database. The period of approval is included on the form, but will not exceed one year. The initial approval period will begin on the date of the

meeting at which the application was approved. 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.

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." Such unapproved changes must be promptly reported to the IRB, and will be duly considered.

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. 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. 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 types of changes are considered to be minimal risk changes and 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 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 a description of the amendment in their meeting book. 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.

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 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.

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. 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 and 21CFR56.110. 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. The re-approval application and the current consent form 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 seconded, 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. 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. 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 routinely conducts random 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 are conducted in conjunction with the Office of Compliance Programs HIPAA compliance audits. 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

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.

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.

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. The report is provided to Board members in their meeting books and the report is assigned to a primary reviewer for presentation to the Full Board. Following discussion at the meeting, the Board determines whether any additional corrective action not taken by the sponsor is to be recommended. If action is required, the investigator and institution are notified. The investigator is responsible for informing the sponsor of the Board's decision.

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 determine whether corrective action or substantive changes must be made in the study.

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. Implementation of additional procedures for monitoring subjects;
4. Suspension of enrollment of new subjects;

5. Suspension of research procedures in currently-enrolled subjects;
6. Modification of informed consent documents to include a description of newly-recognized risks; and
7. Provision of additional information about newly-recognized risks to previously-enrolled subjects.

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 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, sponsors and performance sites.

4.8 Non-compliance by investigators

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.

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 that is the case, 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 subjects are being placed at risk, then the study will be administratively suspended and 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 the "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.

At the conclusion of the investigation, the results are presented to the Board at a convened meeting of the IRB. 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 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. 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.

Per federal policy, any serious or on-going non-compliance with DHHS human subjects regulations or the determinations of the IRB will be promptly reported to the sponsor of the study, institutional officials, OHRP, and, if applicable, the FDA.

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. 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.

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/no/Administration/rs/irb/>.

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. 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. 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.

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). 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 IRB Review Process)

Louisiana State University Health Sciences Center–New Orleans (LSUHSC–NO) and the National Cancer Institute (NCI) have initiated an authorization agreement whereby the LSUHSC–NO IRB 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, 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 DCPC. The Ped CIRB may review other trials approved by DCPC, 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 initial and continuing review of studies, as well as any changes to the protocol, and will review all non-local serious adverse events. The LSUHSC–NO IRB will address local context issues, review local serious adverse events and protocol deviations, and monitor conduct of the study at the local site(s).

The LSUHSC–NO IRB will conduct a “facilitated review” of a CIRB-approved protocol in order to determine whether to accept the CIRB approval, whereby the CIRB would become the IRB of record for that protocol. If the determination is made not to accept the CIRB approval; e.g., if more changes are required by the LSUHSC–NO IRB than are acceptable to the CIRB, then the protocol may be reviewed under Full Board procedures by the LSUHSC–NO IRB.

A. Facilitated Review Process

The LSUHSC-NO IRB will perform facilitated reviews of CIRB-approved protocols as follows:

1. The principal investigator who wishes to enroll subjects in a CIRB-approved protocol will download the Local IRB Facilitated Review Packet, and any other documents as desired by the LSUHSC–NO IRB, from the Participant side of the CIRB website www.ncicirb.org and submit these documents to the LSUHSC–NO IRB.
2. The LSUHSC–NO IRB coordinator for CIRB protocols will make a preliminary review of the submitted materials to ensure that the packet is complete and that the ICF is in the proper LSUHSC–NO format with all required local language inserted.
3. At least one voting member of the LSUHSC–NO IRB in conjunction with the LSUHSC–NO IRB Chair will conduct the facilitated review of the study. The reviewer and Chair will determine whether to accept the CIRB review and whether there are local concerns which need to be addressed. The reviewer and Chair examine the materials submitted from the principal investigator, and any additional information as deemed appropriate, in order to decide whether a particular protocol and ICF are acceptable and whether they are appropriate in their local context. The LSUHSC–NO IRB has the option to accept the CIRB approval "as is", accept it with *de minimus* modifications, or decide not to accept the CIRB review. In this case, should the investigator want to open the study, s/he will be required to submit the protocol for local, Full Board review. The reviewer and Chair are authorized by the LSUHSC–NO IRB to make determinations regarding acceptability of the protocol as approved by the CIRB along with any changes which may be deemed necessary to the ICF.
4. The LSUHSC–NO IRB may add local language to the ICF dealing with state and local law, institutional requirements, or IRB policies. No CIRB-approved information may be deleted from the ICF. The LSUHSC–NO IRB may also make minor word substitutions or additions to the ICF, particularly to facilitate better comprehension by the local population, as long as the proposed changes do not alter the meaning of the CIRB-approved contents. Additional risks may be added to the ICF. The reviewer will communicate with the investigator regarding any changes necessary prior to acceptance; the investigator will re-submit any such revisions to the LSUHSC–NO IRB. Revisions/changes

to the local ICF other than those described above require Full Board review at the local level. Facilitated review may not be used, and the CIRB cannot serve as the IRB of record for that protocol at LSUHSC–NO.

5. The LSUHSC–NO IRB will notify the Central IRB Operations Office of its acceptance of the CIRB review of a protocol. The coordinator will accomplish this by clicking on the "Facilitated Review Acceptance Form" button/link within the main menu for each protocol and completing the Facilitated Review Acceptance Form. This form must be completed and submitted for the CIRB to become the Official IRB of Record for a particular study. A separate form will be submitted for each protocol review that is accepted.
6. The LSUHSC–NO IRB will notify the principal investigator of its determination with regard to each protocol submitted.

B. Further Review Procedures

The LSUHSC-NO IRB will perform reviews of further documentation as follows:

1. For all protocols for which the CIRB is the IRB of record, the principal investigator will download any amendments to the CIRB-approved protocol, along with the CIRB approval documentation, and submit them to the LSUHSC–NO IRB for review. The principal investigator will apprise the LSUHSC–NO IRB of continuing review approval of the protocol by the CIRB and will submit the CIRB Continuing Review approval documentation and any revisions to the ICF. The CIRB renewal date becomes the re-approval date of record. The voting member/s retain/s the option not to accept the CIRB review and can choose to request a local Full Board review, in which case the CIRB would no longer be the IRB of record for that protocol. The LSUHSC-NO IRB would then close that study with the CIRB and open the protocol locally under the jurisdiction of the LSUHSC-NO IRB.
2. The LSUHSC–NO IRB will review all local SAEs generated during the conduct of the study, as well as any protocol deviations/violations. Any actions taken as a result of problems identified in these areas will be shared with the CIRB and reported as required by the procedures established by the study's lead organization.

C. Further Responsibilities of the LSUHSC–NO IRB

The LSUHSC-NO IRB will:

1. Maintain a Federalwide Assurance (FWA) and designate the NCI CIRBs under its FWA
2. Maintain a human subjects protection program, as required by the DHHS OHRP
3. Maintain a local IRB whose membership satisfies the requirements of 45CFR46 and 21CRF56

4. Maintain compliance with any additional state, local, or institutional requirements related to the protection of human subjects
5. Ensure that local IRB members and local investigators receive proper initial and continuing education on the requirements related to human subjects protections
6. Notify the CIRB immediately if there is ever a suspension or restriction of the local IRB's authorization to review studies
7. 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
8. Notify the CIRB immediately if there is a suspension or restriction of a local investigator
9. Provide to the CIRB and keep current the names and addresses of local contact persons who have authority to communicate for the local IRB, such as the local IRB administrator.
10. Notify the CIRB if there is ever a change in the acceptance/rejection of the CIRB review for any given protocol
11. Maintain in the local IRB records documentation of the decision reached for each protocol, and evidence that it has received and considered all CIRB material relevant to the study

5.0 ITEMS OF SPECIAL INTEREST

5.1 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). Note that data collected pursuant to the "Emergency Use" criteria may not be used as research data; i.e., may not be used as part of a marketing application to the FDA.

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 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 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.

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.

Planned Emergency Use

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

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.

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. 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>).

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 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.is.lsuhscc.edu/safety/radiation.aspx>). Radiation Safety approval should be submitted to the IRB. This approval must be received prior to IRB approval.

5.5 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.

5.6 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 pro rated, 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.

5.7 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 on-going 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 or be presented on television or radio.

5.8 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.

5.9 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.lsuohsc.edu/no/administration/rs/HIPAA/default.htm> for additional information related to these regulations.

5.10 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 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.

5.11 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. 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.lsuhscc.edu/no/administration/rs/irb/CITI%20Instructions.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 our CITI page are available for this purpose.

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>.

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.

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-Chairs 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.

5.12 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.

5.13 Protocol Deviations

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

5.14 Notification of Termination of the Study

Termination of a research protocol must be reported in writing to the IRB by memo or 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.

5.15 Institutional Bio-safety Committee Review

All research projects conducted at LUSHSC-NO must receive Institutional Biosafety Committee (IBC) approval. The IBC application is available at http://www.lsuhscc.edu/no/administration/rs/IBC_Protocol_Submittal_Form.doc. IBC approval must be provided to the IRB office before IRB approval will be granted

5.16 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.

5.17 Conflicts of Interest (CoI)

The LSUHSC-NO’s financial CoI policy is described in Chancellor’s Memorandum 35 (CM 35) which is available at the following URL:

<http://www.lsuohsc.edu/no/administration/cm/cm-35.aspx> . The LSUHSC-NO Human Subjects Protection Program and IRB expands on this policy in the following manner:

A. Investigators and Study Team Members

1.) All study team members are required to submit a CoI Attestation form at the time of submission of the initial IRB application.

2.) Should any CoI be identified by the study team member through this document, they must engage the CM 35 process and provide a full disclosure to the Office of Research Services. Following review by the Vice-Chancellor for Academic Affairs and determination that a potential CoI exists, the disclosure is forwarded to the Institution’s CoI committee. This committee develops a CoI management plan which, if approved by the Vice-Chancellor for Academic Affairs, is presented to the IRB.

3.) At the time of Board consideration of the human subjects research project, the IRB determines whether the management plan is adequate to protect the welfare of potential subjects who may be asked to participate in the project.

4.) If the management plan is considered adequate, the project may be given approval by IRB. 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. If the management plan is not considered adequate, it is returned to the CoI committee for further development, or the project is disallowed on the basis of an irresolvable CoI.

5.) Conflicts of commitment are handled in a similar manner but would involve input from the PI’s Department Head.

B. IRB Members

1.) As indicated earlier, no member with a CoI may participate in the discussion of or vote on any item under consideration by the Board. Such members may provide information at the request of the Board but must be otherwise recused.

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.

5.18 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.

5.19 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;
- (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; 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) Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent;
- (3) Any additional costs to the subject that may result from participation in the research;
- (4) The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation;
- (5) A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will

be provided to the subject; and

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

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 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.

5.20 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.

5.21 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.

5.22 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).