**SYSTEM-WIDE** - A formal statement of values, intents (policy), and expectations (procedure) that applies to every employee throughout the System.

**MULTIDISCIPLINARY** - A formal statement of values, intents (policy), and expectations (procedure) that applies to more than one discipline and is usually of a clinical nature. Check below all areas to which this applies.

**DEPARTMENTAL** - A formal statement of values, intents (policy), and expectations (procedure) exclusive to a particular department or group of people within a department at one or multiple locations that does not impact any other area.

### Disciplines / locations to which this multidisciplinary policy applies:

- [ ] Health Information Management
- [ ] Pharmacy
- [ ] Acute Care Hospital Nursing
- [ ] Housekeeping
- [ ] Plant Operations
- [ ] Ambulatory Services
- [ ] Information Systems
- [ ] Radiology
- [ ] Home Health
- [ ] Laboratory
- [ ] Rehabilitation Services
- [ ] HPCC
- [ ] Legal Services
- [ ] Respiratory
- [ ] Physician Offices
- [ ] Nutrition
- [ ] Security
- [ ] Rehab Hospital
- [ ] Other ______

**Date Originated:** 8/88  
**Reviewed/No Revision:** 2/08, 12/15  
**Dates Revised:** 8/91, 10/92, 1/93, 2/95, 10/97, 8/00, 4/01, 11/02, 6/03, 10/04, 4/05, 12/08, 3/10, 7/10, 8/10, 12/10, 10/11, 9/13, 12/13, 12/14  
**Next Review Date:** 12/16

**Author(s):** Pam Fowler, RN, BS, CIM

**Reviewed by:**
- Clinical Practice Council

**Clinical Education Council**  
**Education Plan Required:** Yes  No:  
**Education Complete:**  
**Date:**

**Approved by:**
- Policy Administrator: John Armitstead, MS, RPh, FASHP  
**Date:** 12/2/15

**As Needed:**
- Medical Director: Pharmacy & Therapeutics Committee  
**Date:** 11/5/15

### PURPOSE:

The primary purpose of the Lee Memorial Health System Institutional Review Committee (IRC) is to protect the interests (rights and welfare) of human subjects involved in investigational drug, device and biologics clinical trials and other research projects. This is to minimize any physical,
psychological, financial and social risks to the subjects, and when risk is present, to determine that it is justified by the value of the research and agreed to by the subjects. A secondary purpose is to provide procedures and guidelines for the operation of the Institutional Review Committee regarding research.

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   B. Institutional Requirements

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   B. IRC Vice-Chairman
   C. IRC Members
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XX. PROCESS FOR THE LMHS IRC TO ADDRESS INAPPROPRIATE OR CONCERNING RESEARCH INVESTIGATOR BEHAVIOR

XXI. PROCEDURES FOR PEDIATRIC CENTRAL INSTITUTIONAL REVIEW BOARD (CIRB) APPROVAL OF CHILDREN’S ONCOLOGY GROUP (COG) PROTOCOLS

POLICY:

The Institutional Review Committee will take action on all proposed research involving human subjects conducted within Lee Memorial Health System or as requested by members of the Medical Staff or approved Principal Investigators who are not members of the medical staff. The Institutional Review Committee will ensure that the requirements of the U.S. Department of Health and Human Services (DHHS), the Food and Drug Administration (FDA), International Conference on Harmonisation (ICH) guidelines and the Declaration of Helsinki that govern informed consent and protection of the rights and welfare of human subjects involved in research will be followed. The Committee will review and attempt to determine potential hazards, legal rights, and potential benefits to the human subjects involved according to 21 CFR Part 56.111

I. GOVERNANCE OF HUMAN SUBJECT RESEARCH

The Lee Memorial Health System Institutional Review Committee operates within the principles set forth by Lee Memorial Health System Federal-wide Assurance (FWA# 00000167), enacted between Lee Memorial Health System and the Department of Health and Human Services, Office for Human Research Protections (OHRP).

The Lee Memorial Health System Institutional Review Committee implements the regulatory procedures mandated by DHHS as announced in Title 45 CFR Part 46 and 21 CFR Part 50 and 56 of the United States Food and Drug Administration.

The IRC may disapprove, discontinue, suspend, terminate, or limit approved activities at any time it is deemed in the interest of protecting the rights and welfare of human subjects.
II. AUTHORITY / RESPONSIBILITY

An Institutional Review Committee shall be created consistent with Article IX of the medical staff bylaws. The Committee shall follow the procedures as stated in this manual. The Institutional Review Committee shall review and monitor investigational activities in accordance with US Food and Drug Administration rules and guidelines 21 CFR Part 56 and Department of Health and Human Services 45 CFR 46.

A. Institutional Official

The Lee Memorial Health System Institutional Official is the System President and CEO. This individual, along with the LMHS IRC members ensure that Lee Memorial Health System is in compliance with the federal requirements.

B. Institutional Requirements

The institution is required to vest in the IRC those powers required by 45 CFR 46, Federal Regulations 21 CFR 56 and may not overrule decisions of the IRC regarding project disapproval. However, IRC approvals may be overruled by the Institution if the institutional administration determines that it is unable to conduct the study due to staff requirements, inappropriate equipment, financial loss, etc.

The institution must provide resources (staff, office space, meeting space, office equipment, etc) to the IRC sufficient for it to carry out its duties.

III. IRC MEMBERSHIP

The Institutional Review Committee shall, in order to promote complete and adequate review of research activities, contain at least five members with varying backgrounds. The Committee shall be sufficiently qualified through experience, expertise, and diversity of background to promote respect for its advice and counsel in protecting the rights of the subjects involved. (A current IRC membership list is available through the IRC office).

The diversity shall be sufficient to evaluate a study in terms of science, law, professional ethics, and community attitudes.

The Institutional Review Committee may not consist entirely of men, or entirely of women, or entirely of members of one profession.

The Committee shall include at least one member in the nonscientific areas, one member whose primary concern is scientific (physician), and at least one member not associated with the Institution.

No member of the Institutional Review Committee may be involved in reviewing or voting on a project in which the member has a conflicting interest. An IRC member who has a conflict of interest as investigator, sub-investigator or participant on a project, or a financial interest in the project or company sponsoring the project, is required to declare the conflict. In this circumstance the individual may not take an active part in proposal review, except to provide requested information, and will absent him / herself from the final Board discussion and vote.
There is no limit to the number of terms a member may serve. No member will be selected by an investigator. IRC Members may be selected by the chairman, vice-chairman or IRC Administrator as needed to fulfill the requirements as set forth by the FDA. A member may be added to the Committee if that person has expressed an interest in joining the Committee and holds expertise in a specialized area that is commonly involved in research. The IRC Administrator shall serve as Secretary of the Institutional Review Committee.

The chairman, vice chairman, and secretary of the Institutional Review Committee are authorized to sign approval letters, correspondence, and perform material and expedited reviews (when appropriate and requested by the chair). An electronic signature or an image of an electronic signature of the Chairman, Vice Chairman or Secretary is considered a valid signature for ALL LMHS IRC correspondence.

Members of the Lee Memorial Health System Institutional Review Committee will not be paid for their services related to the Institutional Review Committee. Liability coverage for Institutional Review Committee members is provided under the Sovereign Immunity act (this act covers officers, employees and agents of Lee Memorial Health System) In addition, Lee Memorial Health System Board Policy covers all physician members performing administrative committee duties. Indemnity agreements (for the institution and the IRC) are sought from all sponsored, non cooperative research. All members of the LMHS IRC are volunteer (including the Chairman and Vice Chairman) and are not paid for their time or attendance. The non-voting secretary of the IRC is employed by Lee Memorial Health System as the IRC administrator and is paid to oversee the daily operations of the LMHS IRC.

A. IRC Chairman

The IRC chair will be responsible for:

1. Conducting and directing Institutional Review Committee meetings.
2. Appointing and Orientation of new members.
3. Review of protocols, amendments, etc.
4. Issuing formal decisions on applications.
5. Informing the Institutional Officer/FDA/OHRP of serious and continuing non-compliance problems.
6. Informing the research community on new requirements and areas of concern regarding human subjects.
7. Advising investigators on requirements regarding research with human subjects.
8. Ensuring all necessary information on research with human subjects is widely available.
9. Assisting in the development of policies and procedures to implement the Federal Regulations and Assurance.
10. Ensuring projects are in compliance with 45 CFR 46, 21 CFR 56 and the terms of LMHS Assurance with OHRP.

The Chairman may request removal from his/her position by presenting his/her request to the Committee. The Chairman may be removed by the Committee for failure to fulfill his / her duties.

B. IRC Vice-Chairman

The IRC Vice Chairman will be responsible for:

2. *Preparing IRC agenda.
3. *Preparing IRC minutes.
4. *Developing policies and procedures to implement the federal regulations and assurance.
6. Ensuring projects are in compliance with 45 CFR 46, 21 CFR 56 and the terms of LMHS Assurance with OHRP.
7. Assuming chairman responsibilities in the absence of the Chairman

*These items are delegated to the IRC secretary.

The Vice-Chairman may request removal of his/her position by presenting his / her request to the Committee. The Vice-Chairman may be removed by the Committee for failure to fulfill his / her duties.

In the event that both the Chair and Vice-Chair are unable to attend a scheduled meeting. The IRC Secretary will have the authority to Chair the meeting. The Chairman or Vice-Chairman may also appoint another IRB member as temporary chair on a meeting by meeting basis.

C. IRC Members

IRC members are responsible for:

1. Ensuring projects are in compliance with 45 CFR 46, 21 CFR 56 and the terms of LMHS Assurance with OHRP;
2. Reviewing project proposals and evaluating them in terms of the criteria for approval, as well as in any other terms that appear relevant;
3. Attending IRC meetings at a reasonable frequency, and entering into a process of discovery and discussion concerning the issues inherent in each proposal.

5. Recommending improvements in policies and procedures to improve the integrity and adequacy of human protection.

6. Voting to approve or disapprove protocols, or recommending modification in protocols to enable approval; and

7. Informing the Chair of noncompliance problems of which they become aware.

A member may request removal from the committee by presenting their request to the Committee. A member may be removed by the Committee for failure to fulfill their member duties.

D. Alternates

Named alternate members may vote if the person, for whom they are an alternate, is absent or cannot vote by reason of conflict of interest.

All members of the IRC have access to the Lee County Medical Society Library located in the Lee Memorial Hospital and to all references located in the IRC office.

E. Training of New Members / Continuing Education

Orientation of a new IRC member will be carried out by the Chairman, Vice Chairman and / or the Secretary of the Institutional Review Committee. The Chairman or Secretary will review with the member all procedures of the Institutional Review Committee and an IRC member training manual will be presented to and discussed with the new member.

Continuing education will be presented at various meetings throughout the year. This education will include handouts and discussions relevant to human subject protection topics. Various members of the Committee will attend conferences or workshops related to the research field and human subject protection. The information gained at these conferences will be shared with all members of the Committee. All members (regular and alternates) will complete the required human subject protection training prior to participation of the committee and will renew such training every three (3) years.

IV. IRC MEETINGS

To conduct business, a quorum (50%+1) of IRC members will be present at each convened meeting, including at least one member whose primary concerns are in nonscientific areas and one physician member. Alternate members shall be appointed and invited to all Committee meetings. All regular members have full voting rights on all items on the agenda. Alternate members may vote in the absence of a regular member with the same voting rights. There will be no proxy votes. Members must be present to vote. A formal
vote will be taken on each agenda item, unless the item is specifically designated as information only for the committee. Protocol closures, deviations and adverse event reports are to be considered an agenda item and a formal vote must be taken on each item.

To approve, disapprove or take action on an agenda item a majority vote of the members present must be obtained.

Agendas will be sent to all members two weeks prior to the scheduled meeting. The agenda package will include the agenda and all attachments (continuing review study progress reports, safety reports, amendment synopsis, non-compliance issues, consent changes, new protocol synopsis, consent forms, etc. or any item that is not an attachment to the agenda is described in the agenda by line item.)

All members have access to the complete protocols and agenda items.

The Institutional Review Committee may invite individuals with special competence in complicated areas to help the members better understand complex issues. These individuals may not vote with the Institutional Review Committee.

The Institutional Review Committee shall meet monthly. A regular schedule will be announced each year. If a meeting date, place or time is changed or a meeting is cancelled, all members and Investigators with items on that month’s agenda will be notified in writing.

V. IRC RECORDS

The Institutional Review Committee will maintain records of all functions of the Institutional Review Committee.

All correspondence between the IRC, Investigator and Sponsor is filed in the appropriate protocol file. Correspondence includes adverse event reports, continuing reviews, consent forms, protocols and amendments, investigational drug brochures, advertisements, etc. Records are kept according to 21 CFR Part 56.115. All correspondence between the IRC and the Investigator and or Sponsor including email correspondence, hand written correspondence, phone correspondence and verbal communications will be filed in the appropriate protocol file. Phone and verbal communications will be documented either via email or on the LMHS IRC Telecom Log. A copy of the correspondence will be sent to the Investigator/Sponsor and the original filed in the appropriate protocol file.

Minutes are kept for each meeting and reflect a record of IRC decisions, members present, record of voting (numerical votes for and against, abstentions, etc), summary of debates, etc. The minutes are not intended to be an exhaustive or verbatim record. Minutes will be maintained for a period of at least 5 years. (after this time minutes will be stored offsite for a period of at least 5 years- reflecting a retained storage period of at least 10 years).

Minutes of all Institutional Review Committee decisions will be submitted to the Executive Committee of the Medical staff and the Pharmacy and Therapeutics Committee after each convened meeting. A copy of the full minutes will be submitted to the authorized institutional official for his / her review. Any disciplinary or corrective actions taken by the committee are also forwarded to the authorized institutional official for review.
The Institutional Review Committee will assist the institution in tracking and documenting reimbursement issues related to drug / device trials. This assistance is to ensure that appropriate compensation is paid to Lee Memorial Health System (according to agreed contracts) and that charges (that are to be paid by the study sponsor or investigator) are not inadvertently billed to the study subject or their insurance carrier. The Institutional Review Committee secretary will facilitate talks between the study sponsor / investigator and the appropriate institutional individual.

The Institutional Review Secretary is a non-voting member of the committee to alleviate any real or perceived conflicts of interest due to the involvement of the secretary with contracts and billing issues.

A. Investigator Notification

The Institutional Review Committee will inform the investigator in writing of all decisions made concerning the protocol. Any contingencies required to receive approval must be met before the approval document is issued. If additional information is required, the Committee may request that information in written form, by fax or by telephone.

An Investigator may appeal the decision of the Committee by addressing in writing the issues raised during the Committee’s review. The appeal will then go before the Committee for review. The decision of the Institutional Review Committee will be final. The investigator will be informed in writing of the status of the appeal.

VI. PROJECT REVIEW

A. Areas Requiring Institutional Review:

1. Research activity involving human subjects.

2. Investigational devices to be used in human subjects.

3. Investigational drugs to be used in human subjects.

4. Investigational biologics to be used in human subjects.

The Committee will have authority to review and approve, disapprove or, modify all research activities involving investigational drugs, devices or biologics. The Committee will have the authority to place any restrictions on a study in order to protect the subjects rights and welfare and to comply with FDA regulations. This applies to initial and continuing reviews as well as protocol changes or any other item as deemed necessary by the committee.

B. Review System

A primary, secondary reviewer system will be utilized for review of all protocols, amendments, safety reports, etc. The primary and secondary reviewer will review the protocol in its entirety including all necessary documents (protocol, consent, drug brochure, patient information materials, advertisements, etc.) and present the
protocol at the monthly meeting. All new protocol items will be sent to the primary, secondary reviewed at least two weeks prior to the scheduled meeting. All members who are not primary or secondary reviewers for the said protocol will have an abbreviated protocol package (which will include at a minimum: protocol synopsis, informed consent form, any additional subject education materials and protocol advertisements) sent to them for review two weeks prior to the meeting. A full protocol is available to every member either via email or by the member accessing the secured IRC folder on the LMHS computer system.

The Committee will attempt to determine significant risk (SR) and non-significant risk (NSR) device studies according to 21 CFR 812.3 (m) (a SR device study is defined as a study of a device that presents the potential for serious risk to the health, safety or welfare and (1) is intended as an implant; or (2) is used in supporting or sustaining human life; or (3) is of substantial importance in diagnosing, curing, mitigating or treating disease, or otherwise prevents impairment of human health; or (4) otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.) by reviewing the sponsors risk assessment, the FDA listing of SR and NSR devices and review of investigational plan, determination if an Investigational Device Exemption (IDE) is on file and FDA’s ruling of SR or NSR (if available).

The Committee will review the qualifications of the investigator involved when necessary.

A non-staff physician may request review of research by this committee provided that the appropriate application package is submitted and approved by the Committee. (the non-staff physician application package is available through the IRC office) For non-physician investigators, any person who is not an LMHS employee or is not affiliated with a University or School in which LMHS has an affiliation with or business associate agreement with, may present their request to conduct research to the LMHS IRC office. The appropriate determination of the requestor’s affiliation with LMHS or participating University or school will be made. If no affiliation is found, the requestor will be required to add an LMHS employee to their project (i.e., advisor, research assistant, Co-PI or Mentor) and a business associate agreement signed prior to submitting their proposal to the IRC or any of the existing research committees (Nursing Research Council, Cancer Committee, etc.).

The Committee has the authority to seek verification of information from sources other than the investigator. Verification from sources other than the investigator may be sought to ensure that no material changes have occurred since the previous Institutional Review Committee review. This verification may be sought for any study if the committee suspects that the investigator is misrepresenting or withholding information from the committee, if during a random site audit discrepancies are found, if during the process of continuing review, discrepancies were noted or for routine verification that information submitted to the committee is true, accurate and complete. As part of a routine or for cause site audit, verification from the sponsor, etc., will be sought to confirm that all information has been submitted to the Institutional Review Committee.

The Institutional Review Committee recognizes that there are some instances in which the physician receives monetary payment for enrolling patients into studies. In all instances in which an investigator receives monetary payment for his / her
participation in a clinical trial it will be disclosed to the study subjects in the informed consent form. This can take the form of a statement that the investigator is being paid or compensated by the sponsor of the study to conduct this clinical trial.

The IRC may also permit payment to research subjects in return for participation, providing that such payments are not considered coercive.

The Institutional Review Committee recognizes that there are occasions when a physician will order the use of certain prescription drugs for conditions not named in the official labeling or will order a different dosage than is set forth in the official labeling. This would normally be within the law. According to the Food and Drug Administration, "once the new drug is in a pharmacy, the physician may, as part of the practice of medicine, lawfully prescribe a different dosage for his patient, or may otherwise vary the conditions of use from those approved in the package insert, without informing or obtaining approval of the Food and Drug Administration."

The Institutional Review Committee considers certain groups of human subjects to be particularly vulnerable to coercion or undue influence in a research setting, these include children, pregnant women, mentally disabled persons, prisoners, fetuses and economically disadvantaged persons. In reviewing projects that will include these vulnerable populations, the Institutional Review Committee will scrutinize the project to ascertain that their inclusion is adequately justified and additional safeguards are implemented to minimize risks unique to each group.

The Institutional Review Committee will not review or approve any research involving prisoners unless it has already been approved by another IRC which has a prisoner member.

C. Initial Review

Requests for protocol review must be submitted in writing. Upon receipt of a request for review, the Secretary of the Committee shall send the principal investigator a copy of the “LMHS Investigator’s Manual”.

The investigator may not begin a study until written approval has been received from the Institutional Review Committee approving the investigation. An official approval letter and a date stamped consent form will be sent to the investigator stating that the study has been approved and may begin. An approved informed consent form is good for an indefinite period of time or until a revision to the consent is submitted and approved. The consent is reviewed annually at each continuing review and if no changes are required the current approved consent form may continue to be used.

This is in an effort to reduce the number of consents required for a specific protocol and to further ensure that the correct consent form is in use.

The proposed investigational plans submitted by the investigator to the Institutional Review Committee should include at least the following:

1. The name of the primary investigator and how the investigator may be contacted. (Form 1572), Investigator CV and a copy of medical license.
2. Protocol to include:

a. Title of study, sponsor name, address, and telephone numbers.

b. Purpose of the study to include the intended uses of the device or drug, expected benefits / risks, inclusion/exclusion criteria, procedures.

c. Study design and outline to include how the study will be monitored.

d. Expected length of the study.

e. Expected number of subjects involved and a description of the types of subjects.

f. Expected results of the study.

g. Possible adverse reactions to the device or drug involved and how these events are to be managed.

h. Report of prior human investigation.

i. Investigational Drug Brochure.

j. Any compensation to subjects, compensation for injury, additional costs to subjects or a third party.

k. Protection of subject privacy.

l. Copy of Informed Consent Form containing required elements 21 CFR 50.20 and 50.25, Health Insurance Portability and Accountability Act (HIPAA) privacy and confidentiality information. A translated consent form should also be submitted, if applicable.

m. The process of obtaining informed consent by the investigator.

n. Advertisements or subject information

o. Conflict of Interest (Investigator/SubInvestigators/Study staff)

Significant concerns about the oversight and ethical and appropriate compensation of research investigators by the companies sponsoring the research has been raised in the past several years, with consequences including federal sanctions against the researchers and their employing organizations. Because of these concerns about the safety of research subjects, and the potential liability to Lee Memorial Health System and its Institutional Review Committee (“IRC”) if conflicts of interest are not appropriately evaluated and monitored, all projects will be reviewed for possible financial conflicts of interest. A conflict of interest exists when the designated official(s) reasonably determines
that a Significant Financial Interest could directly and significantly affect the design, conduct, or reporting of the research."¹ This definition will be utilized to evaluate all projects presented to the IRC. Each research investigator is responsible for informing the IRC of any potential financial conflicts of interest at the start of any project, and remains responsible to inform the IRC of any changes as long as the project is open with the IRC (see policy S03 03 433).

Procedure:

1. The LMHS Designated Official will review all projects presented for review for any possible conflict of interest, based on information provided by the Primary Investigator ("PI") and other sources provided by him or her.

2. Following that review, the Designated Official will provide an analysis of the presence or absence of a conflict of interest to the IRC as a whole at the time the project is presented to the Committee for review.

3. The IRC is the final determining body of whether a financial conflict of interest exists. The Committee may seek input from others as deemed necessary to complete it determination, including, but not limited to, legal counsel and the PI.

4. If a financial conflict of interest is determined to exist, the IRC can recommend steps to reduce or eliminate that perceived or real conflict to the PI.

5. The final actions decided upon by the PI will be reviewed by the IRC and a determination as to whether they adequately protect the research subjects will be made based on the facts surrounding the conflict of interest.

6. If the conflict cannot be eliminated, the IRC will recommend options to the PI, including but not limited to, full disclosure to the subjects enrolled into the trial will be required or, in certain circumstances, the project may be rejected by the IRC.

7. The final approval or disapproval will be entered in the minutes of the IRC and provided in writing to the PI.

Elements that are considered in reviewing a potential conflict of interest include, but are not limited to, issues such as:

- Is payment realistic in relationship to the work that is performed as part of a clinical study.

- What is the relationship between the PI, other associated persons, and the study sponsor.
• The study sponsor’s history of conflicts of interest.

• The PI’s history of conflicts of interest.

In all instances in which the PI or associates receive payment for participation in a clinical trial, that fact shall be disclosed to the study subjects in the informed consent form. This can take the form of a simple statement that the PI or the associate is being paid or compensated by the study sponsor to conduct this trial.

Reducing or eliminating perceived or real conflict of interests can take many forms including, but not limited to, actions such as requiring that the PI step down as head of the study; ensuring that someone else provides informed consent to the study subjects; or ensuring that the PI is not in charge of reviewing the final safety and efficacy data.

This policy and procedure is subject to change at any time if the federal or state governmental entities require that to occur (see policy S03 03 433 for additional information).

The Committee will ensure that the proposed protocol contains all of the requirements for approval as stated in 21 CFR 56.111.

The Institutional Review Committee has the authority to request additional information as needed for the review of research protocols.

Under certain circumstances if minor revisions in the submitted documents are required (such as minor revisions to the consent form, etc) or a missing document of minor importance is to be obtained, the Institutional Review Committee may vote to approve the protocol with the required changes and may delegate the secretary of the Institutional Review Committee to obtain these corrections and subsequently send the approval letter upon completion of these tasks.

If any item (clarification or recommendation) requested by the committee is not received in the IRC office within 60 days from the date of request, the item will not be accepted for review and resubmission will be required. This will apply to initial protocol reviews as well.

D. Continuing Review

Projects are approved for a term not to exceed 365 days from the date of initial approval. All studies approved through Lee Memorial Health System Institutional Review Committee require a yearly review unless the protocol is determined by the Committee to need more frequent review. The frequency of continuing review will be determined according to the degree of risk present in the study protocol. The continuing review report will specify the number of patients in the study, number of patients withdrawn, determination if the most current approved consent form has been signed by all subjects (and any explanations if they have not), determination if the most current protocol version (including any amendments) is being utilized, any protocol changes that were not previously submitted to the committee and any
adverse reactions or complications to the drug or device employed. The primary reviewer will also review the protocol and consent form to ensure that the consent remains accurate and complete. The committee members will review a summary of adverse events, the number of subjects accrued, withdrawn (and the reason for the withdrawal), and other relevant information. (If the consent form currently in use is determined to be complete and accurate, no requirement for a new consent form will be issued, the existing, approved consent may continue to be utilized until such time as revisions are required. The IRC does not issue an expiration date for consent forms, however we do issue an approval date and upon reapproval verification of utilization of the most current, approved consent form is performed.)

The Institutional Review Committee will provide clinical investigators with the format for submitting reapproval reports. The content of this report will enable the Institutional Review Committee to determine if the research shall continue in original form, be amended, be terminated, or have restrictions enacted. (Forms are available through the IRC office)

The Committee has the authority to conduct Investigative Site audits either for cause or routine as part of the continuing review process.

E. Expedited Review

The investigator may request expedited review of minor changes in previously approved research or changes that involve no more than minimal risk as allowed by the OHRP and the FDA.

Minor changes in previously approved research can include, but are not limited to: editorial, clarification or administrative changes or amendments, revisions to Form 1572, minor revisions to consent forms (such as phone number changes, increase in subject enrollment, typo corrections, clarifications, etc), changes to protocols/amendments that do not increase the risk to study subjects and are considered minor changes in nature (such as adding an additional blood draw or changing the way a participant fills out a patient diary, etc.), advertisements for previously approved studies that conform to the required guidelines for study advertisements.

1. Research activities that
   a. present no more than minimal risk to human subjects, and
   b. involve only procedures listed in one or more of the following categories,

may be reviewed by the IRB through the expedited review procedure authorized by 45 CFR 46.110 and 21 CFR 56.110. The activities listed should not be deemed to be of minimal risk simply because they are included on this list. Inclusion on this list merely means that the activity is eligible for review through the expedited review procedure when the specific circumstances of the proposed research involve no more than minimal risk to human subjects.

2. The categories in this list apply regardless of the age of subjects, except as noted.
3. The expedited review procedure may not be used where identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.

4. The expedited review procedure may not be used for classified research involving human subjects.

5. IRBs are reminded that the standard requirements for informed consent (or its waiver, alteration, or exception) apply regardless of the type of review—expedited or convened—utilized by the IRB.

6. Categories A through G pertain to both initial and continuing IRB review.

VII. RESEARCH CATEGORIES

A. Clinical studies of drugs and medical devices only when condition (a) or (b) is met.

1. Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required. (Note: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.)

2. Research on medical devices for which
   a. an investigational device exemption application (21 CFR Part 812) is not required; or
   b. the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.

B. Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:

1. from healthy, nonpregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week; or

2. from other adults and children\(^2\), considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week.
C. Prospective collection of biological specimens for research purposes by noninvasive means. Examples:

1. hair and nail clippings in a nondisfiguring manner;
2. deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction;
3. permanent teeth if routine patient care indicates a need for extraction;
4. excreta and external secretions (including sweat);
5. uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or by applying a dilute citric solution to the tongue;
6. placenta removed at delivery;
7. amniotic fluid obtained at the time of rupture of the membrane prior to or during labor;
8. supra- and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques;
9. mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings;
10. sputum collected after saline mist nebulization.

D. Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.) Examples:

1. physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subjects privacy;
2. weighing or testing sensory acuity;
3. magnetic resonance imaging;
4. electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography;
5. moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.
E. Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for non-research purposes (such as medical treatment or diagnosis). (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(4). This listing refers only to research that is not exempt.)

F. Collection of data from voice, video, digital, or image recordings made for research purposes.

G. Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies. NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(2) and (b)(3). This listing refers only to research that is not exempt.

H. Continuing review of research previously approved by the convened IRB as follows:
   1. where
      a. the research is permanently closed to the enrollment of new subjects;
      b. all subjects have completed all research-related interventions; and
      c. the research remains active only for long-term follow-up of subjects; or
   2. where no subjects have been enrolled and no additional risks have been identified; or
   3. where the remaining research activities are limited to data analysis.

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

VIII. EXPEDITED REAPPROVALS

A. Expedited reapprovals may be carried out provided that the study meets the stated criteria as described in the guidance provided by OHRP and the FDA:

B. Continuing review of research previously approved by the convened IRB as follows:
   1. where
a. the research is permanently closed to the enrollment of new subjects;
b. all subjects have completed all research related interventions; and
c. the research remains active only for long term follow-up or subjects; or

2. where no subjects have been enrolled and no additional risks have been identified; or

3. where the remaining research activities are limited to data analysis.

C. Expedited reviews shall be carried out by the Chairman of the Institutional Review Committee or his designee (Secretary of the IRC and / or an experienced reviewer).

D. The reviewer(s) may exercise all the authorities of the IRB, except disapproval. Research may only be disapproved following review by the full committee.

E. All expedited review items will be placed on the next scheduled meeting agenda for full board notification.

XIX. PROTOCOL MODIFICATIONS

Approval for any modification to a protocol instrument or consent document under IRC jurisdiction must be approved by the IRC. Modest changes on projects initially approved by full board review may be approved by expedited review at the discretion of the Chair (or his / her designee).

The investigator shall submit to the Institutional Review Committee a request for any change in the original protocol. Before any change can be implemented, the approval of the Institutional Review Committee must be obtained. (Unless the change is necessary to eliminate immediate hazards to the health and welfare of study subjects.) Specific directives are listed in the initial and continuing review letters stating that no protocol changes can occur until IRC has been granted.

Revisions to existing consent forms are considered protocol changes and must be submitted to the IRC for review. Possible changes to the consent form may occur when significant new study findings are required to be relayed to study subjects.

Protocol revisions/modifications/changes are to be submitted to the LMHS IRC within 90 days of receipt by the investigator.

X. PROJECT TERMINATION

The investigator will notify the Institutional Review Committee of the completion or discontinuance of the study as soon as possible. A final study report is required upon study completion. These forms will be provided to the investigator.

XI. ADVERSE EVENT (AE) REPORTING

The investigator must report in writing to the Committee within five days of its discovery, any unexpected adverse reaction that may reasonably be regarded as probably caused
by the drug or device and which was not anticipated in the original proposal. Any serious adverse event that is anticipated due to the nature of the drug or device must also be reported within five days. This should be done in the form of a written statement to the Chairman of the Institutional Review Committee with the adverse event information attached. The Committee will evaluate each adverse event and determine whether further action needs to be taken. Options include seeking further information, temporarily suspending the study, modification of Informed Consent Form or permanent suspension of the project.

The adverse events will be reviewed by the committee as a whole or an AE Review Subcommittee, this committee will consist of persons qualified to review events and determine relationship to study drug or device. The subcommittee will include at a minimum a physician member, pharmacist member, and nurse member, alternates may be appointed for each member. The subcommittee will review the events and report their findings back to the full committee. Any recommendations by the subcommittee will be presented to the full committee for a discussion and vote. Any member of the full committee may have access to and review any of the adverse events. If an event is determined by the subcommittee to need full review the item will be placed on the agenda for full committee review. This subcommittee may also review protocol deviations following the same guidelines as stated above. All members of the subcommittee will have the full AE report, as well as a copy of the risk section of the informed consent and any other items considered pertinent for review of the AE sent to them for their review prior to the subcommittee meeting. The subcommittee will meet at a time that is convenient for all members and will take place prior to the full board Institutional Review Committee meeting date. If the AE subcommittee is used for review of any adverse events, the sub committees’ recommendations will be reported to the full board. The full board will be presented with a brief synopsis of each AE for each protocol. The full board will vote and/or take action on the subcommittee recommendations on a protocol by protocol basis. There will be no block or group voting. Any serious, unanticipated problems involving risks to human subjects or others that occur in a project under the purview of FDA and/or OHRP will also be reported to the appropriate agency (FDA or OHRP) and the appropriate institutional officials.

The FDA does not require the IRC to acknowledge receipt of an SAE or safety report. The Lee Memorial Health System Institutional Review Committee will not provide acknowledgement of these reports unless a revision to the protocol or consent form is required by the committee. If a change is required, the Investigator will be notified in writing.

**XII. EMERGENCY USE OF A TEST ARTICLE**

When emergency care involves investigational drugs, devices or biologics, US Food and Drug Administration requirements must be satisfied.

Under certain circumstances a test article may be administered to a human subject in a life-threatening situation, when there is no standard acceptable treatment available, or the standard treatments have failed, and the subjects is not enrolled or is not eligible to enroll in a research protocol involving the test article and there is not sufficient time to obtain IRC approval. To qualify for emergency use the criteria listed in 21 CFR 56.104 (c) must apply. If these criteria are met the physician may use the test article without prior Institutional Review Committee approval.
The physician will be required to do the following: obtain written consent from subject or subject’s legal representative (exception from informed consent may be appropriate if the conditions of 21 CFR 50.23 (a) exists, the IRC will follow 21 CFR 50.24 regulations concerning emergency consent form exception), use the test article, in the patients record enter a description of the procedure and attach a copy of the informed consent, notify the Institutional Review Committee within 5 days of the article’s use (information should include, patient name, physician administering test article, name of test article, dosage, route, a copy of the informed consent, any adverse effects observed, outcome of subjects treatment and a brief written description of the event).

The Institutional Review Committee will process such notifications and issue an acknowledgement letter. Any subsequent use of the test article will be subject to prior full board review and approval.

DHHS regulations (OHRP) do not permit research activities to be started, even in an emergency, without prior IRC review and approval. When emergency care is initiated without prior IRC approval, the subject may not be considered a research subject. Such care may not be claimed as research, nor any data regarding such care, be included in any report of a prospectively conceived research activity.

XIII. EXEMPT DETERMINATION

The Lee Memorial Health System will attempt to determine what research activities may be considered as exempt by following the exempt categories listed in 45CFR46.101(b)

Unless otherwise required by department or agency heads, research activities in which the only involvement of human subjects will be in one or more of the following categories are exempt from this policy:¹

A. Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as

1. research on regular and special education instructional strategies, or
2. research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

B. Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior; unless:

1. information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and
2. any disclosure of the human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation.

C. Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior that is not exempt under paragraph (b)(2) of this section, if:
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1. the human subjects are elected or appointed public officials or candidates for public office; or

2. Federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.

D. Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.

E. Research and demonstration projects which are conducted by or subject to the approval of Department or Agency heads, and which are designed to study, evaluate, or otherwise examine:
   1. public benefit or service programs;
   2. procedures for obtaining benefits or services under those programs;
   3. possible changes in or alternatives to those programs or procedures; or
   4. possible changes in methods or levels of payment for benefits or services under those programs.

F. Taste and food quality evaluation and consumer acceptance studies,
   1. if wholesome foods without additives are consumed; or
   2. if a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

G. Quality Improvement (QI) or Performance Improvement (PI) Projects
   1. Projects that are submitted to the LMHS IRC that are determined to be QI / PI projects may be considered exempt by the LMHS IRC.

The Lee Memorial Health System IRB will be the determining body as to whether a project may be considered exempt from IRB review, neither the investigator nor any other committee or department within the institution can decide whether the project is exempt from IRB review and regulations.

This policy applies only to projects that are under the purview of OHRP or not subject to FDA rules and regulations. The FDA does not allow the IRB to determine project exemptions unless the project is determined to be exempt by the FDA.

XIV. WAIVER OF INFORMED CONSENT REQUIREMENTS

For research regulated by DHHS (Department of Health and Human Services).

A. There are only two circumstances under which the regulations give IRBs authority to waive the required consent. The first waiver authority is applicable only to
research activities designed to study certain aspects of public benefit or service programs; the conditions under which this waiver may be authorized by an IRB are detailed in 45 CFR 46.116(c) (see below):

An 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:
   a. public benefit or service programs;
   b. procedures for obtaining benefits or services under those programs;
   c. possible changes in or alternatives to those programs or procedures;
   d. 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.

B. The second waiver authority is described in 45 CFR 46.116(d) as follows:

An 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 requirements to obtain informed consent provided the IRB finds and documents that:

1. The research involves no more than minimal risk to the participants.

2. The waiver or alteration will not adversely affect the rights and welfare of the participants.

3. The research could not practicably be carried out without the waiver or alteration.

4. Whenever appropriate, the participants will be provided with additional pertinent information after participation.

All four criteria must be met in order to alter some or all of the consent process under (45 CFR 46.116(d).

**Note:** It is the responsibility of the investigator to ask the IRB for a waiver of the consent process. When requesting a waiver or alteration of consent under 45 CFR 46.116(d), a justification must be provided. The IRB will not grant a waiver without written justification. The investigator must submit a request for waiver of informed consent form along with the initial submission package.
B. Waiver of Documentation of Informed Consent

An IRB may waive the requirement for the investigator to obtain a signed consent form (45 CFR 46.117 (c)) for some or all participants under one of two conditions:

1. The only record linking the participant and the research would be the consent form and the principal risk would be potential harm resulting from a breach of confidentiality. Each participant will be asked whether the participant wants documentation linking the participant with the research, and the participant's wishes will govern.

2. That the research presents no more than minimal risk of harm to participants and involves no procedures for which written consent is normally required outside the research context. In either case, the IRB may require the investigator to provide participants with a written statement regarding the research.

Minors

In addition to the provisions for waiver contained in §46.116, if the IRB determines that a research protocol is designed for conditions or involves a subject population for which parental or guardian permission is an inappropriate requirement (for example, neglected or abused children), it may waive the consent requirements, provided an appropriate mechanism for protecting the children who will participate as subjects in the research is substituted. However, the waiver still must be consistent with the requirements of federal, state, or local law. The choice of an appropriate mechanism would depend upon the nature and purpose of the activities described in the protocol, the risk and anticipated benefit to the research subjects, and their age, maturity, status, and condition.

Note: It is the responsibility of the investigator to ask the IRB for a waiver of informed consent, documentation of consent, or of parental permission.

When requesting a waiver of written documentation of consent under 45 CFR 46.116, 45 CFR 46.117, or 45 CFR 46.408(c), a justification must be provided. The IRB will not grant these waivers without written justification.

A request for waiver or alteration of the informed consent process does not apply to FDA regulated research unless the research meets the criteria for emergency use as outlined in section 10.

XV. WAIVER OF AUTHORIZATION FOR RESEARCH PURPOSES

The Lee Memorial Health System Institutional Review Committee will be the determining body as to whether a waiver of authorization for research purposes should be issued. The committee may consult with other committees or personnel (HIPAA Task Force, Patient Information Privacy Officer) on an as needed basis.

The HIPAA Privacy Rule, 45 CFR 164 512(l) requires that seven conditions must be met in order to grant a waiver of individual authorization for research uses of Protected Health Information (PHI). In addition to these conditions, the federal Common Rule (45
CFR 46 Section 116(d) stipulates that “whenever appropriate, the subjects will be provided with additional pertinent information after participation.”

A. To request a “waiver of authorization” from the Lee Memorial Health System Institutional Review Committee for research purposes the following criteria must be met:

1. The use or disclosure of PHI involves not more than minimal risk.
2. Granting of the waiver will not adversely affect privacy rights and welfare of the individuals whose records will be used.
3. The project could not practically be conducted without the waiver.
4. The project could not practically be conducted without the use of PHI.
5. An adequate plan to protect identifiers from improper use and disclosure is included in the research proposal.
6. An adequate plan to destroy identifiers at the earliest opportunity, or justification for retaining identifiers, is included in the research proposal.
7. The proposal includes written assurances that PHI will not be re-used or disclosed for other purposes.

If all of the above criteria apply, a waiver of authorization MAY be granted by the Lee Memorial Health System Institutional Review Committee. The investigator must request this waiver by submitting a request for waiver application to the committee.

The Lee Memorial Health System Institutional Review Committee may also grant a partial waiver of authorization for recruitment purposes if requested by the investigator. Approval of the partial waiver will be approved based on fulfillment of the above criteria by the investigator. The investigator must submit a request for partial waiver of authorization for recruitment purposes application to the committee.

B. Reviews Preparatory to Research

These are activities for the purpose of preparing a research protocol, developing a hypothesis, screening or writing a grant application. Activities preparatory to research do not require prior approval under HIPAA, however in order to ensure administrative oversight of all uses of PHI, this type of activity must be reported to the committee on the appropriate –review preparatory to research form-. No information that is reviewed under this activity can be removed from the covered entities premises.

XVI. GENE TRANSFER STUDIES

Studies involving insertion of genetic material into the human body will be subject to all applicable federal regulations. In addition, the study must be approved by the Lee Memorial Health System Institutional Biosafety Committee (IBC) as well as the Lee Memorial Health System Institutional Review Committee (IRC) before the study will be allowed to be
implemented. Proposed changes to the protocol must be submitted to both the Institutional Review Committee and the IBC for review and approval, and cannot be implemented by the investigator, except where necessary to eliminate apparent, immediate hazards to the subject, until both IBC and IRC approval is granted. Continuing review will occur at intervals determined by the IRC, but not more than every 12 months. The IBC will also conduct a continuing review of the protocol at intervals specified by the IBC, but not more than every 12 months. Adverse events must be reported to the IBC and IRC as soon as possible, no more than 5 days after they occur. All new gene transfer protocols must be submitted to the Lee Memorial Health System Institutional Review Committee at least 30 days prior to the next scheduled Institutional Review Committee meeting. Gene transfer trials will be subject to all other Institutional Review Committee policies and guidelines.

XVII. INVESTIGATOR RESPONSIBILITY

A. Responsibilities of the investigator include those specified in the Assurance with OHRP and 21 CFR 312

B. Research investigators must acknowledge and accept their responsibility for protecting the rights and welfare of human research subjects and for complying with all applicable provisions of this Assurance. Research investigators are responsible for providing a copy of the IRC-approved informed consent document to each subject at the time of consent and prior to any study specific screening procedures, unless the IRC has specifically waived this requirement. The Institutional Review Committee does not preclude a researcher from discussing the OPTION of enrolling in a research protocol prior to obtaining consent. (However, disclosure of PHI to any third party for recruitment is prohibited unless a written authorization has been received from the study subject or a waiver has been issued by the Institutional Review Committee.)

C. Informed consent is a crucial part of the research process, and as such entails more than obtaining a signature on a form. Investigators must educate potential subjects to ensure that they can reach a truly informed decision about whether or not to participate in the research. Their informed consent must be given freely, without coercion, and must be based on a clear understanding of what participation involves.

The process of educating subjects about the study begins during initial contact and continues for the duration of their participation. Thus, information conveyed through advertisements, recruitment letters, pre-screening phone calls, study description sheets as well as written informed consent documents and discussions must be understandable to the subjects and should contribute to their understanding of the research. The LMHS IRC must approve written and oral information (including recruitment materials) provided to subjects before and during the informed consent process.

Obtaining and Documenting Assent / Consent from Children

Parental permission is usually a prerequisite to the recruitment of human research participants who are children. However, parental permission constitutes only half of the consent process. Assent, the agreement of a child to participate in research, is the second component of the informed consent procedure for children.

The means of obtaining assent from children must be appropriate for the age ranges and levels of mental development found within the proposed participant pool. The
National Commission for the Protection of Human Subjects of Biomedical and Social Science Research expects that assent be requested from children who are 6 years of age or older. However, for children between the ages of 6 and 18, the appropriate method for obtaining assent will vary. The following guidelines were proposed during a panel discussion sponsored by the National Institutes of Health:

**Age 6-7**

A simple oral description of the child's involvement is given to the participant and verbal assent is requested. The procedure may be documented on the informed consent form by the presence of the signature of a witness.

**Age 8-13**

A more complete oral description of the research (in layman's terminology) is given to the participant. Verbal assent is requested. The procedure may be documented on the informed consent form by the signature of a witness.

**Above age 13**

Written assent should be requested from both parent and child, using age-appropriate and background-appropriate documents.

Although age is used as the primary criteria in determining an appropriate means of obtaining assent, factors such as literacy, mental development and medical condition of the child must also be considered. The need for flexibility in the methods for obtaining assent from children is universally recognized. Because a single method of obtaining assent may not be appropriate for all potential participants, investigators may need to be prepared to use different approaches with different participants. As in any consent process, the primary concern is that the participant is able to understand the explanation that is presented. The need for a witness to document verbal assent procedures is dependent upon the complexity of the research and the risks to the participant.

**NOTE:** A parent or guardian may not be the witness for a child's verbal assent document.

Florida law does permit a minor, under certain circumstances, to consent to medical care and treatment. If one of the following exceptions applies, the minor has legal authority to consent to care and treatment.

1. A minor who is, or has been, married.
2. An unwed pregnant minor consenting to the performance of medical or surgical care or services relating to her pregnancy.
3. An unwed minor mother consenting to the medical or surgical care or services of her child.
4. A minor seeking voluntary substance abuse impairment services.
5. A minor with a court order removing the disability of nonage.
6. A minor consenting to the examination and treatment of a sexually-transmitted disease.

7. A minor receiving contraceptive information or services.

The IRB assesses the potential risks and benefits for each research proposal, and the provisions for permission and assent, to determine if an activity satisfies the conditions for a category of research permitted in children, as specified in DHHS 45 CFR 46.404, 46.405, 46.406 46.407 and 46.409, and FDA 21 CFR 50.51, 50.52, 50.53, 50.54 and 50.56.

The research categories are described below.

- Research that does not involve greater than minimal risk may be approved if the IRB finds that adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians (45 CFR 46.404 and 21 CFR 50.51).

For such research the IRB determines whether adequate provisions to solicit the permission of each child's parents or guardian unless one parent is deceased, unknown, incompetent, or not reasonably available, or unless only one parent has legal responsibility for the care and custody of the child is made. Where parental permission is to be obtained, the IRB may find that the permission of one parent is sufficient.

- Research involving greater than minimal risk, but presenting the prospect of direct benefit to an individual participant, or a monitoring procedure that is likely to contribute to the participant's well-being, may be approved if the IRB finds that (45 CFR 46.405 and 21 CFR 50.52):
  - the risk is justified by the anticipated benefit to the participant;
  - the relationship of anticipated benefit to risk is at least as favorable as that presented by available alternative approaches; and
  - adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians.

For such research the IRB determines whether adequate provisions to solicit the permission of each child's parents or guardian, unless one parent is deceased, unknown, incompetent, or not reasonably available, or unless only one parent has legal responsibility for the care and custody of the child, is made. Where parental permission is to be obtained, the IRB may find that the permission of one parent is sufficient.

- Research involving greater than minimal risk with no prospect of direct benefit to individual participants, but likely to yield generalizable knowledge about the participant's disorder or condition, may be approved if the IRB finds that (45 CFR 46.406 and 21 CFR 50.53):
  - the risk represents a minor increase over minimal risk;
  - the intervention or procedure presents experiences to participants that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations;
the intervention or procedure is likely to yield generalizable knowledge about the participant’s disorder or condition which is of vital importance for the understanding or amelioration of the participant's disorder or condition; and

adequate provisions are made for soliciting assent of the children and permission of their parents or guardians.

For such research, the IRB requires the permission of both parents, unless one parent is deceased, unknown, incompetent, or not reasonably available, or unless only one parent has legal responsibility for the care and custody of the child.

Research that is not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children may be approved if the IRB and the Secretary of the Department of Health and Human Services (DHHS), after consultation with a panel of experts in pertinent disciplines and following an opportunity for public review and comment, find that:

- the research in fact satisfies one of the above three conditions (45 CFR 46.407 and 21 CFR 50.54); or
- the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children;
- the research will be conducted in accordance with sound ethical principles; and
- adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians.

For such research, the IRB requires the permission of both parents, unless one parent is deceased, unknown, incompetent, or not reasonably available, or unless only one parent has legal responsibility for the care and custody of the child.

If the IRB has determined that the permission of both parents is required, permission granted by one parent will nevertheless be sufficient if the other parent is deceased, unknown, incompetent, not reasonably available or if the parent granting permission has legal responsibility for the care and custody of the child. In order to establish that only one parent has legal responsibility for care and custody of a child, an order issued by a court from the state in which such parent resides must grant sole custody of the child to such parent. A copy of the court order should be retained with the documentation of the parent's permission.

D. Investigators are responsible for supplying a copy of the IRC approval letters, continuing review letters, etc. to the sponsor of the protocol. The IRC will inform the study sponsor if a protocol is terminated or suspended due to non-compliance or increased risk to human subjects. In addition, investigators must:

1. be directly responsible for the safety (physical and psychological) of each subject;
2. treat subjects with respect as autonomous individuals;
3. comply with 45 CFR 46, LMHS Assurance with OHRP, FDA Regulations and
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stipulations of the IRC;

4. be familiar with the Belmont Report, Declaration of Helsinki and this Policy and adhere to their principles;

5. complete a course in human subject protection with retraining required every 3 years;

6. complete an initial course in good clinical practice guidelines;

7. adhere to the approved protocol and consent process (obtaining the subjects written consent prior to ANY research related activities or disclosure of PHI (personal health information);

8. obtain approval for any changes in advance (except in an unusual circumstance where it is necessary to deviate from the protocol to protect the well-being of a subject); (specific directives will be listed in the initial approval, re-approval letters, etc.)

9. report all deviations, non-compliance and adverse events promptly to the IRC; and

10. ensure that all colleagues and persons working under his / her direction meet the same standards.

E. The investigator shall refrain from exerting undue influence upon potential research subjects.

F. Conflict of Interest (Investigator/Study staff)

A conflict of interest exists when the designated official(s) reasonably determines that a Significant Financial Interest could directly and significantly affect the design, conduct, or reporting of the research.” ¹ This definition will be utilized to evaluate all projects presented to the IRC. Each research investigator is responsible for informing the IRC of any potential financial conflicts of interest at the start of any project, and remains responsible to inform the IRC of any changes as long as the project is open with the IRC.

XVIII. ACCEPTANCE OF OTHER INSTITUTIONAL APPROVALS

A. The Institutional Review Committee may extend recognition to a qualified Institutional Review Board to review and approve protocols and informed consents on a case by case basis.

B. To be "recognized" an IRC must submit:

1. A list of its Committee members,

2. Meeting schedule,

3. General description of policies and procedures
XIX. SANCTIONS

The Committee will have the authority to suspend or terminate ongoing studies that are not being conducted in accordance with the Institutional Review Committee requirements or that have been associated with unexpected, serious harm to patients. Any suspension or termination of IRC approval for a project under the purview of the FDA and/or OHRP will reported to the appropriate agency and appropriate institutional officials.

The Institutional Review Committee may temporarily or permanently suspend a project at any time and this suspension may not be overridden at any level in the institution (45CFR 46). The Institutional Review Committee may take this action in a wide variety of circumstances or if there is any other serious concern for the well being of the subjects or for the reputation of Lee Memorial Health System (see policy S03 03 135 Clinical Research Compliance Monitoring).

XX. Process for the LMHS IRC to address inappropriate or concerning Research Investigator Behavior.

A. Any member of the committee, voting or non-voting, can bring a concern regarding the behavior of an investigator or his/her sub-investigator or agent to the attention of the IRC.

B. When the focus of the concern is a physician who is a member of any LMHS Medical Staff, the Chair of the IRC will forward the concern in writing to the appropriate Facility Medical President for investigation and action (according to the medical staff bylaws).

C. If the concern raised involves the IRC Chair, the Vice-Chair can act to forward the concern.

D. In the event of an Investigator who is not a member of a LMHS Medical Staff, the Chair, shall forward the concern in writing to the appropriate supervisor for investigation and action.

E. Nothing in this process shall prevent the Chair from immediately suspending all investigations associated with an investigator when the actions of that investigator raise questions of patient safety or concerns about ethical and/or quality controls of any study.

XXI. PROCEDURES FOR PEDIATRIC CENTRAL INSTITUTIONAL REVIEW BOARD (CIRB) APPROVAL OF CHILDREN’S ONCOLOGY GROUP (COG) PROTOCOLS

A. Lee Memorial Health System Institutional Review Committee has designated the National Cancer Institute (NCI) Pediatric Central Institutional Review Board (CIRB) (FWA 00002195, Pediatric CIRB Registration Number IRB00004296, Institution Organization Number IORG0000460) as the IRB of record (on a protocol by protocol basis) for certain Children’s Oncology Group protocols (pilot, Phase II or Phase III).

B. Lee Memorial Health System will perform local institutional functions as outlined in the “Division of Responsibilities Between NCI’s CIRB and Local Institutions” and will rely on the NCI CIRB to fulfill their stated responsibilities.
C. **Principal Investigator Responsibilities:**

After determining if he/she wants to participate in a CIRB reviewed COG protocol, the PI or his/her designee:

1. Informs the LMHS IRC Chair of the protocol that they wish to open, this can be done via email – once the Chair has given his email approval the PI or his designee can open the protocol through IRB manager/PED CIRB.

2. Any local Serious Adverse Events that occur for a participant on a PED CIRB approved protocol must still be reported to the LMHS IRC.

D. **LMHS Institutional Review Committee Responsibilities:**

1. Upon receipt of a request to open a new protocol from the Principle Investigator the IRC Chair will review the protocol and give his OK for the protocol to be opened through the PED CIRB. The PED CIRB will then become the IRB of record for that protocol.

2. The LMHS IRC office will review the consent form to ensure that it meets the requirements of the protocol, the institution and the PED CIRB approved boilerplate language.

3. The LMHS IRC Office will maintain a PED CIRB list of active studies.

E. **CIRB Responsibilities**

The CIRB will notify LMHS IRC and the PI (via email) when there are any actions taken on the protocol, e.g., an SAE report provoking a change in the consent form, an approved protocol amendment, a change in the protocol / informed consent resulting from the Continuing Review, etc.

F. **CIRB Procedures**

1. As outlined in the NCI CIRB Operations Office Standard Operating Procedures, the CIRB receives the protocol, the informed consent document(s), a completed CIRB application and, when appropriate, an investigator drug brochure from the Cooperative Group via the Protocol Information Office at NCI. The CIRB staff clarifies any initial issues with the Study Chair of the Cooperative Group, designates the next meeting date for review, and assigns primary reviewers (two for the Adult CIRB and three for the Pediatric CIRB). The CIRB Chair decides if additional expertise (e.g., a consultant) needs to be brought into the review process.

2. The CIRB members meet at least once a month. At the meetings the Board members discuss the protocol and may consult by telephone with the Study Chair to explore any concerns they may have.

3. Per the NCI CIRB Board Standard Operating Procedures, the Board takes one of the following actions for each protocol: approve, approve pending modification, table, or disapprove. Any non-approval is followed up with
communication with the Study Chair to resolve, wherever possible, outstanding issues identified by the Board.

4. After approval or disapproval, the Study Chair and Cooperative Group sponsor are formally notified.

5. For each protocol, the CIRB's primary reviews, minutes, notification letters, and any other correspondence are posted in a separate section of this website for participating institutions to access.

6. In addition to conducting initial reviews, the CIRB conducts Continuing Reviews and reviews of Serious Adverse Events (SAEs), Data Safety Monitoring Board (DSMB) reports, protocol amendments, national subject recruiting materials, etc. These actions are also posted on the website for prompt access by participating institutions.

G. **Adverse Event Reporting**

The PI or his/her designee reports only LOCAL serious adverse events (via email) to the LMHS IRC.

H. **Consent Form**

The CIRB does not allow the CIRB approved language to be deleted but does allow the local institution to comply with local requirements in terms of required consent language.

I. **Amendments, Revisions, and Continuing Reviews**

1. The PED CIRB is the IRB of record for selected COG protocols. This means that LMHS IRC no longer performs as the IRB of record for these protocols.

J. **Division of Responsibilities**

The responsibilities of the NCI CIRB are to:

1) Maintain an NCI CIRB membership that satisfies the requirements of 45 CFR 46 and 21 CFR 56 and provides special expertise as needed to adequately assess all aspects of each study;
   
a) Post the roster of NCI CIRB membership on the public side of the NCI CIRB website;

2) Conduct initial, amendment, and continuing review of studies as well as review of any other study-specific documents submitted by the Study Chair to the NCI CIRB;

3) Conduct review of local context considerations:
   
a) as outlined in the following Worksheets: the Annual Signatory Institution Worksheet About Local Context for NCI CIRB Review, the Annual Principal Investigator Worksheet About Local Context, and the Study-Specific Worksheet About Local Context;
4) Conduct review of potential unanticipated problems and/or serious or continuing noncompliance when the Signatory Institution or other entity reports an incident, experience, or outcome to the CIRB. This review includes the following step:

a) report any unanticipated problem and/or serious or continuing noncompliance determination to OHRP, the FDA, and the NCI Signatory Official;

5) Conduct review of individual Adverse Event Reports for studies without a Data and Safety Monitoring Board (DSMB) or equivalent monitoring body;

6) Post all study-specific documents related to CIRB reviews to the restricted access side of the CIRB website;

a) Notify research staff and institutional designees of all CIRB actions, per written procedures, via institution-specific correspondence, broadcast emails, and access to the restricted area of the CIRB website;

7) Notify the Signatory Institution immediately if there is ever a suspension or restriction of the CIRB’s authorization to review a study; and

8) Post the NCI CIRB Standard Operating Procedures on the public side of the CIRB website.

The responsibilities of the Signatory Institution are to:

1) Comply with the NCI CIRB’s requirements and directives;

2) Report to the NCI CIRB the names of any Component or Affiliate Institutions that rely on the Signatory Institution’s IRB.

a) Component Institutions are defined by the NCI CIRB as meeting all of the following criteria:

• the Component Institution operates under a different name than the Signatory Institution, but the Signatory Institution has legal authority for the Component Institution;

• the FWA number for the Component Institution is the same as the Signatory Institution;

• the local context considerations of the Component Institution are the same as the Signatory Institution. Local context considerations are reported by the Signatory Institution in the Annual Institution Worksheet About Local Context;

• the boilerplate language and institutional requirements of the Component Institution are the same as the Signatory Institution. The boilerplate language and institutional requirements are reported by the Signatory Institution in the Annual Institution Worksheet About Local Context; and
• the conduct of research at the Component Institution is monitored by the same office as the Signatory Institution.

b) Affiliate Institutions are defined by the NCI CIRB as meeting all of the following criteria:

• the local context considerations of the Affiliate Institution are the same as the Signatory Institution. Local context considerations are reported by the Signatory Institution in the Annual Institution Worksheet About Local Context;

• the boilerplate language and institutional requirements of the Affiliate Institution are the same as the Signatory Institution. The boilerplate language and institutional requirements are reported by the Signatory Institution in the Annual Institution Worksheet About Local Context; and

• the conduct of research at the Affiliate Institution is monitored by the same office as the Signatory Institution.

3) Ensure the safe and appropriate performance of the research at the Signatory Institution and at all Components and Affiliates. This includes, but is not limited to:

a) ensuring the initial and ongoing qualifications of investigators and research staff;

b) overseeing the conduct of the research;

c) monitoring protocol compliance;

d) maintaining compliance with state, local, or institutional requirements related to the protection of human subjects;

e) providing a mechanism to receive and address concerns from local study participants and others about the conduct of the research; and

f) investigating, managing, and providing notification to the NCI CIRB of any study-specific incidence, experience, or outcome that seems to rise to the level of an unanticipated problem and/or serious or continuing noncompliance. When notifying the NCI CIRB of a potential unanticipated problem and/or serious or continuing noncompliance, the institution must provide a plan to manage the incident, experience, or outcome, including measures to prevent similar occurrences;

NOTE: As part of ensuring safe and appropriate performance of research the Signatory Institution has the authority to observe any aspect of the research process including observing the consent process. The CIRB retains the authority to direct this to be done when necessary.

4) Provide updates in a timely manner to the NCI CIRB whenever a Signatory Institution Principal Investigator is no longer the responsible party for a study under the purview of the NCI CIRB;
5) Notify the NCI CIRB when a regulatory deficiency has been cited on an audit that occurred during the time that the NCI CIRB was responsible for study review;

6) Complete and submit the Annual Institution Worksheet About Local Context, the Annual Investigator Worksheet About Local Context, and any other worksheets/forms required by the NCI CIRB for participation;

7) Decide on a study-by-study basis whether to open the study through the NCI CIRB or to conduct its own local IRB full Board review. Indicate the decision to open a study through the NCI CIRB by submitting a Study-Specific Worksheet About Local Context;

8) In the local consent form:

   a) incorporate NCI CIRB-approved boilerplate language into the NCI CIRB-approved model consent form;

   NOTE: Including HIPAA Authorization language as part of boilerplate language is permitted. The CIRB does not approve the HIPAA Authorization language as it does not function as a Privacy Board however the CIRB will accept HIPAA Authorization language when submitted as part of the boilerplate.

   b) make no language changes to the consent form with the exception of NCI CIRB-approved boilerplate language;

   c) obtain NCI CIRB approval of changes to the boilerplate language prior to implementation; and

   d) obtain NCI CIRB approval of translations of the consent form prior to implementation;

9) Maintain a regulatory file for each study under NCI CIRB purview as per local institution and sponsor policy; and

10) Conduct full board review of any study enrolling prisoners, since the NCI CIRB is not constituted to review studies enrolling prisoners.

11) Upon receipt of a request to open a new protocol from the Principle Investigator, the IRC Chair will review the protocol and give his agreement for the protocol to be opened through the PED CIRB. The PED CIRB will then become the IRB of record for that protocol.

12) The LMHS IRC Office will maintain a PED CIRB list of active studies.

This policy was approved by the Lee Memorial Health System Institutional Review Committee. Nothing in this document shall be construed as limiting the authority of Lee Memorial Health System, the institutional official, the institutional review committee, or institutional review committee...
members in their duty to protect the interests of human subjects, as provided in 45 CFR 46 and 21 CFR 56 and other pertinent regulations. All questions regarding this policy should be directed to the IRC office.

RELATED POLICIES:

M03 03 135  Clinical Research Compliance Monitoring

M03 03 430  Investigational Research, Medications, and Devices Monitoring

M03 03 710  Pharmacy Investigational Drug Service

S03 03 433  IRC Responsibilities Regarding Investigator Financial Conflicts of Interest

M23 00 065  Billing Procedures for Investigational Drug-Device Trials

REFERENCES:

Code of Federal Regulations 42 CFR 50.605 (a)
45 CFR 46
21 CFR 56
21 CFR 50
21 CFR 54
21 CFR 812
46 CFR 164

International Conference on Harmonisation; Guidelines on General Considerations for Clinical Trials

Declaration of Helsinki

Belmont Report

Florida Medical Consent Law, Section 766.103, Fla. Stat