

Institutional Review Board Policies and Procedures Manual

SECTION 2: LINES OF AUTHORITY, RESPONSIBILITIES, AND OTHER IRB MEETING ATTENDEES

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2.1 LINES OF AUTHORITY AND RESPONSIBILITIES

A. Federal Oversight Agencies

Although protection of human subjects is a concern of all federal agencies that sponsor research, leadership is vested in the Department of Health and Human Services' Office for Human Research Protection (OHRP) and the Food and Drug Administration (FDA).

The OHRP's primary mechanism of regulating compliance with 45 CFR 46 is through "assurances." Our institution is required to conduct human subject research in accordance with a Federalwide Assurance (FWA), which documents an institution's agreement with OHRP to comply with Federal regulations and maintain adequate programs and procedures for the protection of human subjects. Only institutions with an FWA can receive federal funding for research involving human subjects.

The FDA requires that biomedical research involving the experimental use of drugs, devices, and biologics conform to Good Clinical Practice (GCP). GCP is a standard articulated in FDA regulations for the design, conduct, performance, monitoring, auditing, recording, analysis, and reporting of clinical trials. Compliance with this standard assures that the data and reported results are credible and accurate and that the rights, safety, and well-being of research subjects are protected. To ensure compliance with FDA regulations and GCP standards in the conduct and reporting of clinical trials, the FDA performs audits of all parties involved in regulated clinical trials, including clinical investigators, IRBs, sponsors, monitors, and contract research organizations.

B. Institutional Official

The Chief Research Officer (CRO) and President of the Stanley Manne Children's Research Institute is responsible for the designation of the Institutional Official and has designated the Chief Operating Officer of the Stanley Manne Children's Research Institute as the Institutional Official (IO). The IO is authorized to act on behalf of the Institution, in its overall responsibility for the implementation and maintenance of the HRPP. The IO is directly involved in allocation of sufficient resources to the program to ensure that the conditions of the FWA are met. Where the IO is presented with a conflict of interest due to a role as an investigator of human subject research, the CRO and President will preside over all issues concerning the HRPP.

The following are the responsibilities of the IO:

- Assumes, on behalf of the Institution, the obligations of the Federalwide Assurance
- Consistently demonstrates a strong commitment to the protection of human subjects and sets the tone for a culture of respect for human subjects by communicating the importance of human subjects protections
- Possesses a thorough knowledge of the applicable regulations
- Serve as the contact person for the Office of Human Research Protections (OHRP)
- Routinely meets with the IRB Chair and Director, Research Integrity and Compliance (ORIC)
- Provides adequate resources and support to the staff of the Office of Research Integrity and Compliance (ORIC)

- Communicates with other members of the senior leadership on issues relating to human subjects protection as appropriate.
- The IO follows the same education requirement as the IRB members and ORIC staff.

C. Institutional Review Board

i. IRB Mission and Independence

Lurie Children's has established an IRB responsible for reviewing research with human subjects as defined by DHHS and clinical investigations as defined by the FDA. ORIC operates under the leadership of the Director, and guidance of the Chief Operating Officer and IO. The mission of the IRB is to protect the rights and welfare of human subjects involved in research at the Institution. To accomplish this mission, the IRB conducts a thorough review of each research study, at study initiation and at regular intervals, to ensure that the design and conduct of the study conforms to and abides by all applicable ethical principles and federal, state, and Institutional policies and regulations. The IRB has as its primary responsibility the protection of research subjects. No individual, group of individuals, or entity within or outside the Institution can override an IRB decision, unless to add restrictions or to disapprove an already approved activity. The IRB will function independently of other entities in the Institution.

No individual or group of individuals may try to unduly influence the deliberations and decisions of the IRB. Any IRB member may report any attempt to influence the decision of the IRB to the Chief Operating Officer, and/or the Director, ORIC. They, and the Chief Research Officer and President, will investigate and resolve the incident so that no undue influence is placed on the IRB activities and determinations.

ii. IRB Authority

- a. The IRB reviews, and has the authority to approve, to require modification of (to secure approval), or to disapprove all research activities, including proposed changes in previously approved human subject research. Research that has been approved by the IRB may be subject to further appropriate review by officials of the Institution. However, those officials may not approve research that has not been approved by the IRB.
- b. The IRB conducts continuing review of ongoing, approved research at intervals appropriate to the degree of risk, but not less than once per year. At each stage of review, the IRB determines the degree of risk posed by study activities and schedules the next review accordingly.
- c. The IRB has the authority to suspend or terminate the approval of ongoing, previously approved research that is not being conducted in accordance with the IRB, or Institutional, requirements or that has been associated with unexpected, serious harm to subjects. Within 30 days, any suspension or termination of approval shall include a statement of the reasons for the IRB's action and shall be reported promptly to the investigator, the IO, other appropriate Institutional officials, OHRP, and, if applicable, the FDA and funding agency.

- d. The IRB has the authority to observe or have a third party observe the consent process and other research activities.

- iii. Issues Considered by the IRB

To accomplish the mission of protecting the rights and welfare of human subjects, the IRB must conduct adequate review of research protocols by considering the following critical issues:

- a. Scientific Merit and Study Design

Although federal regulations do not directly require review of the study design or the underlying science of the proposed research, the IRB must review the project to determine there are no obvious flaws that might place research subjects at unnecessary risk. Additionally, the IRB must ensure that the study is designed so that there is sufficient potential benefit to justify any risks or inconvenience to which subjects will be exposed. The IRB reserves the right to review the science as it affects the risk/benefit ratio and human subjects protections and assess the following:

1. Aims are clearly defined and specified;
2. Scientific review of preliminary data includes whether available nonclinical and clinical information on an investigational product is adequate to support the conduct of the study/clinical trial;
3. There is appropriate justification for the research;
4. Study design is adequate and allow the investigators to answer the research questions;
5. Study objectives can be achieved; and
6. Randomization of subjects and/or placebo and controls are described and justified, when applicable.

The IRB considers the qualifications of the investigators when reviewing protocols. Protocols are routed to both the respective Division Head(s) and Department Chair(s) to confirm their agreement with the scientific aims, confirmation that the Principal Investigator (PI), Sub-Investigators, and all members of the research staff have had proper training to conduct the study, and their willingness to provide guidance if needed.

- b. Potential Risks and Anticipated Benefits

Federal regulations define minimal risk as “*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.*” (45 CFR 46.102(i) and 21 CFR 56.102(i)) Therefore, the term “risk” refers to both the chance (probability) of experiencing harm and the severity (magnitude) of the potential harm. The term “benefit” is used in the research context to refer to something of positive value related to health or welfare.

The Belmont Report states “*investigators and members of their institutions are obliged to give forethought to the maximization of benefits and the reduction of risk that might occur from the research investigation. In the case of scientific research in general, members of the larger society are obliged to recognize the longer term benefits and risks that may result from the improvement of knowledge and from the development of novel medical, psychotherapeutic, and social procedures.*” Accordingly, the IRB evaluates each study to ensure:

1. 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 might result from the research (as distinguished from risks and benefits of therapies subjects would receive outside of participation in the research);
2. The research risks will be minimized: (i) by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and (ii) whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes;
3. Subjects are provided with a full description of the known risks and the potential benefits of participation in the research;
4. The risks of the research are distinguished from the risks associated with standard therapeutic interventions (to this end, research procedures should be clearly identified in the protocol, consent form, and IRB application); and
5. When appropriate, there are adequate provisions in place for monitoring the data collected to ensure the safety of subjects.

c. Vulnerable Populations

The regulations outline additional protections for three specific populations: children, prisoners, and pregnant women/fetuses/neonates. The IRB follows the appropriate subparts of the regulations for protections of these populations to ensure the research is in compliance, including making the appropriate risk/benefit assessment in accordance with Subpart D (DHHS and FDA).

The IRB recognizes that there are other populations that are vulnerable to coercion or undue influence such as, but not limited to, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons. The IRB will ensure safeguards are in place to protect these populations. In addition to physical risks posed by participation in biomedical research, research has the potential to cause psychological, social, legal, and/or economic harm to subjects. The IRB reviews the precautions to minimize such risks.

d. Subject Compensation, Reimbursement, and Costs

The IRB reviews any payments made to the subjects and any costs the subject may incur due to study participation. Compensation to subjects should not be such

that it would unduly influence participation. When assessing the appropriateness of research compensation, the IRB reviews the complexity and inconveniences of the research. If the compensation exceeds the amount allowed by the Internal Revenue Service regulations to be tax free, the subject will need to provide Accounts Payable with the required information so that the Institution remains compliant with the federal tax regulations.

The investigator should clearly describe in the protocol and the consent documents whether the payment to the subject is compensation or reimbursement. Payments to subjects that are reimbursements of costs incurred due to participation, such as travel, parking, meals, are not considered compensation and thus are not subject to the federal tax law as described above.

The protocol and when appropriate the consent documents should address the following:

1. Payments are described in such a way to clearly indicate what is compensation, reimbursement, gifts, or incentives;
 2. Amount, form, and timing of payment is provided and are reasonable in relation to the study (e.g. Visa gift card at every visit);
 3. If payments will be prorated depending on the duration of study participation;
 4. When research participants are minors, if compensation will be delivered to a parent/guardian and/or to the participants themselves;
 5. The provisions for care and payment related to research related injury are clearly described;
 6. Payments cannot be in the form of a coupon good for a discount on the purchase price of a product once it has been approved for marketing.
- e. Protection of Privacy and Maintenance of Confidentiality

The IRB will review research procedures to ensure that there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data. Privacy refers to a person's desire to control the access of others to themselves. For example, persons may not want to be seen entering a place that might stigmatize them, such as a pregnancy counseling center that is clearly identified as such by signs on the front of the building. The evaluation of maintaining privacy should involve consideration of how potential subjects will be identified and contacted, the setting of any interactions, the appropriateness of the personnel in attendance during research procedures, and the methods used to obtain information about subjects. IRB members must be made aware of all strategies to protect privacy and confidentiality interests of enrolled and potential research subjects.

Confidentiality refers to the researcher's agreement with the subject about how the subject's identifiable private information will be handled, managed, and disseminated. The evaluation of measures to maintain confidentiality should

involve consideration of how the investigator maintains identifiable data, and the controls on storage, handling, and sharing of data.

When “sensitive” information, which includes information collected on drug or alcohol abuse, behavioral or mental health, pregnancy, sexually transmitted illnesses, HIV/AIDs, drug or alcohol treatment,, abuse and neglect, or other potentially stigmatizing issues is collected for research purposes, the IRB will determine that measures for the protection of confidentiality are adequate. The investigator may be advised, when appropriate, to obtain a Certificate of Confidentiality for the conduct of the study.

When evaluating adequate protections in place to ensure the privacy and confidentiality of the subjects and data are maintained, the following items are reviewed:

1. That protections are in place when the investigator or study staff approaches potential subjects
2. Procedures for collecting and recording study data
3. Methods utilized for coding or de-identifying collected data and the storage and destruction of data
4. Plans for appropriate inclusion of data in the medical record
5. Description of who will have access to the data and under what conditions
6. Health Insurance Portability and Accountability Act (HIPAA) provisions and requirement have been met

The IRB also serves as the Privacy Board in matters related to the requirement for authorization for the use of private and identifiable health information (PHI) for research.

f. Selection of Subjects and Additional Safeguards for Vulnerable Populations

The IRB must determine that selection of subjects is equitable. In making this determination, the IRB should take into account the purposes of the research and the setting in which the research will be conducted. The IRB assesses the study to determine the following:

1. The nature of the research justifies the proposed subject population;
2. Potential subjects are recruited in an equitable manner;
3. Inclusion and exclusion criteria take into consideration subject safety and welfare;
4. Adequate justification for excluding prospective subjects based on sexual orientation, age, race, etc.
5. Provision to include non-English speaking individuals or adequate justification if specifically excluded

When some or all of the potential subjects are likely to be vulnerable to coercion or undue influence (e.g., children, prisoners, individuals with impaired decision-

making capacity, or economically or educationally disadvantaged persons), the IRB will examine whether additional safeguards have been included in the study to protect the rights and welfare of these subjects. The federal regulations also require additional safeguards when the research involves pregnant persons and neonates/fetuses.

g. Recruitment

The IRB reviews both the procedures for approaching potential subjects for study recruitment and the content of all recruitment materials, using the following criteria:

1. Recruitment methods are clearly described
2. Timing and location of recruitment is acceptable
3. Materials are clear and do not overstate the benefits of the research or imply a certainty of favorable outcome beyond what is outlined in the consent or protocol and do not include exculpatory language
4. Acceptable screening procedures prior to recruitment
5. Adequate precautions have been taken to eliminate potential coercion
6. Materials and methods to approach the subjects avoid undue influence in deciding whether to participate. For example, advertisements should not emphasize payments or promise free treatment.
7. Advertisements should be limited to the following information: the full study title, the name of the investigator and facility, the purpose of the research or condition under study, the criteria that will be used to determine eligibility, the commitments required of subjects, and investigator or study staff contact information.
8. For studies in which a drug, biologic, or device is under investigation, advertising cannot make claims that are inconsistent with FDA labeling, or use terms such as “new” treatment, “new” medication, or “new” drug without explaining that the test article is investigational.

h. Protocol Procedures

The IRB reviews the study procedures to ensure that research risks are minimized and research benefits maximized. The IRB also reviews what happens with the study data once collected and if the follow-up of subjects is adequate. The following criteria are used:

1. There is adequate rationale for the procedures
2. Procedures are adequately described including the risk and benefits
3. There is clear differentiation between procedures done as standard of care versus those that are being done only for the research study
4. How the information gained from the procedures will be used

5. Provisions for informing the subjects about their data and the data from the study results
6. Care is taken to avoid duplicate procedures and when possible, these are combined with clinical and treatment indicated procedures

i. Drug and Device Studies

The IRB must ensure that protocols involving the use of drugs, devices, or biologics are compliant with all relevant FDA regulations. The following criteria are used:

1. Investigational status of the drug or device is adequately described
2. Supporting documentation (Investigator's Brochure, package insert, FDA IND/IDE/HDE documentation, etc.) is included in the submission
3. Supporting preclinical or clinical data
4. Phase of study if appropriate (Phase 1, 2 or 3)

j. Data Analysis and Data Safety Monitoring Plans

The IRB is responsible for ensuring that the data obtained from the study will be useful and ensure that an appropriate data and safety-monitoring plan is in place as appropriate given the nature of the study.

k. Informed Consent and Assent

Informed consent and/or assent will be sought from each prospective subject, or the subject's legally authorized representative, unless waived by the IRB in accordance with regulations. Additionally, informed consent and/or assent will be appropriately documented, usually with a signed written consent form or an adolescent assent form. In order to ensure that all subjects provide informed consent and/or assent, the IRB will closely examine an investigator's proposed methods for obtaining consent and/or assent, using the following:

1. That person obtaining consent is sufficiently qualified and is authorized to obtain consent and/or assent in accordance with IRB policy
2. That the setting of the consent process allows for obtaining consent and/or assent that is free from undue influence or coercion
3. That subjects are given sufficient opportunity to review the consent and/or assent form, to ask questions, and to carefully consider their decision to participate
4. The language spoken by both the potential subjects, and/or family, and that of the person obtaining consent
5. Whether it is necessary to implement a mechanism to assess the subject's ability to understand the information
6. That the person obtaining consent ensures that the subject understands that they are free to decline participation and to withdraw from the study at any time after it has begun.

D. IRB Chair: Selection, Responsibilities and Evaluation

The Chief Research Officer (CRO) of the Stanley Manne Children's Research Institute appoints the IRB Chair. The IRB Chair is appointed for a one-year term and is eligible for reappointment annually upon mutual agreement.

Candidates for IRB Chair shall be knowledgeable in clinical research, preferably a healthcare professional with a doctorate level degree with extensive clinical and research experience and without conflicts of interest that may limit their ability to serve objectively and in accordance with the mission of the IRB as defined in applicable laws and policies.

It is the responsibility of the IRB Chair to guide IRB members in performing adequate review of research protocols through consideration of all regulations and ethical principles pertaining to the protection of the rights and welfare of human subjects. The IRB Chair should be capable of facilitating discussion, integrating differing points of view, and moving forward consensus on recommendations to be provided to the investigators. The IRB Chair must also promote perception of the IRB as fair and impartial, and their determinations should be unaffected by pressure either by the Institution's administration, the investigators, or other professional or non-professional sources. The IRB Chair works collegially and collectively with Institutional officials to ensure that the IRB is a respected part of our community.

The responsibilities of the Chair include the following:

- Conduct the IRB meetings;
- Confirms assigned reviewers have adequate knowledge and expertise;
- Ensure the IRB functions in accordance with applicable regulations;
- Advise and consult with investigators regarding human subjects protections and IRB requirements;
- Participate in investigations of noncompliance and/or unanticipated problems;
- Contribute to the development of policies and procedures;
- Serve as a liaison between the IRB, investigators, and research leadership;
- Works closely with the Director, ORIC to resolve administrative issues of concern;
- Serves as a voting member of the IRB;
- Appoints the IRB members and on an ongoing basis, and at least annually, evaluates the adequacy of the membership and individual member performance.

E. IRB Vice-Chairs

The IRB Vice-Chairs are appointed by the IRB Chair for a one-year term and are eligible for reappointment annually upon mutual agreement. In the IRB Chair's absence, the IRB Vice-Chairs exert all authorities ordinarily vested in the IRB Chair (see list above). The IRB Vice-Chairs are routinely delegated the responsibility for expedited reviews and review of safety reports or other unanticipated problems. In the event the IRB Vice-Chair

has conflict of interest with a specific review, the IRB Chair or another IRB member will conduct the review.

F. IRB Membership

The CRO has designated the Institution's IRB Chair to appoint the IRB members and alternates. In accomplishing this task, the IRB Chair consults with the IO and Director, ORIC, and others as deemed appropriate. Copies of the CVs/resumés of all IRB members are submitted to the IRB Chair and Director, ORIC for review to aid in evaluating the individual's qualifications. IRB members are appointed for a one-year term to be renewed annually upon mutual agreement of the IRB Chair and the IRB member. The Institution's IRB membership is composed in compliance with federal regulations as set forth by DHHS (45 CFR 46), and FDA (21 CFR 56). The IRB is composed of at least five members, including at least one non-scientist member and at least one member who is not otherwise affiliated with the Institution and does not belong to the immediate family of a person who is affiliated with the Institution. The IRB must have at least one member whose primary concerns are in scientific areas and one member who represents the perspective of research subjects. (Note that the unaffiliated member, the member representing the general perspective of subjects, and the non-scientific member may be the same person, or they may be two or three different persons.)

The IRB must be composed of members with sufficient experience, expertise and diverse backgrounds (taking into account gender diversity, racial and cultural heritage, and sensitivity to issues such as community attitudes). Members must not only possess professional competence to review specific research projects but must also assess the research in terms of Institutional commitments and regulations, applicable state and local law, and standards of professional conduct and community practice. IRB members are expected to review protocols objectively and impartially. The IRB review process must be free of conflict of interest; as such, individuals who are responsible for business development are prohibited from serving as members on the IRB or carrying out day-day operations of the review process. In addition, members are prohibited from owning equity in the Institution.

The IRB membership is constituted of both primary and alternate members. Primary member may request an alternate in lieu of their absence. The appointed alternate represents the same expertise as the primary member. Alternates may attend to and contribute to all meetings; however, in primary member attends. If the primary member is unable to attend, they are to contact the alternate and to inform the ORIC staff and IRB Chair as to whether the alternate will attend. IRB members are not required to have alternates.

The following criteria regarding IRB membership are also considered in addition to federal requirements:

- Representation from the major disciplines at the Institution including the Department of Nursing;
- Individuals who understand the psychological, emotional and behavioral needs of children; and

- Individuals who are capable of identifying safety concerns including evaluating the location where the research takes place.

When IRBs regularly review categories of research that involve vulnerable subjects (such as children, pregnant persons, prisoners, or cognitively impaired persons) the IRB must include a member who is knowledgeable about and has experience working with these populations. Thus, at least one IRB member that represents the general perspective of subjects (i.e., children) must be present at each meeting. This may include, but is not limited to, a parent, a bioethicist, or a child psychologist.

When the IRB finds that a research study poses issues that require expertise beyond, or in addition to, that available among current IRB members, the IRB Chair may invite individuals with the expertise in these special areas to consult in the review of these issues. Such individuals provide opinions only, and do not vote on motions.

The ORIC staff and General Counsel are present at IRB meetings.

The IRB membership and roster, along with the CVs, and confidentiality statements, (described below), are maintained in ORIC files.

i. Confidentiality

IRB members review research proposals, grant applications, confidential materials from pharmaceutical companies, progress reports, and other written materials, in addition to participating in regular convened meetings. All new IRB members are required to sign an IRB Confidentiality Agreement to assure that they will hold all material provided from ORIC staff and all matters discussed at IRB meetings in the strictest confidence. While IRB members may contact the investigators or research staff of the research directly for clarification, they are encouraged to disseminate all concerns through the ORIC IRB staff. IRB Members do not discuss IRB matters with individuals who are not part of the IRB/ORIC staff. ORIC staff will collect any paper documents after IRB meetings for appropriate disposal.

In addition, the identity of each IRB member involved in the review of a research protocol is confidential and is typically not revealed to any individual outside of the review process. It is crucial to the success of the IRB that members feel free to comment candidly on each research proposal without concern for disclosure of their identity or opinions.

All committee members, including the IRB Chair and IRB Vice-Chairs, are responsible for identifying and declaring any potential conflicts that may influence their review of an assigned protocol.

ii. Attendance

Federal regulations outline quorum requirements for IRB meetings, specifying that quorum must be maintained at all times during the meeting and that no proposed research may be reviewed if quorum is lost. IRB members will be encouraged to make every attempt to attend meetings. Members who are unable to attend a meeting may provide written comments on the protocols to be reviewed that will be presented for discussion by the IRB Chair. ORIC staff

monitor quorum at each convened IRB meeting and tally the number of members participating in the vote of each agenda item.

Both DHHS regulations (45 CFR 46.108(b)) and FDA regulations (21 CFR 56.108(c)) require that a convened IRB meeting includes the majority of the members and at least one member whose primary concerns are in the non-scientific area. Reviewer Assignments/Meeting Materials

IRB members serve as reviewers for new protocols, renewals, modifications, adverse events, and any other administrative and ethical issues relating to human subjects protection. The ORIC Staff assigns specific IRB members to serve as the primary and secondary IRB reviewers for each study taking into consideration both the subject matter of the study and the member's area of expertise. The IRB Chair reviews and confirms that the agenda volume is appropriate for the number of IRB members attending the meeting and assignments made are appropriate. A third IRB member, typically a non-affiliated member, is assigned as a consent reviewer to ensure that the consent and assent documents explain the research study clearly, accurately and in lay language. All IRB members are expected to be familiar with all the protocols on the agenda and to participate in the meeting discussions. ORIC staff forwards the meeting agenda to every IRB member electronically in advance of the meeting. All study documents and the completed application are reviewed in electronic IRB system once assigned to the IRB member responsible for that submission as determined by the IRB Chair. These are assigned on the same day that the meeting agenda is provided. Each IRB member reviews these materials to formulate their questions and concerns, which will then be presented to the IRB.

The review materials consist of the IRB submission, the protocol, investigator drug or device brochures (if applicable), pre-review comments and responses, consent forms, recruitment documents, and other documents as applicable.

A copy of the agenda is provided to each IRB member at the meeting. In addition, during the meeting, key documents are projected for viewing and discussion.

iii. Participation

The review of each protocol at the IRB meeting begins with a summary of the research proposal by the IRB members designated as the primary and the secondary reviewers. These reviewers are required to complete checklists that ensure the study meets the criteria for approval. During the convened meeting, assigned reviewers structure their comments in accordance with this reviewer checklist for each submission. In cases where the reviewer is unable to attend the meeting, they may provide written comments to ORIC staff for presentation at the meeting by the IRB Chair. During the discussion by the reviewers, the ORIC staff project the meeting materials for the IRB members to view. Following this summary is discussion by the entire committee of any issues relevant to the protection of human subjects. All members, and particularly the nonscientific and non-affiliated members, are encouraged to ask questions and voice opinions regarding the nature of the research and the extent to which meets the criteria for approval.

iv. Vote

During the convened meeting, all voting members will vote to approve, disapprove, approve with directed contingencies, or defer each protocol reviewed. Votes may be taken during the meeting by a show of hands, voice vote, or electronic polling if the meeting is conducted via telephone or video conferencing. All primary members including those from the Department of Nursing have full voting privileges. Alternate IRB members can only vote (and count toward quorum) if the primary member they are replacing is not present or voting. A member who does not wish to vote for any reason may abstain. There will be no real or perceived coercion for the vote on any project. For research to be approved, it has to receive the approval of the majority of the IRB members present at the meeting.

Often, IRB members participate in discussion and review as non-voting members. Examples of non-voting members of the IRB are an alternate member when the primary member for whom they provide an alternate is present or a representative from the Institution's General Counsel.

v. Conflict of Interest

All IRB members must comply with the Institution's Conflict of Interest Policy. In addition, no IRB member may participate in the committee's review of or vote for a research project in which they have a conflicting interest. Conflicts of interest that might arise for IRB members include non-financial conflicts, such as serving as a PI, Sub-investigator, or consultant on a research project, or financial conflicts such as having a financial interest of any amount in the proposed research.

ORIC staff makes a notation on the meeting agenda for any item to be discussed by the IRB where a member has a conflict. In addition, at the beginning of each IRB meeting, the IRB Chair requests that the members identify any additional conflicts not already referenced. Any IRB member with a conflict of interest is obligated to notify the IRB Chair of the conflict. That member might be present during the initial discussion of the protocol in order to provide information required by other IRB members in the review process. However, they must be recused from participating in the IRB deliberation and vote for the related study and would not count towards quorum. When the IRB Chair has a conflicting interest, they would also be recused from the deliberation and vote and the IRB Vice-chair or another qualified IRB member chairs the meeting in their absence.

A member having a conflict is not assigned as the primary/secondary reviewer for a submission undergoing review. Listed PIs, Sub-investigators, or other research staff is excluded as primary/secondary reviewers. In the event that an IRB member has another type of conflict, they are obligated to notify the IRB Chair of the conflict. The IRB Chair will work with ORIC staff to reassign the review.

vi. IRB Member Evaluation

On an ongoing basis, and at least annually, the IRB Chair in collaboration with ORIC staff evaluate individual IRB member performance, including attendance, participation, and timeliness of reviews and completion of the reviewer checklists. In addition, if there are specific concerns about a member, the IRB Chair will confidentially speak with the individual member. As indicated above, IRB members are also asked to provide feedback regarding the IRB Chair and ORIC staff.

vii. Teleconferencing/Videoconferencing

If unable to attend in person, IRB Members may participate in IRB meetings via telephone conference or videoconference. Their attendance will count towards quorum and they may vote on the agenda items discussed.

If the entire meeting is held via telephone or video conference, the meeting minutes will reflect this. If individual members cannot attend in person, their remote attendance will be noted on the meeting minutes.

G. Office of Research Integrity and Compliance (ORIC)

ORIC is the administrative unit of the IRB. Under the direction of the Director, ORIC, staff members perform critical functions that support the overall function of the IRB.

ORIC staff are responsible for the following duties to promote the protection of the rights and welfare of human subjects involved in research activities conducted at the Institution:

- i. Ensure ready access to the Institution's Federalwide Assurance, all applicable regulations, current policies and guidelines related to the involvement of human subjects in research, and Institutional policies and procedures. New or modified policies and procedures are disseminated through a variety of methods, including e-mail notifications, educational workshops, and posting the policies on the IRB website.
- ii. Advise IO, IRB Chair and Vice-Chairs, and IRB members of new or modified regulations, policies, and guidelines issued by regulatory oversight agencies.
- iii. Coordinate the development of new policies and procedures or the revision of existing policies and procedures to ensure consistency with federal regulations and guidelines, state law, and Institutional policies. The development of new policies and procedures or major modifications to existing policies and procedures is conducted in consultation with ORIC staff, IRB Chairs, and the IO. The dissemination of new or updated policies throughout the Institution.
- iv. Determine whether activities represent research involving human subjects or a clinical investigation.
- v. May determine when studies are exempt from applicable federal, state, and local regulations and the Institutional policies and procedures.
- vi. Educate members of the Institution's research community (IRB members, research administrators, department heads, investigators, clinical research staff, clinical care staff, human subjects, and Institutional officials, etc.) in order to

establish and maintain a culture of compliance with Federal regulations and Institutional policies relevant to the protection of human subjects. Education should focus on maintaining a high level of awareness regarding the ethical and responsible conduct of research, and on safeguarding the rights and welfare of subjects.

- vii. Provide IRB members with educational materials to ensure that they are kept up to date with the changes in regulations and with any news items pertinent to their review activities. IRB members should be provided with all relevant information to ensure that they can provide the most comprehensive and timely review of each research proposal.
- viii. Offer advice to investigators in completing the IRB application, modification and renewal submissions and provide guidance regarding applicable Institutional, state and federal policies, laws, and regulations.
- ix. Implement and maintain a post-approval monitoring program to ensure investigators' compliance with IRB and Institutional requirements and applicable regulations.
- x. Facilitate the prompt review of proposed changes in research activities and reports of unanticipated problems involving risks to subjects and/or serious adverse events related to ongoing research.
- xi. Promptly convey IRB decisions and requirements for modifications to submission to investigators. After the meeting, ORIC staff members are responsible for drafting correspondence to investigators, which accurately reflect all concerns raised by IRB members. ORIC staff will inform investigators of the rationale for suggested changes and, whenever possible, will refer investigators to relevant regulations or guidelines. If investigators raise questions about the IRB's concerns, ORIC staff will advise them of the IRBs expectations and provide suggestions for how they might best respond to the issues of concern.
- xii. Review and issue the final approval letters after certifying that the information contained in the IRB approval letter is true and correct as verified by the minutes and records of the IRB review of the submission.
- xiii. Notify investigators in writing when the IRB disapproves research, indicating the reasons for this decision and providing them the opportunity to reply in person or in writing.
- xiv. Act as liaison between IRB members and investigators while preserving anonymity of IRB members.
- xv. Perform an administrative review of the completeness of all submissions to ensure compliance with regulatory and Institutional requirements. If a submission is missing a necessary component, based on the submission requirements, ORIC staff will not forward the application to the IRB. Rather, ORIC staff will communicate the problem to the investigator and assist them in completing the application so that the proposal may be considered at the soonest possible IRB meeting.

- xvi. Attend and provide administrative support at IRB meetings, including taking notes and monitoring quorum during the length of the meeting.
- xvii. Maintain complete and accurate IRB records that are accessible for inspection and copying by authorized Federal officials. IRB records are retained for at least three years after completion of the research (45 CFR 46.115(b) and 21 CFR 56.115(b)). These records will include:
 - a. Copies of all research protocols reviewed, scientific evaluations that accompany these protocols, approved consent documents, progress reports submitted by research investigators, and reports of injuries to subjects.
 - b. Copies of all minutes of convened IRB meetings.
 - c. Records of continuing review activities.
 - d. Copies of all correspondence between the IRB and the investigators and/or research staff
 - e. A list of IRB members.
 - f. Written procedures for the IRB as required by 45 CFR 46.103(b)(4).
 - g. Statements of significant new findings provided to subjects, as required by 45 CFR 46.116(b)(5).
 - h. The IRB will provide for the maintenance of records relating to a specific research activity for at least three years after completion of the research.
 - i. IRB records will be accessible for inspection and copying by authorized representative of DHHS at reasonable times and in a reasonable manner or shall be forwarded to DHHS when requested by authorized DHHS representatives.
 - j. Federal regulations do not require public or sponsors access to IRB records. In order to protect the confidentiality of materials submitted by investigators, requests from the public or press to review IRB records will not be honored. ORIC staff makes all reasonable attempts to honor requests for copies of relevant documents from study sponsors if the documents cannot be obtained from the investigators. For the purposes of monitoring compliance with clinical trials, sponsors will only be given direct access to IRB records under circumstances reviewed and approved by senior leadership and the Institution's General Counsel as appropriate.
- xviii. Write and maintain minutes of IRB meetings and seek IRB review and approval prior to finalization. The IRB minutes include the following:
 - a. A list of all primary members on the IRB, a list of the voting members present (primary and alternate), and notation of who are scientists/non-scientists in order to verify that quorum requirements are met. The IRB Rosters are maintained in the ORIC files and indicate whether each member is a scientist, affiliated, and their area of expertise.

- b. Separate deliberations, actions, and votes for each protocol undergoing initial review, modification or continuing review;
 - c. A notation of all issues and concerns raised about a protocol;
 - d. A summary of all controverted issues and their resolution;
 - e. A justification of any deletion or substantive modification of information describing risks of or alternatives to participation outlined in any DHHS sample consent document;
 - f. The specific basis for requiring changes in or disapproving research;
 - g. The vote on these actions including the number of members voting for, against, and abstaining, and those present for the vote;
 - h. The names of any members who identified a conflict with the protocol under discussion and were required to leave the room before the final discussion and vote for the protocol;
 - i. Documentation of specific findings required by the regulations, and the protocol-specific rationale supporting the determination, including protocol specific information that justifies the determinations (e.g., justification for waiver of the requirement of informed consent, documentation of the additional determinations made by the IRB for research involving vulnerable populations;
 - j. Significant Risk (SR) vs., Non-Significant Risk (NSR) device determinations and rationale for the decision;
 - k. For review of studies involving vulnerable populations, a member or consultant who is an appropriate representative of the vulnerable population must participate in the review. The expert reviewer will be asked to comment, whether in person or via written comments, on the appropriateness of the investigator's response to any issues raised after the IRB deliberations.;
 - l. Notation of the length of approval granted; and
 - m. The final version of the minutes will be presented for a vote of acceptance at the same IRB at its next scheduled meeting. After the vote of acceptance, the final version of the minutes is stored electronically on the IRB's drive.
- xix. Record and track metrics related to IRB submissions such as: numbers and types of submissions processed; departmental submission rates; timeliness of review; member attendance; and the volume of review at each IRB meeting. These data are reviewed and considered by the Director, ORIC, and the IRB Chair and Vice-Chairs to identify the need for additional IRB members or resources and make recommendations to research administration.
 - xx. Maintain and review IRB rosters.
 - xxi. Field questions, concerns, and complaints from prospective, current, and former research subjects and their representatives. Subject inquiries and concerns are

responded to in a professional and timely manner and escalated to ORIC leadership as appropriate

- xxii. Performing quality improvement and process improvement assessments with ORIC leadership, IRB Chair and Vice-Chairs to ensure smooth and efficient IRB operations. ORIC staff meet regularly to discuss any issues, such as the following:
 - a. Inconsistencies in protocol review or interpretation of IRB policies and guidelines among the IRB committees;
 - b. Questions related to the application of IRB policies, guidelines, and procedures;
 - c. Suggestions to improve services provided by ORIC staff;
 - d. Review of subject complaints, allegations of non-compliance, unanticipated problems, and conflict of interest management plans before forwarding the issue to the IRB for formal review, as required by regulations and Institutional policies: and/or
 - e. Review and revise existing IRB policies and procedures or to develop new IRB policies and procedures as needed.

H. Investigator Questions, Concerns, and Suggestions

There are several avenues through which Institutional investigators and research personnel may obtain answers to questions and bring forward concerns or suggestions regarding the HRPP.

IRB policies and procedures are posted on the ORIC website. Additionally, new policies and procedures are disseminated to investigators by email and regular educational workshops.

Investigators and research personnel should direct questions about the IRB review of particular protocols and general questions about the IRB review process to ORIC staff. However, investigators and research personnel may also consult with ORIC staff by telephone, or by making an appointment to meet with an individual staff person. Investigators should be mindful that ORIC staff and the IRB Chair or IRB Vice-Chairs cannot reverse a decision made by the convened IRB and cannot make most decisions on behalf of the IRB. However, when appropriate, ORIC staff or the IRB Chair or Vice-Chairs, will work with the investigator to bring concerns and/or suggestions to the convened IRB for consideration.

The IRB is charged with the protection of the rights and welfare of human research subjects. ORIC supports these efforts and is committed to providing excellent service to investigators and research personnel. Investigators with suggestions to improve that service or to improve the Institutional HRPP should direct their suggestions to the Director, ORIC, ORIC staff, or the IRB Chair or Vice-Chairs.

Questions, concerns, and suggestions related to the Institution's HRPP, including issues related to the IRB, may also be directed to the Senior Vice-President and Chief Operating Officer of the Research Institute (IO).

2.2 OTHER IRB MEETING ATTENDEES

A. Legal Counsel

The Office of General Counsel supports the IRB and ORIC mission in efforts to maintain an integrated Institutional compliance program and the independence and authority of the IRB under applicable law.

ORIC and the IRB Chair work closely with the Office of General Counsel on issues relating to interpretation and impact of applicable local, state and federal laws and regulations as they relate to the IRB's jurisdiction and responsibility. Counsel provides accurate and timely advice to the IRB and ORIC.

To promote this working relationship, the Assistant General Counsel regularly attends IRB meetings to address issues within the IRB's purview, assists the IRB Chair and ORIC staff in the review of policies, and provides guidance on specific issues as requested by the IRB Chair and ORIC staff.

General Counsel may also be involved in the in the review and resolution of issues concerning legal noncompliance as well as issues that arise under applicable federal laws that affect the conduct of research, such as FDA/OHRP.

General Counsel, and outside counsel if appropriate, advises on issues regarding reporting requirements.

B. Consultants, Observers, and Guests

The Institution is committed to having an IRB with the appropriate expertise to review clinical research protocols and take into consideration the medial, emotional, social, and psychological needs of the research subjects and their families. When necessary, the IRB may seek input by consultants in order to provide a comprehensive review. Consultants may be internal or external to the Institution and may be asked to assist in the review of an individual protocol and/or attend a meeting. The consultant may also provide education on a specific topic of interest to the IRB. A consultant may not have a conflict of interest as defined for IRB members. Consultants, observers, and guests do not count towards quorum and do not vote.

i. Consultants:

The Director, ORIC, and IRB Chair may determine upon the pre-review of a protocol that a consultant is needed, or any IRB member may request at any time during the review process to add a consultant to the review process. This determination is based on the topic of the protocol and expertise of the voting IRB members.

The IRB Chair selects the consultant and in doing so may consult with the department chair or any other individual as appropriate to select a suitable consultant. A consultant may be internal or external to the Institution and may be asked to review a protocol or provide education or guidance on a specific topic. The consultant provides a written report to the IRB Chair and may also be asked to attend a meeting.

Documentation of Use of Consultants:

- a. Consultants are required to complete the IRB member Conflict of Interest disclosure form and the appropriate confidentiality form.

- b. The use of the consultant is documented in the IRB minutes and in the IRB review for that submission.
 - c. The written report provided by the consultant is made available to the IRB members.
- ii. Observers and Guests:

Observers and guest may attend the IRB meeting at discretion of the IRB Chair and are individuals with a particular interest and not regular attendees. Potential IRB members are invited to attend a meeting prior to joining the IRB. They are required to complete the appropriate confidentiality form, do not count towards quorum and may not vote. They are not allowed to observe the IRB final deliberation and vote for any protocols in which they may have a potential or actual conflict of interest.
- iii. Investigators and Research Staff:

On occasion and by invitation from the IRB Chair, a PI and/or member of their research staff may be asked to attend the IRB meeting where their protocol will be discussed in order to address specific concerns of the IRB members. As with consultants and guest, they are also required to complete a confidentiality form. The PI/research staff will be allowed to attend only the portion of the meeting involving the discussion of their protocol and answer questions posed by the IRB. Once they have addressed the issues raised, the PI and/or research staff is dismissed from the meeting and are not present for the deliberation and vote on the protocol.