

3.0 IRB Review Process

3.1 Policy

All human subjects' research in the Institution must meet the criteria for one of the following methods for review:

- Exempt review
- Expedited review
- Full review by a convened IRB

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

The following describe the procedures required for the review of research by the IRB.

3.2 Human Subjects Research Determination

The responsibility for an initial determination as to whether an activity constitutes human subjects research rests with the IRB. The IRB will make this determination based on the definitions of human subject and research contained in Section 1.0, definition of human subject's research. Since the Institutional Official and the IRB will hold the Investigator responsible if the determination is not correct, Investigators are urged to request a confirmation from the IRB office that an activity does not constitute human subjects. The request may be made, by e-mail or through a formal written communication. All research requests must include sufficient documentation of the activity to support a determination by the IRB.

Determinations as to whether an activity constitutes human subjects research will be made according to the definitions in section 1.0 and using Decision Tree(s) at www.hhs.gov/ohrp/policy/checklists/decisioncharts.html. Determinations regarding activities that are either clearly or clearly not human subject's research based on this guidance document will be made in writing and may be made by the IRB Chair (or designee). Determinations regarding less clear-cut activities will be referred to the IRB Chair, who may make the determination or refer the matter for convened IRB review. If a clear determination cannot be made, then, out of an abundance of caution, the activity should be deemed to constitute human subjects research for further review (e.g., exempt, expedited or convened IRB review).

Documentation of all determinations made of whether activity constitutes human subjects research are recorded and maintained by IRB office. Formal submissions will be responded to in writing and a copy of the submitted materials and determination letter/e-mail will be kept on file.

3.3 Exempt Studies

While all research using human subjects must be approved by the IRB, certain categories of research (i.e., “exempt research”) do not require convened IRB review and approval. Exempt research is subject to Institutional review and must be determined and approved by the IRB Chair (or designee). The following sections will describe activity that is exempt and the procedures for conducting exempt review. After a determination that research is exempt, the Investigator is notified in writing of the exemption status. The study is not subject to continuing review on an annual basis; however, the Investigator is asked to let the IRB know when the study is closed.

Documentation of all exemption determinations made are recorded and maintained by the IRB office.

3.3.1 Limitations on Exemptions

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

3.3.2 Categories of Exempt Research

Unless an exception exists, the following categories of research below are considered exempt research and not regulated by the Common Rule or FDA regulations.

1. Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as:
 - a. Research on regular and special education instructional strategies, or
 - b. Research on the effectiveness of, or the comparison among instructional techniques, curricula, or classroom management methods. [45 CFR §46.101(b)(1)]

2. Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, unless:
 - a. Information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and
 - b. Any disclosure of the human subjects responses outside the research could reasonably place the subjects at risk of criminal or civil liability, loss of insurability

or be damaging to the subject's financial standing, employability, or reputation [see 45 CFR §46.101(b)(2) or (b)(3)]

3. 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 (2), if:
 - a. The human subjects are elected or appointed public officials or candidates for public office; or
 - b. Federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter. Any disclosure of the human subjects responses outside the research could reasonably place the subjects at risk of criminal or civil liability, loss of insurability or be damaging to the subject's financial standing, employability, or reputation. [see 45 CFR §46.101(b)(2) or (b)(3)]

4. 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. [45 CFR §46.101(b)(4)]

NOTE: In order to be eligible for this exemption, all of the materials have to exist at the time the research is proposed.

5. Research and demonstration projects which are conducted by or subject to the approval of federal department or agency heads, and which are 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; or
 - d. Possible changes in methods or levels of payment for benefits or services under those programs.
 - e. The program under study must deliver a public benefit (e.g., financial or medical benefits as provided under the Social Security Act) or service (e.g., social, supportive, or nutrition services as provided under the Older American Act).
 - f. The research demonstration project must be conducted pursuant to specific federal statutory authority, there must be no statutory requirements of IRB review, the research must not involve significant physical invasions or intrusions upon the privacy of subjects', and the exemption must be invoked only with authorization or concurrence by the funding agency.

6. Taste and food quality evaluation and consumer acceptance studies,
 - a. If wholesome foods without additives are consumed; or
 - b. 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 US. Department of Agriculture.

Regulations & Guidance: DHHS 45 CFR §46.101(b); 45 CFR §46.401(b); FDA 21 CFR §56.104(c)-(d); OHRP Guidance at 45 CFR §46.101(b)(5): Exemptions for research and Demonstration Projects on Public Benefit and Service Programs

In addition to the federal criteria for exemptions this Institution evaluates whether the proposed research meets the Institution's ethical standards. The following ethical standards are reviewed on proposed research considered for an exemption:

- The research holds out no more than a minimal risk to participants
- The selection of subjects is equitable
- If there is a recording of identifiable information, there are adequate provisions to maintain the confidentiality of data.
- If there are interactions with participants, the IRB should determine whether there should be a consent process that will disclose such information as:
 - The activity involves research
 - A description of procedures
 - The participation is voluntary
 - The name and contact information of the researcher
- There are adequate provisions to maintain the privacy interests of participants.

3.3.3 FDA Exemptions

The following category of clinical investigation is exempt from the FDA requirements of IRB review:

- Taste and Food Quality Evaluations and Consumer Acceptance Studies, if wholesome foods without additives are consumed or if a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural, chemical, or environmental contaminant at or below the level found to be safe, by the FDA or approved by the EPA or the Food Safety and Inspection Service of the U.S. DOA. [FDA 21 CFR §56.104(d)]

3.4 Expedited Review

3.4.1 Definitions

Expedited Review: Process by which designated IRB members, on behalf of the full IRB, approve a limited class of research activities through reviews conducted outside of the convened IRB meeting.

Expedited Review is used by the IRB for either or both of the following:

- Some or all of the research appearing on the list of categories of research eligible for expedited review and found by the reviewer(s) to involve no more than minimal risk; and/or
- Minor changes in previously approved research during the period (of one year or less) for which approval is authorized. (See section 3.4.2)

Minor changes to research are those that in the judgment of the IRB do not affect assessment of the risks and benefits of the study by substantially altering any of the following:

- The level of risk to subjects;
- The research design or methodology;
- The subject population
- The qualifications of the research team;
- The facilities available to support the safe conduct of the research;
- Any other factor which would warrant review of the proposed changes by the convened IRB.
- A minor change does not increase risk more than minimally or add procedures.

Examples of changes to previously approved research that may be considered minor (and may be reviewed using expedited procedures) when they do not alter the risk/benefit ratio include:

1. Changes in study documents, such as recruitment materials, consent forms, questionnaires, etc. that do not materially affect participation of the subject in the study or alter the meaning of the text (e.g., formatting, phone or room numbers, etc.).
2. Clarifications of the study protocol, procedures, or consent language that do not introduce new procedures or information.
3. Changes in wording or deletions of a question(s) on a survey or in the material properties of a stimulus, where the change or deletion does not alter the fundamental meaning of the item for the research or change the nature of the subject's participation in the study.
4. Addition of a standardized survey instrument that does not substantially increase risk to participants or the duration of their study participation.
5. Addition of advertisements or recruitment materials that are not considered coercive and are easily compared to the approved informed consent script or document.

6. Increases in numbers of participants, who are identified and recruited by approved methods from currently approved populations, or increases in local site enrollment in multi-site studies where the increase does not exceed the approved total number of participants across all sites.
7. Decreases in number or frequency of data collection points that do not compromise study integrity or decrease safeguards for participants.
8. Decreasing the amount of blood draw or the frequency of blood draw
9. Reducing the time period of the study
10. Adjusting incentives (as long as they are not coercive or pose undue influence)
11. Response to a conditional approval determination by the convened IRB.

[DHHS 45 CFR §46.110; FDA 21 CFR §56.110(b)]

3.4.2 Categories of Research Eligible for Expedited Review¹

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. The activities listed below should not be deemed to be of minimal risk simply because they are included on this list.

The expedited review procedure may not be used for the following:

- 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 risk.
- The availability of expedited review contained in paragraphs one (1) through nine (9) of this section below apply regardless of the age of subjects, unless specifically excepted as noted.

The standard requirements for informed consent (or its waiver, alteration, or exception) apply regardless of the type of review (i.e., expedited review or convened IRB review) used by the IRB. However, it should be noted that, while research that involves paragraphs one (1) through seven (7) below pertains to both initial review and continuing review, paragraphs eight (8) and nine (9) below only pertain to continuing reviews.

1. Clinical studies of drugs and medical devices only when condition (a) or (b) is met.
 - a. Research on drugs for which an IND [21 CFR Part 312] is not required.

¹ 63 FR 60364-60367, November 9, 1998.

(NOTE: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the produce is not eligible for expedited review.)

- b. Research on medical devices for which (i) an IDE [21 CFR Part 812] is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.
2. Collections of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:
 - a. From healthy, non-pregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week; or
 - b. From other adults and children, considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week.
 3. Prospective collection of biological specimens for research purposes by noninvasive means. Examples:
 - a. Hair and nail clippings in a non-disfiguring manner;
 - b. Deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction;
 - c. Permanent teeth if routine patient care indicates a need for extraction;
 - d. Excreta and external secretions (including sweat);
 - e. Uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gum base or wax or by applying a dilute citric solution to the tongue.
 - f. Placenta removed at delivery;
 - g. Amniotic fluid obtained at the time of rupture of the membrane prior to or during labor;
 - h. Supra-and sub-gingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques;
 - i. Mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings;
 - j. Sputum collected after saline mist nebulization.
 4. Collection of data through non-invasive 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.

5. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.) Examples:
 - a. Physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject's privacy;
 - b. Weighing or testing sensory acuity;
 - c. Magnetic resonance imaging;
 - d. Electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, Doppler blood flow, and echocardiography;
 - e. Moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.
6. 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 DHHS regulations for the protection of human subjects. See exempt categories and 454 CFR §46.101(b)(4). This listing refers only to research that is not exempt.]

7. Collection of data from voice, video, digital, or image recordings made for research purposes.
8. Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies.

[NOTE: Some Research in this category may be exempt from the DHHS regulations for the protection of human subjects. See exempt categories and 45 CFR §46.101(b)(2) and (b)(3). This listing refers only to research that is not exempt.]

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

Of note, category (8) identifies three situations in which research that is greater than minimal risk and has been initially reviewed by a convened IRB may undergo subsequent continuing review by the expedited review procedures.

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

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

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

3.4.3 Expedited Review Procedures

Under an expedited review procedure, the review may be carried out by the IRB Chair or by one or more reviewers designated by the IRB Chair from among IRB members. IRB members who serve as designees to the IRB Chair for expedited review will be

matched as closely as possible with their field of expertise to the study under review. (see section 2.4.A for definition of experienced member)

IRB members with a COI in the research (see section 2.5 – Conflict of Interest for IRB members) will not be selected to serve as expedited reviewers.

When reviewing research under an expedited review procedure, the IRB Chair, or designated IRB member(s), should receive and review all documentation that would normally be submitted for convened IRB review including the complete protocol. This includes review of the following:

1. the complete protocol,
2. for continuing review, an application for continuing review that summarizes research activities since the previous annual review (including modifications and adverse events);
3. notes from pre-screening conducted by the IRB staff;
4. any applicable applications; and
5. the current consent documentation.

Protocols submitted for expedited review will be pre-screened by IRB staff to ensure that the package is complete. The reviewer(s) conducting initial, continuing reviews or modifications to previously approved research will determine whether the research meets the criteria allowing review using the expedited procedure, and if so, whether the research meets the regulatory criteria for approval. If the research does not meet the criteria for expedited review, then the reviewer will indicate that the research requires convened IRB review and the protocol will be placed on the agenda for the next IRB meeting.

In reviewing the research, the reviewers will follow the review procedures described in sections 3.7 and 3.8 and may exercise all of the authorities of the IRB except that the reviewers may not disapprove the research. A research activity may be disapproved only after review in accordance with the non-expedited procedure set forth below.

The IRB Chair (or designee) will indicate approval, required modifications or referral to the convened IRB. If modifications are required, the IRB staff will inform the Investigator. If the modifications are minor, the IRB Chair may determine if the Investigator has sufficiently addressed the modifications. If the modifications are major or if the IRB Chair (or designee) requests, the modified protocol will be sent back to the IRB member(s) for further review at a convened IRB meeting.

Regulations & Guidance: DHHS 45 CFR §46.100; FDA 21 CFR §46.110; Categories of Research that May Be Reviewed by the IRB through an Expedited Review Procedure - FDA & DHHS; OHRP Guidance on Written IRB Procedures; OHRP Guidance on Use of

Expedited Review Procedures; OHRP Guidance on Continuing Review; FDA Information Sheets: Continuing Review after Study Approval

3.4.4 Informing the IRB

All members of the IRB will be apprised of all expedited review approvals that were reviewed by the IRB Chair (or designee). This notification is accomplished by means of a list in the agenda and a list in the monthly IRB meeting minutes. Any IRB member can request to review the full expedited review and all supporting documentation by contacting the IRB office.

3.5 Convened IRB Review

Convened IRB review means review by a fully convened IRB. Except when an expedited review procedure is used, the IRB will conduct initial, continuing reviews and modifications of previously approved research at convened meetings at which a quorum (see section 3.5.5 below) of the members is present.

Regulations and Guidance: FDA 21 CFR §56.108(c)

3.5.1 IRB Meeting Schedule

The IRB meets on a regular basis throughout the year. The schedule for the IRB may vary due to holidays or lack of quorum. The schedule for IRB meetings is given to all IRB members in December before the next calendar year. Additionally, this information is posted on the Pennington Biomedical Research Center HRPP website for the benefit of all Investigators, research coordinators and other research staff when submitting protocol materials. Special meetings may be called at any time by the IRB Chair.

3.5.2 Preliminary Review

All submissions by Investigators to the IRB are stamped to confirm the date of submission.

The IRB staff will perform a preliminary review of all protocol materials submitted to the IRB for determination of completeness and accuracy. Only complete submissions will be referred for further consideration (i.e., exempt, expedited or convened IRB review).

The Investigator will be informed either by e-mail or phone of missing materials and the deadline to resubmit corrections before further review can take place. The Investigator is responsible to provide the IRB with an active e-mail address and current contact information.

Specific questions regarding the IRB policies and procedures; determining whether a particular protocol is human subjects research or not; and which forms are required for a particular study, can be submitted by email, writing and/or via the telephone to the IRB office for further information and/or clarification.

3.5.3 Primary Reviewers

After it has been determined that the protocol submission is complete, the IRB Chair, with the assistance of the IRB Staff, assigns protocols for review based on the scientific content of the protocol, reviewer's area of expertise, and requirements for representation of vulnerable populations involved in the research. A primary reviewer is assigned to each agenda item and a scientific/scholarly reviewer to each agenda item who has expertise in the area of research (one person could do both).

When the IRB is presented with a protocol which, in the opinion of the IRB Chair, may be outside of the knowledge base or representative capacity of all of the IRB members, an outside consultant will be sought (see section 3.6.6, Consultant - Children and section 3.6.7, Consultant - Vulnerable Populations). Proposals for which appropriate expertise cannot be obtained for a given meeting will be deferred to another meeting when appropriate expertise can be achieved.

Primary reviewers are responsible for:

- Having a thorough knowledge of all details of the proposed research;
- Performing an in-depth review of the proposed research and supporting documents;
- Leading the discussion of the proposed research at the convened meeting and presenting both positive and negative aspects of the research. (section 3.6.4 – Initial, Continuing Review and Requests for Modification);
- Making suggestions for changes to the proposed research.
- Completing all applicable IRB Member Reviewer Forms.

If the primary reviewer will be absent from the meeting, a new reviewer with appropriate expertise will be assigned if time allows. If the reviewer is unable to attend the meeting and an alternate is not able to be assigned, the submission will be tabled until the appropriate expertise can be obtained.

It should be noted that all IRB members have access to and are expected to review all IRB proposals, not just the ones they are responsible for reviewing.

During the convened IRB meeting, primary reviewers must complete the appropriate reviewer forms. All reviewer forms will be filed with the appropriate meeting minutes.

3.5.4 Pre-Meeting Distribution of Documents to Reviewers

Documents reviewed by expedited review are not submitted to members.

The following materials will be distributed to primary reviewers:

- Initial submissions – Application for Initial Review (submitted by investigator), any relevant appendices, any relevant grant applications; the protocol; sponsor or DHHS approved protocol (if one exists), the Investigator’s brochure (when one exists); the sample informed consent document (when one exists); the complete consent document and any supporting documents.
- Continuing review submissions - the primary reviewer will receive the continuing review report, the last approved consent, the complete protocol, Investigator brochure (if one exists), all protocol modifications reviewed during the current continuing review timeframe, all adverse events reviewed during the current continuing review timeframe, all protocol deviations reviewed during the current continuing review time frame.
- Modifications – the primary reviewer will receive a tracked copy all items being modified, a final copy of all items being modified, an application for a modification of approved human research.

The following materials will be distributed to all attending members not involved in the primary review:

- Initial submissions – all members will receive the Initial Submission Application, protocol summary, the complete consent document, recruitment materials (if available) and any supporting documentation.
- Continuing review submissions – all members will receive the continuing review summary and the last approved consent.
- Modifications – all members will receive a final copy of all items being modified and the application for modification of approved human research.

Documents are distributed to IRB members at least one week before the IRB meeting to allow adequate review time.

All expedited submissions and other supporting documents are available to all members before, during and after the IRB meeting.

3.5.5 IRB Agenda

While the IRB will make every effort to review all submissions, the IRB has the right to limit the agenda based on IRB member attendance of appropriate expertise.

3.5.6 Quorum

A quorum consists of a simple majority (more than fifty percent (50%) of the voting IRB membership, including at least one member whose primary concern is in a non-scientific area. For research to be approved it has to receive the approval of a majority

of members present at the meeting. If a regular IRB member and his/her alternative are present at a convened IRB meeting, only one counts towards the quorum and the IRB member (not the alternate) is the only one entitled to vote.

Additional quorum requirements include the following:

- If research involving an FDA-regulated article is involved, a licensed physician must be involved in the review. The physician may be a voting IRB member or a consultant who must be present for the discussion and for the review of any studies (including initial review, continuing review, modification, Investigator brochure or report of anticipated problems involving risks to subjects and others) that involve the FDA-regulated article; and
- For research that involves cognitively-disabled persons or persons with impaired decision-making capacity, IRB membership must include at least one member who is an expert in the area of the research.

At meetings of the IRB, a quorum must be established and maintained for the deliberation and vote on all matters requiring a vote. The IRB Chair, with the assistance of the IRB staff, will confirm that an appropriate quorum is present before calling the meeting to order. If an IRB member leaves the meeting due to a conflict of interest or any other reason the IRB Chair and/or IRB staff are responsible for assuring a quorum is maintained. The IRB staff will document in the meeting minutes the quorum determination. If a quorum is not maintained, the proposal or pending action item must be tabled or the meeting terminated. The IRB staff will document the time of arrival and departure for all IRB members and notify the IRB Chair if a quorum is not present. A sign-in sheet is completed by IRB members, guests and ex-officio (non-voting members) guests to document their attendance at a convened IRB meeting and to memorialize that a quorum was appropriately convened and maintained.

IRB members are considered present and participating at a duly convened IRB meeting when either physically present or participating through electronic means (e.g., teleconferencing or video conferencing) that permits them to listen to and speak during IRB deliberations and voting.

When not physically present, the IRB member must have received all pertinent materials prior to the meeting and must be able to participate actively and equally in all discussions.

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

IRB members commit to contact the IRB office by e-mail or phone approximately two weeks before a scheduled IRB meeting date if unable to make the IRB meeting, so IRB staff can ensure appropriate notification of IRB alternate members.

3.6 IRB Meeting Procedures

3.6.1 Call to Order and Quorum

The IRB Chair (or designee in the event that the IRB Chair is absent) will call the IRB meeting to order, once it has been determined that a quorum exists.

3.6.2 Conflict of Interest of IRB Members

Where there is a COI involving an IRB member, the IRB Chair (or designee) will remind the IRB member to recuse him/herself from the discussion and vote by leaving the room when there is a conflict for the particular action item under review. Known conflicts of interest of an IRB member is also noted on the agenda, which is made available to all members prior to the IRB meeting.

3.6.3 Review and Approval of Prior Meeting Minutes

The IRB will review and discuss the IRB meeting minutes from the previous meeting and determine if there are any revisions/corrections to be made. If there are no changes to be made, the minutes will be accepted as presented and considered final. If it is determined that revisions/corrections are necessary, the minutes will be amended and presented for approval at the next IRB meeting. A majority of the members present at a duly constituted IRB meeting are required to accept the minutes.

3.6.4 Initial, Continuing Review and Requests for Modification

The IRB reviews all submissions for initial review and continuing review, as well as requests for modifications. The primary reviewer presents an overview of the research and lead the IRB through a discussion of the criteria approval for research documented on the IRB Member Reviewer Forms. If a primary reviewer is unable to attend the meeting the item will be tabled until the next meeting. All IRB members present at a duly convened IRB meeting have full voting rights, except in the case of a COI (see section 2.5 – Conflict of Interest for an IRB member) and ex-officio members. In order for the research to be approved, it must receive the approval of a majority of those voting members present at a duly constituted IRB meeting.

Regulations & Guidance: DHHS 45 CFR §46.103(b)(4); 45 CFR §46.108(b); 45 CFR §46.109; 45 CFR §46.116(b)(5); FDA 21 CFR §50.25(b)(5); 21 CFR §56.108; OHRP Guidance on Written IRB Procedures; OHRP Guidance on Continuing Review; FDA Information Sheets: Continuing Review After Study Approval

3.6.5 Recording of Proceedings

It is the responsibility of the IRB staff to record the proceedings of the IRB meeting with digital equipment to ensure accuracy of discussion. In addition, the IRB staff is responsible for taking minutes at each IRB meeting.

In order for research activity to be approved, it must receive the approval of a majority of those members present at a convened IRB meeting. The vote is recorded by means of member voting sheets, which records votes for, against, and abstained. IRB voting sheets are filed with the IRB meeting minutes and the voting results are recorded in the IRB minutes.

3.6.6 Consultant - Children

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

3.6.7 Consultant - Vulnerable Populations

When reviewing studies with other vulnerable populations, including pregnant women, fetuses, neonates, handicapped persons, and cognitively impaired, the IRB will request review by expert consultant, as needed. If the IRB regularly reviews research involving a vulnerable category of subjects, one or more individuals who are knowledgeable about and experienced in working with these subjects should be included as IRB members (refer to policy on vulnerable subjects for more detail section 3.7.6 – Vulnerable Subjects).

3.6.8 Guests and Non-Voting Members

At the discretion of the IRB, the Investigator (or designee such as a Co-Investigator) may be invited to the IRB meeting to answer questions about their proposed or ongoing research. The Investigator may not be present for the discussion or vote on the study or action under review by the IRB.

Other invited guests may be permitted to attend IRB meetings at the discretion of the IRB Chair. Invited guests may not speak unless requested by the IRB and must sign a confidentiality agreement prior to the convened meeting.

Certain ex officio individuals (non-voting members, IRB staff) regularly attend IRB meetings as ex-officio guests. While they are not voting members of the IRB, they may participate in the IRB discussion and may provide additional information to the IRB. The IRB Chair may ask the ex-officio individual to formally review an IRB submission if they feel the ex-officio's expertise is warranted. However, the non-voting member will not be

asked to be the primary reviewer; as the non-voting member has no voting rights. They need only sign a confidentiality agreement once.

3.7 Criteria for IRB Approval of Research

At the time of initial, continuing review and review of a modification to previously approved research (if the modification affects the criteria for approval), the IRB must determine that the following requirements are satisfied in order to approve research involving human subjects.

Risks to subjects are minimized:

- By using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk; and
- Whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.
- Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result.
- In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research).
- The IRB should not consider possible long-range effects of applying knowledge gained in the research (e.g., the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.
- Selection of subjects is equitable. In making this assessment, the IRB should take into account the purpose of the research and the setting in which the research will be conducted and should be particularly cognizant of the special problems of research involving vulnerable populations, such as children, pregnant women, cognitively disabled persons, or economically or educationally disadvantaged persons.
- Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by 45 CFR §46.116.
- Informed consent will be appropriately documented, in accordance with, and to the extent required by 45 CFR §46.117.
- When appropriate, the research plan makes adequate provisions for monitoring the data collected to ensure the safety of subjects.
- When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.
- When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, pregnant women, cognitively disabled persons, or

economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects.

Regulations & Guidance: DHHS 45 CFR §46.111; FDA 21 CFR §56.111

3.7.1 Risk-Benefit Assessment

The goal of a risk-benefit assessment is to ensure that the risks to research subjects posed by participation in a research study are justified relative to the anticipated benefits for the subjects or society. The IRB must:

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

The assessment of the risks and benefits of the proposed research involves a series of steps:

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

Based on this assessment, risk associated with the research will be classified as either minimal risk or greater than minimal risk, which will be based on the interpretation of minimal risk.

Regulations & Guidance: DHHS 45 CFR §46.111(a); FDA 21 CFR §56.111(a)

3.7.1.1 Scientific Merit

In order to assess the risks and benefits of the proposed research, the IRB must determine that the research uses procedures consistent with sound research design, the research design is sound enough to reasonably expect the research to answer its proposed question and the knowledge expected to result from this research is sufficiently important to justify the risk.

The IRB considers the following during the initial protocol review:

- Does the protocol accurately describe the following in a clear, detailed method?
 - Objectives of research
 - Background of research
 - Setting of research
 - Procedures of research
 - Data and safety monitoring plan
 - Risks of research
 - Potential benefits of research
 - Alternatives to participation in research
 - The Investigator has demonstrated a potential for recruiting the required number of suitable subjects within the agreed recruitment period
- All research under the purview of Pennington Biomedical Research Center must have a qualified physician, credentialed by Pennington Biomedical that will be responsible for all trial related medical decisions.

Regulations & Guidance: DHHS 45 CFR §46.111(a)(1); FDA 21 CFR §56.111(a)(1)

3.7.2 Equitable Selection of Subjects

The IRB determines by viewing the protocol that the selection of subjects is equitable with respect to gender, age, class, etc. The IRB will not approve a study that does not provide adequately for the equitable selection of subjects or has not provided an appropriate scientific and ethical justification for excluding classes of persons who might benefit from the research. In making this determination, the IRB evaluates:

- the purpose of the research;
- the setting in which the research occurs;
- scientific and ethical justification for including vulnerable populations such as children, pregnant women, cognitively disabled persons, or economically or educationally disadvantaged persons;
- the scientific and ethical justification for excluding classes of persons who might benefit from the research,
- inclusion/exclusion criteria,

- payment amount and timing of payments to participants (see 3.8.9 – Payments to Research Subjects) and
- participant recruitment and enrollment procedures.

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

Regulations & Guidance: DHHS 45 CFR §46.111(a)(3); FDA 21 CFR §56.111(a)(3)

3.7.2.1 Recruitment of Subjects

The Investigator will provide the IRB with all recruiting materials to be used in identifying subjects including recruitment methods, advertisements, and payment arrangements. See Section 3.8.8-Advertisements for a discussion of IRB review of advertisements, and section 3.8.9 - Payments to Research Subjects for a discussion of IRB review of payments/compensation to subjects.

Regulations & Guidance: DHHS 45 CFR §46.111(a)(3); 45 CFR §46.116; FDA 21 CFR §50.20; 21 CFR §56.111(a)(3)

3.7.3 Informed Consent

The IRB will ensure that informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by 45 CFR §46.116 and 21 CFR §50.20, see section 5.0. In addition, the IRB will ensure that the consent will be appropriately documented in accordance with, and to the extent required by 45 CFR §46.117 and 21 CFR §50.27 (see section 5.0 - Obtaining Consent from Research Subjects).

Regulations & Guidance: DHHS 45 CFR §46.111(a)(4) & (a)(5); FDA 21 CFR 56.111(a)(4) & (a)(5).

3.7.4 Safety Monitoring

Pennington Biomedical Research Center requires that all NIH funded research must have a data safety monitoring plan and convene a data safety monitoring board (DSMB) annually. Any reports generated from the DSMB will be submitted to the Medical Staff Committee, after the Medical Staff Committee has reviewed the DSMB reports the documents are given to the IRB for review.

Data safety monitoring plans and DSMB reports that are considered FDA regulated research are submitted directly to the IRB for review.

For all research that is more than minimal risk, the Investigator must submit a safety monitoring plan. This plan can be included in the protocol.

The data safety monitoring plan must describe the procedures for safety monitoring, reporting of unanticipated problems involving risks to subjects or others, descriptions of interim safety reviews and the procedures planned for transmitting the results to the IRB. This description should include information regarding an independent Data and Safety Monitoring Board (DSMB), if one exists, or an explanation why an independent data safety monitor is not necessary.

The IRB determines that the data safety monitoring plan makes adequate provision for monitoring the reactions of subjects and the collection of data to ensure the safety of subjects. The overall elements of the monitoring plan may vary depending on the potential risks, complexity, and nature of the research study. The method and degree of monitoring needed is related to the degree of risk involved. Monitoring may be conducted in various ways or by various individuals or groups, depending on the size and scope of the research effort. These exist on a continuum from monitoring by the Investigator in a small, low risk study to the establishment of an independent DSMB for a large phase III clinical trial.

The factors the IRB will consider in determining whether the safety monitoring plan is adequate for the research are as follows:

1. Monitoring is commensurate with the nature, complexity, size and risk involved.
2. Monitoring is timely. Frequency should commensurate with risk. Conclusions are reported to the IRB.
3. For low risk studies, continuous, close monitoring by the study Investigator or an independent individual may be an adequate and appropriate format for monitoring, with prompt reporting of problems to the IRB, sponsor and regulatory bodies as appropriate.
4. For an individual Safety Monitor, the plan must include:
 - parameters to be assessed,
 - mechanism to assess the critical efficacy endpoints at intervals in order to determine when to continue, modify, or stop a study.
 - frequency of monitoring procedures for reporting to the IRB
5. For a DSMB, the plan must include:
 - name of the Data Safety Monitoring Board, if applicable
 - is independent from the sponsor,
 - availability of written reports,

- composition of the monitoring group (if a group is to be used):
- experts in all scientific disciplines needed to interpret the data and ensure patient safety. Clinical trial experts, biostatisticians, bioethicists, and clinicians knowledgeable about the disease and treatment under study should be part of the monitoring group or be available if warranted.
- frequency and content of meeting reports
- frequency and character of monitoring meetings (e.g., open or closed, public or private).

In general, it is desirable for a DSMB to be established by the study sponsor for research that is blinded, involves multiple sites, involves vulnerable subjects, or employs high-risk interventions. For some studies the National Institutes of Health (NIH) require a DSMB. The IRB has the authority to require a DSMB as a condition for approval of research where it determines that such monitoring is needed. When DSMBs are utilized, IRBs conducting continuing review of research may rely on a current statement from the DSMB indicating that it has and will continue to review study-wide adverse events, interim findings, and any recent literature that may be relevant to the research, in lieu of requiring that this information be submitted directly to the IRB.

Regulations & Guidance: DHHS 45 CFR §46.111(a)(6); FDA 21 CFR §56.111(a)(6)

3.7.5 Privacy and Confidentiality

Under the research regulations, the IRB is required to determine whether adequate procedures are in place to protect the privacy of subjects and to maintain the confidentiality of the data.

3.7.5.1 Definitions

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

Identifiable Information: for research privacy purposes, this means information where the identity of the subject is or may readily be ascertained by the Investigator or associated with the information.

Individually Identifiable Private Information (IIPI): is information where, for research purposes, the identity of the subject is or may readily be ascertained by the Investigator or associated with the information.

Obtain: means to receive or access Individually Identifiable private Information (or identifiable specimens) for research purposes. This includes an Investigator's use,

study, or analysis for research purposes of Individually Identifiable private Information (or identifiable specimens) already in the possession of the Investigator.

Private information: for research privacy purposes, this means information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (e.g., a medical record). [45 CFR §46.102(f)]

3.7.5.2 Privacy

The IRB must determine whether the activities in the research constitute an invasion of privacy. In order to make that determination, the IRB must obtain information regarding how the Investigators are getting access to subjects or subjects' private, identifiable information. Investigators must have an appropriate authorization to access subjects or the subjects' information.

In developing strategies for the protection of subjects' privacy, consideration should be given to:

- Methods used to identify and contact potential subjects;
- Settings in which an individual will be interacting with an Investigator;
- Appropriateness of all personnel present for research activities;
- Methods used to obtain information about subjects and the nature of the requested information;
- Information that is obtained about individuals other than the target subjects, and whether such individuals meet the regulatory definition of human subject (e.g., a subject provides information about a family member for a survey); and
- How to access the minimum amount of information necessary to complete the study.

3.7.5.3 Confidentiality

The level of confidentiality protections should be commensurate with the potential of harm from inappropriate disclosure.

At the time of initial review, the IRB ensures that the privacy and confidentiality of research subjects are protected. The IRB assesses whether there are adequate provisions to protect subject privacy and maintain confidentiality. The IRB does this through the evaluation of the methods used to obtain information:

- About subjects;
- About individuals who may be recruited to participate in studies;
- The use of personally identifiable records; and
- The methods to protect the confidentiality of research data.

The Investigator will provide information regarding the privacy and confidentiality of research subjects at the time of initial review through the completion of the study; Pennington Biomedical Research Center approved HIPAA Authorization Form, and/or other submitted, applicable materials. The IRB will review all information received from the Investigator and determine whether or not the privacy and confidentiality of research subjects is sufficiently protected. In some cases, the IRB may also require that a certificate of confidentiality be obtained to additionally protect research data from compulsory disclosure.

In reviewing confidentiality protections, the IRB shall consider the nature, probability, and magnitude of harm that would be likely to result from a disclosure of collected information outside the research. It shall evaluate the effectiveness of proposed de-identification techniques, coding systems, encryption methods, storage facilities, access limitations, and other relevant factors in determining the adequacy of confidentiality protections.

Regulations & Guidance: DHHS 45 CFR §46.111(a)(7); FDA 21 CFR §56.111(a)(7)

3.7.6 Vulnerable Populations

At the time of initial review, the IRB will consider the scientific and ethical reasons for including vulnerable subjects in research. The IRB may determine and require that, when appropriate, additional safeguards are put into place for vulnerable subjects, such as those without decision-making capacity.

For an extensive discussion about the IRB's review and approval process for individual populations of vulnerable subjects, please refer to Section 6.0-Vulnerable Subjects in Research.

Regulations & Guidance: DHHS 45 CFR §46.111(b); 45 CFR 46 Subpart B, Subpart C & Subpart D; 45 CFR §46.205; FDA 21 CFR §50.3; 21 CFR §56.111(b)-(c); 21 CFR Subpart D

3.8 Additional Considerations during IRB Review and Approval of Research

3.8.1 Determination of Risk

At the time of initial review and continuing review, the IRB will make a determination regarding the risks associated with the research proposals. Risks associated with the research will be classified as either minimal risk or greater than minimum risk based on the absolute interpretation of minimal risk. The meeting minutes will reflect the IRB's determination regarding risk levels.

3.8.2 Frequency of Review

At the time of initial review and at continuing review, the IRB will make a determination regarding the frequency of review of the research protocols. All protocols will be reviewed by the IRB at intervals appropriate to the degree of risk but no less than once per year. In some circumstances, a shorter review interval (e.g. semi-annually, quarterly, or after accrual of a specific number of subjects) may be required (see 3.8.3 Review More Often Than Annually). The meeting minutes will reflect the IRB's determination regarding review frequency.

Regulations & Guidance: DHHS 45 CFR §46.109(e); FDA 21 CFR §56.109(f).

3.8.3 Review More Often Than Annually

Unless specifically waived by the IRB, research that meets any of the following criteria will require review more often than annually:

- Significant risk, as determined by the IRB, to research subjects (e.g., death, permanent or long lasting disability or morbidity, severe toxicity) without the possibility of direct benefit to the subjects;
- The involvement of especially vulnerable populations likely to be subject to coercion (e.g., terminally ill); or
- A history of serious or continuing non-compliance on the part of the Investigator.

The following factors also will be considered when determining which studies require review more frequently than on an annual basis:

- The probability and magnitude of anticipated risks to subjects;
- The likely medical condition of the proposed subjects;
- The overall qualifications of the Investigator and other members of the research team;
- The specific experience of the Investigator and other members of the research team in conducting similar research;
- The nature and frequency of adverse events observed in similar research at this and other Institutions;
- The novelty of the research making unanticipated adverse events more likely; or
- Any other factors that the IRB deems relevant.

In specifying an IRB approval period of less than one year, the IRB may define the period with either a time interval or a maximum number of subjects either studied or enrolled. If a maximum number of subjects studied or enrolled is used to define the approval period, it is understood that the approval period in no case can exceed one year and that the number of subjects studied or enrolled determines the approval period only when that number of subjects is studied or enrolled in less than one year.

If an approval period of less than one year is specified by the IRB the reason for more frequent review must be documented in the minutes.

3.8.4 Independent Verification That No Material Changes Have Occurred

The IRB recognizes that protecting the rights and welfare of subjects sometimes requires that the IRB independently verify utilizing sources other than the Investigator that no material changes occurred during the IRB designated approval period. Independent verification from sources other than the Investigator may be necessary at times (e.g., in cooperative studies, or other multi-center research).

The IRB will determine the need for verification from outside sources on a case-by-case basis and according to the following criteria:

- Protocols where concern about possible material changes occurred without IRB approval have been raised based on information provided in continuing review reports or from other sources;
- Protocols conducted by Investigators who have previously failed to comply with federal regulations and/or the requirements or determinations of the IRB;
- Protocols randomly selected or for cause audits conducted internally; or
- Whenever else the IRB deems verification from outside sources is relevant.

The following factors also will be considered when determining which studies require independent verification:

- The probability and magnitude of anticipated risks to subjects;
- The likely medical condition of the proposed subjects; or
- The probable nature and frequency of changes that may ordinarily be expected in the type of research proposed.

In making determinations about independent verification, the IRB may prospectively require that such verification take place at predetermined intervals during the approval period, or may retrospectively require such verification at the time of continuing review, review of amendments and/or unanticipated problems.

If any material changes have occurred without IRB review and approval, the IRB will decide the corrective action to be taken. (see section 10.0-Non-Compliance)

3.8.5 Consent Monitoring

In reviewing the adequacy of subject informed consent procedures for proposed research, the IRB may on occasion determine that special monitoring of the consent process by an impartial observer (i.e., a consent monitor) is required to reduce the possibility of coercion and undue influence.

Such monitoring may be particularly warranted when the research presents significant risks to subjects, or if subjects are likely to have difficulty understanding the information that will be provided. Monitoring may also be appropriate as a corrective action where the IRB has identified problems associated with a particular Investigator or a research project.

Regulations & Guidance: DHHS 45 CFR §46.109(e); FDA 21 CFR §56.109(f)

3.8.6 Investigator Conflicts of Interest

The research application asks protocol-specific questions regarding conflict of interests for Investigators and key research personnel. As part of its review process, the IRB notifies the Director of Legal and Regulatory Compliance of the potential conflict. (see Policy 401.00 – Individual Financial Conflict of Interest).

Regulations & Guidance: 42 CFR §50.603; 42 CFR §50.606(a); FDA 21 CFR §50.606(a); 21 CFR §54.1; 21 CFR §54.2; 21 CFR §54.4; 21 CFR §312.64(d); 21 CFR §812.110(d); 45 CFR §690

3.8.7 Significant New Findings

During the course of research, significant new knowledge or findings about the medication and/or the condition under study may develop. The Investigator must report any significant new findings to the IRB and the IRB will review such findings with regard to potential impact on the subjects' rights and welfare. Since the new knowledge or findings may affect the risks or benefits to subjects or subjects' willingness to continue in the research, the IRB may require, during the ongoing review process that the Investigator contact the currently enrolled subjects to inform them of the new information. The IRB will communicate this to the Investigator. The informed consent should be updated and the IRB may require that the currently enrolled subjects be re-consented, acknowledging receipt of this new information and for affirming their continued participation.

Regulations & Guidance: OHRP Guidance on Written IRB Procedures; OHRP Guidance on Continuing Review; FDA Information Sheets: Continuing Review After Study Approval

3.8.8 Advertisements

The IRB must approve any and all recruitment materials and/or advertisements prior to posting and/or distribution for studies that are conducted under the purview of the Institutional IRB. The IRB will review:

- The information contained in the advertisement;

- The mode of its communication;
- The final copy of printed advertisements, prior to posting; and
- The final audio/video taped advertisements,

The IRB reviews the material to assure the material is accurate, and not coercive or unduly optimistic, creating undue influence to the subject to participate which includes, but is not limited to:

- Does NOT state or imply a certainty of favorable outcome or other benefits beyond what is outlined in the consent document and the protocol
- Does NOT promise “free treatment,” when the intent is only to say subjects will not be charged for taking part in the research
- Does NOT include exculpatory language
- Does NOT emphasize the payment or the amount to be paid, by such means as larger or bold type

The advertisement is limited to the information prospective subjects need to determine their eligibility and interest, such as:

- The name and address of the Investigator or research facility
- The condition under study or the purpose of the research
- In summary form, the criteria that will be used to determine eligibility for the study
- A brief list of participation benefits, if any
- The time or other commitment required of the subjects
- The location of the research and the person or office to contact for further information

For FDA-Regulated research, the advertisement:

- Does NOT make claims, either explicitly or implicitly, that the drug, biologic or device is safe or effective for the purposes under investigation
- Does NOT make claims, either explicitly or implicitly, that the test article is known to be equivalent or superior to any other drug, biologic or device
- Does NOT use terms, such as “new treatment,” “new medication” or “new drug” without explaining that the test article is investigational.
- Does NOT include a coupon good for a discount on the purchase price of the product once it has been approved for marketing.

Once approved by the IRB, an advertisement cannot be altered or manipulated in any way without prior IRB approval.

Regulations & Guidance: DHHS 45 CFR §46.111(a)(3); 45 CFR §46.116; FDA 21 CFR §50.20; 21 CFR §56.111(a)(3)

3.8.9 Payment to Research Subjects

Payment to research subjects may be an incentive for participation or a way to reimburse a subject for time, travel, parking, and other expenses incurred due to participation. However, payment for participation is not considered a research benefit. Regardless of the form of remuneration, Investigators must take care to avoid coercion of subjects. Payments should reflect the degree of risk, inconvenience, or discomfort associated with participation. The amount of compensation must be proportional to the risks and inconveniences posed by participation in the study.

All payments are described in the protocol including:

- Amount
- Method
- Timing of disbursement
- Credit for payment accrues as the study progresses.

The following must be addressed in the consent or protocol:

- The consent and/or protocol cannot have a statement stating payment is contingent upon completing the entire study.
- The amount of payment and the proposed method and timing of disbursement is neither coercive nor presented undue influence.
- Any amount paid as a bonus for completion is reasonable and not so large as to unduly induce subjects to stay in the study when they would otherwise have withdrawn.
- All information concerning payment, including the amount and schedule of payments, is in the informed consent document.
- Compensation does not include a coupon good for a discount on the purchase price of the product once it has been approved.
- The subject will be informed through the consent process that all payments will come from the LSU payroll department. Subjects may be paid with gift cards; as long as the value of the gift card is not coercive.

Pennington Biomedical Research Center has a standard payment schedule for compensation to subjects based on number of visits, type of procedure and time to complete visit procedures. Most studies consider this uniform compensation schedule when assigning a compensation amount for subjects. While the IRB does not approve the Pennington Biomedical compensation schedules; the IRB has the final authority to determine whether compensation is considered coercive.

3.8.10 Recruitment Incentives

Payment arrangements among sponsors, Institutions, Investigators, and those referring research subjects may place subjects at risk of coercion or undue influence or cause

inequitable selection. Payment in exchange for referrals of prospective subjects from researchers (physicians) (finder's fees) is not permitted and may be considered illegal under federal or state law. Similarly, payments designed to accelerate recruitment that is tied to the rate or timing of enrollment (bonus payments) also is not permitted. Investigators are strongly encouraged to consult with the IRB office if they have any questions or concerns about recruitment incentives.

3.9 Compliance with all Applicable Laws and Regulations

The IRB follows and adheres to all applicable federal, state and local laws in the jurisdictions where the research is being carried out. The IRB relies on the Pennington Biomedical Research Center Director of Regulatory and Compliance for interpretation and application of federal and state law and the laws of any other jurisdiction where research is conducted as they apply to human subject research.

3.10 Possible IRB Actions

The IRB or reviewer(s) may arrive at the following decisions:

- Approval - see Section 3.10.1;
- Conditional Approval (requiring minor modifications) - see Section 3.10.2;
- Withheld (the IRB has requested major modifications in order to secure approval) - see Section 3.10.3;
- Disapprove - see Section 3.10.4;
- Suspension or Termination - see 3.11

The following Sections provide clarification with respect to each of these decision options.

3.10.1 Approval

Approved: means the determination by the IRB that the investigation and protocol, as submitted, has been reviewed and may be conducted at an institution within the constraints set forth by the IRB and other Institutional and federal regulations. The research may begin as of the IRB approval date.

[DHHS 45 CFR §46.102(h); FDA 21 CFR §56.103(m)].

3.10.2 Conditional Approval

3.10.2.1 Definitions

Conditional Approval: is a situation where the IRB cannot approve the research as submitted or the proposal and/or consent require minor revisions (e.g., wording changes, with replacement language provided). For proposals submitted for convened

IRB review, the needed revisions are agreed upon at the IRB meeting. For proposals submitted expedited review, the needed revisions are designated by the IRB Chair (or designee). None of the required modifications can be related to the regulatory criteria for approval. These revisions are presented to the Investigator for incorporation by simple concurrence. Revisions must be made exactly as designated by the IRB or IRB reviewer(s).

3.10.2.2 Policy

An IRB decision to conditionally approve a study includes situations where the IRB cannot approve the research as submitted and where the protocol and/or consent require minor revisions (e.g., wording changes, with replacement language provided). For protocols submitted for convened IRB review, the needed revisions are agreed upon at the IRB meeting. For proposals submitted expedited review, the needed revisions are designated by the reviewer(s). None of the required modifications can be related to the regulatory criteria for approval. These revisions are presented to the Investigator for incorporation by simple concurrence. Revisions must be made exactly as designated by the IRB or reviewer(s).

In order to receive an approval following a conditional approval determination the Investigator's response, the revised protocol and the previously submitted protocol is given to the IRB Chair, and/or a designee of the IRB for review. The reviewer(s) may approve the study upon receipt and approval of the revisions without further action by the IRB. For protocols initially submitted for expedited review, the Investigator's response, the revised proposal and the previously submitted proposal is given to the same reviewer(s) for re-review. The date of the final approval of the submission is the date the conditions were determined to be met.

Approval of the protocol application will not be granted and certification will not be issued until all deficiencies, if any, are corrected to the satisfaction of the IRB or the reviewer(s).

The outcome of the IRB's deliberations or reviewer(s) findings is communicated to the Investigator in writing. The Investigator may not proceed with the research until receipt of notice of IRB approval of the research.

The IRB's determination concerning the revision will be documented in the minutes of the next regularly scheduled IRB meeting.

An Investigator asking the IRB for review of a "Just-In-Time" grant for funding purposes, should submit an abstract of the project and a statement stating the review is required for funding purposes. If the IRB Chair or designated reviewer determines the study is one the IRB would support in concept, the IRB Chair will issue a letter of support. The

Investigator is required to prospectively submit the developed study for IRB review and approval prior to identifying, recruiting or enrolling any subjects in accordance with Department of Health and Human Services (DHHS) 45 CFR 46 (Common Rule), DHHS Standards for Privacy of Individually Identifiable Health Information 45 CFR 160 and 164 (Privacy Rule), and the U.S. Food and Drug Administration (FDA) 21 CFR, parts 50, 56, and 312.

3.10.3 Withheld Approval

3.10.3.1 Definitions

Withheld Approval: Made when the research does not qualify for approval or conditional approval. When making this motion, the assigned primary reviewer describes the IRB members' reasons for the decision and describes recommendations to make the research approvable.

Descriptions include:

1. the protocol and/or consent require major modification or clarification; or
2. insufficient information is provided to adequately judge the protocol application (e.g., the risks and benefits cannot be assessed with the information provided).

IRB approval of the proposed research must not occur until subsequent review of the material is reviewed by the convened IRB.

3.10.3.2 Policy

This IRB action is taken if major modification or clarification is required, or insufficient information is provided to adequately judge the protocol application (e.g., the risks and benefits cannot be assessed with the information provided). IRB approval of the proposed research must not occur until subsequent review of the material the Investigator submitted by the convened IRB or the expedited reviewer(s).

For protocols initially submitted for convened IRB review, in order to receive approval for a Withheld Approval (Major Modifications), the Investigator's response must be submitted for review at a subsequent, convened meeting of the IRB. The IRB staff provides the IRB with the Investigator's response, the revised protocol and the previously submitted protocol. The item is placed on the agenda for re-review at the next meeting.

IRB approval of the protocol will not be granted and an approval letter will not be issued until all deficiencies, if any, are corrected to the satisfaction of the IRB.

The IRB's determination concerning the subsequent amended protocol will be documented in the minutes of the IRB meeting. The outcome of the IRB action is communicated to the Investigator in writing.

3.10.3.3 Time Limit for Submitting Requested Changes for New Research Protocol Application with Conditional Approval or a Withheld Determination

Failure to submit a response to IRB stipulated changes or inquiries related to new research protocols with a conditional approval or withheld approval within 90 days will result in deactivation of the new research protocol application. The Investigator will receive written notification of the closure of the IRB file including an explanation for this action. Investigator's wishing to re-open their file must re-apply to the IRB following procedures outlined in this document. An extension beyond 90 days may be granted by the IRB if sufficient cause is provided by the Investigators. After the 90-day deadline, the IRB staff will send e-mail notification of the time lapse to the Investigators requesting a withdrawal of the study application. If changes or e-mail notification of the circumstances surrounding the delay are not received by the IRB staff within one week of issuance of this notice, the study may be withdrawn by the IRB staff.

3.10.4 Disapproved

The IRB action of Disapproved means that it cannot approve the protocol as written. The IRB has determined that the research cannot:

1. be conducted on Institutional or Pennington Biomedical Research Center premises, or other facilities;
2. cannot involve Pennington employees;
3. be conducted on or by Pennington Biomedical employees.

Written notice of the Disapproval will be issued by the IRB in writing.

3.10.4.1 Policy

The IRB will not review research given a Disapproval determination more than twice in a calendar year.

3.11 Study Suspension, Termination and Investigator Hold

3.11.1 Suspension or Termination

IRB approval may be suspended or terminated if research is not being conducted in accordance with IRB or regulatory requirements or has been associated with unexpected problems or serious harm to subjects. (see section 8.0 for a discussion of unanticipated problems and section 10.0 for a discussion of non-compliance)

Suspension of IRB approval is a directive of a convened IRB or the IRB Chair to temporarily stop either some or all previously approved research activities to ensure protection of the rights and welfare of study subjects or for non-compliance. Suspension directives made on an urgent basis by the IRB Chair must be reported to a meeting of the convened IRB. Suspended protocols remain open and require continuing review.

Termination of IRB approval is a directive of the convened IRB to permanently stop some or all activities in a previously approved research protocol. If all research activities are terminated, the research no longer requires continuing review.

The IRB shall notify the Investigator in writing of such suspensions or terminations and shall include an explanation of the reasons for the decision. The Investigator shall be provided with an opportunity to respond in person or in writing.

When a study is suspended or terminated, the convened IRB or authorized individual will:

- Have any unanticipated problems reported to the IRB;
- Consider actions to protect the rights and welfare of subjects;
- Consider whether procedures for withdrawal of enrolled subjects take into account their rights and welfare; and
- Consider informing current subjects of the suspension or termination.

All suspensions or terminations must be reported to the Institutional Official and reporting agency (if applicable).

Suspension or termination of research that involves an IRB approved protocol also can be issued by Institutional Officials on matters unrelated to the IRB (i.e., not necessarily related to protecting the rights and welfare of study subjects). Such actions can be made by the Executive Director and the Associate Executive Director of Clinical Research and will be reported to the IRB.

Regulations & Guidance: DHHS 45 CFR §46.113; FDA 21 CFR §56.113

3.11.2 Investigator Hold

An Investigator or sponsor may request an Investigator hold on a protocol when the Investigator/sponsor wishes to temporarily or permanently stop some or all approved research activities. Investigator holds are not suspensions or terminations.

3.11.2.1 Procedures

Investigators must notify the IRB in writing: providing a description of the research activities that will be stopped; describing proposed actions to be taken to protect current

subjects; and describing actions that will be taken prior to IRB approval of proposed changes in order to eliminate apparent immediate harm.

Upon receipt of written notification from the Investigator, the IRB staff places the research study on the agenda for review. The IRB Chair, in consultation with the Investigator, determines whether any additional procedures need to be followed to protect the rights and welfare of current subjects as described in Protection of Currently Enrolled Subjects below in section 3.11.2.2.

The IRB Chair, in consultation with the Investigator, determines how and when currently enrolled subjects will be notified of the administrative hold.

Investigators may request a modification of the administrative hold by submitting a request for a modification to previously approved research.

3.11.2.2 Protection of Currently Enrolled Subjects

Before an Investigator hold, termination or suspension is put into effect, the convened IRB, IRB Chair (or designee) considers whether any additional procedures need to be followed to protect the rights and welfare of current subjects. Such procedures might include:

- Transferring subjects to another Investigator;
- Making arrangements for clinical care outside the research;
- Allowing continuation of some research activities under the supervision of an independent monitor;
- Requiring or permitting follow-up of subjects for safety reasons;
- Requiring adverse events or outcomes to be reported to the IRB and the sponsor;
- Notification of current subjects; and/or
- Notification of former subjects.

3.12 Continuing Review

The IRB will conduct a continuing review of ongoing research at intervals that are appropriate to the level of risk for each research protocol, but not less than once per year. Continuing review must occur as long as the research remains active for long-term follow-up of subjects, even when the research is permanently closed to the enrollment of new subjects and all subjects have completed all research-related interventions. Continuing review of research must occur even when the remaining research activities are limited to the analysis of private identifiable information.

Regulations & Guidance: DHHS 45 CFR §46.109(e); FDA 21 CFR §56.109(f).

3.12.1 Approval Period

Determination of the approval period and the need for additional supervision and/or participation is made by the IRB on a protocol-by-protocol basis.

For each initial or continuing approval the IRB will indicate an approval period with an approval expiration date specified. IRB approval is considered to have lapsed at close of business on the expiration date of the approval. For a study approved by the convened IRB, the approval period starts on the date that the IRB conducts its final review of the study; that is, the date that the convened IRB approved the research. For a study approved under expedited review, the approval period begins on the date the IRB Chair (or designee) gives final approval to the protocol.

The approval date and approval expiration date are noted on initial approvals and subsequent continuing review approvals sent to the Investigator and must be strictly adhered to. Investigators should allow sufficient time for development and review of renewal submissions.

Review of a change in research ordinarily does not alter the date by which continuing review must occur. This is because continuing review is review of the full protocol, not simply a change to it.

The regulations make no provision for any grace period extending the conduct of research beyond the expiration date of IRB approval. Therefore, continuing review and re-approval of research must occur by close of business of the date when IRB approval expires.

3.12.2 Continuing Review Process

To assist Investigators, the IRB staff generates courtesy reminders to Investigators approximately 45 days in advance of the study expiration date so that they timely submit continuing reviews. It is the Investigator's responsibility to ensure that the continuing review of ongoing research is approved prior to the expiration date. By federal regulation, no extension to that date can be granted.

Information and documentation to be sent to the IRB office by Investigators includes the following:

- Continuing review report
- The current consent
- Newly proposed consent with redline edits (i.e., changes are to be highlighted, deletions are to be lined through) to reflect any changes from the prior submission

- The full protocol or a protocol summary containing the relevant information necessary to determine whether the proposed research continues to fulfill the criteria for approval
- A status report on the progress of the research that includes:
 - A summary since the last IRB review of:
 - Unanticipated Problems Involving risks to subjects or others;
 - Adverse Events, untoward events, and adverse outcomes experienced by subjects.
 - Subject withdrawals;
 - The reason for withdrawals;
 - Complaints about the research;
 - Amendments or modifications;
 - Any relevant recent literature; and
 - Any interim findings;
 - Any relevant multi-center trial reports;
 - The Investigator's current risk-potential benefit assessment based on study results;
 - The gender and minority status of those entered into the protocol, including:
 - Number of subjects considered as members of specific vulnerable populations; and
 - An assurance that all serious and unexpected adverse events had been reported as required.

In conducting continuing review of research not eligible for expedited review, all IRB members will have the last approved consent and the continuing review report. The primary reviewer receives all the previous listed materials (see section 3.5.4). At the meeting, the primary reviewer leads the IRB through the completion of the regulatory criteria for approval. See section 3.5.3 - Primary Reviewers

The IRB staff attends the convened meetings and ensures that the proposed study documents (consent, protocol, IB, application, supporting documents) for each protocol on the agenda have been distributed to the IRB members appropriately. The IRB staff will retrieve any additional materials should the IRB members or reviewer(s) request.

In the case of expedited reviews, the IRB members may request the IRB staff to provide them with additional materials required for the review.

Review of currently approved or newly proposed consent documents must occur during the scheduled continuing review of research by the IRB. However, informed consent documents should be reviewed whenever new information becomes available that would require modification of information in the IRB approved informed consent

document. Changes to consent documents are modifications and will be reviewed according to the procedures in section 3.13 – Modification of an Approved Protocol.

Continuing review of a study must continue until:

- The research is permanently closed to the enrollment of new subjects
- All subjects have completed all research related interventions
- Collection and analysis of private identifiable information has completed.

3.12.3 Expedited Review of Continuing Review

In conducting continuing review under expedited review, the reviewer(s) shall have access to all of the above materials specified in section 3.4.3 - Expedited Review Procedures.

Generally, if research did not qualify for expedited review at the time of initial review, it does not qualify for expedited review at the time of continuing review, except in limited circumstances described by expedited review paragraphs (8) and (9) found in section 3.4.2 -Expedited Review Categories. It is also possible that research activities that previously qualified for expedited review in accordance with 45 CFR §46.110, have changed or will change, such that expedited review would no longer be permitted for continuing review.

3.12.4 Lapse in Continuing Review Approval

The regulations permit no grace period or approval extension after approval expiration. Research that continues after the approval period has expired and is considered to be research conducted without IRB approval. If the continuing review approval does not occur within the timeframe set by the IRB, this is a lapse in continued review approval. All research activities must stop. This includes cessation of subject recruitment (e.g., media advertisements must be pulled), enrollment, consent, interventions, interactions, and data collection, unless the IRB finds that it is in the best interests of individual subjects to continue participating in the research interventions or interactions. This will occur even if the Investigator has provided the required information for continued review before the expiration date. Therefore, Investigators must allow sufficient time for IRB review and approval.

It is the responsibility of the Investigator to ensure that a lapse in approval does not occur. The IRB staff will notify the Investigator of the expiration of approval and that all research activities must cease.

If research subjects are currently enrolled in the research project and their participation is ongoing, once notified of the expiration of approval, the Investigator must immediately

submit to the IRB Chair a list of research subjects for whom suspension of the research would cause harm. Enrollment of new subjects cannot occur and continuation of research interventions or interactions for already enrolled subjects will only continue when either the IRB or IRB Chair upon consultation with the Institutional Official finds that it is in the best interest of the individual subjects to do so.

Failure to timely submit continuing review information is considered non-compliance by the Investigator and will be handled according to the non-compliance policy (See Section 10.0-Non-Compliance).

Once approval has expired (i.e., lapse in continuing review approval), IRB review and re-approval must occur prior to re-initiation of the research. If the study approval has lapsed more than 30 days and the Investigator has not submitted an application for continuing review, the study will be closed by the IRB.

If the IRB requires revisions to obtain continuing review approval and no response has been received from the Investigator within 60 days following IRB correspondence, the study will be closed unless the IRB determines that study closure will harm subjects.

3.13 Modification of an Approved Protocol

Investigators who wish to modify or amend their approved applications must seek IRB approval before making any changes in approved research. This requirement exists even though the changes are planned for the period for which IRB approval has already been given. One noteworthy exception are for changes necessary to eliminate an immediate hazard to the subject, in which case the IRB must then be notified at once.

Modifications may be approved if they are within the scope of what the IRB originally authorized. For example, if a researcher wishes to add a population to an existing study, but not alter the study procedures or purpose, a modification request is appropriate. Likewise, modifying a procedure without changing the study's purpose or study population may also be appropriate. If, however, the researcher wishes to add a population and revise study procedures, he or she will need to submit a new application for research in human subjects.

Investigators must submit documentation to inform the IRB about the changes in the status of the study. To this end, Investigators are required to submit the changes to the IRB office. The following completed forms must be turned in:

- Application for a modification; revised sponsor's protocol (if applicable)
- Revised approved consent /assent documents (if applicable) or other documentation that would be provided to subjects when such information might relate to their willingness to continue to participate in the study

- Revised or additional recruitment materials; or any other relevant documents provided by the Investigator.

The IRB Chair will determine whether the proposed changes may be approved through an expedited review process, if the changes are minor, or whether the modification warrants convened IRB review. The reviewer(s) using the expedited procedure has the ultimate responsibility to determine that the proposed changes may be approved through the expedited review procedure and, if not, must refer the protocol for convened IRB review. (see 3.13.1 Expedited Review of Protocol Amendments/Modifications)

Regulations & Guidance: OHRP Guidance on Written IRB Procedures.

3.13.1 Expedited Review of Protocol Amendments/Modifications

An IRB may use expedited review procedures to review minor changes in ongoing previously approved research during the period for which approval is authorized. An expedited review may be carried out by the IRB Chair and/or designee(s) among the IRB members.

The reviewer(s) determine whether the modifications meet the criteria allowing review using the expedited procedure, and if so, whether the research with the proposed modifications continues to meet the regulatory criteria for approval.

The reviewer will also consider whether information about those modifications might relate to subjects' willingness to continue to take part in the research and if so, whether to provide that information to subjects.

3.13.2 Convened IRB Review of Protocol Modifications

When a proposed change in a research study is not minor (e.g., procedures involving increased risk or discomfort are to be added), then the IRB must review and approve the proposed change at a convened meeting before the change can be implemented. The only exception is a change necessary to eliminate apparent immediate hazards to the research subjects. In such a case, the IRB should be promptly informed of the change following its implementation and should review the change to determine that it is consistent with ensuring the subjects' continued welfare.

All documents provided by the Investigator are given to the primary reviewer (see section 3.5.3 - Primary Reviewer)

At the meeting, the primary reviewer presents an overview of the modifications and leads the IRB through the completion of the regulatory criteria required for approval. The IRB will determine whether the research with the proposed modifications continues to meet the regulatory criteria for approval.

When the IRB reviews modifications to previously approved research, the IRB consider whether information about those modifications might relate to subjects' willingness to continue to take part in the research and if so, whether to provide that information to subjects.

3.13.3 Changes in the Informed Consent Document

When a modification makes it necessary to change the informed consent document, regardless of whether any subjects are enrolled, two copies of the revised consent document are to be submitted to the IRB. One tracked copy should show all changes from the previous version (i.e., highlighting all additions and striking through all deletions). The one clean copy will contain the IRB approval stamp without any outdated text.

3.14 Closure of Protocols

The completion or termination of a study is a change in activity that must be reported by the Investigator to the IRB on the closure report. Although subjects will no longer be at risk under the study, a final report to the IRB allows it to close the study files as well as provide information that may be used by the IRB in the evaluation and approval of related studies involving the Investigator.

The Investigators should submit the closure report to the IRB office. IRB staff will review the closure application for completeness and will notify the IRB. Closure applications in which the protocol will expire prior to the next scheduled IRB meeting will be closed and the final report will be included on the next agenda as a closure item. Closure applications in which the expiration date of the protocol is after the next scheduled meeting will be placed on the agenda as a closures item and closed effective the date of the meeting.

3.15 Notice to Investigators of IRB Actions

Barring extraordinary circumstances, all IRB action letters are prepared by IRB staff in writing and sent to the Investigator and research team within ten (10) working days. For an approval, along with written notification of approval, a copy of the approved consent document(s) containing the stamped approval with the dates of the approval and expiration on each sheet will be attached. For required modifications, the notification will include the information that is required, the basis for requiring those modifications, and a deadline for response submission. For a disapproval, termination or suspension, the notification will include the basis for making that decision.

All correspondence between IRB and Investigators are retained in the study file.

The IRB reports its findings and actions to the Institution in the form of its minutes, a copy of which is distributed by IRB staff to Institutional Officials with a copy stored in the IRB files.

3.16 Appeal of IRB Decision to Disapprove

When an IRB protocol presented at a convened meeting is Disapproved, given a Conditional Approval, or Withheld Approval, the IRB will notify the Investigator in writing about the specific deficiencies and the modifications that are necessary for appropriate IRB approval. The IRB shall include in its written notification a statement of the reasons for its decision and give the Investigator an opportunity to respond in writing. The Investigator also is given the opportunity to schedule a meeting with the IRB to discuss this matter.

In cases where there is disagreement between the IRB and the Investigator regarding the nature and extent of the requested changes and these disagreements cannot be resolved amicably in an informal manner, the Investigator and/or the IRB may make an appeal to the Institutional Official for a resolution of the matter. The Institutional Official may organize a meeting to help facilitate discussion between the IRB and the Investigator. While the Institutional Official may provide input and make recommendations to the IRB for expeditious resolution of the matter, final recommendations for approval remain under the purview of the IRB.

Regulations & Guidance: DHHS 45 CFR §46.109(d); FDA 21 CFR §56.109(e)