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

Investigators relying on the institution for IRB review of human subjects research are required to complete an IRB application to receive confirmation that an activity does not constitute human subjects. The IRB Chair or designee is responsible for making determinations of exemption from the requirements of federal regulations on whether an activity constitutes human subjects research based on the definitions of human subjects research. The request must be made through IRBManager. All 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 Not Human Subjects Research submission form and using Decision Tree(s) at www.hhs.gov/ohrp/policy/checklists/decisioncharts.html. After a determination by the IRB Chair (or designee) that the project is not human subjects research, the Investigator is notified in writing.

Regulations & Guidance: DHHS 45 CFR 46.101 (pre-2018); 46.104 (2018 new common rule); FDA 21 CFR 56.101

3.3 Exempt Studies

Exempt research is subject to Institutional review and must be determined and acknowledged by the IRB Chair (or designee). The following sections will describe activity that is exempt and the procedures for conducting exempt review. Investigators will submit an Application for Initial Review and protocol to the IRB for an exempt

determination. After a determination that research is exempt the Investigator is notified in writing. The study is subject to a status report every five years; 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

- Exemption for research involving educational tests, 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. The exemption also does not apply to research involving children when information is recorded with identifiers or code linked to identifiers.
- Pennington does not conduct research involving prisoners. However, the exemptions do not apply to research involving prisoners except for research aimed at involving a broader subject population that only incidentally includes prisoners.
- Exempt research categories do not apply to research that involves FDA-regulated products (studies using investigational drugs, biologics, or devices for which the FDA has granted an investigational new drug [IND] or investigational device exemption [IDE], or non-significant-risk devices).

3.3.2 Categories of Exempt Research (Pre-Common Rule)

Unless an exception exists, the following categories of research below are considered exempt research and not regulated by the Common Rule or FDA regulations if approved prior to January 21, 2019.

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 [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; of
   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. [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.

When exempt research involves an interaction with participants, the reviewer will review the consent process to ensure that subjects are (1) informed that the activity is research and that their participation is voluntary; and (2) given a description of the research activity and the name and contact information for the investigator conducting the research. The reviewer uses checklists to document review and exemption determinations. The IRB notifies the PI in writing that the research is exempt and that the PI may not make changes to the research activity without first discussing the changes with the IRB to ensure that the changes are within the parameters for exemption. If the research no longer meets the criteria for exemption, the investigator must resubmit the research for review by the IRB at a convened meeting or using the expedited review procedure, whichever is appropriate to the research activities.

3.3.3 Categories of Exempt Research (New Common Rule)

Unless an exception exists, the following categories of research below are considered exempt research and not regulated by the Common Rule or FDA regulations if approved on or after January 21, 2019.

1. Research, conducted in established or commonly accepted educational settings, that specifically involves normal educational practices that are not likely to adversely impact students' opportunity to learn required educational content or the assessment of educators who provide instruction. This includes most research on regular and special education instructional strategies, and research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.
   [45 CFR 46.101(b) (1)]

2. Research only includes interactions involving the use of educational tests, survey procedures, interview procedures or observation of public behavior (including visual or auditory recording), if at least one the following criteria is met:
   a. the information recorded cannot be readily linked back to the subjects in such a manner that subjects' identity can be readily ascertained, directly or through identifiers linked to the subjects; or
   b. any disclosure of this information would not place the subjects at risk of certain harms, or
   c. the information is recorded in an identifiable manner, even if sensitive, provided that an IRB determines through limited review that , when appropriate, there are adequate privacy and confidentiality protections in the study.
   d. any disclosure of the participants' responses outside the research would not reasonably place the participants at risk of criminal or civil liability or be damaging to the participants' financial standing, employability, educational advancement, or reputation.
   [45 CFR 46.101(b)(2)]

3. Research involving benign behavioral interventions through verbal, written responses, (including data entry or audiovisual recordings) from adults who prospectively agrees and one of the following is met:

   a. the information recorded cannot be readily linked back to the subjects in such a manner that subjects' identity can be readily ascertained, directly or through identifiers linked to the subjects;

b. any disclosure of the human participants' responses outside the research would not reasonably place the participants at risk of criminal or civil liability or be damaging to the participants' financial standing, employability, educational advancement, or reputation; or

c. If the research involves deception of participants regarding the nature or purposes of the research:

- The participant authorizes the deception through a prospective agreement to participate in research in circumstances in which the participant is informed that he or she will be unaware of or misled regarding the nature or purposes of the research.

Benign behavioral interventions are defined as "brief in duration, harmless, painless, not physically invasive, not likely to have a significant adverse lasting impact on the subjects, and the investigator has no reason to think the subjects will find the interventions offensive or embarrassing."

Exemption 3 is not applicable to biomedical research. Additionally, it applies only to research with adults; it is not applicable to research with children. [45 CFR 46.101 (b)(3)]

4. Secondary research for which consent is not required: Secondary research uses of identifiable private information or identifiable biospecimens, if at least one of the following criteria is met:

    a. The identifiable private information or identifiable biospecimens are publicly available; or
    b. Information, which may include information about biospecimens, is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained directly or through identifiers linked to the subjects, the investigator does not contact the subjects, and the investigator will not re-identify subjects; or
    c. The research involves only information collection and analysis involving the investigator's use of identifiable health information when that use is regulated by HIPAA [under 45 CFR parts 160 and 164, subparts A and E, for the purposes of "health care operations" or "research" as those terms are defined at 45 CFR 164.501 or for "public health activities and purposes" as described under 45 CFR 164.512(b);] or
    d. The research is conducted by, or on behalf of, a Federal department or agency using government-generated or government-collected information

obtained for non-research activities if the research generates identifiable private information that is or will be maintained on information technology that is subject to and in compliance with section 208(b) of the E-Government Act of 2002, 44 U.S.C. 3501

Regulations [Privacy Act of 1974, 5 U.S.C. 552a, and, if applicable, the information used in the research was collected subject to the Paperwork Reduction Act of 1995, 44 U.S.C. 3501]

5. Research and demonstration projects that are conducted or supported by a Federal department or agency, or otherwise subject to the approval of department or agency heads (or the approval of the heads of bureaus or other subordinate agencies that have been delegated authority to conduct the research and demonstration projects), and that are designed to study, evaluate, improve, or otherwise examine public benefit or service programs, including procedures for obtaining benefits or services under those programs, possible changes in or alternatives to those programs or procedures, or possible changes in methods or levels of payment for benefits or services under those programs.

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.

Exemption categories 7 and 8 do not apply to PBRC studies.

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) (6): 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.

When exempt research involves an interaction with participants, the reviewer will review the consent process to ensure that subjects are (1) informed that the activity is research and that their participation is voluntary; and (2) given a description of the research activity and the name and contact information for the investigator conducting the research. The reviewer uses checklists to document review and exemption determinations. The IRB notifies the PI in writing that the research is exempt and that the PI may not make changes to the research activity without first discussing the changes with the IRB to ensure that the changes are within the parameters for exemption. If the research no longer meets the criteria for exemption, the investigator must resubmit the research for review by the IRB at a convened meeting or using the expedited review procedure, whichever is appropriate to the research activities.

Regulation (45CFR46.104)

3.3.4 Limited IRB Review

Limited IRB review is a process that is required only for certain exemptions and does not require an IRB to consider all the IRB approval criteria in §46.111. In limited IRB review, the IRB must determine that certain conditions, which are specified in the regulations, are met. Limited IRB review may be done via the expedited review mechanism, that is, by the Chair or an experienced IRB member designated by the Chair (although it can also be conducted by the full IRB).

The two exemptions that require limited IRB review at PBRC are exemptions (d)(2)(iii), (d)(3)(i)(C).

Research that has progressed to the point that it involves only one or both of the following, which are part of the IRB-approved study are eligible for limited review: (A) Data analysis, including analysis of identifiable private information or identifiable biospecimens, or (B) Accessing follow-up clinical data from procedures that subjects would undergo as part of clinical care. [DHHS 45 CFR 46.104]

Written materials specify the information that researchers must submit for limited IRB review, including:

- The full protocol, application, or a protocol summary containing the relevant information to determine whether the proposed research fulfills the criteria for approval.

- Proposed consent document. Written materials specify that IRB members conducting limited IRB review may not disapprove research.

Written materials must specify the required determinations when conducting limited IRB review.

- For exemption Categories 2 and 3, there are adequate protections for privacy interests of participants and the confidentiality of identifiable data.
- The Institution evaluates whether the proposed research under limited IRB review meets the Institution's ethical standards.
- Continuing review is not required for studies that qualify for a limited review.
- PBRC retains the authority to suspend or terminate IRB approval of research approved with limited review.

3.3.5 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)]

The exemption at 21 CFR 56.104(c) does not apply to human-subjects research regulated by the DHHS. FDA-regulated research determined to be exempt from 21 CFR 56 IRB requirements is subject to 21 CFR 50 Informed Consent of Human Subjects. When providing ethical review of exempt research, the reviewer is also responsible for determining that the research meets the institution's ethical principles for human subject protection, specifically the Ethical Principles and Guidelines for the Protection of Human Subjects of Research (the "Belmont Report") and the requirements of the Health Insurance Portability and Accountability Act (HIPAA) of 1996. Specifically, the IRB is responsible for determining that (1) the research presents no more than minimal risk to subjects; (2) the selection of subjects is equitable; and (3) if applicable, there are adequate provisions to protect the privacy of subjects and maintain the confidentiality of identifiable data.

Clinical investigations governed by FDA regulations may only be determined to be exempt from IRB review/oversight if category 6 applies or in the case of emergency use.

3.4 Expedited Review

The IRB uses the expedited review procedure for review and approval of certain categories of human subjects research that involves no more than minimal risk and for review and approval of minor changes in approved research during the period of IRB approval [DHHS 45 CFR 46.110 and FDA 21 CFR 56.110].

When the IRB is not required to conduct continuing review (for studies approved under the new common rule), records must provide a rationale for any decisions to conduct done continuing review of research otherwise eligible for review using the expedited procedure.

The IRB Chair or designee may use expedited review procedures to approve a limited class of research activities involving human subjects. Expedited IRB review procedures may be used for the following:

- Initial or continuing review of specific categories of research not greater than minimal risk
- Continuing review of research previously approved by the convened IRB, under specified circumstances.
- Review of minor changes to previously approved research.

This policy describes the situations in which research may qualify for expedited review, as well as the process by which the IRB reviews research by expedited procedures.

When reviewing non-exempt human subjects research and clinical investigations using the expedited review procedure, the IRB Chair and designee are subject to the policy on IRB member conflicts of interest.

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 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: Research that in the judgment of the IRB does not affect the 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.

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 do not pose undue influence and are easily compared to the approved informed consent script or document.
6. 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 Review

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 unless the reviewer determines otherwise for a study. 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. (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.

   (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.

5. 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.]

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

7. 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.]

8. 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 protocol, an expedited review procedure may be used by the IRB at a particular site whenever the conditions of category (9) (a), (b), or (c) are satisfied for that site. However, with respect to category 9(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.

9. 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.

Research in any of these categories may require review at a convened meeting of the IRB if the circumstances of the proposed research involve more than minimal risk. The expedited review procedure may not be used where identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that the risk related to invasion of privacy and breach of confidentiality is no greater than minimal. In addition, the expedited review procedures may not be used for classified research involving human subjects. Classified research is research that has a security classification established by an authorized agency of the federal government.

When the IRB is not required to conduct continuing review (for studies approved under the new common rule), records must provide a rationale for any decisions to conduct done continuing review of research otherwise eligible for review using the expedited procedure.

The IRB Chair or designee is responsible for reviewing and determining whether the research is eligible for review using the expedited review procedure. Reviewers use the reviewer checklist that includes the applicability of expedited review and the categories of research eligible for expedited review published in the Federal Register at 63 FR 60364-60367 to document that:

- The research is applicable for expedited review.
- The research is minimal risk.
- The research activities fall within one or more of the research categories eligible for expedited review; and
- The consent form includes the basic elements of informed consent or a waiver or alteration of informed consent is approved. If the proposed research is not eligible for review using the expedited review procedure, the reviewer requests the research activity be scheduled for full board review at a convened meeting of the IRB.
- The Chair or designee may approve, require modifications in (to secure approval), or defer action pending receipt of additional information from the Principal Investigator. The Chair or designee may not disapprove a research activity using the expedited review procedure; a research activity can only be disapproved by the IRB at a convened meeting.

3.4.3 Submission Requirements

A. When submitting applications for initial or continuing review using the expedited procedure, investigators must submit all applicable materials: protocol, consent, assent, and any other protocol related documents.

B. When submitting amendment requests for expedited review, investigators must submit all applicable materials (revised tracked and clean copies of modified documents) listed in HRPP policy [IRB Submission and Pre-Review].

C. Upon receipt of an application for expedited review, an IRB staff member pre-reviews the submission (e.g., to verify whether the materials are complete, required education has been completed, etc.) and makes an initial determination as to whether the submission is eligible for expedited review.

D. Continuing review of the research is required until the research has been completed or has been closed prior to completion. The investigator must submit the continuing review form in IRBManager to document that the study has been completed or is being closed prior to completion. For multi-site research, the research may be considered completed or may be closed prior to completion

when the investigator at this site is no longer collecting, receiving, or analyzing identifiable data.

E. During the trial the investigator should provide to the IRB all documents subject to review.

3.4.4 Expedited Review Procedures

Under an expedited review procedure, the review may be carried out by the IRB Chair designee. 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. Only experienced IRB members may conduct reviews using the expedited procedure.

IRB members with a COI in the research (see IRB Member Conflict of Interest section in Policy 2) 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 or any protocol related documents
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 IRB applications.
5. The current consent document.
6. The investigator's current curriculum vitae, biosketch or other documentation evidencing qualifications.
7. Any newly proposed consent document.
8. Recruitment materials; and

9. A status report on the progress of the research including the following:

    a. number of participants accrued.

    b. a summary since the last IRB review of the following:

        i. unanticipated problems involving risks to participants or others.

        ii. participant withdrawals and the reasons for withdrawals.

        iii. complaints about the research.

        iv. any relevant recent literature.

        v. any interim findings.

        vi. any relevant multi-center trial reports.

        vii. the researcher's current risk-potential benefit assessment based on study results.

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 convened IRB review 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 research involving an FDA-regulated article is involved, a licensed physician must be involved in the review, unless the expedited submission is an administrative change and does not alter the risk/benefit ratio. See section 3.4.1 for examples of expedited

review that do not alter the risk/benefit ratio. The physician may be a voting IRB member or a consultant.

Research for which limited IRB review is a condition of exemption under §46.104(d)(2)(iii) and (d)(3)(i)(C) is permitted through an expedited review process.

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 and 45CFR 46.108(a)(3) and (4); OHRP Guidance on Use of Expedited Review Procedures; OHRP Guidance on Continuing Review; FDA Information Sheets: Continuing Review after Study Approval

3.4.5 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/or 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 3.5.6) 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

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

The IRB obtains a copy of the following documents, if applicable: the protocol, the amendment, written informed consent form(s) and consent form updates that the investigator proposes for use in the trial, subject recruitment procedures (e.g. advertisements), written information to be provided to subjects, Investigators Brochure (IB), available safety information, information about payments and compensation available to subjects, the investigator's current curriculum vitae and/or other documentation evidencing qualifications, and any other documents that the IRB may need to fulfill its responsibilities. The IRB considers the qualifications of the investigator for the proposed trial, as documented by a current curriculum vitae and/or by any other relevant documentation the IRB requests.

The Investigator will be informed either by IRBManager, e-mail or phone of missing materials and the deadline to resubmit corrections before further review can take place.

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, requirements for representation of vulnerable populations involved in the research, and study procedures described in the protocol and the experience and expertise of the members attending the meeting. The qualifications, experience, and expertise, as well as representative capacity of each member are documented in the IRB roster. 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, may be outside of the knowledge base or representative capacity of all of the IRB members, an outside consultant will be sought (see sections 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 give the IRB staff the completed and appropriate reviewer forms. All reviewer forms will be filed with the appropriate meeting.

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 DHHS approved sample consent (if one exists), the Investigator's Brochure (when one exists); the sample informed consent document (when one exists); the complete consent document , recruitment materials (if available), any supporting documents and any other protocol related documents (including, if applicable, a summary of findings from nonclinical studies that potentially have clinical significance and from clinical trials that are relevant to the trial.)
- Continuing review submissions - the primary reviewer will receive the following:
    - the continuing review report,
    - the last approved consent,
    - the complete protocol, protocol summary or application containing the relevant information necessary to determine whether the proposed

research continues to fulfill the criteria for approval. 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 copy of all items being modified, and 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 or protocol, the complete consent document, recruitment materials (if available) and any supporting documentation. All members have access to all documents via IRBManager.
- Continuing review submissions – all members will receive the continuing review submission form (which includes a status report), 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, and the most recently approved consent document. All members have access to all documents via IRBManager.
- Modifications – all members will receive the modification submission form; a copy of items being modified or a summary of the modifications containing the relevant information necessary to determine whether the modification meets the criteria for approval. All members have access to all documents via IRBManager.

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

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

Human subjects research and clinical investigations that cannot be reviewed using the expedited review procedure are reviewed at a convened meeting of the IRB at which a quorum has been confirmed. 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, and one unaffiliated. 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 alternate 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. The review can be provided via email, fax, mail or the reviewer may be present for the discussion and for the review of any studies (including initial review, continuing review, modification, investigator's brochure or report of unanticipated problems involving risks to subjects and others) that involve the FDA-regulated article; and
- For research that involves, individuals 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 arrival and departure for all IRB members and notify the IRB Chair if a quorum is not present. The IRB staff documents attendance of IRB members, guests and ex-officio (non-voting members) guests.

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 who have an alternate member should 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 conflict of interest 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. If the IRB member is a member of the research team, the member may provide additional information if requested by the board but exits the room before final discussion and vote. Known conflicts of interest of an IRB member are 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 Chair will conditionally approve the minutes and approve the final version with the requested changes. 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. If a primary reviewer is unable to attend the meeting and an alternate with the appropriate expertise is not available, 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 conflict of interest (see IRB Member Conflict of Interest section in Policy 2), ex-officio members, and alternate members present at the same meeting which the regular member for which they alternate is also present (see section 3.5.6 – Quorum). 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.

The primary reviewer presents a brief synopsis of the research protocol, with the expectation that the other members have reviewed the protocol materials. The primary reviewer is responsible for covering the scientific background and rationale, study design, how the research differs from and compares to standard care, appropriateness of the study population and the inclusion/exclusion criteria, the risks and potential benefits to subjects, alternative treatments or procedures, as well as the criteria for IRB approval and, when applicable, additional protections for pregnant women, human fetuses, and neonates; children; and individuals with impaired decision-making capacity.

Secondary reviewers are asked to present any additional clarifications or commentary on the study plan, and any questions or concerns, or modifications he/she would require for approval.

Both the primary and secondary reviewers are expected to provide an in-depth review of the consent form and identify missing required elements and when, applicable, additional elements for informed consent. Additionally, reviewers may comment on the reading level and style of the consent form and provide detailed suggestions for improvement. Consent form comments may be handwritten on the form or provided in written commentary as part of the review.

When applicable, both the primary and secondary reviewers are responsible for reviewing the investigational drug brochure or investigational device information, or NIH or other federal grant application or proposal for funding.

Reviewers are encouraged, although not required, to contact the principal investigator prior to the meeting if they have questions about the study, particularly if they have significant concerns about the study or believe additional information is needed for the IRB to be able to assess the risks and anticipated benefits, if any, to subjects and the importance of the knowledge that may be expected to result from the research.

Reviewers are encouraged to provide written comments to ensure that the IRB staff convey the modifications required and/or questions and concerns raised by the IRB completely, accurately and precisely. After the primary and secondary reviewers have presented the study and their review comments, the Chair opens the protocol up for discussion by the membership. The Chair and members may direct specific questions to the assigned reviewers or to other members with specific expertise or viewpoints. Only members who participate in the IRB review and discussion are allowed to vote.

At the end of the discussion, one of the reviewers or another member makes a motion to approve, require modifications in the research (to secure approval), defer action on (pending receipt of additional information), or disapprove the protocol. The IRB may request more information be given to subjects when, in the judgement of the IRB, the additional information would add meaningfully to the protection of the rights, safety and/or well-being of the subjects. A vote on the motion is taken (for, against, or abstain) by show of hands or voice vote and recorded in the Minutes. All motions are decided by majority vote of the members present for the review. A quorum of the members of the IRB (more than one-half the members) must be present in order for the IRB to take a vote.

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 and 45CFR 46.108(a)(3) and (4); 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. All recording of proceedings is destroyed upon approval of the minutes. 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 signifying for, against, and abstained by show of hands. The vote is recorded by the staff and reflected on the IRB meeting 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 individuals with impaired decision-making capacity, the IRB will request review by an 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 Populations).

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 the 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.

Potential new IRB members may be invited to attend IRB meetings as a guest 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 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.

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 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 consider 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, individuals with impaired decision-making capacity, 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 or 21 CFR 50.20.
- Informed consent will be appropriately documented, in accordance with, and to the extent required by 45 CFR 46.117 or 21 CFR 50.27.
- 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 the subjects are likely to be vulnerable to coercion or undue influence, such as children, pregnant women, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects.
- Research studies have the resources necessary to protect participants:
    - Adequate time for the researchers to conduct and complete the research.
    - Adequate number of qualified staff.
    - Adequate facilities.
    - Access to a population that will allow recruitment of the necessary number of participants.
    - Availability of medical or psychosocial resources that participants may need as a consequence of the research.

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 and the purpose of research

    - References to literature and data that are relevant to the trial, and that provide background for the 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.
- Is the available non-clinical and clinical information on an investigational product adequate to support the proposed clinical trial?
- All research involving DXA and medical procedures 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), ICH GCP guidance E6

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, individuals with impaired decision-making capacity, 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 – Payment to Research Subjects); and
- participant recruitment and enrollment procedures.

At the time of the continuing review, the IRB will determine if 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 - Payment 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 determine the following:

- 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.

In addition, the IRB will ensure that the consent will be appropriately documented according to legal requirements in accordance with, and to the extent required by 45 CFR 46.117 and 21 CFR 50.27 (see Policy 5 - Obtaining Informed Consent from Research Subjects for further information on Informed Consent elements).
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 research must have a data safety monitoring plan. Any reports generated from the data safety monitoring plan will be submitted to the IRB and forwarded to the Medical Staff for review.

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 provisions 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 be 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,
    - methods and timing for assessing, including the 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
    - recording of safety parameters

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. 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), CFR 46.108(a)(3)(iii)

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: 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.

Certificates of Confidentiality are issued by the National Institutes of Health (NIH) and other HHS agencies to protect identifiable research information from forced or compelled disclosure. The requirements for obtaining a certificate of confidentiality are as follows:

- Research is automatically covered by a certificate of confidentiality whenever the study is funded in whole or in part by the NIH and involves identifiable, sensitive information.
- The term “identifiable sensitive information” means information is considered "sensitive" if the loss of confidentiality, integrity, or availability could be expected to have a serious, severe or catastrophic adverse effect on organizational operations, organizational assets, or individuals. Personally identifiable data is sensitive if disclosure of such data would pose increased social/reputational, legal, employability, or insurability risk to subjects. For the purposes of the Policy, consistent with subsection 301(d) of the Public Health Service Act (42 U.S.C 241), the term “identifiable, sensitive information” means information about an individual that is gathered or used during biomedical, behavioral, clinical, or other research, where the following may occur:
    - An individual is identified; or
    - For which there is at least a very small risk, that some combination of the information, a request for the information, and other available data sources could be used to deduce the identity of an individual.

- Examples of research automatically covered by a certificate of confidentiality include:
    - Biomedical, behavioral, clinical, or other research, including exempt research, except where the information obtained is recorded in such a manner that human participants cannot be identified or the identity of the human participants cannot readily be ascertained, directly or through identifiers linked to the participants.
    - The collection or use of biospecimens that are identifiable to an individual or for which there is at least a very small risk that some combination of the biospecimen, a request for the biospecimen, and other available data sources could be used to deduce the identity of an individual.
    - The generation of individual level, human genomic data from biospecimens, or the use of such data, regardless of whether the data is recorded in such a manner that human participants can be identified, or the identity of the human participants can readily be ascertained.
    - Any other research that involves information about an individual for which there is at least a very small risk, as determined by current scientific practices or statistical methods, that some combination of the information, a request for the information, and other available data sources could be used to deduce the identity of an individual.
- Researchers may also apply for a certificate of confidentiality for non-federally funded research.
- When research is covered by a certificate of confidentiality, researchers:
    - May not disclose or provide, in any federal, state, or local civil, criminal, administrative, legislative, or other proceeding, the name of such individual or any such information, document, or biospecimen that contains identifiable, sensitive information about the individual and that was created or compiled for purposes of the research, unless such disclosure or use is made with the consent of the individual to whom the information, document, or biospecimen pertains; or
    - May not disclose or provide to any other person not connected with the research the name of such an individual or any information, document, or biospecimen that contains identifiable, sensitive information about such an individual and that was created or compiled for purposes of the research.
    - May disclose information only when:

- Required by federal, state, or local laws (e.g., as required by the Federal Food, Drug, and Cosmetic Act, or state laws requiring the reporting of communicable diseases to state and local health departments), excluding instances of disclosure in any federal, state, or local civil, criminal, administrative, legislative, or other proceeding.
- Necessary for the medical treatment of the individual to whom the information, document, or biospecimen pertains and made with the consent of such individual.
- Made with the consent of the individual to whom the information, document, or biospecimen pertains; or
- Made for the purposes of other scientific research that is in compliance with applicable federal regulations governing the protection of human subjects in research.

- When research is covered by a certificate of confidentiality, researchers must inform participants (for example, in the consent document) of the protections and limitations of certificates of confidentiality:
  - For studies that were previously issued a Certificate, and participants were notified of the protections provided by that Certificate, NIH does not expect participants to be notified that the protections afforded by the Certificate have changed, although IRBs may determine whether it is appropriate to inform participants.
  - If part of the study cohort was recruited prior to issuance of the Certificate, but are no longer actively participating in the study, NIH does not expect participants consented prior to the change in authority, or prior to the issuance of a Certificate, to be notified that the protections afforded by the Certificate have changed, or that participants who were previously consented to be re-contacted to be informed of the Certificate, although IRBs may determine whether it is appropriate to inform participants.
- Researchers conducting NIH-supported research covered by a certificate of confidentiality must ensure that if identifiable, sensitive information is provided to other researchers or organizations, regardless of whether or not the research is federally funded, the other researcher or organization must comply with applicable requirements when research is covered by a certificate of confidentiality.

- Researchers conducting research covered by a certificate of confidentiality, even if the research is not federally funded, must ensure that if identifiable, sensitive information is provided to other researchers or organizations, the other researcher or organization must comply with applicable requirements when research is covered by a certificate of confidentiality.

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, when appropriate, additional safeguards 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 Policy 6 - 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 section 3.8.3 - Review More Often than Annually). The meeting minutes will reflect the IRB's determination regarding review frequency.

3.8.2.1 Exempt and Expedited

For studies approved after January 21, 2019 under the exempt and expedited review categories, a status report is required.

For expedited studies, a status report is required every five years.

For exempt studies, a status report must be received every five years. Modifications are submitted in cases when the change alters the risk, the scope of the project, or falls under a limited review category.

3.8.2.1 Full Board

For full Board studies approved after January 21, 2019, continuing review is required annually, except in the following circumstance:

- The research that is not FDA regulated, interventions have concluded, and the study is only:
- Analyzing data, including identifiable private information or identifiable biospecimens, and
- Accessing follow-up clinical data from clinical care procedures.

A status report is required every 5 years for these studies.

Regulations & Guidance: DHHS 45 CFR 46.109(e); FDA 21 CFR 56.109(f); CFR 115

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.

The IRB must determine which clinical investigations need verification from sources other than the clinical investigator that no material changes in the research have occurred since the previous IRB review. The IRB should consider:

- The vulnerability of the participants.
- The projected rate of enrollment.
- Whether the study involves novel therapies.

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 Policy 10 - 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. The subject or the subject's legally acceptable representative should be informed in a timely manner if new information becomes available that may be relevant to the subject's willingness to continue participation in the trial. The communication of this information should be documented.

Regulations & Guidance: OHRP Guidance on Written IRB Procedures and 45CFR 46.108(a)(3) and (4); 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, including internet-based recruitment.
- 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 on the subject to participate which includes, but is not limited to:

- Does not make claims, either explicitly or implicitly, about the drug, biologic, or device under investigation that are inconsistent with FDA labeling.
- 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. Subjects are not paid to assume risk but can be compensated for time and effort.

The following regarding payments are described in the protocol and/or initial application:

- Amount
- Method
- Timing of disbursement
- Schedule of all payments
- 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 presents 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 clin cards

or checks as long as the value of the clin card or check is not coercive. Gift cards and coupons are not acceptable forms of payment.

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. The IRB will review payments to determine that credit for payment accrues as the study progresses.

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.

3.8.11 Multi-Site Trials Where the Researcher is the Lead Researcher

When the Researcher is the lead Researcher of a multi-site study, the protocol must:

1. Include a plan for how information relevant to the protection of participants will be managed across sites, such as:
    - Unanticipated problems involving risks to participants or others.
    - Interim results
    - Protocol modifications
2. Describe the data and safety monitoring plan that will oversee conduct of the study at all sites. For example,
    a. The frequency of site monitoring visits, who will conduct them and what will occur at each visit.
    b. Schedule of required telephone contacts/conference calls with collaborating site investigators, if applicable. Where and how the data will be stored and for how long. Indicate how the subjects' confidentiality is protected during the transmission of data to other sites.
    c. If records or files are to be transmitted via the internet or shipped to another site, describe how the subjects' confidentiality will be protected.

3.8.12 Transnational Research

Research conducted outside the United States or its territories will generally be subject to approval of a local IRB or Ethics Committee (EC) and/or governmental officials, such as the Ministry of Health. When the research is federally funded, IRB/EC approval must be obtained from an institution/entity in that country that has a current approved FWA and a registered IRB/EC. The IRB will require documentation of the site's IRB approval and FWA/IRB registration status. A database of registered international IRBs searchable by country can be found on the OHRP website at http://ohrp.cit.nih.gov/search/. In addition, OHRP has compiled a listing of the laws, regulations and guidelines that govern human subjects research in many countries around the world (see The International Compilation of Human Subject Research Protections).

3.8.13 Good Clinical Practices

The institution will comply with ICH GCP guidance (E6) only to the extent that it is compatible with NIH, FDA and DHHS regulations in respects to clinical research.

In addition to the requirements outlined in section 3.7.1.1, the IRB considers the following during the initial protocol review:

- Description of the population to be studied.
- References to literature and data that are relevant to the trial, and that provide background for the trial.
- A specific statement of the primary endpoints and the secondary endpoints, if any, to be measured during the trial.
- A detailed description of the objectives and the purpose of the trial.
- A description of the type/design of trial to be conducted (e.g., double-blind, placebo-controlled, parallel design) and a schematic diagram of trial design, procedures and stages.
- A description of the measures taken to minimize/avoid bias, including randomization and blinding.
- A description of the trial treatment(s) and the dosage and dosage regimen of the investigational product(s). Also include a description of the dosage form, packaging, and labelling of the investigational product(s)
- The expected duration of subject participation, and a description of the sequence and duration of all trial periods, including follow-up, if any.
- A description of the "stopping rules" or "discontinuation criteria" for individual subjects, parts of trial and entire trial.

- Accountability procedures for the investigational product(s), including the placebo(s) and comparator(s), if any.
- Maintenance of trial treatment randomization codes and procedures for breaking codes.
- The identification of any data to be recorded directly on the CRFs (i.e., no prior written or electronic record of data), and to be considered to be source data.
- Subject inclusion criteria.
- Subject exclusion criteria.
- Subject withdrawal criteria (i.e., terminating investigational product treatment/trial treatment) and procedures specifying:
    - When and how to withdraw subjects from the trial/investigational product treatment.
    - The type and timing of the data to be collected for withdrawn subjects.
    - Whether and how subjects are to be replaced.
    - The follow-up for subjects withdrawn from investigational product treatment/trial treatment.
- The treatment(s) to be administered, including the name(s) of all the products(s), the dose(s), the dosing schedule(s), the route/mode(s) of administration, and the treatment period(s), including the follow-up period(s) for subjects for each investigational product treatment/trial treatment group/arm of the trial.
- Medication(s)/treatment(s) permitted (including rescue medication) and not permitted before and/or during the trial.
- Procedures for monitoring subject compliance.
- Specification of safety parameters.
- The methods and timing for assessing, recording, and analyzing safety parameters.
- Procedures for eliciting reports of and for recording and reporting adverse event and intercurrent illnesses.
- A description of the statistical methods to be employed, including timing of any planned interim analysis (ses).
- The number of subjects planned to be enrolled. In multicenter trials, the numbers of enrolled subjects projected for each trial site should be specified. Reason for choice of sample size, including reflections on (or calculation of) the power of the trial and clinical justification.
- The level of significance to be used.
- Criteria for the termination of the trial.
- Procedure for accounting for missing, unused, and spurious data.

- Procedures for reporting any deviation(s) from the original statistical plan (any deviation(s) from the original statistical plan should be described and justified in protocol and/or in the final report, as appropriate).
- The selection of subjects to be included in the analyses (e.g., all randomized subjects, all dosed subjects, all eligible subjects, evaluable subjects).
- Specification of the efficacy parameters.
- Methods and timing for assessing, recording, and analyzing of efficacy parameters.

Regulations & Guidance: ICH GCP guidance E6

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 to secure approval) - see Section 3.10.3.
- Disapprove - see Section 3.10.4.
- Suspension or Termination - see Section 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 approval period begins as of the IRB approval date.

Research that has been reviewed and approved by the IRB may be subject to further review depending upon the scope of the research, For example, the Institutional

Biosafety Committee and Institutional Radiation Safety Committee review projects for compliance with biosafety and radiation safety guidelines. The research may be subject to additional institutional requirements before the study can commence.

[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 protocol and/or informed consent document 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

To receive an approval following a conditional approval determination the Investigator's response, the revised document(s) (i.e., protocol, informed consent document, etc.) and the tracked document(s) 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 document(s) and the tracked document(s) 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 research 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 initial application with a protocol and informed consent document. 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.

If the IRB approves research with conditions and the research expires before the conditions are reviewed and approved, all research activities must stop until approval is obtained.

3.10.3 Withheld Approval

3.10.3.1 Definitions

Withheld Approval: Made when the research does not meet the IRB criteria for 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.

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, 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.

3.10.4 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.

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.

3.10.5 Submitting Requested Changes for New Research Protocol Application with Conditional Approval or a Withheld Determination

If the investigator fails to submit a response to IRB stipulated changes or inquiries related to new research protocols with a conditional approval or withheld approval, the study will remain inactive. The project cannot commence without IRB approval.

3.10.6 Time Limit for Submitting Requested Changes for Continuing Review or Modifications with Conditional Approval or a Withheld Determination

If the IRB approves research with conditions and the research expires before the conditions are reviewed and approved, all research activities must stop until approval is obtained.

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 Policy 8 for a discussion of unanticipated problems and Policy 10 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:

- Consider actions to protect the rights and welfare of subjects.
- Consider whether procedures for withdrawal of enrolled subjects consider their rights and welfare; and
- Consider informing current subjects of the suspension or termination.
- Have the Investigator report any adverse events or outcomes to the IRB.

Investigators must report to the IRB when a study is suspended or terminated:

- New information that might adversely affect the safety of the participants or the conduct of the clinical trial.
- Any changes significantly affecting the conduct of the clinical trial or increasing the risk to participants.

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 will be reported to the IRB.

The corrective action(s) and stipulations necessary for the IRB to consider reinstatement of the research must be decided by the convened IRB. The approval will be described in written correspondence to the Principal Investigator.

Regulations & Guidance: DHHS 45 CFR 46.113; FDA 21 CFR 56.113; ICH-GCP (E6)

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.

An administrative hold is a voluntary interruption of research enrollments and ongoing research activities by the researcher.

Suspension of research is defined as a temporary or permanent halt to some or all research procedures until the IRB determines whether the research may recommence (with or without modifications to the research) or whether the research must be terminated. Termination of research means a permanent stop to the research and all research-related activities.

An administrative hold does not apply to interruptions of research related to concerns regarding the safety, rights, or welfare of human research participants, researchers, research staff, or others. If there is an unanticipated problem involving risks to participants or others, the study is not eligible for an administrative hold.

An administrative hold must not be used to avoid reporting deficiencies or circumstances that otherwise require reporting by regulatory agencies.

Activities placed under administrative hold remain subject to continuing review and all organizational policies, such as policies on reporting problems.

An administrative hold cannot be used to extend IRB approval beyond the expiration date of a protocol without IRB approval of continuing review.

An administrative hold may be granted, such as when a researcher goes on extended vacation or takes a leave of absence.

If unavailable to conduct or direct this research personally, as when on leave or vacation, to: (1) arrange for a co-investigator to assume research related responsibilities in the researcher’s absence, and (2) to notify the IRB in writing of this change prior to the absence. If employment with the university is discontinued, to do one of the following with each approved/active study prior to leaving the university: (1)

transfer the study to a new principal investigator or (2) close the project. These changes must be sent in writing to the IRB by submitting either a formal revision or a Continuing Review/Study closure report. This notification must be submitted in advance (prior to the termination of employment).

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 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 60 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 submission form which includes:
    - A summary since the last IRB review of:
        - Number of Participants accrued.
        - 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.
        - Any interim findings.
        - Any relevant multi-center trial reports; and
        - The Investigator's current risk-potential benefit assessment based on study results.
- An assurance that all serious and unexpected adverse events had been reported as required. The current IRB-approved informed consent document.
- Newly proposed consent with redline edits (i.e., additions are to be underlined, deletions are to be lined through) to reflect any changes from the prior submission.
- The current IRB-approved protocol.

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)

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.

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 or private identifiable information has completed.

3.12.3 Expedited Review of Continuing Review

In conducting continuing review under expedited review, at least one qualified IRB member is provided and reviews the Continuing Review submission form and complete protocol. At least one reviewer receives and reviews the same materials that the IRB receives for protocols reviewed by the convened IRB:

- Current consent document, if applicable.
- A status report on the progress of the research (broader than modifications and adverse events).

The status report on the progress of the research must include:

- Number of participants accrued.
- A summary since the last IRB review of:
    - Unanticipated problems involving risks to participants or others.
    - Participant withdrawals.
    - The reasons for withdrawals.
    - Complaints about the research.
    - Any relevant recent literature.
    - Any interim findings.
    - Any relevant multi-center trial reports.
    - The researcher's current risk-potential benefit assessment based on study results.
    - A summary of modifications previously approved, if applicable.
    - Deviation log, if applicable.

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.

Additionally, continuing review of research previously approved by the convened IRB may be conducted using the expedited review procedure where the research is not conducted under an investigational new drug application (IND) or investigational device exemption (IDE) where categories two (2) through eight (8) do not apply but the IRB determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified since the last 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 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 unless the IRB determines that stopping the intervention would cause immediate harm subjects.

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 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 Policy 10 - 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.

3.13 Modification of an Approved Protocol

Investigators who wish to modify or amend their approved research 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 is 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.

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 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 and 45CFR 46.108(a)(3) and (4).

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.

One tracked copy or a summary should show all changes from the previous version (i.e., underlining all additions and striking through all deletions). The protocol must include the title and version date.

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 (no longer than within 30 days) 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 Reviewers)

At the meeting, the primary reviewer presents an overview of the modification(s) 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 considers 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.

One tracked copy or a summary should show all changes from the previous version (i.e., underlining all additions and striking through all deletions). The protocol must include the title and version date.

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., underlining 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 Investigator 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. If the study is closed prematurely, it must be reported to the IRB.

3.15 Notice to Investigators of IRB Actions

Barring extraordinary circumstances, all IRB action letters are generated through IRBManager 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 conditional approval requiring modifications, the notification will include the information that must be modified. For a disapproval, termination or suspension, the notification will include the basis for making that decision.

Before initiating a trial, the investigator should have written and dated approval from the IRB for the protocol, written informed consent form, consent form updates, subject recruitment procedures (e.g., advertisements), and any other written information to be provided to subjects.

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

When the IRB requires modifications to research, investigators' responses will be reviewed to verify that the conditions for approval have been satisfied. Depending on the nature of the modifications, this subsequent review/verification may be performed by the IRB Chair and/or designee or a consultant with specific expertise. Questions about whether the conditions for approval have been satisfied will be forwarded to the IRB Chair. When the conditions for approval are not met the submission will be reviewed again by the same method as the original review (i.e., convened, or expedited review).

The IRB reports its findings and actions to the Institution in the form of IRB 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 Decisions

When an IRB protocol presented at a convened meeting is disapproved or given a Withheld Approval, the IRB will notify the Investigator in writing about the specific deficiencies and/or 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. If the matter will be presented to the convened board, the IRB staff will notify the researcher of the convened board meeting date.

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.

Specific questions regarding the IRB policies and procedures can be submitted by email, writing and/or via the telephone to the IRB office for further information and/or clarification.

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