



Investigator Manual

Version Date: September 26, 2008

Dear Researcher:

Aspire Independent Review Board (Aspire IRB) is dedicated to the ethical protection of human subjects in research. Aspire IRB shall be a leader in the field of ethical review; promoting the rights and welfare of human subjects, facilitating timely completion of responsible research, and fostering a customer-oriented environment based on relationships, quality and efficiency. Our company shall approve and monitor research study protocols that include but are not limited to drugs, biologics, devices and behavioral research. It is also our goal to oversee early drug development with the use of human subjects.

Aspire IRB's business philosophy is to build lasting relationships with business partners who have a dedication to research integrity and the ethical protection of human subjects. We are committed to providing timely and efficient service without sacrificing quality or ethical integrity. We emphasize communication and teamwork between our staff and business associates.

This manual has been written to assist you in utilizing the services of Aspire IRB and to inform you of our standards and requirements. It is necessary that you read all of the information provided to you in this manual. It is also recommended that all members of your study staff read and understand the information in this manual.

We are here to assist you with your study from start to finish. If at any time you need additional assistance or information in this manual is not clear, please do not hesitate to contact a member of our qualified staff.

Sincerely,

Alycia Huston, BA, BS, CIP

Chief Executive Officer

Aspire IRB, LLC

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Please visit our website at www.aspire-irb.com for the following:

IRB Meeting Schedule

Fee Schedule

Submission Forms

BOARD MEMBERSHIP

A current IRB membership roster is updated as needed and maintained in the Aspire IRB office at all times. A current IRB membership roster will be sent out with all new study approval notifications and upon request.

The IRB will consist of at least one member whose primary interests are in a scientific area, one member whose primary interests are in a non-scientific area and at least one member who is non-affiliated with Aspire IRB.

Aspire IRB practices diversity and non-discrimination in terms of race, gender and cultural differences in its membership.

Aspire IRB has an experienced and seasoned Board. Qualities of an Aspire IRB member include:

- Concern for the good and welfare of people who volunteer for the purpose of research.
- Willingness to spend the time that is needed to adequately review the research.
- Understanding of the concept of representing someone who cannot represent himself/herself.
- Experience as a working professional in some field required for scientific and non-scientific members.
- Possession of good listening and verbal communication skills.
- Basic understanding of scientific principles.
- Confidence to express self in a group setting and not intimidated by others.
- Personal or professional experience working with one or more of the following groups:
 - Children, elderly, minorities, cognitively impaired, physically challenged, and non-English speaking individuals.

An ad hoc consultant may be included if necessary because of the special knowledge or experience he/she possesses or by virtue of his/her expertise. An ad hoc consultant in attendance will not be permitted to vote or be counted toward the quorum.

INVESTIGATOR RESPONSIBILITIES

As a Principal Investigator (PI) conducting research projects with Aspire IRB, you must agree to conduct responsible research in accordance with all applicable federal regulations and requirements of Aspire IRB. Following initial approval, the PI is required to submit to Aspire IRB the following for review:

- **Amendments or changes to the protocol.** Approval must be obtained from the Board prior to implementation except as necessary to eliminate an immediate hazard to the subjects. Sponsor closure of the study will be considered a change in the research activity; if subjects are taken off the study, the PI must report discontinued subjects to the IRB and the reason(s) for discontinuance.
- **Requests for changes to the informed consent document.** Approval must be granted by the Board prior to the use of any revised informed consent document.
- **Requests for enrollment changes.** This includes increases in enrollment, suspensions / re-openings, etc. The PI must submit dates of these actions.
- **Notification of the PI's decision to not conduct the study.** This includes notification of the PI's decision to withdraw from the conduct of the study.
- **Continuing review and periodic site monitoring.** For continuing review, Research Status Report Forms should be submitted 30 days prior to the study approval expiration date. For site status reports, Site Status Report Forms should be submitted by their designated due dates.
 - These reports will include at a minimum:
 - The completed form and attachments.
 - Any new information since the IRB's last review.
- **Changes to the protocol that are implemented without prior IRB approval** to eliminate an apparent immediate hazard to subjects must be reported **within 24 hours** of implementation.
- **Within 5 days** from the date of discovery:
 - Serious adverse events.
 - Unexpected and related adverse events.
 - Unanticipated adverse device effects.
- **Within 10 days** from the date of discovery:
 - Information that indicates a change to the risks or potential benefits of the research.
 - Findings or allegations of non-compliance.

- Breaches of confidentiality.
- Changes in FDA labeling or withdrawal from marketing of a drug, device, or biologic used in a research protocol.
- Incarceration of a subject in a protocol overseen by Aspire IRB.
- Events that require reporting to the Sponsor.
- Sponsor-imposed suspensions for risk.
- Complaints from subjects when the complaints indicate unexpected risks or cannot be resolved by the research team.
- Significant protocol deviations/violations.
- FDA 483s, Warning Letters and/or other correspondence resulting from an inspection by a regulatory agency, the PI's written response to the findings and corrective action (if applicable).
- Any other reports by a regulatory agency, Sponsor, CRO or IRB.
- Any other problem that the PI considers to be unanticipated and indicates subjects or others are at increased risk of harm.

CONFLICTS OF INTEREST

It is the policy of Aspire IRB that IRB members may not participate in the initial or continuing review of any research study in which a member has a conflicting interest, except to provide information as requested by the IRB. The IRB member shall abstain from deliberation and voting on any research review with which the member has a conflict of interest.

At the beginning of each IRB meeting, members will be asked if they have any conflicts of interest with any of the agenda items. If it is determined that any member has a conflict of interest with an agenda item, he/she will be asked to leave the room during the deliberation and voting on that item.

FINANCIAL DISCLOSURE

The PI and study staff must disclose any financial arrangements they or their immediate family members might have that could potentially pose a conflict of interest, not including payment for the conduct of the research. Examples include but are not limited to speaking fees or consultation fees exceeding \$25,000, and stock ownership or any equity interests exceeding \$50,000.

The FDA's Financial Interest Disclosure form can be found at:

<http://www.fda.gov/opacom/morechoices/fdaforms/cder.html>

It is the responsibility of the PI to revise the Financial Interest Disclosure form and inform the IRB of any changes to disclosable financial arrangements.

The American Medical Association Code of Ethics, Section 6.03 states that it is unethical for physicians to offer or accept payment for referrals of patients to research studies. In accordance with the AMA, Aspire IRB does not support physicians accepting payment for referrals of patients to research studies.

INVESTIGATOR NON-COMPLIANCE

Aspire IRB follows written procedures for suspension and termination of approval of research not being conducted in accordance with federal regulations or Aspire IRB's requirements or that has been associated with unexpected serious harm to subjects.

- The IRB identifies a significant problem that has been associated with a subject safety concern or indicates non-compliance with Aspire IRB policies or federal regulations, justifying possible suspension or termination of study approval.
- The Chief Operating Officer, in consult with the Quality Assurance & Compliance Administrator and IRB Chairman, determines if further attempts should be made to attain compliance before placing the problem on an IRB meeting agenda. These individuals will also determine whether immediate suspension of enrollment is merited to protect the rights and welfare of subjects.
- All serious or continuing non-compliance is reviewed by the full IRB. The full IRB decides whether a suspension or termination of study approval is warranted.
- The IRB will notify the PI of any decision to suspend or terminate study approval in writing, explaining the reasons for the action, and if appropriate, what measures need to be taken in order to lift the suspension or avoid termination.
- The PI will be sent a letter detailing the IRB's determination, length of suspension or termination of study approval, any additional requirements, sanctions or restrictions, and a request for a response in writing.
- The statement will include a deadline (not to exceed 30 days) for complying with the IRB's requests. If the corrective action is completed within the specified time and found to be adequate, the suspension or termination process ends.

- If the corrective action is not completed or the PI fails to respond within the specified time, then the study file will go to the IRB meeting for a vote of action.
- The Food and Drug Administration (FDA) and/or Office of Human Research Protection (OHRP) will be notified of any determination to suspend or terminate approval in addition to the Sponsor and other parties.
- Requests for reinstatement are reviewed by the full IRB.

INVESTIGATOR AND STAFF TRAINING AND EDUCATION

Aspire IRB requires that the PI receive ongoing training and education in the area of human subject protection/Good Clinical Practice (GCP) at least every two years. This includes training on federal regulations in human subject protection/GCP, reporting requirements and guidelines, ethical principles of conducting research involving human subjects, and other topics related to GCP.

Aspire IRB believes that ongoing training and education for the PI and key research staff is important to ensure that research studies are conducted in accordance with applicable federal regulations/GCP guidelines and that the PI and the research staff have a solid understanding of their respective responsibilities.

To assist you, Aspire IRB recommends visiting the following web sites that offer online training for clinical investigators:

1. OHRP Human Subject Assurance Training:

<http://137.187.172.153/cbts/assurance/login.asp> (No charge)

2. Clinical Research Training – National Institutes of Health:

http://www.nihtraining.com/crtpub_508/index.html (No charge)
(You do not have to be an NIH Investigator to take this course.)

3. Additional educational resources are located on these websites:

FDA Information Sheets: www.fda.gov/oc/ohrt/irbs/

CDER Guidance Documents: www.fda.gov/cder/guidance/index.htm and <http://www.gpoaccess.gov/cfr/about.html> for the Code of Federal Regulations and to obtain copies.

CENTRAL IRB SERVICES

Aspire IRB provides central IRB services and is able to handle an unlimited amount of investigators/sites. Standard turnaround time for documents is 3-5 business days following IRB approval.

Steps for reviewing PIs who are part of a multicenter submission and using Aspire IRB as their central IRB are as follows:

- Protocol is submitted by the Sponsor or Contract Research Organization (CRO) as a multicenter study.
- Protocol, Informed Consent Document, Investigator's Brochure/Package Insert (if applicable) are reviewed by the fully convened IRB unless eligible for expedited review.
- PIs that are part of a multicenter study are reviewed individually at a fully convened IRB meeting or by expedited review. Additional PIs may qualify for expedited review if certain conditions are met.

IRB REVIEW

Aspire IRB shall review and have authority to approve, require modifications in (to secure approval), or disapprove all research activities covered by federal regulations. A written agreement between the PI and Aspire IRB verifies that Aspire IRB has the authority to oversee the study. This agreement is established when:

- The PI completes and signs the Initial Study Application or Initial Device Study Application as part of consideration for study approval.
- There is a change in PI, which requires that a new investigator agreement be signed and attached to the Initial Study Application.

Aspire IRB will inform the PI in writing of his/her responsibilities for the conduct, oversight and continuing review of the research.

The PI and/or Sponsor have the right to appeal the IRB's decision. (See *IRB Appeal Process*.)

Full Board Review

Any research involving human subjects that does not qualify for an exemption or expedited review must be reviewed and approved by a full Board at a convened IRB meeting. The review will result in one of the following actions:

- Approval
- Conditional approval / approval with modifications
- Deferral (until further information is provided)
- Disapproval

Continuing Review

Aspire IRB performs continuing review of previously approved research at intervals appropriate to the degree of risk and the vulnerability of the study subject population, but not less than once per year.

Not less than once per year means that the research must be reviewed before the expiration date of the last IRB study approval, even though the research activity may not begin until a later date.

A Research Status Report Form is a written summary submitted by the Sponsor/CRO or PI regarding the status of the study. Continuing review must occur within 12 months from the time of initial approval. Aspire IRB may limit study approval, if warranted, to a shorter period as specified when the study was initially approved or at renewal time.

Aspire IRB sends a blank Research Status Report Form to the Sponsor/CRO or PI approximately sixty days prior to expiration of study approval. Continuing review is the responsibility of the PI. The Research Status Report Form must be received by the IRB office by the designated due date in order for the IRB to have sufficient time to perform its review prior to the expiration date.

Failure to meet the continuing review due date may result in a warning notice being sent to the PI and/or Sponsor/CRO stating that approval of the research will expire unless the report is received and reviewed prior to the expiration date.

Expedited Review

The IRB Chairman or an experienced and qualified member of the IRB designated by the Chairman is authorized to perform expedited review of certain kinds of research involving no more than minimal risk. The expedited procedure may be used for the review of minor changes to previously approved research during the period for which approval is authorized. "Minor changes" are defined as modifications that do not involve an increase in risk that is more than minimal and in which all added procedures fall into the list of eligible research categories (1)-(7) published in the Federal Register.

Study Closure

Aspire IRB requires that written notification be submitted when all research activities at the approved research facility or facilities have been completed. Once the IRB has received a Final/Study Completed Report or Research Status Report Form indicating study closure, a letter of confirmation is issued to the PI informing him/her that his/her records will be maintained for no less than a period of three years.

IRB Appeal Process

Any PI and/or Sponsor/CRO wishing to appeal Aspire IRB's decision shall submit a written statement describing in detail the basis for the appeal and addressing all concerns raised by the IRB in its review. This information is considered by the IRB and a determination is made within 30 days upon review. This decision of the IRB is final. The PI, Sponsor/CRO, and all applicable regulatory agencies are notified by certified mail and/or courier of the final decision. A copy of the appeal request and the IRB decision is maintained in the study record.

IRB SUBMISSIONS

IRB meetings are held each week on Tuesdays and Thursdays. All study materials must be received by the IRB office on the Monday a week prior to the meeting date to be guaranteed review. The submission must be complete in order to meet the Monday deadline. If a submission is received on Monday and determined to be incomplete and will not meet the deadline, you will be notified. For complete submissions that meet the deadline, standard turnaround time is 7-10 days for full IRB review.

Following the IRB meeting, necessary consent revisions will be made by the Aspire IRB staff. Approval documents will be mailed promptly. If the study is disapproved, either the Chairman or Chief Operating Officer will contact the PI. The PI will be informed of the reasons for disapproval and suggestions for re-submission. Otherwise, approval documentation will be generated and mailed in a timely manner.

Administrative amendments, advertisements, additional facilities, and additional sub-investigators can often be reviewed using the expedited procedure. Review of submissions that qualify for expedited review takes approximately 3-5 days.

The following items must be received to complete a full IRB review of a study:

- Initial Study Application or Initial Device Study Application
- Protocol (or Protocol Signature Page signed by the PI for multicenter investigator submissions)
- Investigator's Brochure(s) or Package Insert (if applicable)
- Informed Consent Document(s) (E-mailed or sent on a diskette)
- Form FDA 1572 (or 1572 Equivalent for non-IND studies, including the location(s) where the study will be conducted, name and address of PI, and name(s) of sub-investigator(s))
- Curriculum Vitae for PI and sub-investigator(s) (signed and dated within 2 years)
- Current Medical License for PI only (if applicable)
- Site Information Form (one per site required every two years)
- Waiver/Deference of Review Form (if applicable)
- Cooperative Review Form (if applicable)
- Community Consultant Review Form (if applicable)

In addition to the above standard requirements, Aspire IRB must perform the following activities for investigational sites located in the state of Massachusetts:

- Conduct an on-site review within (30) days of the study start date when the PI has not previously been approved by Aspire IRB for a research project.
- Conduct an annual on-site review of each research project approved by Aspire IRB.
- Verify that any PI planning to conduct a study involving an IND in Massachusetts has or has applied for his/her Massachusetts Research Registration Number.

INFORMED CONSENT FORM (ICF)

For studies that are subject to the requirements of the FDA and OHRP regulations, the informed consent documents should meet the necessary requirements of these regulatory agencies. IRBs have the final authority for ensuring the adequacy of the information in the informed consent document.

Aspire IRB follows the procedures listed below for informed consent document submissions:

- All informed consent document(s) are entered into the computer system upon receipt. A copy of the informed consent document(s) on diskette (MS Word) or e-mail must be provided.
- If there are any revisions to the informed consent document(s) requested by the IRB for approval, they will be made by the staff the day following the meeting.
- The staff will generate a customized informed consent document for each PI. Since all informed consent documents are maintained in the Aspire IRB computer system, the Aspire IRB staff will generate revisions.
- If a sample informed consent form is not available, one can be developed for an additional fee.
- If the sample informed consent form is not provided on a diskette or sent via e-mail, there will be an additional informed consent fee applied for additional formatting.

If you would like a copy of the Aspire IRB template informed consent document, please contact the IRB office.

Financial Incentives

Financial incentives are often used when health benefits to subjects are remote or non-existent. The amount and schedule of all payments should be presented to the IRB at the time of initial review. The IRB should review both the amount of payment and the proposed method of timing of disbursement to assure that neither are coercive nor present undue influence [21 CFR 50.20].

Witness Signature

FDA does not require the signature of a witness when the subject reads and is capable of understanding the ICF, as outlined in 21 CFR 50.27(b)(1). When the subject lacks the capacity to read and understand the ICF and the information provided, the signature of a witness is required per 21 CFR 50.27(b)(2). The intended purpose is to have the witness present during the entire consent interview and to attest to the accuracy of the presentation and the apparent understanding of the subject. If the intent of the regulation were only to attest to the validity of the subject's signature, witnessing would also be required when the subject reads the ICF.

Pediatric Assent

Aspire IRB will take additional steps as necessary to safeguard and protect the well-being of children participating in research.

Children are considered to be a vulnerable research population and require special ethical and regulatory consideration by the IRB. This complies with the Children's Health Act of 2000, 21 CFR 50 Subpart D, and 45 CFR 46 Subpart D.

The IRB determines what the assent process should involve and how the child's assent (or dissent) will be documented. It is the PI's responsibility to explain the assent process and obtain the permission of the parents or legal guardian.

If you would like a copy of the Aspire IRB template assent document, please contact the IRB office.

TRANSLATION SERVICES

To meet the federal requirements of 21 CFR 50.20 and 45 CFR 46.116, the ICF should be in a language understandable to the subject (or authorized representative). When the consent interview is conducted in English, the ICF should be in English. When the study subject population includes non-English speaking people or the PI or the IRB anticipates that the consent interviews will be conducted in a language other than English, the IRB should require a translated ICF to be prepared and assure that the translation is accurate.

As required by 21 CFR 50.27, a copy of the ICF must be given to each subject. In the case of non-English speaking subjects, this would be the translated ICF. While a translator may be helpful in facilitating conversation with a non-English speaking subject, routine ad hoc translation of the ICF should not be substituted for a written translation.

It is Aspire IRB's policy that the ICF must be in a language understandable to the subject. Non-English speaking study subjects must be provided an IRB-approved certified translation of the ICF in the subject's primary language.

- There will be an administrative review charge for the approval of submitted ICFs that have been translated into a foreign language by a certified translator. A cover letter verifying the translation, which includes a copy of the name and certification of the translator, is required.
- If a translation of the ICF is requested, Aspire IRB will provide that service for the cost of the translator plus a processing fee.

REPORTING REQUIREMENTS:

The PI is responsible for reporting the following problems and events to Aspire IRB:

- Changes to the protocol that are implemented without prior IRB approval to eliminate an apparent immediate hazard to subjects **within 24 hours** of implementation.
- Within **5 calendar days** from the date of discovery:
 - Serious adverse events.
 - Unexpected and related adverse events.
 - Unanticipated adverse device effects.
- Within **10 calendar days** from the date of discovery:
 - Information that indicates a change to the risks or potential benefits of the research.
 - Findings or allegations of non-compliance.
 - Breaches of confidentiality.
 - Changes in FDA labeling or withdrawal from marketing of a drug, device, or biologic used in a research protocol.
 - Incarceration of a subject in a protocol overseen by Aspire IRB.

- Events that require reporting to the Sponsor.
- Sponsor-imposed suspensions for risk.
- Complaints from subjects when the complaints indicate unexpected risks or cannot be resolved by the research team.
- Significant protocol deviations/violations.
- FDA 483s, Warning Letters and/or other audit correspondence and the PI's written response to the findings and corrective action (if applicable).
- Any other audit report by a regulatory agency and/or Sponsor or IRB.
- Any other problem that the PI considers to be unanticipated and indicates that subjects or others are at increased risk of harm.

REPORTING GUIDELINES:

Adverse Events and Unanticipated Adverse Device Effects

The PI is responsible for reporting serious adverse events, unexpected and related adverse events, and unanticipated adverse device effects to Sponsors and Aspire IRB; however, he/she may delegate the communication of such events to appropriate clinical site research personnel. Such events should be reported within 5 calendar days from the date of discovery using the Adverse Event / Unanticipated Adverse Device Effect Report Form. The PI must sign the report prior to submission to Aspire IRB. Assignment of cause and effect of a serious adverse event may not be clear. All serious adverse events should be reported to the IRB regardless of the probability of cause. Deaths should be reported immediately, but in no less than 5 calendar days from the date of discovery. In addition, the PI or designee should supply the Sponsor and IRB with any additional requested information (e.g., hospital records or autopsy reports).

Protocol Deviations/Violations

The PI is responsible for reporting protocol deviations/violations to Sponsors and significant protocol deviations/violations to Aspire IRB; however, he/she may delegate the data collection and communication of such problems and events to appropriate clinical site research personnel. Such problems and events should be reported within 10 calendar days from the date of discovery using the Significant Protocol Deviation / Violation Report Form. The PI or designee on the clinical study must sign the protocol deviation/violation report prior to submission to Aspire IRB.

A significant protocol deviation/violation is defined as any change from the approved protocol that affects the scientific design or integrity of the study and/or the rights and welfare of the study subjects. Protocol deviations/violations that only affect the administrative aspects of the study are not considered significant, and therefore, do not require reporting to the IRB.

Unanticipated Problems Involving Risks to Subjects or Others

All unanticipated problems involving risks to subjects or others must be reported to Aspire IRB. Such unanticipated problems may be reported by PIs or Sponsors depending on the nature of the event and should be reported within 10 calendar days from the date of discovery using the Unanticipated Problem Involving Risk to Subjects or Others Report Form. These may also be reported as adverse events, unanticipated adverse device effects, protocol deviation/violations, or complaints.

IND Safety Reports

For multicenter studies, the Sponsor/CRO is required to submit IND Safety Reports on behalf of the PIs. Once received, Aspire IRB will review and provide documentation acknowledging this review to the submitting party (Sponsor/CRO). In order to avoid duplication of review, PIs on multicenter studies should not submit IND Safety Reports. It is the responsibility of the Sponsor/CRO to provide confirmation of the review of IND Safety Reports to the individual PIs/sites.

MEDICAL DEVICE REVIEW

Aspire IRB has written guidelines for compliance with 21 CFR 812 when determining the level of risk for device studies. Aspire IRB has the responsibility of determining whether a device poses a significant risk or non-significant risk and whether a study utilizing the device poses a minimal or more than minimal risk.

Medical Device is defined, in part, as any health care product that does not achieve its primary intended purpose by chemical action or by being metabolized. Examples of medical devices include, among other things, wheelchairs, surgical lasers, vascular grafts, and diagnostic aids such as reagents and test kits for medical conditions. (Refer to the Appendix for FDA Classification of Medical Devices).

Significant Risk Device (SR) is an investigational device that: (1) is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject; or (2) is for use in supporting or sustaining human life and represents a potential for serious risk to the health, safety, or welfare of a subject; or (3) is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety, or welfare of a subject; or (4) otherwise presents a potential for serious risk to a subject.

Non-significant Risk Device (NSR) is an investigational device that does not meet the definition for significant risk. An IDE is not required provided that (1) the device is not a banned device and the Sponsor follows 21 CFR 812.2(b) or (2) the FDA notifies the Sponsor that an IDE is required.

Investigational Device Exemptions (IDE) is an application to the FDA, requesting approval to utilize a significant risk device in a clinical investigation in accordance with 21 CFR 812.

Pre-market Approval Application (PMA) is the FDA process to evaluate the safety and effectiveness of some Class III devices that are subject to pre-market approval requirements in accordance with 21 CFR Part 814. Examples of Class III devices that require PMA include: replacement heart valves; silicone gel filled breast implants and implanted cerebella stimulators. An approved PMA is a license granted to the applicant to market a particular medical device.

Class III devices that are substantially equivalent to devices legally marketed before May 28, 1976 may be marketed through the 510K processes.

510(k) or Pre-market Notification (PMN) is a marketing application submitted to the FDA to demonstrate that a medical device is as safe and effective or substantially equivalent to a legally marketed device that was or is currently on the U.S. market and does not require pre-market approval.

The Sponsor or PI submits to Aspire IRB all the necessary information on the Initial Device Study Application.

SPECIAL CONSIDERATIONS FOR VULNERABLE POPULATIONS

Aspire IRB will take additional steps towards safeguarding and protecting the rights and welfare of vulnerable populations participating in human research.

Children

Aspire IRB follows applicable federal regulations when reviewing pediatric studies to safeguard and protect children participating in research. The vulnerability of children as research subjects requires special ethical and regulatory consideration by the IRB.

Decisionally Impaired Individuals

Aspire IRB shall determine that adequate consideration has been given to the manner in which subjects are selected and assure that adequate provisions have been made for monitoring of the informed consent process for clinical studies involving decisionally impaired individuals.

Pregnant Women and/or Fetuses

Aspire IRB shall determine that adequate consideration has been given to the manner in which subjects are selected and assure that adequate provisions have been made for monitoring of the informed consent process for clinical studies involving pregnant women and/or fetuses.

In addition to the vulnerable categories stated above, Aspire IRB also considers the following populations to be vulnerable: terminally ill individuals, traumatized or comatose individuals, educationally and/or economically disadvantaged individuals, students of the PI and/or site, and employee volunteers. Aspire IRB shall determine that adequate consideration has been given to the manner in which subjects are selected and assure that adequate provisions have been made for monitoring of the informed consent process for clinical studies involving these populations.

Health Insurance Portability and Accountability Act (HIPAA)

Aspire IRB will review research materials to determine whether adequate measures are in place to protect subjects' privacy interests and maintain the confidentiality of their protected health information (PHI) in accordance with applicable laws and regulations. The responsibility of HIPAA compliance rests with the covered entity.

Sites that are covered entities and do not request a waiver of authorization may satisfy the HIPAA requirement to obtain authorization to use and disclose PHI by utilizing one of the following alternatives:

- Obtain a HIPAA-compliant signed authorization from the research subject using a stand alone document that the covered entity has created; or
- Incorporate the HIPAA language into the ICF and submit to Aspire IRB for review in accordance with applicable laws and regulations; or
- Attach an addendum that contains the HIPAA language to the ICF and submit to Aspire IRB for review in accordance with applicable laws and regulations.

If you would like a copy of the Aspire IRB HIPAA authorization template document, or if you would like Aspire IRB to serve as your Privacy Board, please contact the IRB office.

CHANGES TO PREVIOUSLY APPROVED RESEARCH

Aspire IRB requires PIs to report any changes in research activity. This includes, but is not limited to, protocol amendments, updated Investigator's Brochures, recruitment materials, and changes in research staff and/or facilities.

Changes must be submitted in writing by electronic submission, facsimile or by mail to the Aspire IRB office. Changes are reviewed by the IRB staff prior to full IRB review or expedited review for adherence to Aspire IRB policies and regulatory compliance. The IRB Chairman is notified if the request for review is urgent due to subject safety concerns.

The following are examples of what may be considered by Aspire IRB to be a minor change:

- Recruitment materials
- A change in grammar or wording that improves the clarity of a statement but does not change the intended meaning
- Correction of typographical error(s)
- A change in sub-investigator(s) or site contact information

A qualified voting IRB member with signature authority is authorized by the IRB Chairman to review and approve these changes using the expedited procedure.

Changes that are determined to involve more than a minor change may not be eligible for expedited review. These changes will be sent to a fully convened IRB meeting for discussion and voting.

COOPERATIVE REVIEW & WAIVER/DEFERENCE OF REVIEW

Aspire IRB will have a written agreement that describes the respective responsibilities of Aspire IRB and any institution that chooses to engage in cooperative review or waive/defer oversight of its research studies. The purpose is to avoid duplication of research review. This policy is in accordance with the FDA and Department of Health and Human Services (DHHS) regulations.

The respective review responsibilities for each institution will be described, agreed to and documented using the Cooperative Review Form (or suitable equivalent) or Waiver/Deference of Review Form (or suitable equivalent) as applicable. The delegating institution remains responsible for ensuring that the research conducted is in full accordance with the determinations and requirements of Aspire IRB.

NON-LOCAL REVIEW

Regulations require that the IRB be sufficiently qualified through the diversity of members, including consideration of race, gender, and cultural backgrounds and sensitivity to issues such as community attitudes, to promote respect for its counsel and ability to ascertain the acceptability of the research in terms of regulations, applicable laws and standards of professional conduct and practice. This responsibility exists regardless of the geographic location of the IRB relative to the geographic location of the site(s) at which the research will be conducted.

Adequate knowledge of community attitudes, information on conditions surrounding the conduct of the research and the continuing status of the research for each location is ascertained by one or more of the following:

- The PI completes the Aspire IRB Site Information Form for each study site, including site additions.
- The PI is responsible for providing updates to the Site Information Form. The IRB will maintain copies of the Site Information Form in the study file.
- As part of the continuing review process, the IRB will determine whether the site has submitted any changes to its Site Information Form and verify that it is current.

The IRB may ask for the name and contact information of a layperson in the community who is not affiliated with the organization. This person may be contacted for additional information about community attitudes and local context. This information may be requested at any time during the review process if the IRB finds it is necessary.

IRB SITE VISITS

Aspire IRB is authorized to conduct site visits or arrange for an outside agency to make a site visit. If travel is not feasible, consultation via teleconference or other technologies that allow for real time conversational interaction between the remote auditor and the IRB members is permitted at a convened IRB meeting.

Aspire IRB conducts periodic site visits to obtain additional knowledge of community attitudes, assess conditions surrounding the conduct of the research, and/or evaluate whether the research is being conducted in accordance with regulatory and IRB requirements, and/or to ensure that risks to subjects are minimized.

Please note that Aspire IRB will charge for site visits required by the state of Massachusetts in addition to "for cause" site visits/audits. There will be no charge for routine site visits.

SUBJECT RECRUITMENT GUIDELINES

All advertisements/recruitment materials must be submitted to Aspire IRB for review and approval before they are used. Advertisements/recruitment materials should be reviewed and approved by the IRB as part of the package for initial review, as FDA considers direct advertising for study subjects to be the start of the informed consent and subject selection process. However, when the PI decides at a later date to advertise for subjects, the advertisements may be considered an amendment to the ongoing study. Advertisements/recruitment materials submitted for review and approval should include the PI's name, protocol number, and name and contact information for the person submitting them. Radio and television advertisement scripts must be first submitted to Aspire IRB for approval. After the script has been approved and a final tape produced, a copy of the final tape should be submitted to Aspire IRB for review before the advertising begins. Any time revisions are made to approved advertisements/recruitment materials, they must be submitted to Aspire IRB for review and approval prior to use.

For multicenter studies, the Sponsor/CRO may submit a package of advertisements/recruitment materials for review and approval for use by the sites. Then, each site choosing to use the approved materials should insert its site-specific information such as site name, location, telephone/contact information, compensation information and any other specific information pertaining to the site, taking care not to alter the layout or the size of the approved content. These materials may be considered approved and do not need to be submitted to Aspire IRB for additional review and approval.

When proposed advertisements/recruitment materials are easily compared to the approved consent document, the IRB Chairman or other designated IRB member may review and approve them by expedited means, as provided by 21 CFR 56.110(b)(2). When the expedited reviewer has concerns or other complicating issues are involved, the materials should be reviewed at a convened meeting of the IRB. FDA expects IRBs to review advertisements/recruitment materials to assure that they are not unduly coercive and do not promise a certainty of cure beyond what is outlined in the consent document and the protocol. Generally, FDA believes that advertising content for clinical trials should be limited to the information the prospective subjects need to determine their eligibility and interest.

Advertisements/recruitment materials submitted for investigational drug, biologic or device studies should not include:

- Terms such as “new treatment,” “new medication,” or “new drug” without explaining that the test article is investigational.
- References to “free medical treatment,” when the intent is only to say that subjects will not be charged for taking part in the investigation.
- Any claims, either explicitly or implicitly, about the drug, biologic or device under study that are inconsistent with labeling.
- Emphasis on compensation or the compensation amount by means such as larger or bold type.
- Any statement or implication of a certainty of favorable outcome.
- Exculpatory language.
- Compensation for participation in a study offered by a Sponsor that includes a coupon good for a discount on the purchase price of the product once it has been approved for marketing.
- Any elements that may be considered coercive or unduly influential.
- Testimonials.

Telephone screening scripts submitted for review and approval should be accompanied by a completed Phone Screen Info Form, unless one has been completed and submitted previously and all responses therein still apply. Telephone screening scripts should meet the following guidelines:

- The prospective subject should be informed that any answers he/she provides will remain confidential.
- The prospective subject should be advised as to what happens to the information he/she provides during the call if he/she does not qualify for the study (e.g., it will be destroyed or retained in a database for determining eligibility for future studies if permission is given by the prospective subject).
- If there are plans to retain information provided by the prospective subject to determine his/her eligibility for future studies, his/her permission must be obtained before this may be done.
- In the event someone does not want his/her information to be retained, he/she should be told that the information he/she has provided will be destroyed.

HOLIDAY OBSERVATIONS

Aspire IRB will be closed on the following holidays:

New Years Day

Martin Luther King, Jr. Day

Presidents Day

Memorial Day

Independence Day

Labor Day

Thanksgiving Day

The Day after Thanksgiving

Christmas Eve

Christmas Day