Institutional Review Board Member Handbook
A guide for members of the Institutional Review Board
March 2011
Member Handbook
As the Vice President for Research and Development at Prairie View A&M University, I would like to welcome you as a member of the university’s Institutional Review Board (IRB). The goal of the university is to ensure that the highest ethical standards are maintained in the review process for human research. I am available to support you in the research process.

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Welcome to the Institutional Review Board (IRB)

On behalf of Prairie View A&M University, thank you for your willingness to serve as a member of the IRB. To provide background information on the IRB and the roles and responsibilities of its members, as well as to remind you of the serious nature of this responsibility, this handbook has been specifically designed for IRB members. Your comments are welcome.

The IRB and Protection of Human Subjects

National and international communities have adopted ethical principles to guide the use of human subjects in research. The packet you receive as a member contains copies of the most important of these: the Belmont Report, the Nuremberg Code and the Declaration of Helsinki. These ethical principles have been incorporated into regulations that provide for the protection of human subjects in research.

The IRB was created by federal regulations as the institutional body charged with implementing the regulations on a local level. IRB activities are subject to review by a variety of groups, chief among which is, the Office for Human Research Protections (OHRP) and the Food and Drug Administration (FDA) in the Department of Health and Human Services (DHHS). The university negotiates with OHRP to provide a document called a Federal-wide Assurance (FWA), which acts as a guide for its human subjects’ research protections.

Generally, OHRP audits IRB activities when a particular problem or set of problems has been identified. The FDA may also audit for cause, but they primarily conduct periodic unannounced, on-site audits. These audits can include any FDA-regulated areas, such as the pharmacy and investigator files, as well as all IRB activities. They may include review of IRB policies, handbooks and standard operating procedures, meeting minutes, agendas, protocol files and other pertinent materials.

The Vice President for Research and Development (VPRD) at Prairie View A&M University serves as the Institutional Official (IO) for issues related to the protection of human subjects. The IRB chair, the director for regulatory compliance, associate vice president for research and the institutional official/vice president for research and development are responsible for ensuring compliance with federal, Prairie View A&M University, and other applicable regulations; for interpreting those regulations and determining local policy and procedures; and for developing new policy as science and its ethical implications change.

The IRB and Protection of Privacy (HIPAA)

Recent federal regulations (Health Insurance Portability and Accountability Act of 1996: HIPAA) provide additional guidance and restrictions on privacy and the use of protected health information (PHI). These regulations require institutions to name a privacy board, whose primary responsibility is to ensure that research protocols comply with the HIPAA Privacy Rule. At Prairie View A&M University, the IRB serves as the Privacy Board in addition to its IRB duties.

The member packet includes copies of the HIPAA Regulations, as well as various local policies that were developed to address the specific requirements of the privacy regulations. The Prairie View A&M University Privacy Officer serves as the Institutional Official responsible for
ensuring that the institution is in compliance with the regulations and serves as a point of contact for any questions or concerns regarding PHI.

**IRB Preview**

The IRB is responsible for reviewing all research in which humans participate as research subjects at Prairie View A&M University. This includes the involvement of healthy volunteer subjects in behavioral and medical research, as well as patients recruited as subjects in clinical trials of new drugs and devices. It includes the use of surveys, questionnaires, interviews, tissue, body fluids and other materials both with and without identifiers, as well as the use of individual and aggregate data, patient charts, x-rays, etc. Federal regulations recognize differences between types of research and provide three categories of review. While the default is review by the full committee at a scheduled meeting, certain minimal risk projects may be eligible for expedited review or may be exempt from review requirements. IRB members other than the chair and vice-chair are not generally involved in determining if a protocol is eligible for the exemption or for expedited review. A list of criteria for determining if a protocol may qualify as exempt or for expedited review is included in the submission form.

**Composition of the IRB**

The Prairie View A&M University has a single FWA (FWA00000561) from OHRP that covers the operation of one IRB to review social, biomedical and behavioral research. The IRB is appointed with at least five and not more than twenty-one voting members, including a chair. Members, appointed by the VPRD for three-year renewable terms, will have varying backgrounds necessary to promote complete and adequate review of human research activities commonly conducted by the institution. The membership is reappointed annually by the institutional official. The IRB, in addition, may have a variable number of alternates to assure a quorum with adequate expertise for the applications under review. The current committee roster may be found on the Human Subjects Protection Program (HSPP) Office web site. The committees include community members, scientists, non-scientists, and others to provide needed diversity. The committees also include members who can represent the interests of special and vulnerable populations, such as children, prisoners or pregnant women and fetuses and neonates. On occasion, additional individuals with expertise in a particular field may be invited to a meeting to provide consultation on specific protocols; such individuals are not included in the quorum nor do they have voting rights.

**Your Responsibility as a Member or Alternate**

The Vice President for Research and Development, or designee, appoints members and alternates (collectively referred to as member) for a renewable term of three years. Initially, but not always, most members are appointed as alternates. During your tenure on the committee, you may be asked to serve as primary reviewer on protocols, amendments, adverse events and continuing reviews. In addition, you will be asked to serve on subcommittees of the IRB as it confronts emerging issues. Although the committee has a chair and vice chair to provide leadership, from time to time, you may also be asked to serve as ad hoc chair. Finally, as a member of the IRB, you may be asked to assist in providing educational seminars to the local and research community or to serve as a resource to those within and outside your department or community as they develop protocols or have questions regarding IRB-related issues.

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1 When the Prairie View A&M University has a potential institutional conflict of interest that cannot be managed by the Oversight Committee for Management of Institutional Financial Interests in Research (OCMIFIR), an IRB outside the university may be utilized to provide appropriate oversight. Individual conflicts of interest may be managed by the Committee for Review of Individual Financial Interests in Research (CRIFIR) and may also recommend the use of an IRB outside the university.
Non-Voting Members

The Vice President for Research and Development may, at his/her discretion, recruit non-voting (ex officio) members from among the academic or administrative staff of the Prairie View A&M University, whose presence at the meetings of the IRB would aid the IRB in conducting its duties. These members may take part in all meetings of the IRB, participate in the discussions, and make recommendations to influence decisions, but they may not vote on the decisions. Non-voting members are not included in determining or establishing a quorum at the meetings. IRB meeting minutes reflect the presence of non-voting members and Human Subjects Protection Program Office (HSPPO) staff.

Consultants/Ad hoc Reviewers

At its discretion, the IRB may invite scientists or non-scientists from within or outside the Prairie View A&M University, who have special expertise, to function as consultants and ad hoc reviewers of a project application. These individuals have access to all documents submitted to the IRB relevant to the specific project under review, may participate at the deliberations and make recommendations on the project, but may not vote.

Confidentiality

As a member of the IRB, you have access to research ideas, confidential information of companies, pre-marketing data and many other kinds of confidential and sensitive personal and business materials. At the beginning of your term, you will be asked to sign a confidentiality agreement. Access to this information is for IRB purposes only, and members are reminded that any use of such information for any other purpose would be a violation of the ethical principles by which the university is bound. In addition, Texas state law provides that, in some instances, some parts of the deliberations of the IRB may be considered privileged and confidential while other parts may be available to the public through the Texas Open Records and Open Meetings Acts (TRS 61.870 to TRS 61.884).

Anonymity

IRB members may conduct their reviews of protocols in an anonymous fashion. However, it is the prerogative of reviewers to contact principal investigators (PIs) or research staff directly, breaking anonymity, to seek additional information or clarification. Except as required by law, IRB staff will not divulge the identity of the reviewers to investigators.

Member Conflict of Interest

All members of the IRB have multiple institutional commitments and are active in various roles that have many potentially overlapping relationships. This is also true of members of the IRB who participate in research projects and who are members of departments and sections whose faculty and or staff or scientist colleagues may be submitting protocols for IRB review. As an ethics, privacy and regulatory committee, it is essential that the IRB avoid even the appearance of conflict of interest. Accordingly, as a general principle, the IRB chair and members must adhere to the following standards:
• The chair and/or members may not serve as reviewers on new or continuing review of protocols, on which they have a role, as PI, key personnel or subject.

• The chair and/or members are required to recuse themselves from IRB discussion for those protocols on which they serve as PI or key personnel. The IRB reserves the right to invite them into the discussion to provide additional information or clarification.

• The chair and/or members may not vote on protocols on which they serve as PI, key personnel or subject. Members may vote on protocols from their sections if they do not have a substantive interest in the protocol.

• The chair and/or members may not serve as scientific or scholarly reviewer of a protocol for their department, primary reviewer of the protocol for IRB discussion and approval and vote to approve or disapprove the submitted protocol.

**Member Liability**

IRB members function as employees and/or agents of the Prairie View A&M University. As such, when acting in accordance with the Prairie View A&M University IRB’s Standard Operating Procedures, their actions are covered by the Prairie View A&M University general liability coverage. Community members when acting in accordance with the Prairie View A&M University’s IRB Standard Operating Procedures are covered either by 1) the Prairie View A&M University’s general liability coverage or 2) by insurance from the other affiliated institutions.

**Training**

There are various mechanisms by which new members receive training and become oriented to the committee’s functions, policies, and procedures. New members are invited to an orientation with IRB staff and chair and given a packet of information that includes: copies of regulations, including 45 CFR 46; 21 CFR 50, 56, 312, and 812, ethical principles such as the Belmont Report, Declaration of Helsinki and Nuremberg Code, committee rosters, FDA Information Sheets, OHRP Findings and Determinations, and copies of current forms. These are also available on the Human Subjects Protection Program Office (HSPPO) web site.

New IRB members are required to complete the same training required of investigators at the Prairie View A&M University within one year of appointment. The committee believes that the best way to prepare for being a fully functioning member of the committee is to participate in committee discussions. New members begin service at meetings immediately upon appointment. New members generally are not included as primary reviewers until after observing and participating in several meetings. Members receive periodic updates on key or troublesome issues.

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3 Key personnel are individuals who are directly involved in the design, conduct, management, and reporting of the research.
4 Department chairs are requested not to utilize IRB members from their departments as scientific or scholarly reviewers of protocols submitted to the IRB for review and approval.
5 Beginning August 1, 2009
as well as information on new and emerging areas of concern at committee meetings. Members are routinely invited to all training activities of the IRB for the Prairie View A&M University community.

Members are encouraged to take advantage of the opportunity to attend regional meetings sponsored, in part, by OHRP or national meetings such as the Public Responsibility in Medicine and Research (PRIM&R) and Society of Research administrators (SRA). The HSPPO has many reference materials, including dvds/videos that can be used by new members.

Educational IRB meetings are held the second Monday of every other month. All IRB members are expected to attend. These meetings are organized to allow time for training, policy development and discussion of current issues identified in regular IRB meetings.

Meetings
Currently, the IRB meetings are held the second Monday of the month beginning at 10.00 a.m. CST. Meetings are held in Coleman Library, executive conference room 518. The chair reserves the right to call ad hoc meetings for particular issues. Meeting dates are posted on the HSPPO website.

Meeting Attendance and Quorum
No legally valid IRB action may be taken without a properly constituted quorum. A quorum consists of more than half the number of regular members, including at least one non-scientist. If a quorum is lost during a meeting, then the committee cannot conduct official business until the quorum is restored. If the quorum is not restored, the meeting is concluded and remaining business continues at the next scheduled meeting. Meeting attendance is one of the most critical services of committee members and alternates. It is crucial that members and alternates notify the HSPPO staff of their availability for meetings. This is important to allow appropriate assignment of protocols to available reviewers and that a quorum of members will be present. Generally, this is accomplished by e-mail or phone call (936.261.1588) to the HSPPO office.

Removal of Member
When a committee member consistently fails to attend IRB meetings or fails to meet expectations, the IRB chair and Director, HSPP, meet with the committee member to determine the cause. If the IRB member indicates an inability to continue to function effectively as an IRB member, the IRB chair or Director, Research Regulatory Compliance, will work with the Dean, Director and/or department chair in obtaining a replacement member to serve on the IRB. Members who do not adequately fulfill their responsibilities, as judged by the IRB chair, may be asked to step down from IRB membership by the Vice President for Research and Development.

Meeting Agendas
At each meeting, the committee reviews a combination of new submissions and amendments to existing protocols and conducts continuing review for active protocols, as required by the regulations. In addition, the committee is advised of research protocols 1) approved at time of initial or continuing review and 2) minimal risk changes in research protocols, that have received expedited approval since the previous meeting. The chair will inform the committee of any unusual adverse event reports and any problems with investigators or protocols, and will lead discussion on emerging issues, education, and policy changes, etc.

Meeting Packets
Approximately seven (7) days prior to each meeting, IRB members are sent a packet, which contains the following information: draft agenda of protocols and amendments to be reviewed
and a draft list of those protocols for which annual (or more frequent) review will be conducted. In addition, packets include a notation regarding meeting location, policy materials for discussion, and supplemental materials, as necessary. Continuing review materials may be reviewed in the IRB office prior to the meeting.

**Protocol Assignment**
All protocols submitted for full review are reviewed for completeness by the HSPPO staff and/or the IRB chair or designee. Often, the staff or chair will try to resolve administrative issues prior to the distribution of protocols to reviewers. The IRB chair or designee reviews all protocols and the list of members available to attend a given meeting. Based on this review, the chair or designee will make assignments of protocols and amendments in accordance with member areas of expertise, interest, and/or conflicts of interest. Packets for the primary reviewer will be sent 9-10 days prior to the committee meeting at which they will be reviewed. The packet contains a copy of the protocol submission on which the member will serve as primary reviewer. Each protocol file includes an initial review checklist and a reviewer consent form checklist.

**Reviewing Protocols in Advance of the Meeting**
The designated reviewer will conduct an in-depth, comprehensive review of each assigned protocol or amendment prior to the meeting. This review will look at the many detailed aspects of the protocol and consent form but also ensure that the core principles of research with human subjects are upheld. These key issues include:

- **Respect for persons:** each individual is treated as autonomous, and any persons with diminished autonomy are entitled to special protections;
- **Justice:** selection of subjects should be scrutinized to ensure that some groups are not being systematically selected or excluded; and
- **Beneficence:** do no harm, minimize risk, and maximize benefit.

A review will determine:

- the risk level (minimal to significant).
- if risks have been reduced to the maximum extent possible.
- that risk have been disclosed and benefits outweigh the risks of the project.
- if subject selection is equitable.
- if the consent process and document is sufficient to allow for “informed consent”.

The issue of equipoise, the balance between risk and benefit, will be considered at the meeting. Risks may be physical in nature but may also extend to financial and emotional risk, insurability, reputation, confidentiality, etc. Reviewers are requested to contact investigators, when appropriate, to resolve all outstanding questions before presenting the study to the committee for discussion.
Review
There is no single correct approach to reviewing a protocol, but it is important that every review cover the following issues: study design, risks and benefits, equitable selection of subjects, identification of subjects and confidentiality, the informed consent process, qualifications, additional review, conflict of interest, financial conflict of interest in research, surveys, questionnaires, interview materials, or other testing instruments, deception, and recruitment tools.

• Review of Grant/Protocol Application
The grant/protocol application should provide a comprehensive and robust summary of the research. The application questions are designed to highlight areas of special IRB concern. The completeness and adequacy of the application form is critical, as is the level of consistency among it, the grant/protocol, consent form (if applicable), and any other materials submitted. When responses signal a special concern, the reviewer should note this in their comments and suggest additional safeguards.

• Review of Grant/Protocols
The grant/protocol should be sufficiently detailed to permit the IRB to evaluate the soundness of the procedures proposed and the potential risks and benefits to research subjects. For industry-sponsored research, the latest version of the company protocol and/or investigator brochure must be available to the IRB for review.

❖ As a general guide the following basic elements of a protocol are appropriate:

- background and prior pertinent experimental findings or animal data, if any. This is especially important in protocols for studies of investigational drugs or devices.

- purpose or hypothesis of the study, including potential knowledge to be gained. This should include bibliographic references to support the hypothesis and the justification for the use of human subjects and in particular the inclusion of any special or vulnerable populations.

- description of protocol methodology.

- probable duration of protocol.

- exact location where research is to be conducted (building, room #, etc.).

- modifications for biomedical protocols or confidentiality precautions.

- description of experimental controls and use of placebos for biomedical protocols.

- type and number of experimental subjects, including method of subject selection, randomization, and inclusion and exclusion criteria, if any.

- if applicable, a description of the statistical analysis to which the data will be subjected, allowing the IRB to ensure that the study will produce statistically valid conclusions to justify the research on human subjects.

- potential risks and benefits to subjects.
payment to subjects: normal volunteers, research subjects acting as a control group in an experiment, or other research subjects may be offered a reasonable, but not coercive, payment to participate in the research as compensation for inconvenience, travel, etc. All projects that promise to provide payments to subjects must include details regarding the amount. The reasonableness of the amount offered will depend on the degree of participation by the subjects, the character of the research, the population likely to be attracted by the protocol, the method in which the protocol will be advertised, the duration of the protocol, and other related considerations. In addition, such protocols and consents must describe the plan for prorated payment to subjects if subjects withdraw voluntarily from the protocol or if, upon the suggestion of a physician or investigator, early withdrawal is necessary.

procedures to obtain and record informed consent and consent document.

procedures that will be used to maintain confidentiality of research and subject materials.

a description of recruiting methods, including copies of advertisements and other recruiting materials.

as appropriate, in biomedical research, a description of how, or if, the subject's primary physician will be contacted regarding involving their patient population in a study and what additional role or information might be provided to the subject’s primary physician. If applicable, this should include a description of how subjects would be contacted through the primary physician.

description of anticipated coordination, if any, between appropriate inter-departmental faculty, and, where necessary, inclusion of those faculty as participants.

if applicable, the protocol should clarify if subjects will be required to have a pregnancy test before or during the study.

if applicable, a rationale for excluding women, minorities, and children from participation. It is a policy of National Institutes of Health (NIH) that all research involving human subjects includes women, minorities and children. All protocols that explicitly exclude these populations must provide sufficient rationale for the exclusion of such. Sufficient rationale might include inappropriate study population with respect to the health of the subjects or the purpose of the research. The expectation that additional costs or increased legal liability may be incurred by including women, minorities and children cannot be a reason for excluding these populations.

if applicable, the protocol should state who will infuse the subjects with drugs, how will it be done, where will it be done, and what is the individual’s background and training.

copies of surveys, questionnaires, interviews or other written testing instruments.

assurance that subjects be given the opportunity to withdraw at any time without feeling that it will adversely affect them.
Disclosure of Significant Financial Interest

Faculty and their staff may have financial relationships with outside organizations, which might create the potential for financial conflicts of interest. While the IRB can be helpful in identifying potential conflicts, it is the faculty or staff member’s responsibility to comply with the university’s Disclosure of Significant Financial Interest policy.

When a potential conflict is identified, the Committee for Review of Individual Financial Interests in Research (CRIFIR) works with the individual, the appropriate Department Chair and Dean as well as the VPRD offices to ensure that the conflict is disclosed and, if necessary, managed. Once the management strategy has been developed and approved, the AVPR office works with the Dean’s office to ensure that the faculty member fully implements the plan, including applying special safeguards (alteration of the consent form, protocol modifications, etc) when human subjects are involved in the research. The IRB will not provide approval until the conflict of interest issues have been resolved.

Informed Consent Procedure

Informed consent of the subject is one of the fundamental principles of ethical research with human subjects. While the IRB reserves the right to observe the consent process, the signing of consent form, and the research procedures, such audits are rare and the IRB relies on a thorough review of the proposed consent process and form, as well as on the integrity of the investigator and their staff. It is understood that informed consent will always involve, or be based on, one or more conversations between the investigator and the subject and/or the subject’s legally authorized representative (LAR) or research surrogate (RS). This is true if the requirement for written consent is waived, if a short form or oral consent process is used or if full written consent is sought. In the case of short form and written consent, the written document which the subject signs serves as documentation that a dialogue has taken place and also as a record that the subject

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6 Informed consent by a subject is one of the key cornerstones of the system protecting human subjects in research. It has traditionally been recognized that consent by someone other than the subject is not the same as the subject’s own consent. There are instances, however, in which a subject may be unable to consent. Federal regulations allow for consent by the individual or his/her LAR. Kentucky statutes do not currently define who can act as a research subject’s “legally authorized representative” or “research surrogate” to make research-related decisions on the subject’s behalf. Consent by a LAR or RS should involve all the same considerations that informed consent from a competent subject involves. It also involves identifying a proper representative and ensuring to the extent known that the research decision reflects the wishes of the subject.
has agreed to participate in the research. In addition to providing the subject with a signed copy of
the consent form, the investigator must retain a copy of the consent form and, as necessary,
document the consent process. Prairie View A&M University IRB policy dictates that
investigators must sign these consent forms within two weeks of obtaining the subject’s signature.
Members are encouraged to reference Chapter 4: Informed Consent Requirements in the
Investigator Guide for a better understanding of the informed consent process.

Regulations prohibit any investigator from involving a human being as a subject in research
unless the investigator has obtained the legally effective informed consent of the subject or the
subject's LAR or RS. Accordingly, the IRB carefully reviews the consent process and consent
documents. In considering a consent process, a reviewer should bear in mind the requirement that
consent should be sought only under circumstances that provide the prospective subject or the
representative sufficient opportunity to consider whether or not to participate, and that minimize
the possibility of coercion or undue influence. The information that is given or orally
communicated to the subject or the representative shall be in language understandable to the
subject or the representative (6th and 8th grade level). Informed consent, whether oral or written,
may not include any exculpatory language, through which the subject or the representative is
made to waive or appear to waive any of the subject's legal rights. It may also not release or
appear to release the investigator, the sponsor, the institution or its agents from liability for
negligence.

All consent processes should include the basic elements of consent:

- a statement that the study involves research, an explanation of the purposes of the
  research, the expected duration of the subject's participation, a description of the
  procedures to be followed, and identification of any procedures, that are experimental.

- a description of any reasonably foreseeable risks or discomforts to the subject.

- a description of any benefits to the subject or to others, which may reasonably be
  expected from the research.

- a disclosure of appropriate alternative procedures or courses of treatment, if any,
  (including no treatment), that might be advantageous to the subject. A statement under
  alternatives similar to: "Other treatments for your disease include different drugs and
  drug combinations with similar side effects. You may choose to continue whatever
  treatment you are receiving. Another alternative treatment plan is comfort care only,
  where treatments are directed only at reducing symptoms, relieving suffering, and
  maximizing comfort, dignity, and control. (In comfort care only, treatment is not directed
  at curing, slowing, or reversing your disease)".

- a statement that confidentiality will be maintained and the mechanisms being used to
  preserve it. It should also state, however, the rights of study sponsors, others and
  regulatory agencies, such as OHRP or the FDA, to review study data, including records
  identifying subjects.

- for research involving more than minimal risk, an explanation as to if any compensation,
  and an explanation as to if any medical treatments are available, if injury occurs and, if
  so, what they consist of, or where further information may be obtained.
• an explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and of whom to contact in the event of a research-related injury to the subject.

• a statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits, to which the subject is otherwise entitled.

The following additional statements may be required by the IRB:

• a statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject may become pregnant), which are currently unforeseeable.

• anticipated or unanticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent.

• any additional costs to the subject that may result from participation in the research.

• the consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject.

• a statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject.

• the approximate number of subjects involved in the study.

• a provision for subjects to be given a signed copy of the consent form, if the consent is written.

• identification of the sponsor in sponsor-initiated studies.

• if blood is to be withdrawn, the consent form should include blood withdrawal information, such as; amount of blood to be withdrawn (in teaspoons or tablespoons), number of times, period of time covered, potential hazards, such as "a bruise at the site of vein puncture, inflammation of the vein and possible infection," and a statement that "care will be taken to avoid these complications."

• if subjects are recruited from multiple sites, then list the names of hospitals or other local sites where the study will be conducted.

• if subjects are being followed for survival, the consent form must indicate the investigator’s intent to do so.

• toxicities, and that these are more likely to occur as the doses get higher; and that the study will be discontinued when specified toxicities occur.
• reviewer should consider, given the target recruitment populations, the necessity of consent forms in languages other than English.

An IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth above, or waive the requirements to obtain informed consent provided the IRB documents why the requirement(s) may be waived.

While a written consent including all elements of consent prescribed in 45 CFR 46.116(a) and (b) is held to be standard consent, short form consent, surrogate consent, and oral consent provide alternative methods of consent. The requirement for informed consent will depend on the nature of the research protocol. Reviewers should note that multifaceted studies might require more than one method of consent.

Federal regulations and state law do allow for a waiver of consent in certain, limited situations. To assist reviewers in considering if a proposed method of consent or a waiver of consent is appropriate, the categories are described below.

**Informed Consent with Minors**
For research involving the participation of minors (ages 7-18), a subject assent document is required. The investigator will prepare and submit for approval a document that describes the research detail in general terms understandable to the minor subjects participating in the proposed project. The IRB may determine that the informed consent document requires a single parental signature or dual parental signatures for a particular project based on the level of risk involved.

**Waiver of Informed Consent in Non-Emergency Research**
The IRB can approve a request for waiver of the informed consent procedure and documentation requirements (please note: the use of other consents such as those for surgical procedures, etc. may still be required) only when the IRB finds and documents that a project fulfills all four of the following criteria:

• the research presents no more than minimal risk of harm to subjects.

• the waiver or alteration will not adversely affect the rights and welfare of the subjects.

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

• whenever appropriate, the subjects will be provided with additional pertinent information after participation.

A reviewer should ensure that a protocol satisfies each of these criteria. In instances where consent is waived, it is still essential that appropriate procedures for maintenance of confidentiality be described in the protocol. It is the prerogative of the IRB to request that the researcher provide the subject with a written statement regarding the research. Reviewers should consider if this is necessary.

**Waiver of Consent in Emergency Situations**
Federal regulations provide a narrow exception to the standard requirement for obtaining informed consent from each subject or his/her LAR/RS for a limited class of research activities involving human subjects in need of emergency medical intervention, but unable to consent because of their life-threatening medical condition. The first step in determining if this regulation would be applicable is to determine that:
• the subject is not competent to provide consent.

• the medical condition is truly life threatening.

• there exists a therapeutic window of such short duration that obtaining proxy consent would be impossible.

Waiver of Documentation of Informed Consent
Under certain conditions the IRB may allow oral consent with a waiver of the requirement for documentation. This calls for an oral consent process and the IRB may require an approved written script and it should contain the basic elements of informed consent. The subject will either verbally agree or not agree to participate in the study. Investigators are not required to secure written documentation of these informed consent activities. To qualify for oral consent, a reviewer should ensure that one of the following criteria applies:

• the only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from breach of confidentiality. Each subject will be asked if the subject wants documentation linking the subject with the research and subject's wishes will govern; and/or

• the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.

In cases in which the documentation requirement is waived, the IRB may require the investigator to provide subjects with a written statement regarding the research.

Short Form Consent
Another consent possibility for minimal risk research is the short form consent in which the consent process takes place, but the traditional requirements of a written consent form are waived. To conduct short form consent, a researcher must prepare a document stating that the elements of informed consent have been presented orally to the subject or the subject's LAR/RS. When this method is used, there must be a witness to the oral presentation. Also, the IRB must approve a written summary of what is to be said to the subject or the representative. The subject (or LAR/RS) must sign the short form. The person obtaining consent must sign the summary. The witness should be an individual not involved in the research. Finally, copies of both the short form and the summary should be given to the subject or the representative. The researcher must maintain originals. Reviewers should ensure that the protocol is minimal risk and that it provides for the basic elements of informed consent outlined above.

Documentation of Informed Consent
In most circumstance, a signed consent form is required as part of the consent process. The signed consent form serves as written documentation that the required dialogue has taken place. Often in cooperative group or sponsor-initiated studies, the organization will provide a sample consent document. While this may form the basis of the IRB-approved consent document, the consent form must be modified to conform to IRB practice and expectations. In addition, the IRB has developed a sample consent form to aid investigators. All investigators are encouraged to use this consent template because it offers the best prognosis for a speedy approval by the IRB.
The informed consent document should address those elements applicable to the research as discussed in Informed Consent Procedure.

The document should be printed in no less that a twelve (12) font and all pages are to be numbered. Each document and their subsequent revisions are to display the date of approval by the IRB and the expiration date of the document.

IRB staff will review consent documents to ensure that they comply with the IRB requirements regarding format and boilerplate. Overall, reviewers should ensure that a written consent document is expressed in lay language at a 6th and 8th grade level.

Consent by a Legally Authorized Representative (LAR) or Research Surrogate (RS)
Generally the subject gives written consent, but there are two exceptions. The first involves minors: consent of one or both parents or guardians is generally required depending on the risk/benefit of the research to the minor. The assent of the minor is also necessary in most cases. The second involves the use of LAR or RS consent in cases that may preclude an incompetent subject from participating in the consent process.

Documentation of Primary Review
The IRB Initial Review Checklist and Consent Form Checklist are provided to aid the reviewers in the organization and documentation of their concerns in preparation for their discussion and in the IRB minutes. As the sheets may or may not be updated to reflect the conversations of the meetings, the sheets are merely to provide guidance in initiating the review process.

Review at the IRB Meeting
Reviewers should bring their original protocol files to the scheduled meeting. At the beginning of the meeting, the reviewers receive a copy of the finalized agenda for new protocol submissions, new amendments, and continuing reviews.

During the meeting, the chair calls upon primary reviewer(s) to lead discussion of their assigned protocol, and all members and alternates are encouraged to participate in open discussion of the proposed study. Members, who declare a conflict, may be asked to leave the room at the discretion of the IRB.

As a result of the discussion, the IRB can:

- approve a protocol for a period of one year or less.
- approve the protocol pending non-substantive changes (approval with changes) requesting that either the chair or designee review the investigator’s response.
- impose substantive conditions, which must be met and re-presented at a convened meeting prior to approval (tabled).
- disapprove, disallowing any further discussion of the protocol.

At the conclusion of the committee’s deliberations on each protocol, the chair conducts a vote of the members and voting alternates. Alternates vote only in the absence of a member. Committee actions require a simple majority of a convened quorum. Members voting against must give an explanation for the record.
The committee vote is recorded, as well as an indication of how frequently continuing review should be conducted. Although other institutional committees share the responsibility for following guidelines in the collective effort to protect human subjects, ultimately the final authority for participation of human subjects in research falls on the IRB. Researchers are not required to wait for the approval of the other U of L institutional review committees before submitting a proposal to the IRB. However, IRB final approval will be held until documentation of approvals from other institutional review committees has been forwarded to the IRB.

Other items reviewed during the IRB meeting include, but are not limited to:

- educational reading as assigned by the chair or designee.
- review and approve minutes of previous meetings.
- review and accept expedited approvals completed by the chair since the last scheduled IRB meeting.
- review and accept the report of the Subcommittee on Adverse Events.
- review and approve requests for continuation of previously approved research protocols;
- review and approve amendments to previously approved research protocols.
- review submitted protocol deviations and protocol violations.
- review prepared audit reports and determine any required actions and to whom these actions are reported.
- any other business deemed appropriate by the IRB.

**Establishing Continuing Review Parameters for Approved Protocols**

In approving a protocol, the IRB determines how frequently the protocol should be submitted for continuing review or oversight. Federal Regulations state that approvals may be granted for no longer than a one-year period, but the IRB may recommend more frequent review based upon time intervals or enrollment numbers for high-risk protocols. When determining the interval for continuing review, members should consider:

- studies that are pilot studies and for which little preliminary data exists.
- the experience of the investigator.
- studies that pose a special risk to the subject.
- studies where there may be little preliminary human data.
- emergency waiver of consent protocols.
- studies in which the subjects are gravely ill and the risk/benefit ratio is unclear (e.g. sepsis trials).
• studies in which the preliminary data indicate a special element of risk for the subject.

**Continuing Review Procedures**

IRBs must review proposed research at a convened meeting at which a majority of the members of the IRB are present, including at least one member whose primary concerns are in nonscientific areas and an IRB must conduct continuing review of research at intervals appropriate to the degree of risk, but not less frequently than once per year. The IRB should decide the frequency of continuing review for each study protocol necessary to ensure the continued protection of the rights and welfare of research subjects. When continuing review occurs annually and the IRB performs continuing review within 30 days before the IRB approval period expires, the IRB may retain the anniversary date as the date by which the continuing review must occur.

Sixty and thirty days before study expiration, an expiration reminder letter is sent to the investigator. Once completed continuing review materials are received, a determination is made whether the continuing review is eligible for expedited review (item 3) or if it should be scheduled for full-board review. The continuing review will be scheduled for review at the first regular meeting within 30 days of the study expiration date. The continuing review will not be reviewed more than 30 days prior to expiration.

At each meeting, members may conduct continuing reviews of ongoing, approved protocols. This is designed to ensure that the rights and welfare of subjects continue to be protected. Reviews include protocols, which were determined to require more than annual review, as well as those with annual review requirements. Reviewers receive the annual progress report, including a revised informed consent document and HIPAA Research Authorization. The report includes information on number of subjects’ enrolled, adverse reactions, any protocol violations, proposed changes, confirmation on informed consent process, subjects not completing the study, description of preliminary results, and a brief description of the research project. These materials allow reviewers to determine that the project continues to conform to the study as approved and to any special conditions placed on it by the IRB.

Reviewers are asked to review the annual progress report and supporting documents to ensure compliance with current regulations and standards. Reviewers should:

- consider if new or additional risks have been identified (e.g. number of serious adverse reactions) which would require changes to the protocol, consent form, review frequency, etc.

- verify that applicable requirements of the HIPAA Privacy Rule have been met.

- determine that changes in research were reported to and approved by the IRB.

- identify protocols that should be suspended or terminated because research is not being conducted in accordance with IRB requirements.

- identify studies that might require verification that no material changes have been made since the previous IRB review.

- determine if new IRB policies might necessitate changes in the protocol.
In conducting a review, members should ensure that the same standards as applied in the original review are still valid (e.g. minimize risk, risks reasonable in relation to anticipate benefits, equitable selection, adequate informed consent process and documents, monitoring data to ensure subject safety, privacy protections, and appropriate safeguards for vulnerable populations).

The continuing review provides an important opportunity to ensure that changes in federal or state policy or IRB practices and expectations are reflected in the protocol and especially the new consent form.

If an investigator has failed to provide continuing review information to the IRB or the IRB has not reviewed and approved a research study by the continuing review date specified by the IRB, the research must stop, unless the IRB finds that it is in the best interests of individual subjects to continue participating in the research interventions or interactions. Enrollment of new subjects cannot occur after the expiration of IRB approval.

When continuing review of a research protocol does not occur prior to the end of the approval period specified by the IRB, IRB approval expires automatically. Such expiration of IRB approval does not need to be reported to OHRP as a suspension of IRB approval under HHS regulations.

Investigators are notified in writing of the decision of the IRB and any changes required. Continued approval is not granted until all required changes have been made and submitted for review and approval. Once approved, the investigator is sent a continuing approval letter indicating the date of the next study expiration. The continuing approval letter reminds investigators that changes in research activity may not be initiated without IRB review and approval except when necessary to eliminate apparent immediate hazards to subjects.

**Review of Protocol Amendments**

Changes (amendments) in protocols must be approved by the IRB prior to the initiation of such changes, except when necessary to eliminate apparent immediate hazards to subjects. Reviewers should assess the requirements of the amendment and determine if the amendment changes the risk/benefit ratio for the subjects negatively or substantially changes the way the research is conducted. The essence of the study should be summarized by the reviewer for

IRB members and the reviewer should state how the amendment will affect the conduct of the study, the risk/benefit ratio, and whether or not the amendment should be approved as written. If the amendment requires a change in the informed consent document, then the reviewer must review that change and recommend appropriate committee action. Some minimal risk changes (See finding 21) in previously approved research may be approved by expedited review.

**Minimal Risk Changes approved by Expedited Review**

Minimal risk changes (e.g., study location change, contact information change, addition or deletion of study personnel, change in number of subjects to be recruited, substitution of specific words and/or phrases etc.) may be approved by the IRB chair or his/her designee without return for full IRB review.

**Auditing Activities**

Professional staff in the Human Subjects Protection Program Office, acting on behalf of the IRB, may conduct a monitoring visit. The reason(s) for on-site review may include, for example, (1) random selections, (2) complex projects involving unusual levels or types of risks to subjects, (3) projects conducted by an investigator who previously failed to comply with IRB determinations,
or (4) projects where continuing review or reports from other sources have indicated that changes without IRB approval may have occurred or subjects were consented inappropriately, (5) HIPAA non-compliance or (6) subject or whistleblower complaints.

**Additional Information**

This Member’s Handbook provides basic, but critical information for members. Key aspects of the regulations governing the use of human subjects and relevant IRB policies and procedures with which all members should become familiar have been highlighted in the text. Familiarity with the Handbook is no substitution for knowledge of the IRB SOPs, federal regulations and ethical principles. You are urged to review the materials provided in the member’s packets and to seek additional information or clarification from the HSPPO staff. In addition, if there are topics you would like to see added, please contact the HSPPO staff at 936.261.1553/1588 or refer to your roster for current chair and staff information.
**DEFINITIONS**

**Adjuvant Therapy** – Therapy provided to enhance the effect of a primary therapy; auxiliary therapy.

**Adverse Event** – An undesirable, unintended and not necessarily unexpected result of therapy or other intervention (e.g., a headache following a spinal tap or intestinal bleeding associated with aspirin therapy).

**Assent** - Agreement by an individual not competent to give legally valid informed consent (e.g., a child or cognitively impaired person) to participate in research.

**Assurance** – A formal written, binding commitment that is submitted to a federal agency in which an institution promises to comply with applicable regulations governing research with human subjects and stipulates the procedures through which compliance will be achieved.

**Authorized Institutional Official** - An officer of an institution with the authority to speak for and legally commit the institution to adherence to the requirements of the federal regulations regarding the involvement of human subjects in biomedical and behavioral research.

**Autonomy** – Personal capacity to consider alternatives, make choices, and act without undue influence or interference of others.

**Belmont Report** - A statement of basic ethical principles governing research involving human subjects issued by the National Commission for the Protection of Human Subjects in 1978.

**Beneficence** - An ethical principle discussed in the Belmont Report that entails an obligation to protect persons from harm. The principle of beneficence can be expressed in two general rules: (1) do not harm; and (2) protect from harm by maximizing possible benefits and minimizing possible risks of harm.

**Benefit** - A valued or desired outcome; an advantage.

**Biologic** - Any therapeutic serum, toxin, anti-toxin, or analogous microbial product applicable to the prevention, treatment, or cure of diseases or injuries.

**Chair** – Chair, Co-Chair, or Vice-Chair, as designated on IRB roster submitted to OHRP, unless otherwise indicated.

**Children** - Persons who have not attained the legal age for consent to treatment or procedures involved in the research, as determined under the applicable law of the jurisdiction in which the research will be conducted [45 CFR 46.401(a)]. In Texas, generally a person under the age of eighteen.

**Clinical Trial** - A controlled study involving human subjects, designed to evaluate prospectively the safety and effectiveness of new drugs or devices or of behavioral interventions.

**Cognitively Impaired** - Having either a psychiatric disorder (e.g., psychosis, neurosis, personality or behavior disorders, or dementia) or a developmental disorder (e.g., mental retardation) that affects cognitive or emotional functions to the extent that capacity for judgment and reasoning is significantly diminished. Others, including persons under the influence of or
dependent on drugs or alcohol, those suffering from degenerative diseases affecting the brain, terminally ill patients, and persons with severely disabling physical handicaps, may also be compromised in their ability to make decisions in their best interests.

**Cohort** - A group of subjects initially identified as having one or more characteristics in common who are followed over time. In social science research, this term may refer to any group of persons who are born at about the same time and share common historical or cultural experiences.

**Compensation** - Payment or medical care provided to subjects injured in research; does not refer to payment (remuneration) for participation in research.

**Competence** - Technically, a legal term, used to denote capacity to act on one's own behalf; the ability to understand information presented, to appreciate the consequences of acting (or not acting) on that information, and to make a choice. (See also: Incompetence, Incapacity.)

**Confidentiality** - Pertains to the treatment of information that an individual has disclosed in a relationship of trust and with the expectation that it will not be divulged to others without permission in ways that are inconsistent with the understanding of the original disclosure.

**Conflict of Interest** – an IRB member may not vote on a project, and is not counted towards a quorum, when s/he or an immediate family member has a conflict of interest with a project being reviewed, defined as:

- Serving as a co-investigator or other member of the research team; or
- Receiving payments in excess of $10,000 including salary, consulting fees, royalty or licensing payments from intellectual property, honoraria and/or gifts from the study sponsor over the past 12 months or anticipated for the next 12 months (excluding salary and other payments for services from the Prairie View A&M University); or
- Having equity interest worth more than $10,000 or more than 5% of the business entity as determined by reference to publicly listed prices (excluding mutual funds); or
- Having any equity interest if the value cannot be determined by reference to publicly listed prices (e.g., start-up companies); or
- Holding a position as director, officer, partner, trustee, employee, or any other position of management; or
- Holding patent rights or royalties from such rights whose value may be affected by the outcome of the research, including royalties under any royalty-sharing agreements involving the Prairie View A&M University.

**Consent Summary** – A summary of the information contained in the complete informed consent document; used with short form consent.

**Contract** - An agreement; as used here, an agreement that a specific research activity will be performed at the request, and under the direction, of the agency providing the funds. Research performed under contract is more closely controlled by the agency than research performed under a grant.
**Contraindicated** - Disadvantageous, perhaps dangerous; a treatment that should not be used in certain individuals or conditions due to risks (e.g., a drug may be contraindicated for pregnant women and persons with high blood pressure).

**Cross-over Design** - A type of clinical trial in which each subject experiences, at different times, both the experimental and control therapy. For example, half of the subjects might be randomly assigned first to the control group and then to the experimental intervention, while the other half would have the sequence reversed.

**Data and Safety Monitoring Board** – committee of scientists, physicians, statisticians, and others that collects and analyzes data during the course of a clinical trial to monitor for adverse effects and other trends (such as an indication that one treatment is significantly better than another, particularly when one arm of the trial involves a placebo control) that would warrant modification or termination of the trial or notification of subjects about new information that might affect their willingness to continue in the trial.

**Debriefing** – Giving subjects previously undisclosed information about the research project following completion of their participation in research. (Note that this usage, which occurs within the behavioral sciences, departs from standard English, in which debriefing is obtaining rather than imparting information.)


**De-identified Health Information** - De-identified health information neither identifies nor provides a reasonable basis to identify an individual. There are two ways to de-identify information; either: 1) a formal determination by a qualified statistician; or 2) the removal of specified identifiers of the individual and of the individual’s relatives, household members, and employers is required, and is adequate only if the covered entity has no actual knowledge that the remaining information could be used to identify the individual.

**Descriptive Study** - Any study that is not truly experimental (e.g., quasi-experimental studies, correlational studies, record reviews, case histories, and observational studies).

**Diagnostic (Procedure)** - Tests used to identify a disorder or disease in a living person.

**Double-masked Design** - A study design in which neither the investigators nor the subjects know the treatment group assignments of individual subjects. Sometimes referred to as "double-blind."

**Drug** - Any chemical compound that may be used on or administered to humans as an aid in the diagnosis, treatment, cure, mitigation, or prevention of disease or other abnormal conditions.

**Emancipated Minor** - A legal status conferred upon persons who have not yet attained the age of legal competency as defined by state law (for such purposes as consenting to medical care), but who are entitled to treatment as if they had by virtue of assuming adult responsibilities such as being self-supporting and not living at home, marriage, or procreation. (See also: Mature Minor.)

**Embryo** - Early stages of a developing organism, broadly used to refer to stages immediately following fertilization of an egg through implantation and very early pregnancy (i.e., from conception to the eighth week of pregnancy).
**Emergency use** - the use of an FDA-regulated test article on a human subject in a life-threatening situation in which no standard acceptable treatment is available, and in which there is not sufficient time to obtain IRB approval.

**Equitable** - Fair or just; used in the context of selection of subjects to indicate that the benefits and burdens of research are fairly distributed.

**Ethnographic Research** - Ethnography is the study of people and their culture. Ethnographic research, also called fieldwork, involves observation of and interaction with the persons or group being studied in the group's own environment, often for long periods of time.

**Existing Data** – Data that existed prior to the initiation of a research project.

**Expedited Review** - Review of proposed research by the IRB chair or a designated voting member or group of voting members rather than by the entire IRB. Federal rules permit expedited review for certain kinds of research involving no more than minimal risk and for minor changes in approved research.

**Experimental** - Term often used to denote a therapy (drug, device, procedure) that is unproven or not yet scientifically validated with respect to safety and efficacy. A procedure may be considered "experimental" without necessarily being part of a formal study (research) to evaluate its usefulness.

**Federal-Wide Assurance (FWA)** —An agreement between a federally funded institution and OHRP that stipulates method(s) by which the organization will protect research participants. (66 Fed. Reg. 19139, 19141 (April 13, 2001)).

**FDA** – Food and Drug Administration, an agency of the federal government established by Congress in 1912 and presently part of the Department of Health and Human Services.

**Fetal Material** - The placenta, amniotic fluid, fetal membranes, and umbilical cord.

**Fetus** - The product of conception from the time of implantation until delivery. If the delivered or expelled fetus is viable, it is designated an infant [45 CFR 46.203(c)]. The term "fetus" generally refers to later phases of development; the term "embryo" is usually used for earlier phases of development.

**Fieldwork** - Behavioral, social, or anthropological research involving the study of persons or groups in their own environment and without manipulation for research purposes (distinguished from laboratory or controlled settings).

**Full-Board Review** - Review of proposed research at a convened meeting at which a majority of the membership of the IRB are present, including at least one member whose primary concerns are in nonscientific areas. For the research to be approved, it must receive the approval of a majority of those members present at the meeting.

**Gatekeeper** – An individual or organization that controls access to research records, documents or specimens.

**Gene Therapy** - Human gene transfer is the process of transferring genetic material (DNA or RNA) into a person. At present, human gene transfer is experimental and is being studied to see
whether it could treat certain health problems by compensating for defective genes, producing a potentially therapeutic substance, or triggering the immune system to fight disease. Human gene transfer may help improve genetic disorders, particularly those conditions that result from inborn errors in a single gene (for example, sickle cell anemia, hemophilia, and cystic fibrosis). It may also hold promise for diseases with more complex origins, like cancer and heart disease. Gene transfer is also being studied as a possible treatment for certain infectious diseases, such as AIDS. This type of experimentation is sometimes called “gene therapy” research.

**Genetic Screening** - Tests to identify persons who have an inherited predisposition to a certain phenotype or who are at risk of producing offspring with inherited diseases or disorders.

**Genotype** – The genetic constitution of an individual.

**Good Clinical Practice (GCP)** — Good Clinical Practice (GCP) is an international ethical and scientific quality standard for designing, conducting, recording and reporting trials that involve the participation of human subjects. Compliance with this standard provides public assurance that the rights, safety and well being of trial participants are protected, consistent with the principles that have their origin in the Declaration of Helsinki, and that the clinical trial data are credible (International Code of Harmonization for Good Clinical Practice (ICH GCP)).

**Guardian** - An individual who is authorized under applicable state or local law to give permission on behalf of a child to general medical care.

**HIPAA (Health Insurance Portability and Accountability Act of 1996)** - HIPAA governs the use and disclosure of protected health information (PHI) that is created or received by a covered entity that relates to:

- the physical or mental health of an individual (living or deceased)
- the provision of health care
- the payment for health care
- identifies the individual or reasonably may be used to identify the individual

Gives individuals the following rights

- right to request restrictions on use or disclosure of their PHI
- right to access medical records (including research records)
- right to amend medical records
- right to an accounting of disclosure of their PHI
- right to request alternate confidential communications
- right to lodge complaint with covered entity and / or the Department for Health and Human Services

Administrative Requirements
Version 3/11/11 ii Member Handbook
• Covered Entity must designate a Privacy Official
• Covered Entity must develop policies and procedures that are HIPAA compliant
• Covered Entity must provide privacy training to the workforce
• Covered Entity must implement administrative, technical and physical safeguards to protect the privacy of PHI • Covered Entity must develop sanctions for violations of the HIPAA Privacy Rule
• Covered Entity must meet the documentation requirements
• Covered Entity must develop sanctions for violations of the HIPAA Privacy Rule
• Covered Entity must meet the documentation requirements

**Human Research Protection Program (HRPP)** — A system that includes all structural units, policies, and activities critical to protecting individuals studied in research and that is managed in accordance with these standards and with applicable federal, state and local laws. Some components of the HRPP may be external to the organization seeking accreditation, but the essential components of an HRPP should be identifiable in all cases.

**Human subject** – a living individual about whom an investigator (whether professional or student) conducting research obtains a) data through intervention or interaction with the individual, or b) identifiable private information. Individuals whose physiologic or behavioral characteristics and responses are the object of study in a research project.

**Humanitarian Device Exemption (HDE)** - A Humanitarian Device Exemption (HDE) is an application that is similar to a pre-market approval (PMA) application, but exempt from the effectiveness requirements of a PMA. An approved HDE authorizes marketing of a Humanitarian Use Device (HUD).

**Humanitarian Use Device (HUD)** - A device that is intended to benefit patients in the treatment and diagnosis of diseases or conditions that affect or is manifested in fewer than 4,000 individuals in the United States per year.

**Informed Consent** - A person's voluntary agreement, based upon adequate knowledge and understanding of relevant information, to participate in research or to undergo a diagnostic, therapeutic, or preventive procedure. In giving informed consent, subjects may not waive or appear to waive any of their legal rights, or release or appear to release the investigator, the sponsor, the institution or agents thereof from liability for negligence.

**Institutional Review Board (IRB)** - any board, committee, or other group formally designated by an institution to review, to approve the initiation of, and to conduct periodic review of, biomedical or behavioral/social science research involving human subjects. The primary purpose of such review is to assure the protection of the rights and welfare of the human subjects.

**Interaction** - includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.
**Intervention** - includes communication or inter-personal contact between investigator and subject.

**Investigational Device Exemption (IDE)** - Exemptions from certain regulations found in the Medical Device Amendments that allow shipment of unapproved devices for use in clinical investigations

**Investigational New Drug or Device** - A drug or device permitted by FDA to be tested in humans but not yet determined to be safe and effective for a particular use in the general population and not yet licensed for marketing.

**Investigator** - In clinical trials, an individual who actually conducts an investigation

**IRB Committee Member (Member)** - An individual appointed by the Vice President for Research and Development or designee to serve on the IRB.

**IRB approval** - the determination of the IRB that the research study has been reviewed and may be conducted at an institution within the constraints set forth by the IRB and by other institutional and Federal requirements.

**Justice** - An ethical principle discussed in the Belmont Report requiring fairness in distribution of burdens and benefits; often expressed in terms of treating persons of similar circumstances or characteristics similarly.

**Key Personnel** – Participants in a research team who contribute in a substantive way to the scientific development or execution of a project, including the principal investigator

**Legally Authorized Representative** - A person who, by relation or legal appointment, acts in the best interest of an individual who is deemed incapable, by law, of giving informed consent.

**Longitudinal Study** - A study designed to follow subjects forward through time.

**Major modifications** – Modifications to a research project and/or consent documents that present additional risk to subjects such as dosage escalation, additional procedures or tests, significant increases in time commitment by subject, etc. Substantive protocol revisions also are considered major modifications.

**Medical Device** - A diagnostic or therapeutic article that does not achieve any of its principal intended purpose through chemical action within or on the body. Such devices include diagnostic test kits, crutches, electrodes, pacemakers, arterial grafts, intraocular lenses, and orthopedic pins or other orthopedic equipment.

**Mentally Disabled** – See Cognitively impaired.

**Minimal risk** – the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

**Minor modifications** – modifications to a research project and/or consent documents that pose no additional risk to subjects such as changes in title, co-investigator(s), funding sources; addition
or modification of procedures that fall into one of the categories eligible for expedited review; or modifications that maintain similar or increased safeguards to protect the subject.

**Monitoring** - The act of overseeing the progress of a research study to ensure that the rights and well-being of participants are protected, that the data are accurate, complete and verifiable, and that the conduct of the research is in compliance with the protocol, with applicable regulatory requirements and with standards of the field.

**New Drug Application (NDA)** - Request for FDA approval to market a new drug. [21 CFR 312.3]. Any interventions (e.g., drugs) involved in the study are administered to subjects under the immediate direction of the investigator.

**Non-affiliated Member** - A member of an Institutional Review Board that has no ties to the parent institution, its staff or faculty. This individual is usually from the local community (e.g., minister, business person, attorney, teacher, home maker).

**Non-significant Risk (NSR)** - An NSR device investigation is one that does not meet the definition for a significant risk study. NSR device studies, however, should not be confused with the concept of "minimal risk," a term utilized in the IRB regulations to identify certain studies that may be approved through an "expedited review" procedure.

**Normal Volunteers** - Volunteer subjects used to study normal physiology and behavior or who do not have the condition under study in a particular protocol, used as comparisons with subjects who do have the condition. "Normal" may not mean normal in all respects. For example, patients with broken legs (if not on medication that will affect the results) may serve as normal volunteers in studies of metabolism, cognitive development, and the like. Similarly, patients with heart disease but without diabetes may be the "normals" in a study of diabetes complicated by heart disease.

**Null Hypothesis** - The proposition, to be tested statistically, that the experimental intervention has "no effect," meaning that the treatment and control groups will not differ as a result of the intervention. Investigators usually hope that the data will demonstrate some effect from the intervention, thereby allowing the investigator to reject the null hypothesis.

**Nuremberg Code** - A code of research ethics developed during the trials of Nazi war criminals following World War II and widely adopted as a standard during the 1950s and 1960s for protecting human subjects.

**Office of Human Research Protections (OHRP)** – The office within the Department of Human and Human Services responsible for implementing DHHS regulations governing research involving human subjects.

**Open Design** - An experimental design in which both the investigator(s) and the subjects know the treatment group(s) to which subjects are assigned.

**Paternalism** - Making decisions for others against or apart from their wishes with the intent of doing them good.

**Phase 1, 2, 3, 4 Drug Trials** - Different stages of testing drugs in humans, from first application in humans (Phase 1) through limited and broad clinical tests (Phase 3), to post marketing studies (Phase 4).
• **Phase 1 Drug Trial** - Phase 1 trials include the initial introduction of an investigational new drug into humans. These studies are typically conducted with healthy volunteers; sometimes, where the drug is intended for use in patients with a particular disease, however, such patients may participate as subjects. Phase 1 trials are designed to determine the metabolic and pharmacological actions of the drug in humans, the side effects associated with increasing doses (to establish a safe dose range), and, if possible, to gain early evidence of effectiveness; they are typically closely monitored. The ultimate goal of Phase 1 trials is to obtain sufficient information about the drug's pharmacokinetics and pharmacological effects to permit the design of well-controlled, sufficiently valid Phase 2 studies. Other examples of Phase 1 studies include studies of drug metabolism, structure-activity relationships, and mechanisms of actions in humans, as well as studies in which investigational drugs are used as research tools to explore biological phenomena or disease processes. The total number of subjects involved in Phase 1 investigations is generally in the range of 20-80.

• **Phase 2 Drug Trial** - Phase 2 trials include controlled clinical studies conducted to evaluate the drug's effectiveness for a particular indication in patients with the disease or condition under study, and to determine the common short-term side effects and risks associated with the drug. These studies are typically well controlled, closely monitored, and conducted with a relatively small number of patients, usually involving no more than several hundred subjects.

• **Phase 3 Drug Trial** - Phase 3 trials involve the administration of a new drug to a larger number of patients in different clinical settings to determine its safety, efficacy, and appropriate dosage. They are performed after preliminary evidence of effectiveness has been obtained, and are intended to gather necessary additional information about effectiveness and safety for evaluating the overall benefit-risk relationship of the drug, and to provide and adequate basis for physician labeling. In Phase 3 studies, the drug is used the way it would be administered when marketed. When these studies are completed and the sponsor believes that the drug is safe and effective under specific conditions, the sponsor applies to the FDA for approval to market the drug. Phase 3 trials usually involve several hundred to several thousand patient-subjects.

• **Phase 4 Drug Trial** - Concurrent with marketing approval, FDA may seek agreement from the sponsor to conduct certain post marketing (Phase 4) studies to delineate additional information about the drug's risks, benefits, and optimal use. These studies could include, but would not be limited to, studying different doses or schedules of administration than were used in Phase 2 studies, use of the drug in other patient populations or other stages of the disease, or use of the drug over a longer period of time [21 CFR §312.85].

**Phenotype** - The physical manifestation of a gene function.

**PHS (Public Health Service)** - Part of the U.S. Department of Health and Human Services, it includes FDA, NIH, CDC, SAMHSA, and HRSA.

**Placebo** - A chemically inert substance given in the guise of medicine for its psychologically suggestive effect; used in controlled clinical trials to determine whether improvement and side effects may reflect imagination or anticipation rather than actual power of a drug.
**Principal Investigator** - A qualified person who directs a research project or program, may write the protocol, and oversees the scientific, technical and day-to-day management of the research.

**Prisoner** - An individual involuntarily confined in a penal institution, including persons: (1) sentenced under a criminal or civil statute; (2) detained pending arraignment, trial, or sentencing; and (3) detained in other facilities (e.g., for drug detoxification or treatment of alcoholism) under statutes or commitment procedures providing such alternatives to criminal prosecution or incarceration in a penal institution

**Privacy** - Control over the extent, timing, and circumstances of sharing oneself (physically, behaviorally, or intellectually) with others.

**Private Information** - includes 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 (for example, a medical record). Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects.

**Protected Health Information (PHI)** — Individually identifiable health information including demographic data that relates to:

- the individual’s past, present or future physical or mental health or condition,
- the provision of health care to the individual, or
- the past, present, or future payment for the provision of health care to the individual,
- and that identifies the individual or for which there is a reasonable basis to believe can be used to identify the individual. Individually identifiable health information includes many common identifiers (e.g., name, address, birth date, Social Security Number).

**Protocol** - The formal design or plan of an experiment or research activity; specifically, the plan submitted to an IRB for review and to an agency for research support. The protocol includes a description of the research design or methodology to be employed, the eligibility requirements for prospective subjects and controls, the treatment regimen(s), and the proposed methods of analysis that will be performed on the collected data.

**Quality Improvement (QI)** — Periodic examination of organizational activities, policies, procedures and performance to identify best practices and target areas in need of improvement; includes implementation of corrective actions or policy changes where needed.

**Quorum** — a majority of voting members of an IRB, including at least one member whose primary expertise is in a nonscientific area.

**Radioactive Drug** - Any substance defined as a drug in §201(b)(1) of the Federal Food, Drug and Cosmetic Act that exhibits spontaneous disintegration of unstable nuclei with the emission of nuclear particles or photons [21 CFR 310.3(n)]. Included are any nonradioactive reagent kit or nuclide generator that is intended to be used in the preparation of a radioactive drug and "radioactive biological products," as defined in 21 CFR 600.3(ee). Drugs such as carbon-
containing compounds or potassium-containing salts containing trace quantities of naturally occurring radionuclides are not considered radioactive drugs.

**Randomization** - Assignment of subjects to different treatments, interventions, or conditions according to chance rather than systematically (e.g., as dictated by the standard or usual response to their condition, history, or prognosis, or according to demographic characteristics). Random assignment of subjects to conditions is an essential element of experimental research because it makes more likely the probability that differences observed between subject groups are the result of the experimental intervention.

**Recombinant DNA Technology** - "The ability to chop up DNA, the stuff of which genes are made, and move the pieces, [which] permits the direct examination of the human genome," and the identification of the genetic components of a wide variety of disorders. Recombinant DNA technology is also used to develop diagnostic screens and tests, as well as drugs and biologics for treating diseases with genetic components.

**Remission** - A period in which the signs and symptoms of a disease are diminished or in abeyance. The term "remission" is used when one cannot say with confidence that the disease has been cured.

**Research** - a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. Activities that meet this definition constitute research even if they are a component of a larger non-research activity (e.g., instruction, demonstration).

**Retrospective Studies** - Research conducted by reviewing records from the past (e.g., birth and death certificates, medical records, school records, or employment records) or by obtaining information about past events elicited through interviews or surveys. Case control studies are an example of this type of research.

**Risk** – the probability of harm or injury (physical, psychological, social, or economic) occurring as a result of participation in a research study. Both the probability and magnitude may vary from minimal to significant.

**Serious adverse experience (SAE)** – Any adverse experience associated with the use of the drug/device that results in any of the following outcomes: death, a life-threatening adverse experience, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant disability/incapacity, or a congenital anomaly/birth defect. Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered a serious adverse experience when, based upon appropriate medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed above.

**Significant Risk (SR) Device** - An SR device study is defined as a study of a device that presents a potential for serious risk to the health, safety, or welfare of a subject and (1) is intended as an implant; or (2) is used in supporting or sustaining human life; or (3) is of substantial importance in diagnosing, curing, mitigating or treating disease, or otherwise prevents impairment of human health; or (4) otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.
**Single-masked Design** - Typically, a study design in which the investigator, but not the subject, knows the identity of the treatment assignment. Occasionally the subject, but not the investigator, knows the assignment. Sometimes called "single-blind design."

**Site Visit** - A visit by agency officials, representatives, or consultants to the location of a research activity to assess the adequacy of IRB protection of human subjects or the capability of personnel to conduct the research.

**Sponsor** - a person or other entity that initiates a research study, but that does not actually conduct the investigation, i.e., the test article is administered or dispensed to, or used involving, a subject under the immediate direction of another individual. A person other than an individual (e.g., a corporation or agency) that uses one or more of its own employees to conduct an investigation that it has initiated is considered to be a sponsor (not a sponsor-investigator), and the employees are considered to be investigators.

**Statistical Significance** - A determination of the probability of obtaining the particular distribution of the data on the assumption that the null hypothesis is true. Or, more simply put, the probability of coming to a false positive conclusion.

**Surveys** - Studies designed to obtain information from a large number of respondents through written questionnaires, telephone interviews, door-to-door canvassing, or similar procedures.

**Therapy** - Treatment intended and expected to alleviate a disease or disorder.

**Unanticipated Problems (UP)** — Any unplanned occurrence that may affect the risks and/or potential benefits involved in the research study. Unplanned occurrences are usually related to study design or methods. Such occurrences can be favorable or unfavorable to participants and may or may not influence the study objectives or results (e.g., loss of identifiable data). Some adverse events in clinical trials are a subset of unanticipated problems.

**Unexpected adverse experience (UAE)** — Any adverse experience associated with the use of the drug/device, the specificity or severity of which is not consistent with the current investigator brochure; or, if an investigator brochure is not required or available, the specificity or severity of which is not consistent with the risk information provided to subjects and the IRB.

**Vaccine** - A biologic product generally made from an infectious agent or its components — a virus, bacterium, or other microorganism — that is killed (inactive) or live attenuated (active, although weakened). Vaccines may also be biochemically synthesized or made through recombinant DNA techniques.

**Vulnerable Subjects/Participants** — Individuals who lack the capacity to provide informed consent or whose willingness to participate in research may be unduly influenced by others. Vulnerable subjects include, for example, children, prisoners, individuals with emotional or cognitive disorders/impairments, and economically or educationally disadvantaged persons. (45 CFR 46.111 (a)(3); 45 CFR 46.111 (b); 45 CFR 46 Subparts B, C and D).

**Witness** – Impartial, non-involved observer of the consent process for enrollment into a research study.
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