## I. GENERAL ADMINISTRATION

<table>
<thead>
<tr>
<th>SOP Code</th>
<th>Description</th>
<th>Version Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>001</td>
<td>PRIME IRB SOP 001 Definitions</td>
<td>Version 0.4; 13-June-2017</td>
</tr>
<tr>
<td>100</td>
<td>PRIME IRB SOP 100 Overview, Introduction and Statement of Authority and Purpose</td>
<td>Version 0.1, 02-June-2017</td>
</tr>
<tr>
<td>101</td>
<td>PRIME IRB SOP 101 Maintenance of Standard Operating Procedures</td>
<td>Version 0.1; 05-June-2017</td>
</tr>
<tr>
<td>102</td>
<td>PRIME IRB SOP 102 HRPP Training and Education for IRB Members and Staff</td>
<td>Version 0.1; 05-June-2017</td>
</tr>
<tr>
<td>103</td>
<td>PRIME IRB SOP 103 Management of IRB Office Personnel</td>
<td>Version 0.1; 05-June-2017</td>
</tr>
<tr>
<td>104</td>
<td>PRIME IRB SOP 104 IRB Review Process</td>
<td>Version 0.1; 05-June-2017</td>
</tr>
<tr>
<td>105</td>
<td>PRIME IRB SOP 105 Research That Must Be Reviewed by the Prime Review Board Services</td>
<td>Version 0.1; 05-June-2017</td>
</tr>
<tr>
<td>106</td>
<td>PRIME IRB SOP 106 RESERVED for Department of Defense, when needed</td>
<td></td>
</tr>
<tr>
<td>107</td>
<td>PRIME IRB SOP 107 Annual Evaluation of the Human Research Protection Program</td>
<td>Version 0.1; 16-May-2017</td>
</tr>
<tr>
<td>108</td>
<td>PRIME IRB SOP 108 Monthly Evaluations of the Human Research Protection Program</td>
<td>Version 0.1; 16-May-2017</td>
</tr>
<tr>
<td>109</td>
<td>PRIME IRB SOP 109 Daily Tasks</td>
<td>Version 0.1; 17-May-2017</td>
</tr>
<tr>
<td>110</td>
<td>PRIME IRB SOP 110 Expiration of IRB Approval</td>
<td>Version 0.1; 17-May-2017</td>
</tr>
<tr>
<td>111</td>
<td>PRIME IRB SOP 111 Institutional Conflicts of Interest</td>
<td>Version 0.1; 16-May-2017</td>
</tr>
</tbody>
</table>

## II. PRIME REVIEW BOARD SERVICES ORGANIZATION

<table>
<thead>
<tr>
<th>SOP Code</th>
<th>Description</th>
<th>Version Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>200</td>
<td>PRIME IRB SOP 200 IRB Formation</td>
<td>Version 0.2; 06-June-2017</td>
</tr>
<tr>
<td>201</td>
<td>PRIME IRB SOP 201 Membership Addition</td>
<td>Version 0.2; 06-June-2017</td>
</tr>
<tr>
<td>202</td>
<td>PRIME IRB SOP 202 IRB Meeting Scheduling and Notification</td>
<td>Version 0.2; 06-June-2017</td>
</tr>
<tr>
<td>203</td>
<td>PRIME IRB SOP 203 Composition and Management of the IRB</td>
<td>Version 0.2; 06-June-2017</td>
</tr>
<tr>
<td>204</td>
<td>PRIME IRB SOP 204 Duties of IRB Members</td>
<td>Version 0.1; 06-June-2017</td>
</tr>
</tbody>
</table>

## III. PRIME REVIEW BOARD SERVICES FUNCTIONS AND OPERATIONS

<table>
<thead>
<tr>
<th>SOP Code</th>
<th>Description</th>
<th>Version Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>300</td>
<td>PRIME IRB SOP 300 Research Submission Requirements</td>
<td>Version 0.1; 06-June-2017</td>
</tr>
</tbody>
</table>
PRIME IRB SOP 301  Incoming Items Directed to the IRB [Version 0.2; 17-May-2017]
PRIME IRB SOP 302  Pre-Review [Version 0.2; 17-May-2017]
PRIME IRB SOP 303  Research Exempt From IRB Review [Version 0.1; 17-May-2017]
PRIME IRB SOP 304  Determining When a Proposal Meets the Definition of Human Subjects Research [Version 0.1; 07-June-2017]
PRIME IRB SOP 305  IRB Meeting Administration [Version 0.1; 07-June-2017]
PRIME IRB SOP 306  IRB Meeting Preparation [Version 0.1; 16-May-2017]
PRIME IRB SOP 307  IRB Meeting Conduct [Version 0.1; 16-May-2017]
PRIME IRB SOP 308  IRB Meeting Attendance Monitoring [Version 0.1; 16-May-2017]
PRIME IRB SOP 309  IRB Meeting Minutes [Version 0.1; 17-May-2017]
PRIME IRB SOP 310  Conflicting Interests of IRB Members [Version 2.0; 31-December-2018]
PRIME IRB SOP 311  Consultation to the IRB [Version 0.1; 17-May-2017]
PRIME IRB SOP 312  Post Review [Version 0.1; 17-May-2017]
PRIME IRB SOP 313  Documentation and Document Management [Version 0.1; 07-June-2017]
PRIME IRB SOP 314  Prime Review Board Services Records [Version 0.1; 07-June-2017]
PRIME IRB SOP 315  Standard Operating Procedures [Version 0.1; 07-June-2017]
PRIME IRB SOP 316  Prime Review Board Services Record Retention [Version 0.1; 22-May-2017]

IV. IRB REVIEW OF RESEARCH
PRIME IRB SOP 400  Determinations and Motions [Version 0.1; 07-June-2017]
PRIME IRB SOP 401  Criteria for PRIME IRB Approval [Version 0.1; 07-June-2017]
PRIME IRB SOP 402  Modifications Required to Secure Approval [Version 0.1; 16-May-2017]
PRIME IRB SOP 403  Expedited Review Procedures [Version 0.1; 07-June-2017]
PRIME IRB SOP 404  Modifications to Previously Approved Research and New Information [Version 0.1; 09-June-2017]
V. ADDITIONAL PROTECTIONS FOR SPECIAL POPULATIONS

500 PRIME IRB SOP 500 Vulnerable Subjects [Version 0.2; 17-July-2017]
501 PRIME IRB SOP 501 Research Involving Pregnant Women, Fetuses and Neonates [Version 0.2; 17-July-2017]
502 PRIME IRB SOP 502 RESERVED for Research Involving Prisoners, when needed
503 PRIME IRB SOP 503 Research Involving Children [Version 0.2; 17-July-2017]
504 PRIME IRB SOP 504 Minors Who Are Not Children in the Research Context [Version 0.2; 17-July-2017]
505 PRIME IRB SOP 505 RESERVED for Community Based Participatory Research, when needed

VI. INFORMED CONSENT

600 PRIME IRB SOP 600 Required Elements of Consent and Documentation of Consent [Version 1.1; 1-February-2019]
601 PRIME IRB SOP 601 Assent and Parental Permission [Version 0.2; 17-July-2017]
602 PRIME IRB SOP 602 Legally Authorized Representatives, Children, and Guardians [Version 0.2; 17-July-2017]
603 PRIME IRB SOP 603 Review of Recruitment Methods, Materials, and Compensation [Version 0.2; 17-July-2017]
604 PRIME IRB SOP 604 Payment to Subjects [Version 0.2; 18-July-2017]
605 PRIME IRB SOP 605 Waiver of Elements of Consent and Waiver of HIPAA Authorization [Version 0.4; 26-March-2018]
606 PRIME IRB SOP 606 Requirements for and Documentation of HIPAA Authorization [Version 0.2; 18-July-2017]
VII. INVESTIGATOR RESPONSIBILITIES

700  PRIME IRB SOP 700  Investigator Responsibilities Related to Human Research Subject Protections [Version 0.2; 18-July-2017]

701  PRIME IRB SOP 701  Data and Safety Monitoring Plan [Version 0.2; 18-July-2017]

VIII. RESEARCH COMPLIANCE

800  PRIME IRB SOP 800  Non-Compliance with Human Research Subjects [Version 0.1; 04-January-2018]
1 PURPOSE

1.1 This policy establishes the definitions followed by the human research protection program.

2 REVISIONS FROM PREVIOUS VERSION

2.1 None

3 POLICY

3.1 Administrative Hold: A voluntary action taken by an investigator to temporarily or permanently stop some or all approved research activities. The administrative hold may be either initiated by the principal investigator or it may be in response to a request by the convened IRB or IRB designee to take such action. Administrative holds are not suspensions or terminations.

3.2 Adverse Event (AE): Any untoward or unfavorable medical occurrence in a human subject, including any abnormal sign (for example, abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the subject’s participation in the research, whether or not considered related to the subject’s participation in the research. Adverse events encompass both physical and psychological harms. They occur most commonly in the context of biomedical research, although, they can occur in the context of social and behavioral research.

3.2.1 Expected Adverse Event: Any event that does not meet the definition of unexpected adverse event.

3.2.2 External (Off-Site) Adverse Events: Adverse events experienced by subjects enrolled by investigators at other institutions engaged in a multi-center clinical trial, or a different ongoing clinical trial involving the same intervention.

3.1.3 Internal (On-Site) Adverse Events: Adverse events experienced by subjects enrolled by the investigator(s) at their research site.

3.1.4 Related to Participation: Adverse events at least partially caused by participation in the research. Relatedness is assessed using the following terms: Definitely related, Probably related, Possibly related, Unlikely to be related or Unrelated. Possibly related means there is a reasonable possibility
that the adverse event may have been caused by the procedures involved in the research. In this document, related to the research means at least possibly related

3.3 Allegation of Non-Compliance: An unproved assertion of Non-Compliance.

3.4 Amendment: Any change in the research activity from what was approved by the IRB, including but not limited to modifications to the protocol, consent document, recruitment material, or Investigator’s Brochure

3.5 Assent: Assent refers to the research participant’s emotional reaction to the research procedures or environment. After being given basic information about the research and included in the conversation, participants unable to consent for themselves may agree or disagree to take part. Assent differs from consent as consent refers to the informed decision to participate in or refuse participation in research.

3.6 Capacity to Consent: An adult’s ability to understand information relevant to making an informed and voluntary decision to participate in research. This includes the ability to understand the purpose of the research and the procedures involved, the consequences of participation (including the risks and benefits) and the ability to decide and effectively communicate a choice about participation.

3.7 Capacity to Consent (lacking or diminished): Prospective research participants lack “consent capacity” when the capacity to consent is not present or is impaired to a degree that the potential participant is unable to give informed consent to enroll in or to continue in a study. All persons who are individually adjudicated or classified by law as “incompetent” shall be deemed to lack “consent capacity.”

3.8 Capacity to Consent (Fluctuating): In many individuals, consent capacity is not static. A research participant’s consent capacity may improve, deteriorate or fluctuate during the course of a research study. Study protocols, consent forms and procedures should anticipate and address this phenomenon. Safeguards must be in place prior to participant enrollment and, as appropriate, throughout the course of research participation. Consent must be continuously present during the course of a study.

In that consent must be continuously present during a study, the research plan must address the situation of maintaining consent in the event that a consenting participant suffers a medical, psychiatric or toxic event during a study that causes the capacity of consent to become critically diminished or absent during the study.

3.9 CLIA: Clinical Laboratory Improvement Amendments (1992) established standards for accuracy and precision of laboratory tests. Certification is required for all clinical-diagnostic laboratories.
3.10 **Clinical Trial**: A research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes.

3.11 **Clinically significant**: means situations in which knowledge of the test result will alter or result in the institution of a currently available, validated therapy. To be clinically significant, the test procedure must have established accuracy, precision, and reproducibility. In general, this means that the test was performed in a CLIA-certified laboratory.

3.12 **Conflicting Interest for HRPP Managed Scientific Assessors**: An individual involved in HRPP managed scientific assessment is automatically considered to have a conflicting interest when any of the conditions for **Conflicting Interest for IRB Members** has been met. The following also apply:

3.12.1 Subordinate relationship to an immediate supervisor who is also an investigator on the protocol.

3.13 **Conflicting Interest for IRB Members**: An individual involved in research review is automatically considered to have a conflicting interest when the individual or the individual’s spouse, domestic partner, children, and dependents have any of the following interests in the sponsor, product or service being tested, or competitor of the sponsor held by the individual or the individual’s immediate family:

3.13.1 Involvement in the design, conduct, or reporting of the research. Note, in cases where the Investigational Drug Services (IDS) Pharmacist (who is also an IRB member) is listed on the FDA Form 1572 as a sub-investigator and that role is limited to the preparation and/or labeling of the drug(s) where no design, subject contact or analysis of data is performed by the IDS Pharmacist, that individual does not have a conflict of interest with the review or approval of a protocol.

3.13.2 Ownership interest, stock options, or other ownership interest of any value exclusive of interests in publicly-traded, diversified mutual funds.

3.13.3 Compensation of any amount in the past year or of any amount expected in the next year, excluding compensation for costs directly related to conducting research.

3.13.4 Proprietary interest including, but not limited to, a patent, trademark, copyright or licensing agreement.

3.13.5 Board or executive relationship, regardless of compensation.
3.13.6 Reimbursed or sponsored travel by an entity other than a federal, state, or local government agency, higher education institution or affiliated research institute, academic teaching hospital, or medical center.

3.13.7 Other nonfinancial interests that may be conflicting interests, such as the following: (a) An IRB member is a participant in a study under review; (b) An IRB member is considered a personal or professional adversary of the investigator (e.g. direct competitor of the investigator for limited resources, in dispute with the investigator, etc.); or (c) An IRB member has a close personal relationship with the investigator. For the above examples, the IRB member must disclose the circumstances to the IRB Chair or HRPP Director for determination of whether a conflicting interest exists.

3.13.8 Any other reason for which the member independently, or in consultation with the IRB Chair or HRPP Director, believes that he or she cannot be independent.

3.14 Continuing Non-Compliance: A pattern of Non-Compliance that suggests the likelihood that, without intervention, instances of Non-Compliance will recur, a repeated unwillingness to comply, or a persistent lack of knowledge of how to comply.

Continuing Noncompliance: means a pattern of noncompliance that indicates a lack of understanding about the regulations or ethical requirements that may affect the rights and welfare of participants. The pattern of noncompliance is assessed by the number of incidents occurring during the course of a protocol, or across multiple protocols, and whether the same noncompliant action was repeated or many different noncompliant events occurred especially after education or training has been provided to the researcher or research staff.

3.15 Court-approved guardian of a child: a person, other than the biological parent or adoptive parent, who is appointed or confirmed by a Court to assume responsibility for the care and welfare of a child. A court can appoint a guardian through a formal legal hearing process, or confirm a guardian upon petition filed by a person named as a guardian in a parent’s will or health care directive.

3.16 Data and Safety Monitoring Plan (DSMP): The DSMP includes all aspects for ensuring the integrity of the data and for protecting the safety of current and future participants.

3.16.1 DSMB or DMC or DMB: Data Safety Monitoring Board, Data Monitoring Committee or Data Monitoring Board.
3.16.2 **Internal DMC**: A committee composed of representatives of the study investigators and sponsors who are empowered to monitor the progress, safety and integrity of a study.

3.16.3 **Independent DMC**: A committee composed of individuals with no connection or conflicts of interest related to the current study and organized to provide oversight of the emerging data and safety during the progress of a clinical trial. One of the primary purposes of the Independent DMC is to preserve the integrity of a randomized blinded trial

3.17 **Designated Reviewer**: The IRB chair or an Experienced IRB Member designated by the IRB chair to conduct Non-Committee Reviews.

3.18 **Document Management System**: The Prime Review Board Services uses an electronic submission system for submitting all protocols to the Prime Review Board Services Operations Office for review. The document management system is a web-based system accessible anywhere with an Internet connection that supports electronic submissions of new Prime Review Board Services studies along with Amendment and Continuing Review for submissions originally completed in the system. It is also a fully interactive client portal that includes and accepts documents submitted to the Prime Review Board Services, approval memos, informed consents, expirations, electronic signatures, automated email notifications, tracking and Prime Review Board Services distribution. The document management system is a 21 CFR, Part 11 compliant system and contains a verification process for new users.

All study documents submitted to the Prime Review Board Services will be maintained in the system and be accessible by Users given access to the study. Investigators have access to see the protocols they're investigating as well as attachments, events and documents generated for their study but do not have the authority to edit them. This includes studies for which they are the Sub-Investigator.

3.19 **Effective Approval Date**: The date of confirmation that all of the IRB’s requested clarifications and modifications have been satisfactorily completed and that all ancillary approvals or other conditions for approval (e.g., evidence of FDA approval, receipt of a Certificate of Confidentiality, etc.) have been met. The date at which all required modifications or contingencies have been satisfied. This may be at a convened meeting or, for changes that are not substantive, by the Chair or designee using expedited procedures.

3.20 **Engaged**: The term used by the Office of Human Research Protections (OHRP) to identify that IRB oversight is required for a site or personnel participating in a research
study or project. (See “WORKSHEET: Engagement Determination” for guidance on engagement.)

3.21 **Expanded Expedited Review Categories:** The procedures and categories of research not listed in the Federal Register Expedited Review Categories that have been determined by the Prime IRB to be no more than minimal risk.

3.22 **Expeditied Review:** Review of proposed research by the IRB Chair or designee rather than by the convened IRB.

3.23 **Expeditied Review Categories:** The listing of procedures and categories of research published periodically by the Secretary HHS in the Federal Register (See Prime IRB SOP 403; Appendix 1).

3.24 **Experienced IRB Member:** An IRB member is considered experienced if the IRB chair considers the IRB member to have sufficient experience in and knowledge of conducting IRB reviews.

3.25 **Expiration Date:** The first date that the protocol is no longer approved. The date after the end date of the approval period.

3.26 **External IRB:** An IRB that is not affiliated with the EMMES Corporation or does not fall under the EMMES Corporation’s IRB authority. An example of an External IRB is an IRB at another institution or entity, e.g., another university, or an independent IRB, e.g., Quorum Review IRB.

3.27 **Finding of Non-Compliance:** Non-Compliance in fact.

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

3.29 **Guardian of a child:** a person, other than the biological parent or adoptive parent and generally a family member, who is responsible for the care and welfare of a child. The guardian may assume responsibility because the parent: a) authorizes the guardian to do so; b) is absent from the child’s life; or c) is unable to care for the child or authorize another to do so.
3.30 **Human Research**: Any activity that either:¹

3.30.1 Is Research as Defined by DHHS and involves Human Subjects as Defined by DHHS; or

3.30.2 Is Research as Defined by FDA and involves Human Subjects as Defined by FDA.

3.31 **Human Subject as Defined by DHHS**: A living individual about whom an investigator (whether professional or student) conducting research obtains (1) data through **Intervention** or **Interaction** with the individual, or (2) information that is both **Private Information** and **Identifiable Information**. For the purpose of this definition:

3.31.1 **Intervention**: 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.

3.31.2 **Interaction**: Communication or interpersonal contact between investigator and subject.

3.31.3 **Private Information**: 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).

3.31.4 **Identifiable Information**: Information that is individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information).

3.32 **Human Subject as Defined by FDA**: An individual who is or becomes a subject in research, either as a recipient of the test article or as a control. A subject may be either a healthy human or a patient. A human subject includes an individual on whose specimen a medical device is used.

3.33 **Immediate Family**: Spouse, domestic partner; and dependent children; any other family member whom the covered individual reasonably knows may benefit personally from actions taken by the covered individual on behalf of the University.

3.34 **Individual Investigator Agreement (IIA)**: An agreement used when an institution’s IRB agrees to serve as the IRB of record for external personnel or collaborators **engaged in Human Research**, but who are not affiliated with an institution that has its own IRB. This document is issued only when studies are federally conducted or

¹ The terms “Human Subject Research,” “Research Involving Human Subjects,” “Clinical Research,” “Clinical Investigation,” “Clinical Study” and similar phrases are considered to be synonyms for the term **Human Research**.
supported. If an IIA is needed, the HRPP Office facilitates the processing of such agreements.

3.35 **Individually Identifiable Health Information**: means a subset of health information, including demographic information collected from an individual, and (1) is created or received by a health care provider, health plan, employer, or healthcare clearinghouse; and (2) relates to the past, present, or future physical or mental health or condition of an individual; the provision of health care to an individual; or the past, present, or future payment for the provision of healthcare to an individual; and (a) that identifies the individual; or (b) with respect to which there is a reasonable basis to believe the information can be used to identify the individual.

3.36 **Institutional Official**: The President and CEO of Emmes Corporation is the Institutional Official for Prime Review Board Services.

3.37 **Institutional Review Board (IRB) Types**:

3.37.1 **Institution**: An IRB may be based at an institution, academic or other, such as a university (e.g., EMMES Corporation IRB), an academic medical center (e.g., Cincinnati Children’s IRB), or an independent research institution (e.g., National Donor Marrow Program®).

3.37.2 **Commercial/independent**: An IRB may be a commercial/independent IRB (e.g., Quorum Review IRB) which is free-standing IRB with no direct or permanent affiliation to a research institution. (In some cases, these IRBs are for-profit companies.)

3.37.3 **Federal central IRB**: A federally funded freestanding IRB (e.g., NCI CIRB).

3.38 **Interpreter**: For consent interviews involving non-English speaking subjects: A person that (a) understands both English and the subject's native language and (b) is not part of the study team or otherwise involved with the study. This individual may also serve as the witness when the Short Form Consent process is used. Trained Medical Interpreters are individuals who have completed a minimum of forty hours of formal training in the techniques, ethics and cross-cultural issues related to medical interpreting.

3.39 **Investigational Device Exemption (IDE)**: Clinical evaluation of medical devices not cleared for marketing, unless exempt, requires an approved IDE. An approved IDE application permits a medical device, which would otherwise be subject to marketing clearance, to be shipped lawfully for the purpose of conducting a clinical study. This allows a researcher to use a device in studies undertaken to develop safety and effectiveness data for that medical device when such studies involve human subjects.
3.40 **Investigational New Drug (IND):** Investigational new drug means a new drug, antibiotic drug, or biological drug that is used in a clinical investigation. The term also includes a biological product that is used in vitro for diagnostic purposes. An investigator who desires to pursue FDA regulated human research using new medical products, drugs, biologics, or genes requires prior notification of the FDA before clinical investigations using these products in humans can begin. These investigators must make application to the FDA for an IND.

3.41 **Investigator:** means someone who participates in the planning, design, execution, analysis and reporting of a research study (See Principal Investigator).

3.42 **Investigative Team Member:** means all investigators, faculty, trainees, study coordinators, research assistants or other staff who interacts with a human subject directly through an interaction, intervention, or identifiable health information (including data and biological specimens).

3.43 **IRB Authorization Agreement (IAA):** An agreement that authorizes one institution to provide IRB review for another institution. An agreement may be developed to cover a single Human Research study, categories of Human Research, or Human Research within a research program. See also Reliance Agreement.

3.44 **IRB of Record:** An IRB that assumes IRB responsibilities for the review of Human Research. The IRB of Record will be at the EMMES Corporation unless established elsewhere through a Reliance Agreement. Similar terms include Single IRB (sIRB) and Central IRB (cIRB).

3.45 **IRB Reliance:** A term to describe agreements between or among institutions engaged in Human Research to identify the reviewing IRB and the roles and responsibilities of each institution. These agreements are documented in Reliance Agreements. Similar terms include cede review and deferred review.

3.46 **Legally Authorized Representative (LAR):** “An individual or judicial or other body authorized under applicable law to consent on behalf of a prospective research participant to the research participant's participation in the procedure(s) involved in the research).” (45 CFR 46.111, 46.102(c) and 21 CFR 50.3(1)).

The individual with the legal authority to provide proxy consent for a person who lacks the capacity or legal status to function autonomously.

3.47 **Local Context/Local Research Context:** Knowledge of the institution and community environment in which Human Research will be conducted. In order for an IRB to agree to serve the IRB of Record for another institution or entity, it must have adequate
knowledge of that institution’s or entity’s local context. This may include local research policies and other institutional requirements.

3.48 **Master Reliance Agreement**: A Reliance Agreement involving two or more institutions setting out terms, conditions, and roles and responsibilities for the institution agreeing to serve as the IRB of Record and the institution(s) agreeing to cede IRB review and oversight. A Master Reliance Agreement is usually entered into in order to avoid negotiating an agreement for each individual study as the parties to the agreement rely on the terms of the Master Reliance Agreement for all studies, including future studies (unless otherwise indicated). This agreement also includes a set of standard operating procedures detailing roles and responsibilities of study teams, the IRB of Record, and the relying institution(s). Also called “umbrella agreements, this mechanism often takes much longer to establish but it virtually eliminates any need to negotiate an agreement for future studies that fall underneath it.

3.49 **Material Change**: A modification to the research-related documentation that impacts the conduct of the research or the assessment of the risks and benefits of the study. Non-material changes do not require IRB review or approval.

3.50 **Medical Device**: An instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component, part, or accessory, which is recognized in the official National Formulary, or the United States (U.S.) Pharmacopoeia, and intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man, or intended to affect the structure or any function of the body of man, and which does not achieve any of its primary intended purposes through chemical action within or on the body of man and which is not dependent upon being metabolized for the achievement of any of its primary intended purposes.

3.51 **Meeting Date**: means the date of the convened meeting where the research was approved. This includes studies approved with modifications that will be reviewed using expedited procedures. For studies approved using expedited review procedures, the meeting date is the date of the review at which the Chair or designee approves the research.

3.52 **Minimal Risk**: The probability and magnitude of harm or discomfort anticipated in the research that 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.²

---

² The phrase “ordinarily encountered in daily life or during the performance of routine physical or physiological examinations or tests” should not be interpreted to include the inherent risks certain categories of subjects face in their everyday life. For example, the risks imposed in research involving human subjects focused on a special...
3.52.1 For research involving prisoners **Minimal Risk** is the probability and magnitude of physical or psychological harm that is normally encountered in the daily lives, or in the routine medical, dental, or psychological examination of healthy persons.

3.52.2 When following Department of Defense regulations, the definition of minimal risk based on the phrase “ordinarily encountered in daily life or during the performance of routine physical or physiological examination or tests” shall not be interpreted to include the inherent risks certain categories of human participants face in their everyday life. For example, the risks imposed in research involving human participants focused on a special population should not be evaluated against the inherent risks encountered in their work environment (e.g., emergency responder, pilot, soldier in a combat zone) or having a medical condition (e.g., frequent medical tests or constant pain).

3.53 **Minor Amendment**: A proposed change in the research-related activities that does not materially affect assessment of the risks and benefits of the study and does not substantially change the specific aims, objectives or design of the study. A modification may not be considered “minor” if the changes involve the addition of a procedure that is more than minimal risk or a procedure that cannot be reviewed under Expedited Categories (as outlined in Prime IRB SOP 403 Appendix 1: A and B) Representative minor modifications are included in the Prime IRB SOP 403 Appendix 2.

3.54 **Multi-Site Research**: Human Research involving more than one institution. The components of the research project may be distributed across more than one institution OR some or all of the research activities may occur at more than one site. Also called “cooperative research” or “collaborative” research. Each institution remains responsible for safeguarding the rights and welfare of human subjects as detailed in the Reliance Agreement, if any, and in the protocol.

3.55 **Non-Committee Review**: Any of the following:

3.55.1 Determination of whether an activity is Human Research.

3.55.2 Determination of whether Human Research is exempt from regulation.

3.55.3 Reviews of non-exempt research using the expedited procedure.

3.55.4 Determinations of which subjects can continue in expired research.
3.56 **Non-Compliance**: Failure to follow the regulations, or the requirements or determinations of the IRB. Noncompliance is defined as a violation of any federal, state, or local regulation that governs human research; any institutional policy on human research; any deviation from the protocol approved by the IRB or stipulations imposed by the IRB as a condition of approval.

3.56.1 In the case of research funded or conducted by the Department of Defense (DOD), Non-Compliance includes failure of a person, group, or institution to act in accordance with Department of Defense (DOD) instruction 3216.02, its references, or applicable requirements.

3.57 **Parent**: A child’s biological or adoptive parent.

3.58 **Parental Permission**: The agreement of parent(s) or guardian to the participation of their child or ward in research.

3.59 **Principal Investigator**: An individual who conducts human subjects research and, in case of the human subjects research being conducted by a team of individuals, is the responsible leader of that team (generally referred to as the “Principal Investigator”).

3.60 **Prisoner**: Any individual involuntarily confined or detained in a penal institution. The term is intended to encompass individuals sentenced to such an institution under a criminal or civil statute, individuals detained in other facilities by virtue of statutes or commitment procedures which provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing.

3.60.1 For Department of Defense (DOD) research the term includes military personnel in either civilian or military custody.

3.61 **Privacy Rule (HIPAA)**: means the federal regulations at 45 CFR 160 and 164

3.61.1 **Written Authorization**: means written permission for the use or disclosure of PHI.

3.61.2 **Waiver of Authorization**: means waiver from the requirements of the Privacy Rule to obtain written permission for the use or disclosure of PHI.

3.61.3 **Alteration of Requirement of Authorization**: means a waiver of one or more of the requirements of the Privacy Rule.

3.62 **Private Information**: Includes information about data or behavior that occurs in a setting in which an individual can reasonably expect that no observation or recording is taking place. It includes information, which has been provided for specific purposes by an individual, and the individual can reasonably expect will not be made public (e.g., a
medical record). Private information must be individually identifiable in order to be considered information to constitute research involving human subjects. This may include identifiable private information obtained from a primary subject about a third party.

3.63 **Protected Health Information (PHI):** Individually Identifiable Health Information transmitted by electronic media, maintained in electronic media, or transmitted or maintained in any other form or medium. There are 18 PHI identifiers of individual patients, their relatives, household members or employers. These include: name; all geographic identifiers smaller than a state, including address and zip codes; dates except for years (including birth, admission, discharge or death dates); Social Security numbers; telephone and fax numbers; e-mail addresses; and medical record and health plan numbers.

3.64 **Quorum:** Quorum is a majority of the IRB members (more than half), including at least one member whose primary concerns are in scientific areas, and one member whose primary concerns are in non-scientific areas. When FDA-regulated research is reviewed, there shall be at least one member who is a physician. An appropriate IRB alternate may attend an IRB meeting in the place of an absent member in order to meet quorum requirements.

3.65 **Recruitment:** The process by which an investigator conveys information to a prospective subject to in order to allow the individual to determine whether or not they are interested in participating in the research.

3.66 **Recruitment Methods:** includes recruiting materials, advertised compensation, and other means and methods used to attract potential participants for research.

3.67 **Recruitment Materials:** Web sites, flyers, posters, newspaper advertisements, television scripts, radio advertisements, brochures, and doctor-to-patient letters and any other material that participants will see or hear that is used as part of the recruitment process. Recruitment materials do not include information conveyed as part of in-person or telephone recruitment, unless the conversation adheres to a written script.

3.68 **Reimbursement:** A payment to research subjects/families for direct, out-of-pocket research-related expenses based on actual expenses (e.g., transportation, parking, lodging, meals, childcare, etc.) incurred as a result of their participation in research. The actual expenses must be based upon 1) receipts (or other valid, acceptable documentation) that are collected and submitted for the exact amount as the original expense, or 2) allowances for lodging or meals and incidental expenses up to the IRS-set per diem rates.
Reimbursement for actual expenses is not considered taxable income. Note: Payments for expenses that are not based on receipts or actual costs incurred (flat-rate payment) are considered compensation by the IRS and are therefore taxable income.

3.68.1 Compensation or Incentive Payments: A predetermined payment of cash or cash equivalent provided to research subjects for the time, effort, inconvenience, and general expense of participating in a research activity. Payment may be made on a one-time basis or several payments may be made over a period of time. Compensation is considered taxable income.

3.68.2 Tokens of Appreciation: Tokens of appreciation are small gifts of appreciation that include tangible items of nominal value such as T-shirts, mugs, calendars, books, stuffed animal, tote bag, etc. In order to ensure compliance with tax reporting requirements, a maximum value of $100 has been set for Tokens of Appreciation. Tokens of Appreciation are neither compensation/incentive nor reimbursement and are not considered taxable income.

3.68.3 Wage-Payment Model: A method of determining the amount of payment by using a standardized hourly wage and an estimated time for completing the research task.

3.69 Related to the Research: A financial interest is Related to the Research when the interest is in:

3.69.1 A sponsor of the research;
3.69.2 A competitor of the sponsor of the research;
3.69.3 A product or service being tested; or
3.69.4 A competitor of the product or service being tested.

3.70 Reliance Agreement: The formal written agreement between two or more entities that documents respective authorities, roles, responsibilities, and communication between an institution/organization serving as the IRB of Record and the institution relying on that IRB. This term includes: IRB Authorization Agreement (IAA), cooperative agreement, Master Services Agreement (MSA), Master Joint Agreement (MJA), or umbrella agreement.

3.71 Relying Institution: Also called “Relying Organization.” The institution or organization that has ceded IRB review to another IRB to provide IRB review and oversight for a specific study or set of studies. Relying on another IRB to provide IRB oversight also is referred to as ceding or deferring IRB review.
3.72 **Research as Defined by DHHS:** A systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.

3.73 **Research as Defined by FDA:** Any experiment that involves a test article and one or more Human Subjects, and that meets any one of the following:

3.73.1 Must meet the requirements for prior submission to the Food and Drug Administration under section 505(i) of the Federal Food, Drug, and Cosmetic Act meaning any use of a drug other than the use of an approved drug in the course of medical practice;

3.73.2 Must meet the requirements for prior submission to the Food and Drug Administration under section 520(g) of the Federal Food, Drug, and Cosmetic Act meaning any activity that evaluates the safety or effectiveness of a device; OR

3.73.3 Any activity the results of which are intended to be later submitted to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit.

3.74 **Restricted:** Applies to investigators who are delinquent in meeting IRB requirements.

3.75 **Reviewing IRB:** The External IRB or entity taking on the role of providing IRB review and oversight may also be called the “Central IRB (cIRB),” “Single IRB (sIRB),” or **IRB of Record.**

3.76 **Screening:** The screening process starts the moment an investigator seeks information from an individual to determine if they are eligible for the research. 45 CFR 46.102 (f) defines a human subject as “a living individual about whom an investigator (whether professional or student) conducting research obtains (1) Data through intervention or interaction with the individual, or (2) Identifiable private information.” Screening that involves collection of data from an interaction with an investigator and an individual, requires prior informed consent and (usually) HIPAA of the subject.

3.77 **Serious Adverse Event (SAE):** Any adverse event that meets any of the following conditions:

3.77.1 Results in death;

3.77.2 Is life threatening (places the subject at immediate risk of death from the event as it occurred);
3.77.3 Requires inpatient hospitalization or prolongation of existing hospitalization; (hospitalization for a protocol-specified activity or for an elective, pre-planned procedure is not considered an SAE);

3.77.4 Results in persistent or significant disability/incapacity;

3.77.5 Results in a congenital anomaly or a birth defect; or

3.77.6 Based upon appropriate medical judgment, may jeopardize the subject’s health and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition (examples of such events include allergic bronchospasm requiring intensive treatment in the emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse).

3.78 **Serious Non-Compliance**: Non-Compliance that adversely affects the rights or welfare of subjects. **Serious Noncompliance** means noncompliance that may affect subject safety, increase risks to subjects, affect the integrity of the data, violate the rights and welfare of subjects, or affect the subject’s willingness to participate in research.

3.78.1 For Department of Defense (DOD) research **Serious Non-Compliance** includes failure of a person, group, or institution to act in accordance with Department of Defense (DOD) Instruction 3216.02 and its references such that the failure could adversely affect the rights, safety, or welfare of a human subject; place a human subject at increased risk of harm; cause harm to a human subject; affect a human subject’s willingness to participate in research; or damage or compromise the scientific integrity of research data.

3.79 **Short Form Consent Document**: A brief document, written in the subject's native language. The short form consent document must contain the following:

3.79.1 a description of the required elements of informed consent;

3.79.2 an explanation that the purpose of the research, the study procedures and the other required elements in the consent form will be presented to the subject, or legally authorized representative in their native language.

3.80 **Significant Risk Device**: means an investigational device that is (1) intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject; (2) is purported or represented to be for a use in supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a subject; (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 the health, safety, or welfare of a subject. (21 CFR 812.3(m))

3.81 **Single IRB (sIRB):** The single IRB of Record for Multi-Site Research. The sIRB can be of several different models, such as institution-based, independent, or a federal central IRB. This is the term used by NIH. Other terms may include IRB of Record, Reviewing IRB, or Central IRB (cIRB).

3.82 **Sound Research Design:** means that the study has (1) well defined goals and objectives which have scientific and social value, (2) scientific validity consistent with the stated objectives, (3) is feasible, (4) the researcher is capable of successfully conducting the proposed research and (5) the plan provides sufficient evidence to ensure the likelihood of fruitful results.

3.83 **Sponsor-Investigator:** An individual who both initiates and actually conducts, alone or with others, a clinical investigation, i.e., under whose immediate direction the investigational device, biologic or drug is administered, dispensed, or used. The term does not include a corporation or agency. The obligations of a sponsor-investigator include the responsibilities of an investigator and the responsibilities of a sponsor.

3.84 **Summary Document:** A document used in the consent process with Non-English speaking subjects when the short form process is implemented. The IRB-approved English version of the informed consent form can be used to create the summary document (e.g. by attaching additional signature pages).

3.85 **Suspension of IRB Approval:** An action of the IRB, IRB designee, Institutional Official, or designee of the Institutional Official to temporarily or permanently withdraw IRB approval of some or all research procedures short of a Termination of IRB Approval. Suspended studies remain open and are subject to continuing review.

3.86 **Termination of IRB Approval:** An action of the IRB, IRB designee, Institutional Official, or designee of the Institutional Official to permanently withdraw IRB approval of all research procedures (except for those follow up procedures which are necessary to protect the health or welfare of the subjects). Terminated studies are permanently closed and no longer require continuing review.

3.87 **Translator:** A person who translates written documents from one language into another.

3.88 **Unanticipated adverse device effect:** Any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of...
incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

3.89 **Unanticipated Problem Involving Risks to Subjects or Others:** Any information that is (1) unanticipated, (2) related to the research, and (3) indicates that subjects or others are at increased risk of harm.

3.89.1 For Department of Defense (DOD) research the term **Unanticipated Problem Involving Risks to Subjects or Others** includes any incident, experience, or outcome that meets ALL three of the following conditions:

3.89.1.1 Is unexpected (in terms of nature, severity, or frequency) given the procedures described in the research protocol documents (e.g., the IRB-approved research protocol and informed consent document) and the characteristics of the human subject population being studied.

3.89.1.2 Is related or possibly related to participation in the research (in this Instruction, possibly related means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research).

3.89.1.3 Suggests that the research places human subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized, even if no harm has actually occurred.

3.90 **Unexpected Adverse Events:** Any adverse event occurring in one or more subjects in a research protocol, the nature, severity, or frequency of which is not consistent with either:

3.90.1 the known or foreseeable risk of adverse events associated with the procedures involved in the research that are described in (a) the protocol–related documents, such as the IRB-approved research protocol, any applicable investigator brochure, and the current IRB-approved informed consent document, and (b) other relevant sources of information such as product labeling and package inserts; or

3.90.2 the expected natural progression of any underlying disease, disorder, or condition of the subject(s) experiencing the adverse event and the subject’s predisposing risk factor profile for the adverse event.

3.91 **Vulnerability:** Vulnerable research participants are vulnerable to coerced consent to research or to exploitation during research. Vulnerability is a power imbalance and
thereby differs from impaired consent capacity. Not every person in a vulnerable group is susceptible to coercion or exploitation. Situations in which vulnerability may be relevant include fear of stigmatization, communication impairment, deferential or formal power relationships, dire medical need, and relational dependence.

3.92 **Witness:** A third party present during the oral presentation of the consent form and the consent interview. The IRB may require a witness to the consent process based on the nature and risks of research.

3.92.1 For consent interviews involving non-English speaking subjects: A person that (a) understands both English and the subject's native language and (b) is not part of the study team or otherwise involved with the study, and witnesses the consent process. This can be an interpreter assisting the person obtaining consent. For illiterate subjects, the witness must be impartial.

4 **RESPONSIBILITIES**

4.1 Individuals writing policies and procedures are to indicate terms defined in this policy with a double underline.

4.2 Individuals using policies and procedures are to consult this policy for the definitions of double underlined terms.

5 **PROCEDURE**

5.1 None

6 **MATERIALS**

6.1 None

7 **REFERENCES**

7.1 45 CFR §46.102.

7.2 21 CFR §50.3, 21 CFR §56.102, 21 CFR §312.3, 21 CFR §812.2(a), 21 CFR §812.3(p)
<table>
<thead>
<tr>
<th>Version 0.6</th>
<th>Name</th>
<th>Status (Pending, Reviewed, Approved)</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Written by:</td>
<td>Karl Nelson</td>
<td></td>
<td>13-July-2017</td>
</tr>
<tr>
<td>Reviewed by:</td>
<td>Jennifer Neal-Jimenez</td>
<td></td>
<td>5-January-2018</td>
</tr>
<tr>
<td>Approved by:</td>
<td>Jennifer Neal-Jimenez</td>
<td>Approved</td>
<td>8-January-2018</td>
</tr>
</tbody>
</table>
# 1. PURPOSE

1.1. To give a general overview, Introduction, & Statement of Authority and Purpose for the Prime Review Board Services governing board.

## 2. REVISIONS FROM PREVIOUS VERSION

2.1. None

## 3. POLICY

### 3.1. Overview

3.1.1. The EMMES Corporation ("Emmes") is committed to ensuring an institutional culture where research is conducted in an ethical and scientifically rigorous manner and where safeguards to subjects who participate in clinical studies are of paramount importance. Ensuring an institutional culture of research excellence begins with the establishment of a strong and dynamic Institutional Review Board (Prime Review Board Services) with committed members who are well-trained in regulatory requirements, ethical conduct and sound implementation of research and have the support and resources necessary to effectively review and oversee proposed human subject research. In furtherance of this institutional commitment, Emmes has created the Prime Review Board Services.

3.1.2. The mission of The Prime Review Board Services is to ensure that all human subject research which is conducted under the oversight of the Prime Review Board Services is conducted in accordance with applicable law and regulations (national, state, local, and institutional), as well as research ethics. The rights of individuals who are participants or potential participants will be protected by the Prime Review Board Services through the thoughtful consideration of research risks and benefits, including scientific merit; by ensuring appropriate informed consent is obtained from each participant (or the legal representative).
in a process which is ongoing, voluntary and non-coercive; by requiring appropriate training of Prime Review Board Services members, Investigators and research staff; and by monitoring and re-reviewing research at appropriate intervals, based on the risks posed. Research conducted at Emmes must meet the ethical standards of respect for persons, beneficence, and justice.

3.1.3. Regulations require that Prime Review Board Services have written policies and procedures and that Prime Review Board Services oversight of research is carried out as described in those policies and procedures documents. These Standard Operating Policies and Procedures (SOPs) are written to enable the Prime Review Board Services to maintain a system of compliance. These SOPs reflect not only the laws and regulations, but also the underlying ethical principles that are the basis of the Prime Review Board Services's mandate. Finally, these policies also reflect our overarching commitment to provide protection for all the human subjects involved in research at this and affiliated facilities. The forms, checklists, and other documents that are part of the SOPs are included in order to assure that the procedures are integrated into the daily activities of not only Prime Review Board Services members and staff, but also into the activities of each research team.

3.2. Introduction

3.2.1. Federal regulations require review and oversight of federally sponsored research by a body committed to protecting human research subjects – the Institutional Review Board. These regulations also require the Prime Review Board Services to have written policies and procedures which describe the operation of the Prime Review Board Services, and which permit the Prime Review Board Services to ensure compliance with laws and regulations, as well as the underlying ethical principles that are the basis of the Prime Review Board Services's mandate. These policies also reflect the overarching commitment of Emmes and its affiliated organizations to provide protection for all human subjects involved in research conducted under the supervision of the Prime Review Board Services. The ethically responsible researcher is expected to carry the dual burden of advancing existing or generating new knowledge that can improve the human condition and, at the same time, of recognizing the absolute imperative to treat human research subjects with the utmost care and respect. In no event can the anticipated outcomes of research be used to excuse the unethical treatment of study participants.

3.2.2. The responsibility imposed on researchers is shared with others. All those involved in the conduct of research are responsible for ensuring compliance with legal and ethical mandates.
3.2.3. This responsibility also falls to the men and women who sit on Institutional Review Boards. They are expected to act as custodians of the research, to manage the research enterprise to enable the advancement of science, and have as their overriding concern the protection of the human subjects of the research.

3.2.4. These Standard Operating Policies and Procedures (SOPs) apply to all of the day-to-day operations of the Prime Review Board Services. The SOPs apply to each member who serves on the Prime Review Board Services, each individual who supports the Prime Review Board Services and all others who must comply with its decisions and its requirements (for example, Investigators, research managers/coordinators, research nurses, support staff, etc.).

3.2.5. The forms, checklists, and other documents that are part of the SOPs are included in order to assure that the procedures are integrated into the daily activities of not only Prime Review Board Services members and staff, but into the activities of the research team as well. These SOPs will be reviewed periodically to ensure that they are current, that new legislation, regulations or ethical standards are reflected and that daily activities are being performed as described in the Sops. These policies are based on current regulations, ethical principles, and guidelines for the protection of the human subjects of biomedical and behavioral research. The policies state what this institution requires for the ethical conduct of clinical research. The procedures detail how these policies are carried out.

3.2.6. These policies and procedures are the framework upon which research reviewed by the Prime Review Board Services is conducted. Therefore, all members of the research enterprise under the jurisdiction of the Prime Review Board Services are expected to read, understand, and comply with them. Everyone who engages in or supports research at Emmes must be committed to conducting sound, effective and ethical research.

3.3. Statement and Authority of Purpose

3.3.1. Governing Principles

3.3.1.1. The Prime Review Board Services is guided by the same ethical principles as are applied to all federally-supported research in the United States involving humans as subjects, as set forth in the report of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, titled: Ethical Principles and Guidelines for the Protection of Human Subjects of Research (the
"Belmont Report"). These principles are defined in the Belmont Report as follows:

3.3.1.1.1. **Respect for Persons** -- Respect for persons includes two ethical convictions: that individuals capable of autonomy should have the right to agree, freely and without coercion, to participate or not participate in research; and that persons with diminished autonomy are entitled to protection. The expression of the ethical principle of Respect for Persons is seen most clearly in requirements for a legally effective informed consent, unless the requirements for waiver of informed consent are met by adequate and appropriate methods in accordance with the provisions of applicable regulations.

3.3.1.1.2. **Beneficence** -- The sum of the benefits to the subject and the importance of the knowledge to be gained so outweigh the risks to the subjects as to warrant a decision to allow the research to go forward; benefits have been maximized and risks have been minimized, to the extent possible.

3.3.1.1.3. **Justice** -- The selection of subjects is equitable. To the extent possible, subjects are representative of the group that will benefit from the research. Those subjects, who are particularly vulnerable, such as children, pregnant women and fetuses, and prisoners, are provided special protections.

3.4. **Authority**

3.4.1. The Prime Review Board Services is established and empowered by the executive management of Emmes and by the Institution’s Federal Wide Assurance with the federal Office for Human Research Protections ("OHRP"). All Prime Review Board Servicess at Emmes subscribe to the same underlying principles and authorities, and all are subject to these SOPs.

3.4.2. Emmes' Prime Review Board Servicess have been established to review all human subject biomedical and behavioral research which involves funds, assets, employees, students, patients, or otherwise has a significant connection with Emmes, the Emmes Foundation, or any affiliate or subsidiary of either. All research involving human subjects, and all other activities
which even in part involve such research, regardless of funding or sponsorship, are subject to Prime Review Board Services review and oversight and these SOPs, unless the only involvement of humans as subjects is in one or more of the categories exempted or waived under 45 CFR §§ 46.101(b)(1-6) or 101(i).

3.4.3. Prime Review Board Services review and approval is required if:

3.4.3.1. The research is sponsored, in whole or in part, by Emmes, or any entity with a prior Prime Review Board Services Affiliation Agreement with the Prime Review Board Services, regardless of whether the research is conducted at Emmes or at another institution; the research is conducted by or under the direction of any employee, faculty, staff, student or agent of Emmes;

3.4.3.2. The research is conducted by and/or at other institutions or organizations and that institution/organization has requested Prime Review Board Services review, approval and oversight of the Research and the Prime Review Board Services has accepted the request;

3.4.3.3. The research is conducted by or under the direction of any employee, faculty, staff, student or agent of Emmes using any property or facility of Emmes; and/or the research involves the use of nonpublic information (including patient information) of Emmes, or any affiliate or subsidiary, including use of such information to identify or contact potential research subjects;

3.4.3.4. Emmes information, including identifiable patient information, is provided to an Investigator or used to identify possible study subjects;

3.4.3.5. Emmes serves as a collating center or statistical center for analysis or retention of data gathered by other study sites; and/or

3.4.3.6. The research is conducted on individuals who have a relationship with Emmes, and the research otherwise has a connection to Emmes.

3.4.3.7. In some cases, Prime Review Board Services may defer oversight to an external Prime Review Board Services (such as a commercial Prime Review Board Services or another institution’s Prime Review Board Services), provided that the Institutional Official or designee performs this designation in accordance with Emmes Research Policy 106 – Designation of
Institutional Review Board. If the external Prime Review Board Services is unable or unwilling to serve as a HIPAA Privacy Board for a given research protocol over which it has oversight, the Prime Review Board Services will retain its ability to serve in the role of a Privacy Board in reviewing HIPAA-related materials.

3.4.4. In the context of research, a person is acting as an agent of Emmes if that person is being compensated by Emmes for the performance of research activities or is under contract with Emmes to provide such services.

3.4.5. The Prime Review Board Services has the authority to ensure that research is designed and conducted in such a manner that protects the rights and welfare of participating subjects. Specifically:

3.4.5.1. The Prime Review Board Services may reject, modify or approve research based solely upon consideration of human subject protection aspects;

3.4.5.2. The Prime Review Board Services reviews, and has the authority to approve, require modification in, reject, suspend, or terminate all research activities that fall within its jurisdiction;

3.4.5.3. The Prime Review Board Services has the authority to conduct continuing review as it deems necessary to protect the rights and welfare of research subjects, including requiring progress reports from the Investigators, auditing the conduct of the study, observing the informed consent process, and/or auditing the progress of any study under its jurisdiction as it deems necessary to protect the rights and welfare of human subjects; and

3.4.5.4. The Prime Review Board Services may place restrictions on a study or on an Investigator.

3.4.6. If federal funding for a study is sought, the application for funding and the protocol must be reviewed by the Prime Review Board Services. Under current regulations, the Prime Review Board Services review can be requested once the application is identified as fundable by the applicable federal agency. The protocol and grant application must be reviewed and approved by the Prime Review Board Services prior to release of any grant funds. In some cases, additional laws, regulations or other requirements, including grant requirements, will apply to research. Examples are research studies funded by the Department of Energy, the Veterans Administration, or the Bureau of Prisons. Similarly, in some cases state law imposes additional requirements.
Compliance with all applicable laws and regulations is required.

3.5. **Relationship of Prime Review Board Services To Other Administrative Entities**

3.5.1. The Prime Review Board Services also has a relationship to other Emmes research review committees, such as various Emmes research feasibility committees. The Prime Review Board Services functions independently of, but in coordination with, those other committees. Projects may require administrative approval in addition to Prime Review Board Services approval, and research that has been reviewed and approved by the Prime Review Board Services may be subject to administrative review and approval or disapproval by institutional officials or other committees. However, those officials or committees may not approve research if it has been disapproved by the Prime Review Board Services. The Investigator is responsible for ensuring all necessary approvals have been received prior to beginning the project.

3.5.2. Other areas of Emmes with responsibility over some aspects of research include executive and administrative leadership, quality assurance, compliance, contracting, training, human resources and contract management. A data safety monitoring board (DSMB) may be used, at the request of the Prime Review Board Services. When appropriate, legal guidance is obtained. As areas of expertise are identified, the Prime Review Board Services may seek guidance from individuals with such expertise to best assure human subject protection.

4. **RESPONSIBILITIES**

4.1. **Activities Subject to Prime Review Board Services Review**

4.1.1. All human subjects research (as defined in Research Defined - Prime Review Board Services Review of Research Prime Review Board Services408), and all other activities, which even in part involve such research, regardless of sponsorship, must be submitted to the Prime Review Board Services(s) and approved in accordance with these policies before any research activity is initiated (see also, Jurisdiction of the Prime Review Board Services – Prime Review Board Services Organization Prime Review Board Services203).

4.1.2. No intervention or interaction with human subjects in research, including recruitment, identification of possible subjects or other activities preparatory to research which require access to personal information, may begin at Emmes or
using Emmes staff or assets until Prime Review Board Services has reviewed and approved the research protocol. Specific determinations as to the definition of “research” or “human subjects,” and their implications for the jurisdiction of the Prime Review Board Services under Emmes policies are determined by the Prime Review Board Services (see Research Defined – Prime Review Board Services Review of Research Prime Review Board Services408). If you are unsure of whether a given activity constitutes human subject research, obtain guidance from the Prime Review Board Services prior to engaging in the activity. The Prime Review Board Services retains final authority over the determination of what constitutes research for which Prime Review Board Services approval is required.

4.1.3. The Prime Review Board Services's purpose and responsibility is to protect the rights and welfare of human subjects. The Prime Review Board Services reviews and oversees human subject research to ensure that it meets well established ethical principles and that it complies with federal regulations at 45 CFR Part 46 and 21 CFR Parts 50 and 56, that pertain to human subject protection, as well as any other pertinent regulations and guidelines, such as the Good Clinical Practice (GCP) Guideline (E6) of the International Conference on Harmonization (ICH).

4.1.4. According to federal regulations, the activities that require Prime Review Board Services review include any human research activities involving the collection of data through intervention or interaction with a living individual, or involving identifiable private information regarding a living individual. Specific activities that require Prime Review Board Services review include, but are not necessarily limited to the following:

4.1.4.1. Clinical investigations, and any experiment that involves a test article and one or more human subjects, and that meets the requirements for prior submission to the Food and Drug Administration (FDA) under relevant investigational drug or medical device provisions of the Food, Drug, and Cosmetics Act, or experiments that need not meet the requirements for prior submission to the FDA, but the results of which are intended to be later submitted to, or held for inspection by, the FDA as part of an application for a research or marketing permit.

4.1.4.2. Collection of data about one or more of standard procedures or treatments for publication, dissemination or generalization of knowledge gained.
4.1.4.3. A patient’s care or assignment to intervention is altered for research purposes in any way (i.e., treatment or other interventions are selected on a basis other than purely based on patient condition).

4.1.4.4. A diagnostic procedure for research purposes is added to a standard treatment.

4.1.4.5. Systematic investigation involving innovative procedures or treatments. For example, if a physician plans to collect information about the innovation for scientific purposes or to repeat the innovation in other patients in order to compare it to standard treatment, it is considered research.

4.1.4.6. Emergency use of an investigational drug or medical device. Note that when emergency medical care is initiated without prior Prime Review Board Services review and approval, the patient may not be considered a research subject, and data generated from such care cannot be included in any report of a research activity.

4.1.4.7. Human cell or tissue (including blood) research that uses newly collected tissue or blood.

4.1.4.8. Human cell or tissue research that involves repositories that collect, store, and distribute human tissue materials for research purposes. However, human cell or tissue repositories activities do not require Prime Review Board Services review if material submitted to the repository satisfies both of the following conditions: (i) The material, in its entirety, was collected for purposes other than submission to the repository (e.g., the material was collected solely for clinical purposes, or for legitimate but unrelated research purposes, with no "extra" material collected for submission to the repository); and (ii) The material is submitted to the repository without any identifiable private data or information, i.e., no codes or links of any sort may be maintained, either by the submitter or by the repository, that would permit access to identifiable private data or information about the living individual from whom the material was obtained. In accordance with HIPAA and the Emmes HIPAA Policies, the requirements imposed by HIPAA do not apply to de-identified information.

4.1.4.9. Investigator-initiated research, where an Investigator both initiates and conducts, alone or with others, a clinical trial. In the case of Investigator-initiated studies, it is the Investigator's responsibility to keep Prime Review Board Services informed of unanticipated non-
serious research related events and unanticipated serious adverse events and other unexpected findings that affect the risk/benefit assessment of the research, even if the event occurred at a location for which the Institution’s Prime Review Board Services is not the Prime Review Board Services of record.

4.1.4.10. Student-conducted research, which includes all activities that meet the definition of research with human subjects and that are conducted by students for a class project or for work toward a degree, must be reviewed by the Prime Review Board Services. These activities include: (i) All master’s theses and doctoral dissertations that involve human subjects; and (ii) All projects that involve human subjects and for which findings may be published or otherwise disseminated. Federal regulations exempt some research from Prime Review Board Services review, even though the research involves human subjects. In furtherance of the Prime Review Board Services's mission, the Prime Review Board Services strongly encourages review of research which is exempt from Prime Review Board Services review per 45 CFR 46 §§ 101(b) (1-6) or 101(i) but involves human subjects or materials, in order to ensure that the subjects are appropriately protected.

4.2. Failure to Submit a Project for Prime Review Board Services Review.

4.2.1. The implications of engaging in activities that qualify as research subject to Prime Review Board Services review without first obtaining such review are serious. Results from such studies may not be published unless Prime Review Board Services approval was obtained prior to collecting the data. To do so is violation of Emmes policy. It is also against Emmes policy to use those data to satisfy thesis or dissertation requirements. If an Investigator begins a project and later finds that the data gathered could contribute to the existing knowledge base or that he or she may wish to publish the results, the Investigator should submit a proposal to the Prime Review Board Services for review as soon as possible. If the Prime Review Board Services does not approve the research, data collected cannot be used as part of a thesis or dissertation, and the results of the research cannot be published. Furthermore, the FDA may reject such data if it is submitted in support of a marketing application. The Prime Review Board Services will adhere to the requirements set forth by the federal government in 45 CFR 46, 21 CFR 56, and all other applicable federal and state laws or regulations regarding the reporting of Investigators who engage in research without first obtaining Prime Review
Board Services approval. **Investigators who engage in research without first obtaining Prime Review Board Services approval will be reported to the Office for Human Research Protections as required by law and regulation.**

4.3. **Assurance of Independence.**

4.3.1. Prime Review Board Services has the mandate to act as an independent entity within the corporate structure of Emmes. The Institutional Official (IO) has established and maintains a federal wide assurance (FWA) between Emmes (Emmes) and the United States Department of Health and Human Services (HHS), through its Office for Human Research Protections (OHRP). In that assurance, Emmes pledges to comply with federal regulations for all federally supported research. The IO, on behalf of Emmes, is authorized to establish and has established an Institutional Review Board (Prime Review Board Services) to assist in complying with applicable laws, regulations and Emmes policy in the review, approval and monitoring of human research. The Prime Review Board Services office is responsible for the day-to-day operation of the Prime Review Board Services. The office functions in coordination with Emmes officials and other review committees but at all times maintains its independence to appropriately review, approve and monitor human research. It is the responsibility of the IO to maintain and enforce the independent nature of the relationship between the Prime Review Board Services and Emmes.

5. **PROCEDURE**

5.1 None

6. **MATERIALS**

6.1 None

7. **REFERENCES**

7.1 None
<table>
<thead>
<tr>
<th>Version 0.2</th>
<th>Name</th>
<th>Status (Pending, Reviewed, Approved)</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Written by</td>
<td>Karl Nelson</td>
<td></td>
<td>14-July-2017</td>
</tr>
<tr>
<td>Reviewed by</td>
<td>Jennifer Neal-Jimenez</td>
<td></td>
<td>5-January-2018</td>
</tr>
<tr>
<td>Approved by</td>
<td>Jennifer Neal-Jimenez</td>
<td></td>
<td>8-January-2018</td>
</tr>
</tbody>
</table>
1 PURPOSE

1.1 Written operating procedures compliant with federal regulations and guidance, and Emmes policies, must be in place to ensure the highest quality and integrity of the review and oversight of research involving human subjects and for the adequate documentation of such oversight.

1.2 Compliance with these operating procedures ensures that the rights and welfare of human subjects participating in clinical research will be overseen and protected in a uniform manner, regardless of changes in personnel.

1.3 This procedure establishes the process to create and update standard operating procedures and associated checklists and worksheets.

1.4 The process begins when the IRB manager or Organizational Official determines that a standard operating procedure needs to be created or modified.

1.5 The process ends when the new or revised standard operating procedure has been approved and filed.

2 REVISIONS FROM PREVIOUS VERSION

2.1 None.

3 POLICY

3.1 Standard operating policies and procedures (SOPs) will be developed, reviewed and maintained in accordance with Emmes policies. These SOPs provide the framework for the ethical and scientifically sound conduct of human research.

4 RESPONSIBILITIES

4.1 Director, Prime Review Board Services: Responsible for establishing and periodically reviewing and modifying (as appropriate) IRB standard operating policies and procedures.
4.2 Chair, Prime Review Board Services: Responsible for establishing and periodically reviewing and modifying (as appropriate) IRB standard operating policies and procedures.

4.3 The IRB staff carries out these procedures.

5 PROCEDURE

5.1 **Review, Revision, Approval of Policies & Procedures**

5.1.1 The Director, Prime Review Board Services with input from the Chair and Vice-Chair Prime Review Board Services, and the IRB Analysts, determines when a new or updated SOP must be generated. The following may warrant changes or additions to the SOPs:

- 5.1.1.1 Changes to federal regulations;
- 5.1.1.2 New or revised federal guidelines;
- 5.1.1.3 Changes to Emmes research practice;
- 5.1.1.4 Modifications to Emmes policies and procedures; or
- 5.1.1.5 Recommendations from external auditors or inspectors.

5.1.2 Policies will be reviewed by the Director, Prime Review Board Services at intervals not less than every two years, in order to determine whether or not they are current.

5.2 **New and updated SOPs**

5.2.1 New and updated SOPs are drafted in collaboration with the appropriate members of the Prime Review Board Services Office, the Prime Review Board Services Chairs and in consultation with the Director of Regulatory Affairs and Research Compliance.

5.2.2 For new standard operating procedure, assign a number.

5.2.3 Assign an author and approver.

5.2.4 Have the author create or update the standard operating procedure following the “TEMPLATE SOP” or update the associated checklist or worksheet.

5.2.5 Have the approver review and approve the document.

5.2.6 Once approved by the approver:

- 5.2.6.1 Update the approval date.
5.2.6.2 File the approved new or revised document in the standard operating procedure files.

5.2.6.3 Post the approved procedure on the Human Research Protection Program Web site.

5.2.6.4 File the old document, if any, in the standard operating procedure files.

5.2.7 Send an email to affected individuals informing them of the change.

5.2.8 The Director Prime Review Board Services reviews the SOP for consistency, accuracy and ability for those affected by the SOP to easily and effectively implement.

5.2.9 The Director Prime Review Board Services and the Chair, Prime Review Board Services will approve all new or revised SOPs. The signature of the Director Prime Review Board Services and Chair are evidence of approval.

5.3. SOP Dissemination and Training

5.3.1. When a new or revised SOP is approved, notice of the changes will be disseminated to all appropriate individuals and departments and the revised SOP will be made available on the CHOP Research intranet.

5.3.2. Training will be provided to all members of the IRB and IRB staff, as appropriate, on each new or revised SOP. Evidence of training must be documented by signed attendance records at training sessions or by documentation in meeting minutes. (SOP 102)

5.3.3. Each new IRB member or staff employee must review the applicable SOPs, prior to undertaking a related IRB responsibility. Evidence of training must be documented following the same procedures as noted in 5.3.2.

5.4. Forms and Checklists

Checklists may be used to facilitate compliance with the regulatory requirements and IRB SOPs. Checklists are reviewed at least every 2 years.

5.4.1. Reviewer forms include checklists for the IRB reviewer to ensure compliance with the regulations, as well as space for written comments, and recommendations for IRB action (e.g., indication of approval or requested modifications).

5.4.2. Analyst’s checklists are tools used by the IRB Office staff to ensure that submissions are complete and ready for review.
6 MATERIALS

6.1 TEMPLATE SOP

7 REFERENCES

21 CFR 56.108; 21 CFR 56.109; 21 CFR 56.113
45 CFR 46.108; 45 CFR 46.109; 45 CFR 46.113
<table>
<thead>
<tr>
<th>Version 0.2</th>
<th>Name</th>
<th>Status (Pending, Reviewed, Approved)</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Written by:</td>
<td>Karl Nelson</td>
<td></td>
<td>14-July-2017</td>
</tr>
<tr>
<td>Reviewed by:</td>
<td>Jennifer Neal-Jimenez</td>
<td></td>
<td>5-January-2018</td>
</tr>
<tr>
<td>Approved by:</td>
<td>Jennifer Neal-Jimenez</td>
<td>Approved</td>
<td>8-January-2018</td>
</tr>
</tbody>
</table>
1 **PURPOSE**

1.1 The purpose of this standard operating procedure is to document the requirements for all personnel reviewing, approving, or supporting research involving human subjects, to demonstrate and maintain sufficient knowledge of the ethical principles and federal, state, and local requirements for protecting research participants.

1.2 Training of Prime Review Board Services staff and members is critical to enable the Prime Review Board Services to fulfill its mandate to protect the rights and welfare of research subjects in a consistent manner.

2 **REVISIONS FROM PREVIOUS VERSION**

2.1 None.

3 **POLICY**

3.1 Prime Review Board Services members, staff and others charged with the responsibility for reviewing, approving, and overseeing human subject research shall receive detailed training in the regulations, guidelines, ethics and policies applicable to human subjects’ research. The required training will be appropriate to the individual’s role and to the nature of the research.

4 **RESPONSIBILITIES**

4.1 Director, Prime Review Board Services: Responsible for establishing, conducting and/or supervising all relevant training programs for Prime Review Board Services members and staff.

4.2 Chair, Prime Review Board Services: Responsible for guiding the development of Prime Review Board Services member training programs, in collaboration with the Director, Prime Review Board Services.
4.3 Prime Review Board Services staff: Responsible for keeping records of all training documentation.

5 PROCEDURE

5.1 Prime Review Board Services Member/Alternate Training

5.1.1 The Director, Prime Review Board Services and Chair, Prime Review Board Services are responsible for identifying training needs for Prime Review Board Services members. The Director, Prime Review Board Services will manage the development of training programs for Prime Review Board Services members.

5.1.2 New Prime Review Board Services Members/Alternates will participate in the required training for new members.

5.1.3 All Prime Review Board Services Office staff and members of each Committee will receive initial and ongoing training regarding the responsible review and oversight of research and these policies and accompanying procedures. Training activities will include, but are not limited to the following:

5.1.3.1 A Prime Review Board Services Member notebook, which includes the Code of Federal Regulations (Common Rule), FDA Information Sheets, and important journal articles and reference materials on human subjects’ research topics.

5.1.3.2 Important regulatory and research ethics documents that are distributed as part of each meeting agenda.

5.1.4 The Director, Prime Review Board Services and the Chair, Prime Review Board Services establish the educational and training requirements for Prime Review Board Services members and staff who review biomedical and behavioral research involving human subjects at this institution and who perform related administrative duties.

5.1.4.1 Educational and training activities include, but are not limited to:

5.1.4.1.1 Periodic educational sessions with speakers from Emmes, as well as outside of Emmes (e.g., FDA or OHRP);

5.1.4.1.2 Prime Review Board Services staff and members are encouraged to participate in the IRBForum, which is a
listserv providing opportunity for discussion on issues and regulation throughout the IRB community.

5.1.4.1.3 CITI training in the protection of human subjects, HIPAA for research, and Conflict of Interest.

5.1.4.2 Initial and ongoing training is provided and documented.

5.1.5 Chairpersons will receive additional training in areas germane to their additional responsibilities as Chairs. These activities include attendance at Prime Review Board Services conferences and receiving publications outlining updates to regulations.

5.1.6 Prime Review Board Services members are encouraged to attend outside workshops and other educational opportunities focused on Prime Review Board Services issues.

5.1.7 The Director, Prime Review Board Services will monitor participation in HRPP training requirements of members and will share observations with the Chair, Prime Review Board Services. The Director and Chair will arrange for any relevant training to be provided to members before assignment of additional reviewer responsibilities.

5.2 Prime Review Board Services Staff Training

Prime Review Board Services staff will receive initial and continuing training in the areas germane to their responsibilities, including all Standard Operating Policies and Procedures (SOP).

5.2.1. Initial training of Prime Review Board Services Staff includes the following:

5.2.1.1. Attendance at Prime Review Board Services meetings as an observer to learn the process of administering a meeting,

5.2.1.2. Instructions to read the federal regulations (Common Rule and FDA regulations), as well the Prime Review Board Services SOPs.

5.2.1.3. Shadowing current staff members to learn Prime Review Board Services Office processes,

5.2.1.4. Taking the online course curriculum for human subjects [Collaborative Institutional Training Initiative (CITI)];

5.2.1.5. One-on-one discussions with the Director, Prime Review Board Services and the Prime Review Board Services chairs related to the Analyst’s assigned protocols.
5.2.2. Continuing Training of Prime Review Board Services staff includes the following:

5.2.2.1. Attendance at local and national conferences relevant to Prime Review Board Services activities,

5.2.2.2. The encouragement of Prime Review Board Services Staff members to become Certified Prime Review Board Services Professionals (CIP) within two years of their tenure in the Prime Review Board Services Office.

5.2.2.3. Review of relevant journal articles, revised regulations and guidelines circulated by the Prime Review Board Services chairs or Director, Prime Review Board Services.

5.2.2.4. Presentations and discussions at monthly staff meetings.

5.3. Documentation

Training and continuing education shall be documented and added to the records of the Prime Review Board Services as described below:

5.3.1. Copies of certifications of achievement will be placed in the Prime Review Board Services staff members’ personnel file within the office.

5.3.2. Prime Review Board Services members and staff attending the on-site, periodic educational training program may receive CME credits.

5.3.3. Prime Review Board Services Meeting minutes will reflect the members and staff who attend the meetings where the educational materials were discussed.

6 MATERIALS

6.1 None

7 REFERENCES

45 CFR 46.107
21 CFR 56.107
Prime Review Board Services Guidebook
NIH Notice: OD-00-039 Required Education in the Protection of Human Research Participants
<table>
<thead>
<tr>
<th>Version 0.2</th>
<th>Name</th>
<th>Status (Pending, Reviewed, Approved)</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Written by</td>
<td>Karl Nelson</td>
<td></td>
<td>14-July-2017</td>
</tr>
<tr>
<td>Reviewed by</td>
<td>Jennifer Neal-Jimenez</td>
<td></td>
<td>5-January-2018</td>
</tr>
<tr>
<td>Approved by</td>
<td>Jennifer Neal-Jimenez</td>
<td>Approved</td>
<td>8-January-2018</td>
</tr>
</tbody>
</table>
1 PURPOSE

1.1 The purpose of this standard operating procedure is to describe the administrative functions associated with the management of Prime Review Board Services staff. The Prime Review Board Services staff provides consistency, expertise, and administrative support to the Prime Review Board Services, and serve as a daily link between the Prime Review Board Services and the research community. In this capacity, the Prime Review Board Services staff are vital for the effective operation of the Prime Review Board Services human subjects’ protection program.

2 REVISIONS FROM PREVIOUS VERSION

2.1 None.

3 POLICY

3.1 The Emmes Institutional Official ensures that the Prime Review Board Services Office has sufficient office staff to support the efficient and effective administration of the Prime Review Board Services and its activities.

4 RESPONSIBILITIES

4.1 Director, Prime Review Board Services: Responsible for establishing personnel requirements and for hiring and evaluating the ongoing performance of the Prime Review Board Services staff.

4.2 Chair, Prime Review Board Services: Responsible for providing feedback to the Director, Prime Review Board Services regarding observations about resources and staffing of the Prime Review Board Services membership and staff.
5 PROCEDURE

5.1 Job Description and Performance Evaluations

5.1.1 The job descriptions for members of the Prime Review Board Services staff will detail the responsibilities expected of their positions. The performance of Prime Review Board Services staff will be reviewed according to current Emmes policy.

5.2 Ensuring Adequate Resources for Prime Review Board Services Operations

5.2.1 The Director, Prime Review Board Services and Chair, Prime Review Board Services in consultation with the Director, Office of Research Compliance and Regulatory Affairs review the metrics related to Prime Review Board Services activities and the required Prime Review Board Services resources and budget at least annually. The reports of these findings are forwarded to the Institutional Official.

5.2.2 The Institutional Official or their designee ensure that the Prime Review Board Services Office has sufficient resources, including staff and space to support the Prime Review Board Services’ activities. Support requirements will be determined in part, by the volume of submissions to the Prime Review Board Services and the type and complexity of the research.

5.3 Hiring and Terminating Prime Review Board Services Staff

5.3.1 The Human Resource policies of Emmes determine the policies for recruiting and hiring staff.

5.4 Documentation

5.4.1 The policies of Emmes Department of Human Resources determine the means of identifying, documenting and retaining formal staff interactions (such as performance reviews, termination procedures).

6 MATERIALS

6.1 None

7 REFERENCES

45 CFR 46.107
21 CFR 56.107
<table>
<thead>
<tr>
<th>Version 0.2</th>
<th>Name</th>
<th>Status (Pending, Reviewed, Approved)</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Written by:</td>
<td>Karl Nelson</td>
<td></td>
<td>14-July-2017</td>
</tr>
<tr>
<td>Reviewed by:</td>
<td>Jennifer Neal-Jimenez</td>
<td></td>
<td>5-January-2018</td>
</tr>
<tr>
<td>Approved by:</td>
<td>Jennifer Neal-Jimenez</td>
<td>Approved</td>
<td>8-January-2018</td>
</tr>
</tbody>
</table>
1 PURPOSE

1.1 The purpose of this standard operating procedure is to describe Prime Review Board Services review processes, including pre-review, review, and post-review procedures.

2 REVISIONS FROM PREVIOUS VERSION

2.1 None.

3 POLICY

3.1 The Prime Review Board Services reviews research involving human subjects via full board review procedures, expedited review procedures, or exempt determinations. Any activity determined to be human subjects research must be reviewed and approved by the Prime Review Board Services prior to any intervention or interaction with human subjects, including recruitment procedures.

4 RESPONSIBILITIES

4.1 Director, Prime Review Board Services: Responsible for establishing and periodically reviewing and modifying (as appropriate) Prime Review Board Services standard operating policies and procedures.

4.2 Chair, Prime Review Board Services: Responsible for establishing and periodically reviewing and modifying (as appropriate) Prime Review Board Services standard operating policies and procedures and for delegating reviews, as required to a designee.

4.3 Prime Review Board Designee: Responsible for conducting reviews or determinations as assigned by the Chair.
5 PROCEDURE

5.1 Determination of Need for Consultation

The Chair determines whether the review of the research requires expertise beyond that available on the Prime Review Board Services. For research that requires additional expertise, the Chair invites an individual with additional expertise to serve as a consultant and assist the Prime Review Board Services in its review as described in *Prime IRB SOP 203: Composition and Management of the Prime Review Board Services*.

5.1.1 Consultants are encouraged to attend Prime Review Board Services meetings; however, when attendance is not feasible, the consultant may participate via telephone conference or confer with the assigned Primary Reviewer(s) or Chair prior to the Prime Review Board Services meeting.

5.1.2 If the consultant presents at the meeting, the minutes will document key information provided by the consultant. If the consultant provides a written report, the report will be included in the Prime Review Board Services records.

5.1.3 Consults who attend Prime Review Board Services meetings will not count toward a quorum.

5.1.4 Individuals with a Conflict of Interest may not serve as consultants to the Prime Review Board Services.

5.2 Review Processes

The Prime Review Board Services ensures that all research submissions receive substantive review.

5.2.1 The Prime Review Board Services Office will ensure that all submissions are complete and available to all Prime Review Board Services members, alternates and consultants no later than five (5) days prior to the scheduled convened meeting. The Chair or the Director, HSR may permit agenda items on shorter notice.

5.2.2 When the research will involve prisoners, it will be scheduled for a meeting in accordance with *Prime IRB SOP 502: Research Involving Prisoners*.

5.2.3 Prime Review Board Services members and alternates are responsible for disclosing any conflicting interests they may have with any research under review in accordance with *Prime IRB SOP 803: Avoiding Conflicts of Interest in IRB Actions*.

5.2.3.1 Once disclosed, Prime Review Board Services members with a Conflict of Interest may remain in the Prime Review Board Services...
meeting to answer questions related to the research at the invitation of the Chair, but will recuse themselves for the deliberation and vote.

5.2.3.1.1 Prime Review Board Services meeting minutes will document the name of each recused Prime Review Board Services member, and will document that a Conflict of Interest is the reason for the absence.

5.2.4 Studies that must be reviewed by the convened Prime Review Board Services will be placed on the next available committee agenda for review.

5.2.4.1 The Prime Review Board Services Analyst, in consultation with the Prime Review Board Services Chair, selects primary reviewers for each submission based on the relevant expertise and availability of the members. Novel studies are usually assigned a primary and secondary reviewer. At least one reviewer has the appropriate scientific and scholarly expertise to review the research.

5.2.4.2 Prime Review Board Services members and alternates are expected to review the materials (described in Prime IRB SOP 300: Research Submission Requirements) in sufficient depth to be familiar with and prepared to discuss the information at the convened meeting. All Prime Review Board Services members have access to the complete submission; those who are not reviewers must review, at a minimum the application, protocol summary and consent documents(s).

5.2.5 Primary and secondary reviewer(s) responsibilities include:

5.2.5.1 Presenting their findings regarding the proposed research activities, including the scientific merit of the research, at the convened Prime Review Board Services meeting.

5.2.5.2 Reviewing and ensuring that the content and format of the informed consent document(s) (and assent document, when applicable) meet all regulatory requirements and are consistent with the information in the study protocol.

5.2.5.3 Completing and submitting all reviews in writing using the electronic Prime Review Board Services system.

5.2.5.3.1 The primary reviewer will be responsible for completing the written review of the protocol
5.2.5.3.2 The secondary reviewer will be responsible for completing the written review of the consent documents.

5.2.5.3.3 When only a primary reviewer is assigned, they will be responsible for written reviews of all of the submitted documents.

5.2.6 Research is reviewed by the convened Prime Review Board Services to ensure that the Investigator has satisfied all the requirements stated in **Prime IRB SOP 401: Criteria for Initial Approval** and **Prime IRB SOP 405: Continuing Review of Approved Research**.

5.2.7 After review and discussion of research, the Prime Review Board Services takes one of the actions described in **Prime IRB SOP 400: Categories of Action** based on the regulatory criteria for Prime Review Board Services approval as described in **Prime IRB SOP 401: Criteria for Initial Prime Review Board Services Approval**.

5.2.8 For each submission, the Prime Review Board Services determines the frequency of continuing review, based on the risks of the research and experience of the Investigator.

5.2.8.1 Federally-funded and FDA-regulated research cannot be approved for more than 1 year.

5.2.8.2 Minimal risk research that is not FDA-regulated and is not supported by a federal grant may be approved for up to three years.

5.2.8.3 For other submissions, including amendments, the Prime Review Board Services will determine if the submission affects the risks of the research and if changes to the frequency of continuing review are necessary.

5.2.9 When applicable, the Prime Review Board Services also makes the following determinations at the time of initial review of the research and may change these determinations during subsequent reviews:

5.2.9.1 Pediatric Research Risk: Benefit Determination (described in **Prime IRB SOP 503: Research Involving Children**).

5.2.9.2 Assent Requirements (described in **Prime IRB SOP 601: Assent and Parental Permission**).

5.2.9.3 Parental Permission (described in **Prime IRB SOP 601: Assent and Parental Permission**).
5.2.9.4 Device Risk Determinations (described in Prime IRB SOP 408: Determination of IND/IDE Requirements);

5.2.9.5 Waiver or alteration of the consent process and authorization (described in Prime IRB SOP 605: Waiver of Elements of Consent and Waiver of HIPAA Authorization and Prime IRB SOP 606: Requirements for and Documentation of HIPAA Authorization).

5.2.9.6 Determinations related to research involving pregnant women, human fetuses, and neonates (described in Prime IRB SOP 501: Research Involving Pregnant Women, Fetuses and Neonates).

5.2.9.7 Determinations related to research involving prisoners (described in Prime IRB SOP 502: Research Involving Prisoners)

5.2.9.8 The Prime Review Board Services retains the authority to observe or have a third party observe the consent process and the research.

5.2.9.9 Determinations related to the need for verification from sources other than the investigators that no material changes have occurred since previous Prime Review Board Services review.

5.3 Post Prime Review Board Services Review

5.3.1 Following Prime Review Board Services review by the convened Prime Review Board Services, the Prime Review Board Services Analyst drafts the meeting minutes as described in Prime IRB SOP 301: Prime Review Board Services Meeting Administration.

5.3.2 Once the meeting minutes have been reviewed and approved by the Prime Review Board Services Chair, the Prime Review Board Services Analyst provides documentation for the Investigator regarding the Prime Review Board Services ‘s determinations.

5.3.2.1 For Prime Review Board Services approvals, the documentation includes the following information:

5.3.2.1.1 Prime Review Board Services Approval and Expiration Dates;

5.3.2.1.2 Type of submission reviewed (for example Initial, Amendments or Continuing Review);

5.3.2.1.3 The date and version number of the protocol, consent document, or any other document submitted for review; and
5.3.2.1.4 Any conditions of approval and additional determinations.

5.3.2.2 For Prime Review Board Services approvals made by the convened Prime Review Board Services with revisions required, the documentation includes a listing of the required changes and clarifications that must be submitted for Prime Review Board Services review. Refer to categories of action *Prime IRB SOP 400: Categories of Action*.

5.3.2.2.1 The documentation will include the date of the Prime Review Board Services review (via convened Prime Review Board Services or expedited review) and the stipulations that must be addressed by the investigator.

5.3.2.2.2 Responses to approval with revisions required may be designated for either review by the Chair or designee or administrative confirmation.

5.3.2.2.3 Administrative confirmation may be performed by appropriately training Prime Review Board Services staff members. If the required confirmations or changes were not made exactly as specified by the Prime Review Board Services, the responses will be forwarded for expedited review.

5.3.2.2.4 When the responses do not comply with the Prime Review Board Services’s required changes or do not confirm the Prime Review Board Services’s understanding, the responses will be forwarded to the convened Prime Review Board Services for review.

5.3.2.3 When the research is disapproved, the documentation will include the date of review, reasons for disapproval, and a description of how the Investigators may respond (either in person or in writing). The responses require review by the convened Prime Review Board Services.

5.3.2.4 When the research is deferred, the documentation will include the date of review, reasons for deferral, and a description of how the investigator may respond. The responses require review by the convened Prime Review Board Services unless the research was determined to be minimal risk.
6 MATERIALS

6.1 None

7 REFERENCES

45 CFR 46.109, 46.111
21 CFR 56.109, 56.111
Prime IRB SOP 203: Composition and Management of the Prime Review Board Services
Prime IRB SOP 300: Research Submission Requirements
Prime IRB SOP 305: Prime Review Board Services Meeting Administration
Prime IRB SOP 400: Determinations and Motions.
Prime IRB SOP 401: Criteria for Prime IRB Approval
Prime IRB SOP 405: Continuing Review of Approved Research.
Prime IRB SOP 408: Determination of IND/IDE Requirements
Prime IRB SOP 501: Research Involving Pregnant Women, Fetuses and Neonates
Prime IRB SOP 503: Research Involving Children
Prime IRB SOP 504: Minors Who Are Not Children in the Research Context
Prime IRB SOP 601: Assent and Parental Permission
Prime IRB SOP 605: Waiver of Elements of Consent and Waiver of HIPAA Authorization
Prime IRB SOP 606: Requirements for and Documentation of HIPAA Authorization
<table>
<thead>
<tr>
<th>Version 0.2</th>
<th>Name</th>
<th>Status (Pending, Reviewed, Approved)</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Written by:</td>
<td>Karl Nelson</td>
<td></td>
<td>14-July-2017</td>
</tr>
<tr>
<td>Reviewed by:</td>
<td>Jennifer Neal-Jimenez</td>
<td></td>
<td>5-January-2018</td>
</tr>
<tr>
<td>Approved by:</td>
<td>Jennifer Neal-Jimenez</td>
<td>Approved</td>
<td>8-January-2018</td>
</tr>
</tbody>
</table>
1 PURPOSE

1.1 To provide guidance on the types of research activities that are subject to review and approval by the Prime Review Board Services.

2 REVISIONS FROM PREVIOUS VERSION

2.1 None.

3 POLICY

3.1 It is the policy of the Prime Review Board Services to assert jurisdiction over all human subject research subject to its Assurance.

4 RESPONSIBILITIES

4.1 Director, Prime Review Board Services: Responsible for initial review of all incoming IRB submissions to determine whether they meet the definition of human subject research.

4.2 Chair, Prime Review Board Services: Responsible for working with the Director, Prime Review Board Services on determining whether a submission meets the definition of human subjects’ research.

4.3 Prime Review Board Services: Responsible for reviewing proposed research activities in accordance with applicable IRB policies and procedures.

5 PROCEDURE

5.1 Determination of Human Subject Research

5.1.1 When an investigator submits a new application; the Director, Prime Review Board Services, the Chair, Prime Review Board Services or their designee will
review the application and determine if the study meets the criteria for human subject research.

5.1.1.1 If the research does meet the criteria of human subject research then the application will be reviewed per Prime IRB SOP 403: Expedited Review Procedures or Prime IRB SOP 104: IRB Review Processes.

5.1.1.2 If the research does not meet the criteria of human subject research the investigator will be notified through eIRB and instructed to resubmit the study under the appropriate review category.

5.2 Review and Approval of Human Subject Research

5.2.1 All research meeting the definition of human subject research regardless of sponsorship, must be reviewed and approved by Prime Review Board Services. The Prime Review Board Services must review all human subjects research if one or more of the following apply:

5.2.1.1 The research is sponsored by Emmes;

5.2.1.2 The research is conducted by or under the direction of any employee, faculty, staff, student, or agent of Emmes in connection with his/her institutional responsibilities, without regard to the location of research;

5.2.1.3 The research is conducted by or under the direction of any employee or agent of this institution using any of its property or facilities;

5.2.1.4 The research involves the use of non-public information maintained by Emmes to identify or contact human subjects or prospective subjects;

5.2.1.5 Emmes receives a direct award and or contract to conduct human subject research by the federal government, even where all activities involving human subjects are carried out by a subcontractor or collaborator; and/or

5.2.1.6 The research is conducted in accordance with an Assurance filed with the Office of Human Research Protections (OHRP) in which the Prime Review Board Services is designated as the IRB of record through an established IRB Authorization Agreement. (Prime IRB SOP 305: Reliance Agreement)

5.2.2 No research involving human subjects, including intervention, interaction, collection of private identifiable information, administration of test articles,
advertising, recruitment, or screening, may begin until the IRB has reviewed and approved the research.

5.2.3 If an investigator begins a non-research project and later finds that the data gathered could contribute to generalizable knowledge, the Investigator must submit a protocol to the IRB for review and approval at the time of the change in intent and prior to publication or presentation of the data (e.g., journal article, poster session, public speech or presentation, or project report).

5.3 Failure to Submit a Project for IRB Review
5.3.1 Failure to obtain prior IRB approval is considered non-compliance.
5.3.2 The IRB will not grant post-hoc approval for research conducted without IRB review and approval.

5.4 Human Subjects Research Review Not Reviewed by the Prime IRB
5.4.1 Research that involves either classified information or is excluded by Prime IRB SOP 106: Department of Defense will not be reviewed by the Prime IRB. The Prime Review Board Services at Emmes cannot provide oversight for this research.

6 MATERIALS
6.1 None

7 REFERENCES
45 CFR 46
21 CFR 50 and 21 CFR 56
Prime IRB SOP 403: Expedited Review Procedures
<table>
<thead>
<tr>
<th>Version 0.2</th>
<th>Name</th>
<th>Status (Pending, Reviewed, Approved)</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Written by:</td>
<td>Karl Nelson</td>
<td></td>
<td>14-July-2017</td>
</tr>
<tr>
<td>Reviewed by</td>
<td>Jennifer Neal-Jimenez</td>
<td></td>
<td>5-January-2018</td>
</tr>
<tr>
<td>Approved by</td>
<td>Jennifer Neal-Jimenez</td>
<td>Approved</td>
<td>8-January-2018</td>
</tr>
</tbody>
</table>
1 PURPOSE

1.1 This procedure establishes the process to conduct annual evaluations of the human research protection program.

1.2 The process begins the first business day of each June.¹

1.3 The process ends when all evaluations have been completed and communicated to those evaluated.

2 REVISIONS FROM PREVIOUS VERSION

2.1 None

3 POLICY

3.1 The human research protection program is evaluated annually.

4 RESPONSIBILITIES

4.1 IRB staff ensure completion of these procedures.

5 PROCEDURE

5.1 Have the Organizational Official evaluate the resources provided to the human research protection program and make adjustments as part of the budgeting process.

5.2 Evaluate whether the number of IRBs is appropriate to the volume and types of research reviewed.

5.2.1 Provide a copy of the evaluation to the Organizational Official.

5.2.2 If the number of IRBs is not appropriate to the volume and types of research reviewed, work with the Organizational Official to modify the IRB structure.

5.3 Have the IRB chair or IRB manager evaluate the knowledge, skills, and performance of each regular and alternate IRB member.

5.3.1 Provide a copy of the evaluation to the Organizational Official.

¹ Modify to coincide with the usual time for annual evaluation of personnel and resources.
5.3.2 Provide a copy of the evaluation to each IRB member.

5.3.3 Send a copy of the “TEMPLATE LETTER: IRB Member Appreciation” to the IRB member’s supervisor.

5.3.4 If needed, work with each IRB member to develop a plan to improve the individual’s knowledge, skills, and performance.

5.4 Have the **Organizational Official** evaluate the knowledge, skills, and performance of each IRB chair.

   5.4.1 Provide a copy of the evaluation to the **Organizational Official**.

   5.4.2 Provide a copy of the evaluation to each IRB chair.

   5.4.3 If needed, work with each IRB chair to develop a plan to improve the individual’s knowledge, skills, and performance.

5.5 Follow the Human Resources annual employee evaluation process to evaluate the knowledge, skills, and performance of IRB staff.

   5.5.1 Provide a copy of the evaluation to the **Organizational Official**.

   5.5.2 Provide a copy of the evaluation to each IRB staff.

   5.5.3 If needed, work with each IRB staff person to develop a plan to improve the individual’s knowledge, skills, and performance.

5.6 Complete the “WORKSHEET: IRB Composition” to evaluate whether the composition of the IRB meets regulatory and organizational requirements.

   5.6.1 Provide a copy of the evaluation to the **Organizational Official**.

   5.6.2 If the composition of an IRB does not meet regulatory and organizational requirements, work with the **Organizational Official** to modify the IRB composition.

5.7 Evaluate the subject outreach plan.

   5.7.1 Provide a copy of the evaluation to the **Organizational Official**.

   5.7.2 If the subject outreach program is not meeting organizational goals, work with the **Organizational Official** to modify the plan.

5.8 Check when the last time each IRB was registered. If more than 2 years, update the registration.\(^2\)

5.9 Check when the last time the federalwide assurance (FWA) was updated or renewed. If more than 2 years, update/renew the FWA.³

6 MATERIALS

6.1 WORKSHEET: IRB Composition

6.2 TEMPLATE LETTER: IRB Member Appreciation

7 REFERENCES

7.1 None

---

<table>
<thead>
<tr>
<th>Version 0.2</th>
<th>Name</th>
<th>Status (Pending, Reviewed, Approved)</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Written by</td>
<td>Karl Nelson</td>
<td></td>
<td>17-July-2017</td>
</tr>
<tr>
<td>Reviewed by</td>
<td>Jennifer Neal-Jimenez</td>
<td></td>
<td>5-January-2018</td>
</tr>
<tr>
<td>Approved by</td>
<td>Jennifer Neal-Jimenez</td>
<td>Approved</td>
<td>8-January-2018</td>
</tr>
</tbody>
</table>
1 PURPOSE

1.1 This procedure establishes the process to conduct quality improvement of the human research protection program.

1.2 The process begins the first business day of each Month.

1.3 The process ends when all evaluations have been completed and communicated to those evaluated.

2 REVISIONS FROM PREVIOUS VERSION

2.1 None

3 POLICY

3.1 The goal of the quality improvement plan is to achieve and maintain compliance and to achieving targeted levels of quality, efficiency, and effectiveness of the HRPP.

4 RESPONSIBILITIES

4.1 IRB staff ensure completion of these procedures.

5 PROCEDURE

5.1 Review the results of “CHECKLIST: Investigator Quality Improvement Assessment” sent out the previous month, track the results, and examine for significant trends.

5.1.1 If the results demonstrate high variability, implement an intervention to reduce variability.

5.1.2 If the results are outside performance target, implement an intervention to achieve performance target.

5.2 Complete “TEMPLATE LETTER: Investigator Quality Improvement Assessment” and Send “CHECKLIST: Investigator Quality Improvement Assessment” to 10 investigators.

5.3 Send revised tracking changes to the IRB manager and organizational official with a description of any proposed interventions.
6 MATERIALS

6.1 CHECKLIST: Investigator Quality Improvement Assessment

6.2 TEMPLATE LETTER: Investigator Quality Improvement Assessment

7 REFERENCES

7.1 None
<table>
<thead>
<tr>
<th>Version 0.2</th>
<th>Name</th>
<th>Status (Pending, Reviewed, Approved)</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Written by</td>
<td>Karl Nelson</td>
<td></td>
<td>14-July-2017</td>
</tr>
<tr>
<td>Reviewed by</td>
<td>Jennifer Neal-Jimenez</td>
<td></td>
<td>5-January-2018</td>
</tr>
<tr>
<td>Approved by</td>
<td>Jennifer Neal-Jimenez</td>
<td>Approved</td>
<td>8-January-2018</td>
</tr>
</tbody>
</table>
1 PURPOSE

1.1 This procedure establishes the process to complete daily tasks required to monitor the research review process.

1.2 The process begins each day.

1.3 The process ends when the tasks have been completed.

2 REVISIONS FROM PREVIOUS VERSION

2.1 None.

3 POLICY

3.1 Receipt deadlines are maintained in the “Prime IRB Document Management System: Awaiting Receipt.”

3.2 Protocol history is maintained in the “Prime IRB Document Management System: Protocol History.”

4 RESPONSIBILITIES

4.1 IRB staff members carry out these procedures.

5 PROCEDURE

5.1 Check the database for individuals whose training will lapse in the next 30 days who have not yet been sent a reminder.

5.1.1 Complete and send “TEMPLATE LETTER: Training Reminder.”

5.2 Check the database for protocols whose continuing review progress report is due in 30 days who have not yet been sent a reminder.

5.2.1 Complete and send “TEMPLATE LETTER: Continuing Review Reminder”
5.3 Check the database for protocols where the IRB requested modifications to secure approval, more than 30 days have lapsed without receipt of the modifications, and the following steps have not taken place:

5.3.1 Send to each affected individual “TEMPLATE LETTER: Failure to Submit Modifications Required to Secure Approval.”
5.3.2 Update the protocol history
5.3.3 Update the database to indicate that protocol was “Withdrawn by IRB.”

5.4 Check the database for continuing review progress reports that have not been submitted 30 days prior to protocol expiration and the following steps have not taken place:

5.4.1 Complete and send “TEMPLATE LETTER: Failure to Submit Continuing Review Progress Report.”
5.4.2 Update the protocol history
5.4.3 Place the individual on the Restricted list.
5.4.4 Process the failure to submit as a Finding of Non-Compliance under “Prime IRB SOP 800: Non-Compliance with Human Subjects Research Policy.”

5.5 Check the database for individuals whose Human research training has lapsed and the where following steps have not taken place:

5.5.1 Send to each affected individual “TEMPLATE LETTER: Failure to Undergo Training.”
5.5.2 Place the individual on the Restricted list.
5.5.3 Process the failure to submit as a Finding of Non-Compliance under “Prime IRB SOP 800: Non-Compliance with Human Subjects Research Policy.”
5.5.4 If the individual is an IRB member, follow “Prime IRB SOP 205: IRB Membership Removal.”

5.6 Check the database for protocols that have expired due to lack of continuing review and where the following steps have not taken place:

5.6.1 Send the “TEMPLATE LETTER: Expiration of IRB Approval.”
5.6.2 Update the protocol history

6 MATERIALS

6.1 Prime IRB Document Management System: Awaiting Receipt
6.3 TEMPLATE LETTER: Continuing Review Reminder
6.4 TEMPLATE LETTER: Expiration of IRB Approval
6.5 TEMPLATE LETTER: Training Reminder
6.6 TEMPLATE LETTER: Failure to Submit Modifications Required to Secure Approval
6.7 TEMPLATE LETTER: Failure to Submit Protocol For Emergency Use
6.8 TEMPLATE LETTER: Failure to Submit Five-Day Report of Emergency Use
6.9 TEMPLATE LETTER: Failure to Undergo Training
6.10 TEMPLATE LETTER: Failure to Submit Continuing Review Progress Report

7 REFERENCES

7.1 Prime IRB SOP 314: Prime Review Board Services Records
7.2 Prime IRB SOP 800: Non-Compliance with Human Subjects Research Policy

<table>
<thead>
<tr>
<th>Version &lt;xx&gt;</th>
<th>Name</th>
<th>Status (Pending, Reviewed, Approved)</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Written by:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reviewed by:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Approved by:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Version 0.2</td>
<td>Name</td>
<td>Status (Pending, Reviewed, Approved)</td>
<td>Date</td>
</tr>
<tr>
<td>------------</td>
<td>---------------</td>
<td>-------------------------------------</td>
<td>----------------</td>
</tr>
<tr>
<td>Written by:</td>
<td>Karl Nelson</td>
<td></td>
<td>14-July-2017</td>
</tr>
<tr>
<td>Reviewed by:</td>
<td>Jennifer Neal-Jimenez</td>
<td></td>
<td>5-January-2018</td>
</tr>
<tr>
<td>Approved by:</td>
<td>Jennifer Neal-Jimenez</td>
<td>Approved</td>
<td>8-January-2018</td>
</tr>
</tbody>
</table>
1 PURPOSE

1.1 This procedure establishes the process for a Designated Reviewer to determine whether current subjects may continue in expired research.

1.2 The process begins when the Designated Reviewer is notified of a request by an investigator of a request for current subjects to continue in expired research.

1.3 The process ends when the Designated Reviewer has communicated a decision and documented the decision in writing.

2 REVISIONS FROM PREVIOUS VERSION

2.1 None.

3 POLICY

3.1 Use the “Prime IRB Document Management System: Protocol History” to update a protocol history.

4 RESPONSIBILITIES

4.1 A Designated Reviewer is responsible to follow these procedures.

5 PROCEDURE

5.1 Determine from the investigator which subjects need to continue in the expired research, what procedures are being requested to continue, and why.

5.2 Under no circumstances can new subjects be enrolled.

5.3 Determine which subjects can continue in the research based on these principles:
   5.3.1 In general, research procedures should be safely discontinued.
5.3.2 In general, the only research procedures that should continue are those that are not available outside of the research context. If the required procedures can be provided as standard of care, these should be provided as such.

5.3.3 In general, research procedures conducted to collect data with no direct benefit to the subject should not continue.

5.3.4 In some cases, an ethical issue may be raised where the above general principles may not be followed.

5.4 In the case of Veterans Administration (VA) research, consult with the Veterans Administration (VA) Chief of Staff to make a final determination.

5.5 Communicate with the investigator using “TEMPLATE LETTER: Continuation of Subjects in Expired Research.”

5.6 Update the protocol history.

5.7 Follow “Prime IRB SOP 314: Prime Review Board Services Records.”

6 MATERIALS

6.2 TEMPLATE LETTER: Continuation of Subjects in Expired Research

7 REFERENCES
7.1 Prime IRB SOP 314: Prime Review Board Services Records
<table>
<thead>
<tr>
<th>Version 0.2</th>
<th>Name</th>
<th>Status (Pending, Reviewed, Approved)</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Written by:</td>
<td>Karl Nelson</td>
<td></td>
<td>14-July-2017</td>
</tr>
<tr>
<td>Reviewed by:</td>
<td>Jennifer Neal-Jimenez</td>
<td></td>
<td>5-January-2018</td>
</tr>
<tr>
<td>Approved by:</td>
<td>Jennifer Neal-Jimenez</td>
<td>Approved</td>
<td>8-January-2018</td>
</tr>
</tbody>
</table>
1 PURPOSE

1.1 This procedure establishes the process to identify institutional financial interests that may cause an institutional conflict of interests.

1.2 The process begins when the Organizational Official is informed of a change in the institution’s financial holdings outside of standard investments.

1.3 The process ends when the IRB staff are provided an updated list of the institution’s financial holdings.

2 REVISIONS FROM PREVIOUS VERSION

2.1 None

3 POLICY

3.1 The Technology Transfer Office, Grants and Contracts Office, and the organization’s legal counsel are to notify the Organizational Official of any change in the institution’s financial holdings not controlled by the institution’s investment managers related to:

3.1.1 Licensing
3.1.2 Investments
3.1.3 Gifts
3.1.4 Other financial interests

3.2 The fiduciary responsibility of the institution’s investment managers is to maintain a diversified portfolio of holdings that meet the institution’s goals in terms of capital appreciation, income, and risk. Institutional officials may not influence the decisions of the institution’s investment managers. This institution considers such investments to be similar to diversified mutual funds and not subject to disclosure under this policy.

4 RESPONSIBILITIES

4.1 The Organizational Official carries out these responsibilities.
5 PROCEDURE

5.1 Upon receipt of information of a change in financial interest update the list of investments that are not controlled by the institution’s investment managers. Include information about the name of the company, the names of related companies, and affected products or services.

5.2 Provide a copy of the updated list to the IRB staff.

6 MATERIALS

6.1 None

7 REFERENCES

7.1 None
<table>
<thead>
<tr>
<th>Version 0.2</th>
<th>Name</th>
<th>Status (Pending, Reviewed, Approved)</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Written by:</td>
<td>Karl Nelson</td>
<td></td>
<td>14-July-2017</td>
</tr>
<tr>
<td>Reviewed by</td>
<td>Jennifer Neal-Jimenez</td>
<td></td>
<td>5-January-2018</td>
</tr>
<tr>
<td>Approved by</td>
<td>Jennifer Neal-Jimenez</td>
<td>Approved</td>
<td>8-January-2018</td>
</tr>
</tbody>
</table>
1 PURPOSE

1.1 This procedure establishes the process to form or rely on a new IRB.

1.2 The process begins when the Organizational Official determines the need for a new IRB.

1.3 The process ends when the IRB is registered, the federalwide assurance is updated, and all members have completed training.

2 REVISIONS FROM PREVIOUS VERSION

2.1 None.

3 POLICY

3.1 IRB rosters are maintained using the “Prime Review Board Services Document Management System: IRB Roster.”

4 RESPONSIBILITIES

4.1 IRB staff members carry out these procedures.

4.2 The Organizational Official appoints IRB members, alternate members, and IRB chairs.

5 PROCEDURE

5.1 Determine from the Organizational Official whether the IRB will conduct all reviews without limitation or will be limited to certain types of reviews. Indicate this on the “IRB Scope” tab of the IRB Roster.

5.2 For external IRBs:

5.2.1 Consult the AAHRPP Web site and ensure that the IRB is AAHRPP accredited.
5.2.2 Update the federalwide assurance with the new IRB.

5.2.3 File the federalwide assurance.

5.3 For internal IRBs:

5.3.1 Select:

5.3.1.1 At least five individuals to serve as IRB members.
5.3.1.2 Additional individuals to serve as alternate IRB members, if needed.
5.3.1.3 At least one of the individuals to be the IRB chair.

5.3.2 Have each individual complete the “FORM: IRB Member Information.”

5.3.3 Obtain a copy of each individual’s résumé or curriculum vita.

5.3.4 Complete the “WORKSHEET: IRB Composition” and revise the selected individuals as needed to ensure that the IRB is appropriately constituted.

5.3.5 Prepare a “TEMPLATE LETTER: IRB Member Appointment” for each individual.

5.3.6 For each individual for review and approval by the Organizational Official:

5.3.6.1 FORM: IRB Member Information.
5.3.6.2 Résumé or curriculum vita.
5.3.6.3 LETTER: IRB Member Appointment

5.3.7 Revise the list of individuals if the Organizational Official does not approve one or more individual.

5.3.8 Once the appointment letter are signed:

5.3.8.1 Send each individual the “IRB Member Appointment” letter.
5.3.8.2 Schedule each previously untrained individual for training.
5.3.8.3 Register the IRB.\(^1\)
5.3.8.4 Update the federalwide assurance with the new IRB.\(^2\)

5.3.9 Update the IRB roster.

5.3.10 File the IRB roster, the federalwide assurance, and all checklists, résumés or curriculum vitae, and appointment letters.

5.3.11 Notify the IRB manager when all individuals have completed training.

---

6 MATERIALS

6.2 FORM: IRB Member Information
6.3 TEMPLATE LETTER: IRB Member Appointment
6.4 WORKSHEET: IRB Composition.

7 REFERENCES

7.1 45 CFR §46.107, 45 CFR §46.103(b)(3), 45 CFR §46.115(a)(5).
7.2 21 CFR §56.107, 21 CFR §56.115(a)(5).

<table>
<thead>
<tr>
<th>Version 0.3</th>
<th>Name</th>
<th>Status (Pending, Reviewed, Approved)</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Written by:</td>
<td>Karl Nelson</td>
<td></td>
<td>14-July-2017</td>
</tr>
<tr>
<td>Reviewed by:</td>
<td>Jennifer Neal-Jimenez</td>
<td></td>
<td>6-January-2018</td>
</tr>
<tr>
<td>Approved by:</td>
<td>Jennifer Neal-Jimenez</td>
<td>Approved</td>
<td>8-January-2018</td>
</tr>
</tbody>
</table>
1 PURPOSE

1.1 This procedure establishes the process to add a new IRB member.

1.2 The process begins when the Organizational Official has appointed a new IRB member to an IRB. (This may be a completely new IRB member, or the addition of a previous member to another IRB.)

1.3 The process ends when the IRB roster is updated with OHRP and the new members has completed training.

2 REVISIONS FROM PREVIOUS VERSION

2.1 None.

3 POLICY

3.1 IRB rosters are maintained using the “Prime Review Board Services Document Management System: IRB Roster.”

4 RESPONSIBILITIES

4.1 IRB staff members carry out these procedures.

4.2 The Organizational Official appoints IRB members, alternate members, and IRB chairs.

5 PROCEDURE

5.1 Determine from the Organizational Official whether the individual will be a regular IRB member, alternate IRB member, or IRB chair.

5.2 Have the individual complete the “FORM: IRB Member Information.”

5.3 For Veterans Administration (VA) representatives, obtain confirmation of the appointment from the Veterans Administration (VA) Medical Center Director.
5.4 Obtain a copy of the individual’s résumé or curriculum vita.

5.5 Update the IRB roster.

5.6 Complete “WORKSHEET: IRB Composition” and revise the membership as needed to ensure that the IRB is appropriately constituted.

5.7 Prepare a “TEMPLATE LETTER: IRB Member Appointment” for the individual.

5.8 Provide to the Organizational Official for review and approval:
   5.8.1 FORM: IRB Member Information.
   5.8.2 Résumé or curriculum vita.
   5.8.3 TEMPLATE LETTER: IRB Member Appointment

5.9 If not approve, select another individual and restart at 5.2.

5.10 Once the appointment letter is signed:
   5.10.1 Send “TEMPLATE LETTER: IRB Member Appointment” to the individual.
   5.10.2 If the individual requires training, schedule the individual for training.
   5.10.3 Update the registration of all affected IRBs.¹

5.11 File the IRB roster, “FORM: IRB Member Information”, and the individual’s résumé or curriculum vita, and “IRB Member Appointment” letter.

5.12 Notify the IRB manager when the individual has completed training.


6 MATERIALS


6.2 FORM: IRB Member Information

6.3 TEMPLATE LETTER: IRB Member Appointment

6.4 WORKSHEET: IRB Composition.

7 REFERENCES

7.1 45 CFR §46.107, 45 CFR §46.103(b)(3), 45 CFR §46.115(a)(5).
7.2 21 CFR §56.107, 21 CFR §56.115(a)(5).
7.3 Prime IRB SOP 314: Prime Services Review Board Records
<table>
<thead>
<tr>
<th>Written by:</th>
<th>Name</th>
<th>Status (Pending, Reviewed, Approved)</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Karl Nelson</td>
<td></td>
<td>14-July-2017</td>
</tr>
<tr>
<td>Reviewed by:</td>
<td>Jennifer Neal-Jimenez</td>
<td></td>
<td>6-January-2018</td>
</tr>
<tr>
<td>Approved by:</td>
<td>Jennifer Neal-Jimenez</td>
<td>Approved</td>
<td>8-January-2018</td>
</tr>
</tbody>
</table>
1 PURPOSE

1.1 This procedure establishes the process to schedule and notify individuals of convened meetings.

1.2 The process begins when there are approximately fewer than six months of meetings on the current schedule.

1.3 The process ends when meetings are scheduled at least six months in advance and individuals in the organization are notified of the schedule.

2 REVISIONS FROM PREVIOUS VERSION

2.1 None.

3 POLICY

3.1 Whenever possible the IRB schedules meetings at least three months in advance.

4 RESPONSIBILITIES

4.1 The IRB manager carries out these procedures.

5 PROCEDURE

5.1 Create a schedule of meetings for each IRB.

5.2 Post the schedule on the organization’s Web site.

5.3 Notify the following individuals of the updated schedule with an email providing a link to the IRB Web page with the schedule information:

5.3.1 IRB members.

5.3.2 Investigators and research staff on the IRB email list.

5.3.3 Organizational Official.
6 MATERIALS

6.1 None

7 REFERENCES

7.1 ICH-GCP E6 3.3.2
<table>
<thead>
<tr>
<th>Version 0.3</th>
<th>Name</th>
<th>Status (Pending, Reviewed, Approved)</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Written by</td>
<td>Karl Nelson</td>
<td></td>
<td>14-July-2017</td>
</tr>
<tr>
<td>Reviewed by</td>
<td>Jennifer Neal-Jimenez</td>
<td></td>
<td>6-January-2018</td>
</tr>
<tr>
<td>Approved by</td>
<td>Jennifer Neal-Jimenez</td>
<td>Approved</td>
<td>8-January-2018</td>
</tr>
</tbody>
</table>
1 PURPOSE

1.1 To describe the procedures used to ensure that Emmes provides the appropriate number of IRBs each with a membership properly composed for the volume and types of human subjects’ research to be reviewed and in accordance with the terms of institutional commitments and policies, federal regulations, applicable law, and standards of professional conduct and practice.

2 REVISIONS FROM PREVIOUS VERSION

2.1 None.

3 POLICY

3.1 The Chair, Prime Review Board Services at Emmes and the Director, Prime Review Board Services, will ensure that a diverse membership is appointed to the Prime Review Board Services, with the scope of expertise required to conduct its scientific review and regulatory functions.

4 RESPONSIBILITIES

4.1. Institutional Official: Responsible for ensuring the Prime Review Board Services has adequate resources to identify and recruit qualified potential members.

4.2. Director, Prime Review Board Services: Responsible for recruiting and installing new Prime Review Board Services members. Responsible for registration of the Prime Review Board Services with OHRP and the FDA as well as renewing/updating the FWA.

4.3. Chair, Prime Review Board Services: Serves as the Executive Chair for the Prime Review Board Services. Responsible for recruiting and evaluating new IRB members.
5  PROCEDURE

5.1  Membership Selection Criteria

5.1.1  The Prime Review Board Services shall consist of at least 5 regular, voting members and may include a variable number of alternates.

5.1.1.1  Prime Review Board Services members are nominated by the Chair, Prime Review Board Services in consultation with the Vice-Chair, Prime Review Board Services, other Prime Review Board Services Chairs and Vice-Chairs (as applicable) and the Director, Prime Review Board Services.

5.1.1.2  The Prime Review Board Services Chairs are nominated by the Institutional Official (or designee), Chair Prime Review Board Services, and Director, Prime Review Board Services.

5.1.1.3  All appointments of Prime Review Board Services members and Prime Review Board Services Chairs are made by.

5.1.2  The members of the Prime Review Board Services shall be sufficiently qualified through experience in their relevant field and expertise for reviewing research proposals with regard to federal regulations, applicable law and standards of professional conduct and practice, and institutional policies and commitments.

5.1.3  In order to adequately assess all aspects of research submitted for review, the membership shall be diverse and selection shall include consideration of race, gender, cultural background, clinical expertise, other relevant healthcare experience and sensitivity to such issues as community attitudes.

5.1.4  Individuals whose primary responsibility is grant management are prohibited from serving as members on the Prime Review Board Services.

5.1.5  A curriculum vitae that is current at the time of a Prime Review Board Services member’s initial appointment will be maintained in the Prime Review Board Services Office.

5.2  Composition of the Board

5.2.1  There shall be at least one member whose primary concerns are in scientific areas and at least one member whose primary concerns are in non-scientific areas. There shall be at least one member who is not otherwise affiliated with Emmes, who is not part of the immediate family of a person who is affiliated with Emmes. Regular members must include:
5.2.1.1 **Non-affiliated member(s):** The member(s), who can be either scientific or non-scientific reviewers, should be knowledgeable about the local community and be willing to discuss issues and research from that perspective. Consideration is given to recruiting individuals who speak for the communities from which Emmes draws its research subjects. The non-affiliated member typically represents the general perspective of the research participants.

5.2.1.2 **Scientific member(s):** The membership will include individuals, such as physicians and Ph.D. level physical or biological scientists.

5.2.1.2.1 When the Prime Review Board Services encounters studies involving science beyond the expertise of the members, the Prime Review Board Services may use a consultant to assist in the review, as described below and provided by 45 CFR 46.107(f) and 21 CFR 56.107(f).

5.2.1.2.2 When FDA-regulated products are reviewed, the convened meeting must include a licensed physician member, therefore, at least one (1) member of the Prime Review Board Services must be a physician.

5.2.1.3 **Non-scientific member(s):** The intent of the requirement for diversity of disciplines is to include members whose main concerns are not in scientific areas. Therefore, non-scientific members are individuals whose education, work, or interests are not solely in medical or scientific areas.

5.2.1.4 **Representatives of special groups of subjects:** Certain types of research may require members or consultants who are knowledgeable about the concerns of certain groups. For example, when the Prime Review Board Services reviews research involving prisoners, a member who can represent the interests of this group, either an ex-prisoner or an individual with specialized knowledge about this group, must be included on the Prime Review Board Services.

5.2.1.5 **Chairs:** The individual Prime Review Board Services Chairs will be highly respected individuals, fully capable of managing the Prime Review Board Services and the matters brought before it with fairness and impartiality.
5.3 Committees

5.3.1 The Prime Review Board Services reviews all human research studies as well as issues of alleged non-compliance.

5.3.2 The Prime Review Board Services will also be charged with serving as an IRB to meet for rapid reviews, and for input regarding matters of general IRB policy.

5.3.3 An evaluation of whether the composition of the Prime Review Board Services is appropriate to the volume and types of human research reviewed will be conducted at least annually. This is to ensure that reviews are accomplished in a thorough and timely manner. This evaluation is conducted via review of benchmark reports completed by the Prime Review Board Services staff and in conjunction with Prime IRB SOP 805: Prime Review Board Services Office Quality Control and Improvement Activities.

5.3.4 The Prime Review Board Services is registered with the Office of Human Research Protection (OHRP) and the FDA. Any changes in membership are reported promptly by the Prime Review Board Services Office to the OHRP and the FDA in accordance with regulatory requirements. The Director, Prime Review Board Services, is responsible for reviewing and adjusting (if necessary) the composition of the Prime Review Board Services to meet regulatory and organizational requirements.

5.3.5 A list of Prime Review Board Services members will be maintained in the Prime Review Board Services office. The list will include each member’s name, earned degrees, representative capacity, experience, licenses, board certifications, employment and any other relationships or affiliations members may have with Emmes.

5.4 Term

Members will serve on the Prime Review Board Services for a term of one year. Reappointment for additional terms may occur, by mutual agreement of the Prime Review Board Services Chairs, the Institutional Official or their designee, and the Director, Prime Review Board Services.

5.5 Appointments

The Director, Prime Review Board Services has the authority to appoint members to the Prime Review Board Services. Members will be solicited from both Emmes and from the national and local communities.
5.6 Alternates

5.6.1 Alternates will be appointed to the committee to substitute for specific members based on expertise.

5.6.2 Members may serve as a member of one committee and as an alternate member of another.

5.6.3 When a member serves as an alternate, he/she will be allowed to vote only if the member for whom they are serving as an alternate is not in attendance.

5.6.4 Alternate members receive and review the same material that the primary member receives.

5.7 Resignations and Removals

5.7.1 A member may resign before the conclusion of his/her term. The vacancy will be filled as quickly as possible.

5.7.2 Members of the Prime Review Board Services or their alternates are required to attend at 80% of regularly scheduled meetings each fiscal year. Failure to meet attendance requirements may result in removal from the Prime Review Board Services.

5.7.3 The Prime Review Board Services Chair, after consultation with the Director, Human Subjects Research and the Institutional Official or their designee, may remove a member of the Prime Review Board Services.

5.8 Compensation

5.8.1 Members of the Prime Review Board Services will be compensated, for their service as Prime Review Board Services members provided the member fulfills his/her agreed upon responsibilities.

5.8.2 Members not affiliated with Emmes shall receive compensation for their service on the Prime Review Board Services provided the member fulfills his/her agreed upon responsibilities.

5.8.3 Emmes consultants engaged for additional expertise will not be compensated for their consulting.

5.9 Liability Insurance

5.9.1 Regular and alternate members have liability insurance coverage as part of their IRB membership in their capacity as agents of Emmes.
5.10 Initial and Continual Training Requirements

5.10.1 Prime Review Board Services Chairs, members and staff will receive continuing education and training in accordance with *Prime IRB SOP 102: HRPP Training and Education for IRB Members and Staff*. Completion of training requirements will be one of the items included as part of performance evaluations.

5.11 Performance Evaluation

5.11.1 Prime Review Board Services member performance will be evaluated, on a no less than annual basis, by the Prime Review Board Services Chair and Vice Chair and the Director of Prime Review Board Services. Formal feedback will be provided by the Chair, Prime Review Board Services. This evaluation will include, but is not limited to, such performance measures as:

5.11.1.1 Attendance at meetings;
5.11.1.2 Communication with the Prime Review Board Services office;
5.11.1.3 Timely completion of assigned reviews;
5.11.1.4 Quality of completed reviews; and
5.11.1.5 Contributions (verbal and written) during the Prime Review Board Services meeting.

5.11.2 Prime Review Board Services Chair performance will be evaluated on a no less than annual basis by the Institutional Official, with input from the Director, Prime Review Board Services, Prime Review Board Services staff and members. Formal feedback will be provided to the Prime Review Board Services Chair by the Institutional Official.

5.12 Prime Review Board Services Registration


5.12.1 Initial registration has already been performed and the institution holds an approved Federalwide Assurance (FWA);

5.12.2 The Registration of the Prime Review Board Services will be renewed at least every 3 years and updated within 30 days of changes to the institution's registration information (e.g., addition of an IRB, new roster of members, a change in Prime Review Board Services Chair).
5.12.3 The FWA of the institution will be renewed at least every 3 years and updated within 30 days of changes in the institution's assurance information on record with OHRP (e.g., change in Signatory Official, addition of an IRB, change in mailing addresses);

5.12.4 OHRP will also be notified within 30 days of the Prime Review Board Services’ decision:
   5.12.4.1 to permanently cease review of HHS-conducted or FDA-regulated research;
   5.12.4.2 to review new types of FDA-regulated research (e.g., drugs products, biologicals, devices, food additives).

6 MATERIALS

6.1 None

7 REFERENCES

21 CFR 56.103(b)(2)
21 CFR 56.103(d)
21 CFR 56.106
21 CFR 56.107
45 CFR 46.103(b)(2)
45 CFR 46.103(d)
45 CFR 46.107
45 CFR 46.501 - 505
FDA Information Sheets, FAQ section II questions 14, 15
Prime IRB SOP 102: HRPP Training and Education for IRB Members and Staff
<table>
<thead>
<tr>
<th>Version 0.3</th>
<th>Name</th>
<th>Status (Pending, Reviewed, Approved)</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Written by</td>
<td>Karl Nelson</td>
<td></td>
<td>14-July-2017</td>
</tr>
<tr>
<td>Reviewed by</td>
<td>Jennifer Neal-Jimenez</td>
<td></td>
<td>6-January-2018</td>
</tr>
<tr>
<td>Approved by</td>
<td>Jennifer Neal-Jimenez</td>
<td>Approved</td>
<td>8-January-2018</td>
</tr>
</tbody>
</table>
1 PURPOSE

1.1 The purpose of this standard operating procedure is to outline the various duties of each IRB Member.

2 REVISIONS FROM PREVIOUS VERSION

2.1 None.

3 POLICY

3.1 Prime Review Board Services Members must fulfill the responsibilities outlined below in order to maintain their membership on the Prime Review Board Services at Emmes.

4 RESPONSIBILITIES

4.1 Director, Prime Review Board Services: Responsible for clearly articulating the scope of Prime Review Board Services members’ duties to potential and current Prime Review Board Services members.

4.2 Chair, Prime Review Board Services: Responsible for clearly articulating the scope of Prime Review Board Services members’ duties to potential and current Prime Review Board Services members.

5 PROCEDURE

5.1 General Duties

The task of making the Prime Review Board Services a respected part of the institutional community will fall primarily on the shoulders of the members and the Prime Review Board Services staff. The Prime Review Board Services must be perceived to be fair and impartial, immune from pressure either by Emmes administration, investigators whose protocols are brought before it, or other professional and non-professional sources.
5.1.1 The Prime Review Board Services is appointed as Institutional Committees. As such, the Prime Review Board Services members serve Emmes, rather than a particular department. Therefore, members must not allow their own interest or that of their department to supersede their duty to protect the rights and welfare of research subjects.

5.1.2 Prime Review Board Services members are expected to commit to a 1-year term and, during that time, to fulfill certain duties. These duties will be described prior to appointment and each Prime Review Board Services member is expected to fully understand the responsibilities of membership prior to accepting appointment as an IRB member.

5.1.3 Prime Review Board Services members shall attend at least 80% of the scheduled meetings per year.

5.1.4 Prime Review Board Services members shall be versed in the federal regulations governing human subjects’ protection, biomedical and behavioral research, research ethics, and the policies of Emmes germane to human subject’s protection, including:

- Prime IRB SOP 305 IRB Meeting Administration
- Prime IRB SOP 403 Expedited Review Procedures
- Prime IRB SOP 401 Criteria for Prime IRB Approval, and
- Prime IRB SOP 405 Continuing Review of Approved Research.

5.2 Specific Duties

5.2.1 Non-scientific members:

- 5.2.1.1 Non-scientific members are expected to provide input on areas germane to their knowledge, expertise and experience, professional and otherwise.

- 5.2.1.2 Non-scientific members should advise the Prime Review Board Services when additional expertise in a non-scientific area is required to assess if the protocol adequately protects the rights and welfare of subjects.

5.2.2 Scientific members:

- 5.2.2.1 Scientific members are expected to contribute to the evaluation of a study on its scientific and statistical merits and standards of practice.
5.2.2 Scientific members should advise the Prime Review Board Services when additional expertise in a scientific area is required to assess if the protocol adequately protects the rights and welfare of subjects.

5.2.3 Prime Review Board Services Chairs:

5.2.3.1 In addition to the above responsibilities (germane to the member's capacity), the Chairs moderate convened meetings of the Prime Review Board Services.

5.2.3.2 Chairs perform or delegate to one or more experienced voting IRB member review of research eligible under expedited review procedures in accordance with *Prime IRB SOP 403: Expedited Review Procedures*

5.2.3.3 Chairs are empowered to suspend human subjects research on an urgent basis as deemed necessary to protect the rights and welfare of participants. (*Prime IRB SOP 409: Suspensions and Terminations of Research*).

5.2.4 Designees of the Prime Review Board Services Chair

5.2.4.1 Designees of the Prime Review Board Services Chair are identified on the Prime Review Board Services Membership Roster and are empowered to perform Prime Review Board Services reviews using expedited review procedures and to make exempt determinations in accordance with *Prime IRB SOP 303: Research Exempt From IRB Review* and *Prime IRB SOP 403: Expedited Review Procedures*

6 MATERIALS

6.1 None

7 REFERENCES

7.1 45 CFR 46.108, 46,100, 46.113

7.2 OHRP IRB Guidebook

7.3 21 CFR 50.108 50.110, 50.113

7.4 FDA Information Sheets FAQ, Section II, question 17.

7.5. *Prime IRB SOP 303: Research Exempt From IRB Review*
7.6. Prime IRB SOP 305: IRB Meeting Administration
7.7. Prime IRB SOP 401: Criteria for Prime IRB Approval, and
7.10. Prime IRB SOP 409: Suspensions and Terminations of Research
<table>
<thead>
<tr>
<th>Version 0.2</th>
<th>Name</th>
<th>Status (Pending, Reviewed, Approved)</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Written by</td>
<td>Karl Nelson</td>
<td></td>
<td>14-July-2017</td>
</tr>
<tr>
<td>Reviewed by</td>
<td>Jennifer Neal-Jimenez</td>
<td></td>
<td>6-January-2018</td>
</tr>
<tr>
<td>Approved by</td>
<td>Jennifer Neal-Jimenez</td>
<td>Approved</td>
<td>8-January-2018</td>
</tr>
</tbody>
</table>
1 PURPOSE

1.1 The purpose of this standard operating procedure is to outline the documentation requirements when seeking Prime Review Board Services approval through the initial, continuing, or amendment review processes. These requirements apply when Prime Review Board Services serves as the IRB of record.

1.2 To enable the Prime Review Board Services members to meet their regulatory obligations, they rely on this documentation to systemically evaluate each research study to assure the protection of human subjects and adhere to the regulatory requirements.

2 REVISIONS FROM PREVIOUS VERSION

2.1 None.

3 POLICY

3.1 The Prime Review Board Services must have adequate information to review and approve all human subject research activity.

4 RESPONSIBILITIES

4.1 Director, Prime Review Board Services: Responsible for maintaining current research submission requirements for interested investigators and for preliminary triage of non-routine submissions. The required requirements and forms will be maintained on the Prime Review Board Services website.

4.2 Prime Review Board Services Analyst: Responsible for preparing member review materials and reviewing submission elements.

4.3 Resource Coordinator: Responsible for submission receipt, tracking and acknowledgements.
5 PROCEDURE

5.1 Submission Requirements for Initial Review

5.1.1 The Prime Review Board Services must review complete information in order to understand the proposed research activities and how the research will be conducted at Emmes. The documents required for initial Prime Review Board Services review include, but are not limited to, the following:

5.1.1.1 The Complete Protocol

5.1.1.1.1 For multi-center research, the protocol prepared by the study sponsor (pharmaceutical company, steering committee, overall PI or data coordinating center) and distributed to all sites, will be considered the official study protocol and must adhere to sound, scientific-design standards. Supplementary materials that augment the protocol may be required by the Prime Review Board Services in order to demonstrate that the research adheres to sound scientific-design standards. These could include items such as a detailed statistical analysis plan, manual of operations or study-specific recruitment materials.

5.1.1.1.2 When a multi-center protocol does not exist (e.g. single center research), the protocol prepared by the Principal Investigator must adhere to sound, scientific design standards.

5.1.1.2 Application completed in the electronic Prime Review Board Services management system.

5.1.1.3 Complete research grant for federally-funded research.

5.1.1.4 Informed consent document(s) and assent document(s) (if applicable).

5.1.1.5 The Sponsor-approved sample informed consent document (when one exists).

5.1.1.6 Investigators’ Brochure or product label (if applicable).

5.1.1.7 Device manual or other supporting information (if applicable).

5.1.1.8 Additional supporting materials (if applicable)

5.1.1.8.1 Key literature articles from the Reference list in the protocol.
5.1.1.8.2 Recruitment materials.

5.1.1.8.3 For Multi-center studies where the Principal Investigator is the Lead Investigator for the study, information about study oversight and operations (data coordinating center activities).

5.2 Submission Requirements for Continuing Review of Previously Approved Research

5.2.1 When conducting continuing review, the Prime Review Board Services applies the same regulatory criteria for approval of research used for initial approval of the research. In order for the Prime Review Board Services to conduct a substantive and meaningful review of the research at the time of continuing review investigators submit documentation to inform the Prime Review Board Services about study progress to date. Required documentation in the Continuing Review Application includes, but is not limited to:

5.2.1.1 Summary of the research activity since the previous initial or continuing review, including a summary of study enrollment and recruitment activities, number and reasons for subject withdrawal or discontinuation, and plans for improving lagging enrollment (when applicable). When the study is conducted at multiple institutions, the summary should include study enrollment, including information regarding equitable subject selection. The most recent study report should be provided.

5.2.1.2 New information documenting changes in the potential for risk or prospect for benefit, including information that appears in the literature, reports of all unanticipated problems involving risk to research subjects or others (see Prime IRB SOP 407: Unanticipated Problems Involving Risks to Subjects), a summary of protocol deviations.

5.2.1.3 A brief summary of significant minor protocol deviation/violations. (Major deviations, including unanticipated problem involving risks to subjects or others, should have been reported promptly; see Section 5.4, below)

5.2.1.4 A summary of any other important adverse event experiences that occurred in the past year, that did not meet the definition of an unanticipated problem involving risks to subjects or others (i.e., did not require prompt reporting to the Prime Review Board)
5.2.1.5 Data Safety Monitoring Reports (if applicable).
5.2.1.6 Audit Reports/FDA correspondence (if applicable).
5.2.1.7 Other materials as specified by the Prime Review Board Services.

5.2.2 Proposed changes to the Prime Review Board Services approved materials, including protocol, consent documents or recruitment materials may not be included in the Continuing Review; investigators must submit these changes via an Amendment.

5.3 Submission Requirements for Modifications to Previously Approved Research

5.3.1 Any proposed change in a protocol, or the conduct of the protocol, must be reviewed and approved by the Prime Review Board Services prior to implementation, except where an immediate change is necessary to eliminate a hazard to the subjects.

5.3.2 Investigators submit the following documents for Prime Review Board Services review:

5.3.2.1 Electronic amendment application
5.3.2.2 Explanation and justification (scientific or other) for the proposed changes;
5.3.2.3 A list of the proposed changes to the protocol including:
   5.3.2.3.1 Current wording in the protocol, recruitment plan or application
   5.3.2.3.2 Proposed new wording;
5.3.2.4 New or revised documents, including protocol and consent form(s) (if applicable). If the amendment includes revised documents, the submission should include both tracked-changes copy and a clean copy.
5.3.2.5 Revised grant application (if applicable).

5.4 Submission Requirements for Unanticipated Events and Protocol Deviations

5.4.1 Investigators are responsible for notifying the Prime Review Board Services of unanticipated problems involving risks to subjects or others.
5.4.1.1. These reportable events will be submitted as described in *Prime IRB SOP 407: Unanticipated Problems Involving Risks to Subjects*.

5.4.1.2. When applicable, the report should include the investigator’s action plans implemented to prevent recurrence.

5.4.2. Investigators are responsible for promptly notifying the Prime Review Board Services of major protocol deviations (non-compliance with the approved research plan). Major deviations include those that produce actual harm or had the potential to produce harm to a participant or others (an AE) and those that negatively impacted the scientific validity of the research. Examples of the latter enrollment of an ineligible subject, events that cause a subject to be withdrawn from the study; events that prevent a subject from being evaluable for the study's primary endpoint; and enrollment of more than the Prime Review Board Services-approved number of subjects.

5.4.2.1. Reports summarizing major protocol deviations will be submitted through the electronic Prime Review Board Services management system.

5.4.1.1 When applicable, the report should include the investigator’s action plan to prevent recurrence of similar events

### 6 MATERIALS

6.1 None

### 7 REFERENCES

Prime IRB SOP 303: Exempt Research
Prime IRB SOP 403: Expedited Review Procedures
Prime IRB SOP 401: Criteria for Prime IRB Approval
Prime IRB SOP 407: Unanticipated Problem Involving Risks to Subjects or Others
<table>
<thead>
<tr>
<th>Version 0.2</th>
<th>Name</th>
<th>Status (Pending, Reviewed, Approved)</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Written by</td>
<td>Karl Nelson</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reviewed by</td>
<td>Jennifer Neal-Jimenez</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Approved by</td>
<td>Jennifer Neal-Jimenez</td>
<td>Approved</td>
<td></td>
</tr>
</tbody>
</table>

Written by: Karl Nelson 14-July-2017
Reviewed by: Jennifer Neal-Jimenez 6-January-2018
Approved by: Jennifer Neal-Jimenez Approved 8-January-2018
1 PURPOSE

1.1 This procedure establishes the process to triage information submitted to the Prime Review Board Services.

1.2 The process begins when any communication is received by the Prime Review Board Services.

1.3 The process ends when a Prime Review Board Services staff member determines the appropriate action for the received information.

2 REVISIONS FROM PREVIOUS VERSION

2.1 None.

3 POLICY

3.1 Contact information is maintained in “Prime Review Board Services Document Management System: Contacts.”


3.3 The list of protocols is maintained in “Prime Review Board Services Document Management System: Protocols.”

3.4 Receipt deadlines are maintained in “Prime Review Board Services Document Management System: Awaiting Receipt.”

4 RESPONSIBILITIES

4.1 Prime Review Board Services staff members carry out these procedures.

5 PROCEDURE

5.1 Date stamp information received by mail. Scan the document and attach to the appropriate Event Instance in the Prime Review Board Services Document Management System.
5.2 Save information received by email. Attach the saved email to the appropriate Event Instance in Prime Review Board Services Document Management System.

5.3 If the submission includes new or modified contact information, create contact information or update the contact information in Prime Review Board Services Document Management System.

5.4 If the information represents a request to Withdraw from Consideration a New Protocol or Modifications to An Approved Protocol with a status of “Submitted” or “Modifications Required to Secure Approval.”

5.4.1 Add an entry to the protocol history in Prime Review Board Services Document Management System.

5.4.2 If the status was “Modifications Required to Secure Approval,” update the item’s receipt deadline in Prime Review Board Services Document Management System as received.

5.5 If the information represents a request for an approval (Approval of New Research, Continuing Review of Research, Or Modification to Previously Approved Research) or a determination whether an activity is exempt Human Research or is not Human Research:

5.5.1 If the item is a new protocol, create a new study in Prime Review Board Services Document Management System.

5.5.2 Add an entry to the protocol history in Prime Review Board Services Document Management System to indicate the current status of the protocol.

5.5.3 Follow “Prime IRB SOP 302: Pre-Review.”

5.6 If the information represents a response to Modifications Required to Secure Approval:

5.6.1 Update the item’s receipt deadline in Prime Review Board Services Document Management System as received.

5.6.2 If the submission includes a new or modified contact, make a new entry in the contact information in Prime Review Board Services Document Management System.

5.6.3 Add an entry to the protocol history in Prime Review Board Services Document Management System to indicate the current status of the protocol.

5.6.4 Follow “Prime IRB SOP 402: Modifications Required to Secure Approval.”
5.7 If the information represents a “FORM: Continuing Review Progress Report” requesting the status of the study be changed to Complete:

5.7.1 Confirm that the research has met the criteria for changing the status to Complete listed on “FORM: Continuing Review Progress Report.”

5.7.2 Add an entry to the protocol history to indicate that the status of the study has been changed to Complete.

5.8 If the information represents a notification of completion of required training, update the item’s receipt deadline as received.

5.9 If the information represents an investigator’s request to continue subjects in expired research:

5.9.1 Add an entry to the protocol history in Prime Review Board Services Document Management System.

5.9.2 Have a Designated Reviewer follow “Prime IRB SOP: Expiration of IRB Approval.”

5.10 If the information represents an item that does not fit into the above categories:

5.10.1 Add an entry to the protocol history in Prime Review Board Services Document Management System.

5.10.2 If the information represents a question, concern, or complaint:

5.10.2.1 Document the nature of the question, concern, or complaint and the contact information of the person contacting the Prime Review Board Services.

5.10.2.2 Answer any questions that are basic or general in nature. For more complicated questions, tell the person that you will call/email him/her once you have been able to find additional information. If necessary, consult with the Director, Prime Review Board Services to identify the best course of action for the question, concern, or complaint.

5.10.3 Follow “Prime IRB SOP 404: Modifications to Previously Approved Research and New Information.”

5.11 Upon completion follow “Prime IRB SOP 314: Prime Review Board Services Records.”
6 MATERIALS


7 REFERENCES

7.1 Prime IRB SOP 110: Expiration of IRB Approval
7.2 Prime IRB SOP 314: Prime Review Board Services Records
7.3 Prime IRB SOP 402: Modifications Required to Secure Approval
7.4 Prime IRB SOP 404: Modifications to Previously Approved Research and New Information
7.5 Prime IRB SOP 302: Pre-Review
<table>
<thead>
<tr>
<th>Version 0.3</th>
<th>Name</th>
<th>Status (Pending, Reviewed, Approved)</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Written by</td>
<td>Karl Nelson</td>
<td></td>
<td>14-July-2017</td>
</tr>
<tr>
<td>Reviewed by</td>
<td>Jennifer Neal-Jimenez</td>
<td></td>
<td>6-January-2018</td>
</tr>
<tr>
<td>Approved by</td>
<td>Jennifer Neal-Jimenez</td>
<td>Approved</td>
<td>9-January-2018</td>
</tr>
</tbody>
</table>
1 PURPOSE

1.1 This procedure establishes the process to pre-review a request for approval (approval of new research, continuing review of research, or modification to previously approved research) or a determination whether an activity is exempt Human Research or is not Human Research.

1.2 The process begins when the Prime Review Board Services receives a request for approval.

1.3 The process ends when the information has been placed on the agenda for a Prime Review Board Services meeting or has been provided to a Designated Reviewer.

2 REVISIONS FROM PREVIOUS VERSION

2.1 None.

3 POLICY


3.2 The addition of a previously approved protocol at a new site or sites that will be overseen by a principal investigator who will take separate and full responsibility for that site or those sites is considered a modification to previously approved research.

4 RESPONSIBILITIES

4.1 Prime Review Board Services staff members carry out these procedures.

5 PROCEDURE

5.1 Use the “WORKSHEET: Submission Materials” and to review the application materials and complete “CHECKLIST: Pre-Review.”

5.2 If the information is not complete, contact the investigator and offer the opportunity to provide additional information.
5.2.1 If the investigator will not provide additional materials, return the application and note in the protocol history that the submission was “Withdrawn.”

5.2.2 If the investigator will provide additional materials, continue processing.

5.3 If the investigator or research staff member is Restricted, contact the investigator. Explain that the investigator or research staff member is Restricted, give the reasons, and indicate that if the protocol goes to the Prime Review Board Services and the activity is Human Research, the IRB policy is to not approve the research except where necessary to maintain protection of current subjects.

5.3.1 If the investigator will not take steps to remove the Restricted status, update the protocol history to note that the submission was withdrawn.

5.3.2 If the investigator will take actions, continue processing.

5.4 Evaluate the most likely level of review:

5.4.1 If the request can be handled as a Non-Committee Review and the investigators and research staff are not Restricted, follow “PRIME IRB SOP: Non-Committee Review Preparation.”

5.4.2 If the request cannot be handled as a Non-Committee Review, place the protocol on the agenda for a convened Prime Review Board Services meeting with appropriate scope. (Do not assign a Veterans Administration (VA) protocol to a commercial IRB.)

6 MATERIALS


6.2 WORKSHEET: Pre-Review

6.3 WORKSHEET: Submission Materials

7 REFERENCES

7.1 None.
<table>
<thead>
<tr>
<th>Version 0.3</th>
<th>Name</th>
<th>Status (Pending, Reviewed, Approved)</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Written by</td>
<td>Karl Nelson</td>
<td></td>
<td>14-July-2017</td>
</tr>
<tr>
<td>Reviewed by</td>
<td>Jennifer Neal-Jimenez</td>
<td></td>
<td>6-January-2018</td>
</tr>
<tr>
<td>Approved by</td>
<td>Jennifer Neal-Jimenez</td>
<td>Approved</td>
<td>9-January-2018</td>
</tr>
</tbody>
</table>
1 PURPOSE

1.1 Define the criteria and procedures by which the IRB makes the determination of whether research is exempt from further IRB review.

2 REVISIONS FROM PREVIOUS VERSION

2.1 None.

3 POLICY

3.1 Emmes does not permit investigators to make an independent determination of exemption and reserves that role for the Prime Review Board Services. The determination of exemption will be made by a member of the Prime Review Board Services based on regulatory and/or institutional criteria and will be documented in the study file.

4 RESPONSIBILITIES

4.1. Chair, Prime Review Board Services: Responsible for evaluating submissions that claim exemption from IRB review or delegating review to designated committee member(s); authorized to make exemption determinations.

4.2. Designee (Prime Review Board Services Member): Responsible for evaluating submissions that claim exemption from IRB review; authorized to make exemption determinations.

4.3. Prime Review Board Services Staff: Responsible for pre-review of study application for completeness and for communicating queries and determination results to the investigative team.

5 PROCEDURE

5.1 After an investigator submits an application conforming to the requirements of *Prime IRB SOP 300: Research Submission Requirements*, the Prime Review Board
Services staff checks it for completeness, and returns incomplete applications with a request for changes outlining any identified deficiencies.

5.2 The application will be evaluated to determine whether or not it qualifies for exemption.

5.2.1 Questions about the application will be sent to the investigator for response.

5.2.2 If the exemption is granted, the investigator will be notified.

5.2.3 If the exemption is not granted, the investigator will be notified that the submission does not meet the criteria and will be advised about how to proceed.

5.3 Exempt Categories

Exempt: Research activities that involve no greater than minimal risk and meet applicable criteria set forth by the federal regulations (45 CFR 46.101(b), 45 CFR 46.201(b), 45 CFR 46.301(a), 45 CFR 46.401(b), and 21 CFR 56.104. For research not subject to FDA regulations or federally funded, Emmes’ expanded exempt categories will apply.

5.3.1. Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as (i) research on regular and special education instructional strategies, or (ii) research on the effectiveness of or on the comparison among instructional techniques, curricula, or classroom management methods.

The purpose of this category is to exempt research on educational practices, in an educational institution. This category does not extend to research conducted in a school setting but not related to the instruction in that institution. For example, an evaluation of two methods of fourth grade classroom instruction in a local school district would qualify as exempt research. A sociometric survey of children's preferences for playmates in the same school, involving the same children, would not qualify as exempt research. As the example indicates, research on minor students can be exempt if it is educational research in the sense intended here.

5.3.2. Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, unless: (i) information obtained is recorded in such a manner that the human subjects can be identified, directly or through identifiers linked to the subjects; and (ii) any disclosure of the subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil
liability or be damaging to the subjects' financial standing, employability, or reputation.

"Educational tests" refers to standardized tests used for educational purposes, such as a scholastic achievement test. It does not refer to personality tests or clinical evaluations. Survey or interview studies qualify as exempt unless the subjects can be identified from the records, and there are risks to the subjects due to the sensitive nature of their responses.

The Federal guideline refers only to risks associated with sensitive aspects of behavior. The Prime Review Board Services has determined that there are other types of information that might be considered sensitive and damaging if revealed, even though the information is not associated with behavior. For instance, knowledge that a person was at risk for a genetically determined disease might be a factor in denying that person employment. Therefore, the Prime Review Board Services will not treat as exempt a survey or interview study where subjects can be identified and any information is collected that could be detrimental to the subject, regardless of whether or not that information is based on the subject's own behavior.

Studies of publicly observable behavior are exempt from Federal regulations unless there are potential risks of the type described and the data are recorded in a way that could be used to identify subjects.

The Prime Review Board Services interprets "public behavior" to mean behavior that is apparent to an unconcealed observer, without the use of any special or surreptitious equipment, such as binoculars, special microphones, or recording devices.

5.3.3. Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior that is not exempt under paragraph (b)(2) of this section, if:
   (i) The human subjects are elected or appointed public officials or candidates for public office or (ii) federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.

5.3.4. Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the Investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.
Historical, literary and journalistic research of the type described earlier as being excluded typically would also be described by point 4. If a research project qualifies as excluded, the Investigator may proceed without further review.

Situations arise in which records may be excerpted from a data source that does contain identified, sensitive information, but are provided to the Investigator without identifiers. For instance, physicians might be asked to provide case summaries without identifiers. Such studies may be exempt, providing that the person excerpting the records already has authorized access to them for research purposes, and the Investigator has no access to the original records.

“Existing” means that the data are “on the shelf” at the time the researcher develops a proposal for their use. Use of data not already on the shelf is not eligible for exemption.

State and federal laws preclude the use of certain kinds of existing data (including health care information, records of drug and alcohol treatment, and records of psychiatric care) from use by researchers without human subjects’ review, regardless of whether they are “existing” or recorded by the Investigator in such a way that subjects cannot be identified.

5.3.5. Research and demonstration projects which are conducted by or subject to the approval of the department or agency heads, and which are designed to study, evaluate or otherwise examine: (i) Public benefit or service programs; (ii) Procedures for obtaining benefits or services under those programs, (iii) possible changes in or alternatives to those programs or procedures; or (iv) possible changes in methods or levels of payment for benefits or services under those programs.

The “department or agency heads” referred to are federal, not state, local, or Prime Review Board Services. This category of exempt research refers to activities sponsored by federal agencies to evaluate their own benefit or service programs.

5.3.6. Taste and food quality evaluation and consumer acceptance studies, (i) if wholesome foods without additives are consumed or (ii) if a food is consumed that contains a food ingredient at or below the level of and for a use found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture
The following five categories of research are not exempt, and always require Prime Review Board Services review: (1) research involving prisoners; (2) studies of pregnant women where the focus of the research is on pregnancy and/or the fetus; (3) research on fetuses in utero; (4) research on minor children unless the research qualifies as educational research in the sense of items 1 and 2 above, or where the research does not involve direct interaction with the child, and (5) research using non-public records.

5.4 Expanded Exempt Categories:

Research that is not funded by the federal government, is not FDA-regulated and that includes one or more of the following categories of research is eligible for a determination of exemption.

5.4.1. In addition to research that is exempt under Category 2, research that involves interviews or questionnaires of adults is exempt even when the subject of the research is a child.

5.4.2. Interviews with adolescents where the IRB would otherwise waive the requirement for parental permission.

5.4.3. In addition to research that is exempt under Category 4, research that involves the use of existing data, documents, records, pathological specimens, or diagnostic specimens collected during a previously approved research study may be eligible for a determination of exemption, provided that the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.

6 MATERIALS

6.1 CHECKLIST: Exemption Determination

7 REFERENCES

7.1 45 CFR 46.101
7.2 21 CFR 56.104, 21 CFR 56.105
7.3 Prime IRB SOP 301: Research Submission Requirements
<table>
<thead>
<tr>
<th>Version 0.2</th>
<th>Name</th>
<th>Status (Pending, Reviewed, Approved)</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Written by</td>
<td>Karl Nelson</td>
<td></td>
<td>14-July-2017</td>
</tr>
<tr>
<td>Reviewed by</td>
<td>Jennifer Neal-Jimenez</td>
<td></td>
<td>6-January-2018</td>
</tr>
<tr>
<td>Approved by</td>
<td>Jennifer Neal-Jimenez</td>
<td>Approved</td>
<td>9-January-2018</td>
</tr>
</tbody>
</table>
1 PURPOSE

1.1 The purpose of this SOP is to outline the procedures in place for determining whether submissions meet the definition of human subjects’ research, including but not limited to case series, quality improvement activities or use of data/specimens that are not readily identifiable.

2 REVISIONS FROM PREVIOUS VERSION

2.1 None.

3 POLICY

3.1 The Prime Review Board Services must review all activities that meet the definition of human subjects’ research but is not required to review activities that are (1) not research or (2) do not meet the regulatory definition of research involving human subjects. When an investigator is uncertain whether or not the federal research regulations apply, the investigator may request the IRB to issue a formal determination.

4 RESPONSIBILITIES

4.1 Director, Prime Review Board Services: Director, Prime Review Board Services (or designee) is responsible for determining whether or not the proposed activity meets the definition of research subject to regulation.

5 PROCEDURE

5.1 Prime Review Board Services Review

5.1.1 Investigators who are uncertain as to whether their proposed activities constitute either research or human subjects research may submit a request to the Prime Review Board Services office for a determination of non-human subjects’ research.
5.1.2 The Director, Prime Review Board Services or designee, will review the submission to determine if the work proposed meets the regulatory definitions of research and if it does, whether or not it meets the definition of human subjects’ research or non-human subjects research.

5.1.2.1 Any proposals that meet the regulatory definition of human subjects’ research are subject to Prime Review Board Services review and approval before any research activities commence.

5.1.2.2 Otherwise, the investigator will be notified of the Prime Review Board Services’s determination that the planned activities are non-human subjects research (i.e., do not meet the definition of research or human subjects research).

5.2. Examples of Activities That Either Do Not Meet the Definition of Research or Are Not Human Subjects Research

5.2.1. Case Report: an unsystematic clinical observation based on a single case. A case report states the outcome or response of a single patient to a diagnostic strategy or treatment. The Prime Review Board Services does not consider illustrative reports of a single patient (case report) to meet the definition of research.

5.2.2. Case Series: an unsystematic retrospective clinical observation about more than one case. A case series sometimes reports on a variety of different diagnostic or therapeutic approaches. These will not be considered research provided there are 5 illustrative cases or fewer. Case series with more than 5 illustrative cases must be submitted to the IRB in order for the IRB to determine whether or not the case series meets the definition of research.

5.2.3. Quality Improvement: systematic, iterative, data-guided activities designed to bring about immediate improvements in health delivery in particular settings. Most QI activities do not meet the definition of human subjects’ research. When there is an overlap, the QI initiative must be reviewed by the IRB prior to initiation.

5.2.4. Secondary Use of De-Identified Data or Specimens: The use of existing data or biospecimens that have been collected for clinical or research purposes and which is not readily identifiable to the investigator does not meet the definition of human subjects’ research and is not subject to Prime Review Board Services review.
6 MATERIALS

6.1 WORKSHEET: Human Subjects Research Determination

6.2 WORKSHEET: Quality Assurance Quality Improvement Determination

7 REFERENCES

7.1 None.
<table>
<thead>
<tr>
<th>Written by:</th>
<th>Karl Nelson</th>
<th>Status (Pending, Reviewed, Approved)</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reviewed by:</td>
<td>Jennifer Neal-Jimenez</td>
<td></td>
<td>6-January-2018</td>
</tr>
<tr>
<td>Approved by:</td>
<td>Jennifer Neal-Jimenez</td>
<td>Approved</td>
<td>9-January-2018</td>
</tr>
</tbody>
</table>
1 PURPOSE

1.1 The purpose of this standard operating procedure is to describe the management of the convened meeting, including the material provided to Prime Review Board Services members for review, and the information documented in the Prime Review Board Services meeting agenda and minutes.

2 REVISIONS FROM PREVIOUS VERSION

2.1 None.

3 POLICY

3.1 Meetings of the Prime Review Board Services will be convened bi-monthly or as necessary, and conducted and documented as described within this SOP and required by the regulations.

4 RESPONSIBILITIES

4.1. Director, Prime Review Board Services: Responsible for ensuring that there are adequate staff assigned and prepared for each Prime Review Board Services meeting.

4.2. Chair, Prime Review Board Services: Responsible for Prime Review Board Services meeting review conduct and leadership.

4.3. Prime Review Board Services Analyst: Responsible for meeting quorum, recording of votes and preparation of minutes.

5 PROCEDURE

5.1 Development of the Meeting Agenda

The Prime Review Board Services agenda lists all items that will be discussed at the convened meeting.
5.1.1 Complete submissions determined to require review at a convened Prime Review Board Services meeting are placed on the next available Prime Review Board Services meeting agenda for review.

5.1.2 The Prime Review Board Services Analyst monitors the items on the agenda to ensure adequate time for discussion.

5.2 **Distribution of Meeting Materials**

5.2.1 Each committee will include scientific members, non-scientific members and non-affiliated members or alternate members who represent the general perspective of subjects. To ensure consistent representation of scientific, non-scientific and non-affiliated members, attendance at meetings will be evaluated at least annually by the Director, HSR and the Prime Review Board Services Chairs, in accordance with *Prime IRB SOP 203: Composition and Management of the IRB*.

5.2.2 Members and alternates participating in a given Prime Review Board Services meeting have access to the protocol, consent documents and other pertinent study materials as described in *Prime IRB SOP 300: Research Submission Requirements*.

5.2.3 Consultants receive the materials specific to the research for which their input is requested.

5.2.4 The Prime Review Board Services Analyst finalizes the Prime Review Board Services meeting agenda which includes:

5.2.4.1 Reminder for members to disclose, at the beginning of each meeting, any actual or potential conflicts of interest they may have with an agenda item.

5.2.4.2 Prime Review Board Services educational materials;

5.2.4.3 The report of actions taken using expedited review procedures;

5.2.4.4 Minutes from the previous convened Prime Review Board Services meeting; and

5.2.4.5 Submissions scheduled for review.

5.2.5 The agenda is distributed via the electronic Prime Review Board Services management system.
5.3. **Prime Review Board Services Meeting**

5.3.1. The meeting may begin when quorum is established; if the quorum is lost during a meeting, the Prime Review Board Services does not deliberate or vote until quorum is restored.

5.3.2. The Prime Review Board Services Analyst is responsible for assuring and tracking quorum.

5.3.3. At the discretion of the presiding Chair, the Principal Investigator may be invited to appear at a convened meeting (in person or by telephone) to provide additional information. Principal Investigators will not be present during the deliberation or vote on agenda items for which they have conflicts.

5.4. **Voting**

5.4.1. The minutes for each Prime Review Board Services meeting will reflect the votes (number for, against, and abstain) of the members and alternates participating in the Prime Review Board Services meeting. Any member or alternate who abstains and is present for the deliberation and vote is counted toward the quorum.

5.4.2. In the case of a conflict of interest, the conflicted member or alternate must recuse him/herself. Recusals are identified in the minutes. A recused member or alternate is not counted toward the quorum.

5.5. **Minutes**

5.5.1. Minutes will contain sufficient detail to show the following:

5.5.1.1. Meeting attendance; including status of each attendee (non-affiliated members, consultants, etc.), guests and staff present; when FDA-regulated research is reviewed, that a physician was present for the review.

5.5.1.2. Summary of the separate deliberations for each action, including:

5.5.1.2.1. The approval period for initial and continuing reviews;

5.5.1.2.2. The action taken by the Prime Review Board Services, including the number of votes for, against, and abstaining;

5.5.1.2.3. That the regulatory criteria for approval were met for submissions the Prime Review Board Services approves or approves with modification;
5.5.1.2.4. The basis for requiring changes in or disapproving research; and

5.5.1.2.5. The discussion of controverted issues (if any) and their resolution. If there are no controverted issues associated with a submission, the minutes will not reference controverted issues.

5.5.1.3. Any protocol-specific information required for specific categories of Research, including:

5.5.1.3.1. Required Consent Documentation (Prime IRB SOP 600: Required Elements of Consent and Documentation of Consent)

5.5.1.3.2. Research involving Children (Prime IRB SOP 503: Research Involving Children)

5.5.1.3.3. Pregnant women, human fetuses or neonates (Prime IRB SOP 501: Research Involving Women, Fetuses, and Neonates)

5.5.1.3.4. Prisoners (Prime IRB SOP 502: Research Involving Prisoners)

5.5.1.3.5. For research involving subjects that might be vulnerable due to diminished mental capability or mental health, their status as wards of the state, social or economic condition or other factor, and any additional safeguards and protections that were deemed appropriate as described in Prime IRB SOP 500: Vulnerable Subjects.

5.5.1.3.6. For research involving investigational medical devices, the Prime Review Board Services’ Significant or Non-Significant risk determination.

5.5.1.3.7. For research involving the investigation of an approved drug(s) or biologic(s), the Prime Review Board Services’ determination as to whether or not the research meets the criteria for exemption from the requirement for an IND in accordance with 21 CFR 312.2.
5.5.1.4. Any discussion related to the report of actions taken using expedited review procedures reported to the committee.

5.5.1.5. Any discussion related to the educational information shared with the Prime Review Board Services.

5.5.2. During the convened Prime Review Board Services meeting the Prime Review Board Services will review the Prime Review Board Services Meeting Minutes from the previous meeting, that were distributed to members prior to the Prime Review Board Services meeting.

5.5.2.1. The Chair approves the final minutes that incorporate the comments and corrections of members, when applicable.

5.6. Participation from Remote Locations

5.6.1. Members unable to attend a Prime Review Board Services meeting in person but able to participate via telephone conference or videoconference are counted toward quorum and their votes are documented.

5.6.2. Members participating by a remote mechanism will receive and have access to Prime Review Board Services submission materials and will be able to participate in the discussion as if they were physically present

6 MATERIALS

6.1 WORKSHEET: Human Subjects Research Determination

6.2 WORKSHEET: Quality Assurance Quality Improvement Determination

7 REFERENCES

45 CFR 46.103, 45 CFR 46.108
FDA Information Sheets, 1998
Prime IRB SOP 203: Composition and Management of the IRB
Prime IRB SOP 300: Research Submission Requirements
Prime IRB SOP 403: Expedited Review Procedures
Prime IRB SOP 500: Vulnerable Subjects
Prime IRB SOP 501: Research Involving Pregnant Women, Fetuses and Neonates
Prime IRB SOP 503: Children (Additional Protections)
Prime IRB SOP 600: Required Elements of Consent and Documentation of Consent
<table>
<thead>
<tr>
<th>Version 0.2</th>
<th>Name</th>
<th>Status (Pending, Reviewed, Approved)</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Written by</td>
<td>Karl Nelson</td>
<td></td>
<td>14-July-2017</td>
</tr>
<tr>
<td>Reviewed by</td>
<td>Jennifer Neal-Jimenez</td>
<td></td>
<td>6-January-2018</td>
</tr>
<tr>
<td>Approved by</td>
<td>Jennifer Neal-Jimenez</td>
<td>Approved</td>
<td>9-January-2018</td>
</tr>
</tbody>
</table>
1 PURPOSE

1.1 This procedure establishes the process to prepare for a convened IRB meeting.

1.2 The process begins when the agenda is closed, approximately ten days before a meeting date.

1.3 The process ends when IRB meeting agenda materials have been sent to IRB members.¹

2 REVISIONS FROM PREVIOUS VERSION

2.1 None.

3 POLICY

3.1 At least one IRB member or consultant is responsible for scientific/scholarly review of research.

3.2 Protocols are reviewed by IRB members and consultants with sufficient expertise.

3.3 When IRB members review research that involves vulnerable subjects, at least one individual who is knowledgeable about or experienced in working with such subjects will be present at the meeting.

3.4 IRB members are provided sufficient information so that each member can provide an opinion on whether the regulatory criteria for approval are met.

3.5 Alternate IRB members serve the same function as other IRB members, except that if the alternate IRB member and the regular IRB member for whom the alternate member is substituting are both present only one member may vote.

¹ If the IRB uses an electronic document management system, then this SOP should be modified to note the process to make agenda items available electronically to IRB members and notify IRB members of their availability. In addition, the “WORKSHEET: Agenda Packet Contents” should be revised to be a tool for IRB members to describe the materials that IRB members are expected to review among all the materials available electronically.
3.6 Agenda materials are provided to all IRB members at least one week before convened meetings.

4 RESPONSIBILITIES
4.1 IRB staff members carry out these procedures.

5 PROCEDURE
5.1 Confirm which IRB members (regular, alternate, and chairs) will be present at the meeting.
5.2 Consult the current IRB roster to be aware of the experience, expertise and representational capacity of the IRB.
5.3 Review all submissions placed on the agenda for a convened IRB meeting.
5.4 Prepare an agenda for the meeting.
   5.4.1 Assign a primary reviewer to each agenda item.
   5.4.2 Assign a scientific/scholarly reviewer to each agenda item who has scientific/scholarly expertise in the area of research. The primary reviewer and scientific/scholarly reviewer may be the same individual.
5.5 Use the “WORKSHEET: Evaluation of Quorum and Expertise” to ensure that the meeting will be appropriately convened and to ensure the IRB will have the appropriate expertise for each protocol.
   5.5.1 If the meeting will not meet the quorum and expertise requirements, take steps to obtain the required attendance members and consultants or cancel the meeting.
   5.5.2 Follow the procedures in “Prime IRB SOP 311: Consultation to the IRB” to obtain consultants. Note any consultants on the agenda.
5.6 Prepare agenda packets for IRB members and consultants using “WORKSHEET: Agenda Packet Contents.”
5.7 Deliver or mail IRB meeting agenda packets to all IRB members and consultants.
5.8 Place a copy of all materials in the protocol file.

6 MATERIALS
6.1 WORKSHEET: Agenda Packet Contents.
6.2 WORKSHEET: Evaluation of Quorum and Expertise
7 REFERENCES

7.1 45 CFR §46.108(b)
7.2 21 CFR §56.108(b)
7.3 Prime IRB SOP 311: Consultation to the IRB.
<table>
<thead>
<tr>
<th>Version 0.2</th>
<th>Name</th>
<th>Status (Pending, Reviewed, Approved)</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Written by</td>
<td>Karl Nelson</td>
<td></td>
<td>14-July-2017</td>
</tr>
<tr>
<td>Reviewed by</td>
<td>Jennifer Neal-Jimenez</td>
<td></td>
<td>6-January-2018</td>
</tr>
<tr>
<td>Approved by</td>
<td>Jennifer Neal-Jimenez</td>
<td>Approved</td>
<td>9-January-2018</td>
</tr>
</tbody>
</table>
1 PURPOSE

1.1 This procedure establishes the process to conduct convened meetings.

1.2 The process begins when the IRB members gather for a convened meeting.

1.3 The process ends when the meeting is adjourned.

2 REVISIONS FROM PREVIOUS VERSION

2.1 None.

3 POLICY

3.1 The IRB reviews research in accordance with the applicable regulatory criteria for approval.

3.2 The IRB chair votes as a regular member.

4 RESPONSIBILITIES

4.1 The IRB chair carries out these procedures.

4.2 Primary reviewers lead IRB members through consideration of the regulatory criteria for approval.

5 PROCEDURE

5.1 Call the meeting to order.

5.2 Ask IRB members whether anyone has a Conflicting Interest in any item on the agenda and note the responses.
5.3 For each business item:

5.3.1 Table the item when notified by IRB staff when requirements for review of a specific item as defined in “WORKSHEET: Evaluation of Quorum and Expertise” are not met.\(^1\)

5.3.2 If there are IRB members with a Conflicting Interest, invite the IRB to ask questions of those members and then ask those members to leave for discussion and voting.

5.3.3 If there is a consultant present, ask the consultant to present his or her review to the IRB.

5.3.4 If a consultant provided written information to the IRB, present that information to the IRB.

5.3.5 If there is a scientific review, ask the scientific member to present his or her review to the IRB.

5.3.6 Ensure that all final contingencies on “CHECKLIST: Pre-Review” will have to be met as a condition of IRB approval.

5.3.6.1 Require any pending conflict of interest review to return to the convened IRB for review.

5.3.7 Have the primary reviewer lead the IRB through the review as described below.

5.3.8 Open the floor for additional discussion.

5.3.9 Review any modifications required by the IRB to secure approval to ensure that the IRB staff has recorded them.

5.3.10 Entertain a motion by an IRB member.

5.3.11 Call for a vote.

5.3.11.1 Only IRB members may vote.

5.3.11.2 If a member and an alternate are both present, only one may vote.

5.3.11.3 Consultants may not vote.

5.3.11.4 For a motion to be approved, it needs the approval of more than half of the members present at the meeting. (If there are 10 or 11 members present at the meeting, 6 votes are required for approval, which is greater than 5 and 5.5, respectively.)

\(^1\) “Tabled” is not an action of the IRB, but is a status based on the inability of the IRB to take an action because of reasons of quorum.
5.3.12 Re-invite IRB members with a **Conflicting Interest** back into the meeting.

5.3.13 Provide any written information provided by a member or consultant to the IRB staff.

5.4 For each protocol requesting approval have the primary reviewer:

5.4.1 Use the “WORKSHEET: Criteria for Approval and Additional Considerations” and all referenced checklists (listed below) to have the convened IRB determine which regulatory criteria are met, which are not met, and which would be met if the investigator modified the protocol as requested by the IRB.

5.4.2 Restate the IRB’s consensus regarding protocol specific findings justifying a determination when required by a checklist.

5.4.3 Make a motion for one of the following actions:

5.4.3.1 Approve (with a specific continuing review interval for initial or continuing review): Made when all criteria for approval are met.

5.4.3.2 Modifications Required to Secure Approval (with a specific continuing review interval for initial or continuing review): Made when IRB members require specific modifications such that the **Designated Reviewer** can determine whether an investigator has made the required changes without judging whether a change meets the regulatory criteria for approval. When making this motion, the assigned primary reviewer restates the modifications required by the IRB members and the IRB member’s reasons for those changes.

5.4.3.3 Defer: Made when the research does not qualify for Approval or Modifications Required to Secure Approval and the IRB has recommendations that might make the protocol approvable. When making this motion, the assigned primary reviewer describes the IRB member’s reasons for the decision and describes recommendation to make the research approvable.²

5.4.3.4 Disapprove: Made when the research does not qualify for Approval or Modifications Required to Secure Approval and the IRB has no recommendations that might make the protocol approvable. When making this motion, the assigned primary reviewer describes the IRB member’s reasons for the decision.

² If desired, “Defer” and “Disapprove” can be combined into one “Disapprove” determination.
5.5 For each Unanticipated Problem Involving Risks to Subjects or Others, Serious or Continuing Non-Compliance, or Suspension or Termination Of IRB Approval have the primary reviewer:

5.5.1 Use the “WORKSHEET: Review of Information Items” to have the convened IRB make any necessary determinations.

5.5.2 Make a motion reflecting any actions required by the IRB members.

5.6 If the IRB approves a motion involving a Suspension of IRB Approval or Termination of IRB Approval follow “Prime IRB SOP 409: Suspension or Termination of IRB Approval.”

5.7 Temporarily adjourn the meeting when notified by IRB staff that quorum has been lost.

5.8 Adjourn the meeting when there is no further business.

6 MATERIALS

6.1 CHECKLIST: Approval Criteria

6.2 CHECKLIST: Short Form of Consent Documentation

6.3 CHECKLIST: Waiver or Alteration of the Consent Process

6.4 CHECKLIST: Waiver of Written Documentation of the Consent Process

6.5 CHECKLIST: Waiver of the Consent Process for Planned Emergency Research

6.6 WORKSHEET: Evaluation of Quorum and Expertise

7 REFERENCES


7.2 45 CFR §46.109, §46.116, §46.117.

7.3 Prime IRB SOP 409: Suspension or Termination of IRB Approval
<table>
<thead>
<tr>
<th>Version 0.2</th>
<th>Name</th>
<th>Status (Pending, Reviewed, Approved)</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Written by:</td>
<td>Karl Nelson</td>
<td></td>
<td>14-July-2017</td>
</tr>
<tr>
<td>Reviewed by:</td>
<td>Jennifer Neal-Jimenez</td>
<td></td>
<td>6-January-2018</td>
</tr>
<tr>
<td>Approved by:</td>
<td>Jennifer Neal-Jimenez</td>
<td>Approved</td>
<td>9-January-2018</td>
</tr>
</tbody>
</table>
1 PURPOSE

1.1 This procedure establishes the process to monitor quorum at convened IRB meetings.

1.2 The process begins when the IRB staff member responsible for monitoring quorum notifies the IRB chair that quorum has been attained.

1.3 The process ends when the meeting is adjourned.

2 REVISIONS FROM PREVIOUS VERSION

2.1 None.

3 POLICY

3.1 None.

4 RESPONSIBILITIES

4.1 IRB staff members carry out these procedures.

5 PROCEDURE

5.1 At meetings consult the “WORKSHEET: Evaluation of Quorum and Expertise” to determine that the meeting is appropriately convened by meeting the “QUORUM REQUIREMENTS” and notify the IRB chair when the meeting is appropriately convened.

5.2 Before each protocol consult the “WORKSHEET: Evaluation of Quorum and Expertise” to determine that the meeting is appropriately convened by meeting the “EXPERTISE REQUIREMENTS” and notify the IRB chair when the meeting is not appropriately constituted for the review of that protocol.

5.3 When a member leaves the meeting room for any reason (including a Conflicting Interest) consult the “WORKSHEET: Evaluation of Quorum and Expertise” to
determine that the meeting continues to be appropriately convened by meeting the “QUORUM REQUIREMENTS” and notify the IRB chair when the meeting is not appropriately convened.

6 MATERIALS

6.1 WORKSHEET: Evaluation of Quorum and Expertise

7 REFERENCES

7.1 45 CFR §46.108(b)
7.2 21 CFR §56.108(c)
<table>
<thead>
<tr>
<th>Version 0.2</th>
<th>Name</th>
<th>Status (Pending, Reviewed, Approved)</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Written by</td>
<td>Karl Nelson</td>
<td></td>
<td>14-July-2017</td>
</tr>
<tr>
<td>Reviewed by</td>
<td>Jennifer Neal-Jimenez</td>
<td></td>
<td>6-January-2018</td>
</tr>
<tr>
<td>Approved by</td>
<td>Jennifer Neal-Jimenez</td>
<td>Approved</td>
<td>9-January-2018</td>
</tr>
</tbody>
</table>
1 PURPOSE

1.1 This procedure establishes the process to record minutes for convened meetings.

1.2 The process begins when the meeting is called to order.

1.3 The process ends when the minutes are approved by the IRB chair or IRB Manager.

2 REVISIONS FROM PREVIOUS VERSION

2.1 None.

3 POLICY

3.1 Minutes are to comply with regulatory and guidance requirements.

3.2 Minutes are to record separate deliberations for each action.

3.3 Minutes are officially approved on behalf of the IRB by the IRB chair or IRB manager.

3.4 IRB members may make corrections to minutes.

3.5 The IRB writes minutes and makes them available for review within three weeks of the meeting date.

3.6 Minutes may not be altered by anyone including a higher authority once accepted by the convened IRB.

4 RESPONSIBILITIES

4.1 IRB staff members carry out these procedures.
5 PROCEDURE

5.1 Use the “TEMPLATE MINUTES” to record observations at meetings.

5.2 Under “Attendance Table” record each voting member (regular members and alternates) present at the meeting at any time: (Do not record non-voting members under “Attendance Table.”)

5.2.1 Name.

5.2.2 Status: E.g., chair, vice chair, scientific member, non-scientific member, unaffiliated member, representative of vulnerable population (specify), prisoner representative, Veterans Administration (VA) representative, or alternate member.

5.2.3 For alternate members who are substituting for a regular member, indicate the name of the regular member for whom the alternate member is substituting.

5.2.4 Whether the member was present by teleconference.

5.3 Record the total number of members present on the current IRB roster. Exclude alternate members in this count.

5.4 Record the number of members required for quorum. Divide the number of members by two and select the next whole number. For example, if there are 10 IRB members on the roster, then 10/2 = 5 and the next whole number is 6. If there 11 IRB members on the roster, then 11/2=5.5 and the next whole number is 6.

5.5 Indicate whether members present by teleconference received all pertinent material before the meeting and were able to actively and equally participate in all discussions. Delete if no members were present by teleconference.

5.6 Record the meeting start time.

5.7 Record a summary of each business item that was discussed.

5.8 For each protocol reviewed record:

5.8.1 Protocol ID

5.8.2 Protocol title.

5.8.3 Investigator name.

5.8.4 Type of review: Initial review, continuing review, or review of modifications to previously approved research
5.8.5 Consultant report: Summarize the key information provided the consultant. Delete if there was no consultant.

5.8.6 Controverted issues (when the IRB members express a difference of opinion among themselves) and their resolution. Indicate “None” or record using the “Controverted Issue/Resolution” table. If there was no resolution, indicate this.

5.8.7 Motion: Approved, Approved with Modifications, Deferred, Disapproved. For initial or continuing review add the period of approval to the motion. If the protocol was tabled, indicate this.

5.8.8 Vote: Record as the number of members for, against, abstaining, absent, or recused. List the names of IRB members who were absent or recused. Do not count votes of consultants. If both a regular IRB member and the alternate IRB member are present at the meeting record the vote of just one.

5.8.8.1 For: Voting for the motion.

5.8.8.2 Against: Voting against the motion.

5.8.8.3 Abstain: Present for the vote, but not voting “For” or “Against.”

5.8.8.4 Absent: Listed under “Members Present” but not present for the discussion and vote on this protocol for reasons other than a Conflicting Interest. List the names of absent members in the vote. For example: “For: 7 Against: 3 Abstain: 2 Absent: 2 (Alice Baker, Charlie Delta) Recused: 0”

5.8.8.5 Recused: Listed under “Members Present” but not present for the discussion and vote on this protocol for because of a Conflicting Interest. List the names of recused members in the vote. For example: “For: 7 Against: 3 Abstain: 2 Absent: 0 Recused: 2 (Evelyn Foxtrot, George India)”

5.8.9 Level of risk determined by the convened IRB: Minimal risk or more than minimal risk.

5.8.10 Regulatory determinations and protocol-specific findings supporting those determinations: If the research involves waiver or alteration of consent, waiver of written documentation of consent, children, pregnant women, pregnant women, neonates, prisoners, or cognitively impaired adults, enter “See IRB Records,” enter “See IRB records for this protocol” and ensure that the corresponding completed checklist is in the IRB records, or include one of more of the “Determination/Protocol Specific Findings” tables in the “TEMPLATE MINUTES.” Delete if the IRB disapproved the research. Otherwise enter “None.”
5.8.11 Justification of any deletion or substantive modification of information concerning risks or alternative procedures contained in the DHHS-approved sample consent document: Delete if a DHHS-approved sample consent form was not reviewed. Otherwise indicate “None” or describe the changes and the rationale.

5.8.12 Rationale for a significant/non-significant device determination: Delete if there were no devices submitted under the abbreviated IDE requirements. Otherwise describe the rationale for the determination.

5.8.13 Modifications required to secure approval: Delete if there were no modifications required to secure approval. Otherwise, include the “Modifications Required to Secure Approval Table” in the “TEMPLATE MINUTES.”

5.8.14 Reasons the IRB tabled the protocol: Delete if the IRB did not table the protocol.

5.8.15 Reasons for the deferral or disapproval and recommended changes: Delete if the IRB did not defer or disapprove the research.

5.9 For each problem reviewed record:

5.9.1 Description of problem.

5.9.2 Protocol ID: Omit if there is no specific protocol.

5.9.3 Individual(s) involved:

5.9.4 Controversial issues and their resolution:

5.9.5 Motion: Include any IRB determination of whether the problem is (1) an unfounded Allegation of Non-Compliance, (2) Non-Compliance that is neither Serious nor Continuing Non-Compliance, (3) Serious or Continuing Non-Compliance, (4) not an Unanticipated Problem Involving Risks to Subjects or Others, (5) an Unanticipated Problem Involving Risks to Subjects or Others.

5.9.6 Vote: Record as the number of members for, against, abstaining, absent, or recused. List the names of IRB members who were absent or recused.

5.9.7 Reasons for Suspension or Termination of IRB Approval.

5.10 Record the meeting end time.

5.11 Within one business day revise minutes for accuracy and provide them to the IRB chair or IRB manager for review and approval.
5.12 Once approved by the IRB chair or IRB manager, provide a copy of the minutes by email to:

5.12.1 Organizational Official.
5.12.2 IRB members.
5.12.3 Veterans Administration (VA) Research and Development Committee

5.13 IRB members have one week to review the minutes.

5.14 Attach the following documents to the approved minutes: (VA)

5.14.1 List of exemptions granted.
5.14.2 List of protocols granted approval using the expedited procedure.
5.14.3 List research approved with modifications to secure approval and granted approval by the chair or designee after confirmation that the modifications were made.


6 MATERIALS

6.1 TEMPLATE MINUTES

7 REFERENCES

7.1 21 CFR §56.115(a)(2)
7.2 45 CFR §46.115(a)(2)
<table>
<thead>
<tr>
<th>Version 0.2</th>
<th>Name</th>
<th>Status (Pending, Reviewed, Approved)</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Written by</td>
<td>Karl Nelson</td>
<td></td>
<td>14-July-2017</td>
</tr>
<tr>
<td>Reviewed by</td>
<td>Jennifer Neal-Jimenez</td>
<td></td>
<td>6-January-2018</td>
</tr>
<tr>
<td>Approved by</td>
<td>Jennifer Neal-Jimenez</td>
<td>Approved</td>
<td>9-January-2018</td>
</tr>
</tbody>
</table>
1 PURPOSE

1.1 The purpose of this policy is to promote objectivity and address the possibility of bias or perceived bias in the review process. To that end, IRB members will not participate in the review and approval process for any project with which they have, or appear to have, a present or potential personal, professional, or financial conflicting interest. The requirement to recuse oneself from review pertains to any type of review conducted by the IRB, including initial or continuing reviews, review of modifications, event reports, unanticipated problems, and potential non-compliance.

2 REVISIONS FROM PREVIOUS VERSION

2.1 Revised in full.

3 POLICY

3.1 It is the policy of Prime Review Board that all IRB member and IRB consultant conflicts of interest are reported to the Prime office in order to ensure the integrity of the review process, and to protect the welfare of research participants. Conflicts must be reported before IRB review of the conflicted research proposal. Conflicts of interest will be eliminated where possible, but will otherwise be promptly disclosed and effectively managed.

4 RESPONSIBILITIES

4.1 IRB members (regular and alternate) and consultants follow these procedures.

5 PROCEDURE

5.1 An IRB member is considered to have a conflict of interest in any of the following circumstances:

5.1.1 Financial Conflicts of Interest:

5.1.1.1 The member has, or has had at any time in the past 24 months, an equity interest, financial interest (including travel reimbursement), or managerial interest in a sponsoring entity or product being evaluated or provided by a commercial entity in the research, or has an immediate family member (i.e. spouse, partner, parent, sibling, child) with such an interest;
5.1.1.2 The member has received or will receive compensation with value that cannot be readily determined but that may be affected by the outcome of the research project under review, or by a competing research project;

5.1.1.3 The member has a proprietary interest in the research, such as a non-provisional patent application, patent, trademark, copyright, or licensing agreement.

5.1.2 Non-Financial Conflict of Interest:

5.1.2.1 The member is or will be an investigator or member of the research team involved in the design, conduct, oversight or reporting of the research under review by the IRB, or has an immediate family member (i.e. spouse, partner, parent, sibling, child) with such an interest;

5.1.2.2 The member has a relationship with an individual who is one of the investigators or member of the research team involved in the design, conduct, or reporting of the research under review by the IRB that could impact, or appear to impact, the ability to review objectively;

5.1.2.3 The member is employed by the same institution as the principal investigator for the research submission under review by the IRB;

5.1.2.4 The member has a role in decision making (e.g. as an executive or director) as the sponsor of research;

5.1.2.5 The member has a nonfinancial interest (personal circumstance, ethical belief, or other factor) that may be conflicting and/or otherwise affect, or appear to affect, the ability to review the research objectively.

5.1.3 Each board member is responsible for disclosing conflicts of interest to the Prime office as soon as the member is aware of the conflict.

5.2 Identification of Conflicts of Interests

5.2.1 All members of the IRB complete a “Conflict of Interest Disclosure Statement” when first appointed to the board, when there are changes in financial circumstances, and annually thereafter.

5.2.1.1 Financial interests will be disclosed to the Director of Prime Review Board via the Conflict of Interest Disclosure Statement

5.2.1.2 Disclosures will be kept on file in the Prime office and made accessible only to the Director of Prime Review Board and Prime office staff.

5.2.2 Consultants to the Prime IRB will complete a “Conflict of Interest Disclosure Statement” upon agreeing to consult on the review. Conflict of interest is defined for consultants as for members in section 5.1.

5.2.2.1 A possible consultant who discloses a COI usually will not provide consultation to the IRB. However, a conflicted consultant may still be asked to provide consultation when:
5.2.2.1.1 The IRB lacks specific expertise that is important to the review AND
5.2.2.1.2 An alternate consultant cannot be located

5.2.2.1.2.1 The consultant will be asked to divulge the details of any financial or non-financial COIs and the COI will be documented and the conflict will be managed as follows:

5.2.2.1.2.1.1 The consultant will be provided with specific questions to address that are as focused and as objective as possible.
5.2.2.1.2.1.2 The IRB will be notified of the consultant’s COI

5.3 Actions and Responsibilities

5.3.1 Upon discovery of a conflict or potential conflict

5.3.1.1 The board member, or consultant, should alert the Prime office to the presence of a conflict, or potential conflict, as soon as the conflict is known,

5.3.1.1.1 In the case of full-board review, disclosure should occur as far in advance of the relevant IRB meeting as possible, or if not previously disclosed, at the beginning of the IRB meeting.

5.3.1.1.2 In the case of expedited review, the reviewer must notify the Prime office immediately so that the item can be reassigned. Upon notification by the Prime office, it is the responsibility of the IRB Chair to assign a new reviewer.

5.3.1.2 If not previously disclosed, the Prime office will send a “Conflict of Interest Disclosure Statement” to collect a brief statement recording the nature of the conflict from the conflicted member.

5.3.1.3 Disclosures made to the Prime office are shared with the IRB Chair. The IRB Chair is responsible for identifying disclosures at the beginning of every IRB meeting, and will confirm that there are no additional conflicts to disclose.

5.3.2 In cases where disclosures constitute a conflict of interest:

5.3.2.1 Conflicted members will be present only to provide information as requested by the Board and will remove themselves from the meeting during the discussion and voting phases of the review and approval process.

5.3.2.1.1 Members who are recused do not count toward quorum for the review in which they are conflicted. Recused members may return after the vote and be added back to the member count for quorum. Prime staff are responsible for monitoring IRB meeting attendance to ensure that quorum is maintained.
5.3.2.2 If the IRB Chair has a conflict of interest, he or she may not chair the meeting during the consideration of the item for which the conflict exists and will appoint an acting chair for the relevant review.

5.3.2.3 IRB members who have a conflict with a site-specific application are recused from review of site-specific materials for that site.

5.3.3 When it is not clear whether a conflict of interest exists, the individuals listed below make a determination whether (1) the disclosure constitutes a conflict of interest; (2) the disclosure does not constitute a conflict of interest, or (3) the disclosure does not constitute a conflict of interest, but requires management to avoid the perception of conflict.

Conflicted IRB member: IRB Chair or Director of Prime Review Board

Conflicted IRB Chair: Director of Prime Review Board

The determination is based on gathering as much information as necessary from relevant sources.

5.3.3.1 If the disclosure does not constitute a conflict of interest but requires management to avoid the perception of conflict, a management plan will be developed in order to avoid the perception of conflict. The management plan is subject to approval by a majority of the IRB members.

5.3.4 The IRB Chair will call attention to the conflict of interest policy at the beginning of each meeting. An entry in each meeting’s minutes will reflect adherence to this policy.

5.3.5 If a previously unrecognized conflict is disclosed after the review is completed, the Board Chair and Director will meet to determine an appropriate course of action and the relevant information documented.

5.4 Documentation

5.4.1 IRB minutes will record:

5.4.1.1 The name of the conflicted member and the review item(s) for which they are conflicted

5.4.1.2 When the conflicted member left the meeting, and will note ‘conflict of interest’ as the reason for leaving.

5.4.1.3 A statement that the member with a COI does not count toward quorum.

5.4.2 Prime IRB will maintain records for at least 3 years for:

5.4.2.1 COI Disclosure Statements

5.4.2.2 Management of COIs

6 MATERIALS

6.1 Conflict of Interest Disclosure Statement
7 REFERENCES

7.1 21 CFR §56.107(e).
7.2 45 CFR §46.107(e).

<table>
<thead>
<tr>
<th>Written By</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gillian Beach</td>
<td>14 December 2018</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Reviewed By</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jennifer Christensen (Vice-Chair, IRB)</td>
<td>19 December 2018</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Approved By</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Toby Schonfeld</td>
<td>31 December 2018</td>
</tr>
</tbody>
</table>
1 PURPOSE

1.1 This procedure establishes the process for the IRB to obtain consultants.

1.2 The process begins when the IRB staff or IRB member has identified the need for consultation.

1.3 The process ends when the consultant has provided additional expertise to the IRB.

2 REVISIONS FROM PREVIOUS VERSION

2.1 None.

3 POLICY

3.1 The IRB invites consultants with competence in special areas to assist in the review of issues which require expertise beyond or in addition to that available on the IRB.

3.2 Consultants with a Conflicting Interest may not provide information to the IRB.

4 RESPONSIBILITIES

4.1 For review by a convened IRB, IRB staff members carry out these procedures.

4.2 For Non-Committee Review, the Designated Reviewer carries out these procedures.

5 PROCEDURE

5.1 Identify a consultant with the required expertise who can provide a review.

Determine whether the consultant has a Conflicting Interest as defined in “SOP: Definitions.” If so, obtain another consultant.

5.2 Contact the consultant and determine availability for review.
5.3 Prepare a packet for the consultant using the “WORKSHEET: Agenda Packet Contents”. The information in the packet may be limited to those needed for the consultant to review in order provide the additional expertise needed. If the additional expertise needed does not require review of any materials, no materials need be provided.

5.4 For review by the convened IRB:

5.4.1 Provide the consultant’s written comments to the IRB members attending the meeting.

5.4.2 If the consultant did not provide a written report or if requested by an IRB member, invite the consultant to the IRB meeting.

5.5 For Non-Committee Review:

5.5.1 Directly obtain the information from the consultant.

5.5.2 Document information received orally with the name of the consultant.

6 MATERIALS

6.1 Prime IRB SOP 001: Definitions

6.2 WORKSHEET: Agenda Packet Contents.

7 REFERENCES

7.1 21 CFR 56.107(f).

7.2 45 CFR 46.107(f).
<table>
<thead>
<tr>
<th>Version 0.2</th>
<th>Name</th>
<th>Status (Pending, Reviewed, Approved)</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Written by</td>
<td>Karl Nelson</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reviewed by</td>
<td>Jennifer Neal-Jimenez</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Approved by</td>
<td>Jennifer Neal-Jimenez</td>
<td>Approved</td>
<td>9-January-2018</td>
</tr>
</tbody>
</table>

Prime Review Board Services
Prime IRB SOP 311: Consultation to the IRB [Version 0.2; 14-July-2017]
Page 3
1 PURPOSE

1.1 This procedure establishes the process for communications after a protocol is reviewed.

1.2 The process begins when:

   1.2.1 A Designated Reviewer has completed a Non-Committee Review and provided completed materials to the IRB staff; OR

   1.2.2 An IRB meeting has adjourned and the IRB chair or IRB manager has approved the minutes.

1.3 The process ends when all correspondence related to IRB determinations and actions have been sent and additional tasks have been completed.

2 REVISIONS FROM PREVIOUS VERSION

2.1 None.

3 POLICY

3.1 The IRB reports its findings and actions to the investigator.

3.2 The IRB reports its findings and actions to the institution.

3.3 When the IRB disapproves research, it provides the investigator with a statement of the reasons for the decision and gives the investigator an opportunity to respond in person or in writing.

3.4 These reporting procedures are to be completed within ten business days of the IRB meeting or receipt of the completed Non-Committee Review materials.

3.5 Contact information is maintained in the “Prime IRB Document Management System: Contacts.”

3.6 The list of protocols is maintained in the “Prime IRB Document Management System: Protocols.”
3.7 Receipt deadlines are maintained in the “Prime IRB Document Management System: Awaiting Receipt.

4 RESPONSIBILITIES

4.1 IRB staff members carry out these procedures.

5 PROCEDURE

5.1 If the Non-Committee Review indicated a Conflicting Interest or a lack of expertise, follow “SOP: Non-Committee Review Preparation.”

5.2 If information about the investigator or research staff were changed, update the contact information.

5.3 If the title, principal investigator, or research staff for a protocol changed, update the list of protocols.

5.4 For approvals for initial or continuing review, add a deadline for receipt of the continuing review application 30 days before study expiration.

5.5 If the review indicated “Modifications Required to Secure Approval,” add a deadline to receive a response within 30 days.

5.6 Refer to “WORKSHEET: Calculation of Approval Intervals” to calculated approval intervals.”

5.7 Stamp all consent documents with the End Approval Date in the “DO NOT SIGN THIS FORM AFTER THIS DATE” section and the date of review in the “Form Date” section.

5.8 Refer to “WORKSHEET: Communication of Review Results” and send all applicable letters.

5.8.1 Have letter signed by the signatory in the template letter.

5.8.2 Send the letter to the inside addresses and cc list as directed by the letter.

5.8.3 Attach stamped consent documents to the letter.

5.9 Update the status of the research in the Prime IRB Document Management System.

5.10 Update the protocol list.

6 MATERIALS

6.1 Prime IRB Document Management System: Awaiting Receipt

6.2 Prime IRB Document Management System: Contacts

6.3 Prime IRB Document Management System: Protocols

6.4 WORKSHEET: Communication of Review Results

6.5 WORKSHEET: Calculation of Approval Intervals and Expiration Dates.

7 REFERENCES


7.2 21 CFR §56.108(a)(1), 21 CFR §50.24(e), 21 CFR §50.54(b), 21 CFR §812.66

7.3 Prime IRB SOP 314: Prime Review Board Services Records
<table>
<thead>
<tr>
<th>Version 0.2</th>
<th>Name</th>
<th>Status (Pending, Reviewed, Approved)</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Written by</td>
<td>Karl Nelson</td>
<td></td>
<td>14-July-2017</td>
</tr>
<tr>
<td>Reviewed by</td>
<td>Jennifer Neal-Jimenez</td>
<td></td>
<td>6-January-2018</td>
</tr>
<tr>
<td>Approved by</td>
<td>Jennifer Neal-Jimenez</td>
<td>Approved</td>
<td>9-January-2018</td>
</tr>
</tbody>
</table>
1 PURPOSE

1.1 The purpose of this standard operating procedure is to describe the Prime Review Board Services’ procedures for documentation and document management.

2 REVISIONS FROM PREVIOUS VERSION

2.1 None.

3 POLICY

3.1 The Prime Review Board Services' records will contain the complete history of all actions related to review and approval of a protocol, including continuing reviews, amendments, changes in personnel and other required reports (SAEs, protocol deviations, and unanticipated problems related to research) reports. All records regarding a submitted study (regardless of whether it is approved) must be retained in an appropriate manner as required by regulatory requirements and/or institutional policy.

3.2 Records must be accessible for inspection and copying by authorized representatives of the Sponsor, funding department or agency, regulatory agencies and institutional auditors at reasonable times and in a reasonable manner.

3.3 Required documents must be submitted to the appropriate funding entity as required.

4 RESPONSIBILITIES

4.1 Director, Prime Review Board Services: Responsible for ensuring that Prime Review Board Services staff adhere to all applicable regulatory compliance requirements and establishing and periodically reviewing and modifying (as appropriate) Prime Review Board Services standard operating policies and procedures.

4.2 Chair, Prime Review Board Services: Responsible for establishing and periodically reviewing and modifying (as appropriate) Prime Review Board Services standard operating policies and procedures.
4.3 Prime Review Board Services Staff: Responsible for maintaining complete files on all research reviewed by or submitted to the Prime Review Board Services and for all applicable regulatory compliance requirements.

5 PROCEDURE

5.1 Protocol-Specific Document Retention

5.1.1 The Prime Review Board Services Office retains records regarding an application (regardless of whether it is approved) for at least three (3) years; for approved research applications, records are retained for at least three (3) years after completion of the research.

5.1.2 Access to Prime Review Board Services records shall be restricted to authorized individuals who have a role or institutional responsibility related to the study. The Prime Review Board Services Document Management System login establishes an individual’s possible role(s) and access.

5.1.3 Prime Review Board Services records are accessible for inspection and copying by representatives of the sponsor of the research, by authorized representatives of federal agencies or departments, and by other authorized agents of regulatory and accrediting agencies, at reasonable times and in a reasonable manner.

5.1.4 Retained documents include but are not limited to:

5.1.4.1 Copies of all original research protocols reviewed, scientific evaluations, if any, that accompany the protocol, approved consent documents, amendments, continuing reviews and progress reports submitted by investigators, and reports of injuries to subjects (including serious adverse events), other unanticipated problems related to research and reports of deviations from the protocol.

5.1.4.2 Minutes of all convened Prime Review Board Services meetings.

5.1.4.3 Copies of all submitted monitoring reports, site visit reports and other continuing review activities.

5.1.4.4 Copies of relevant correspondence between the Prime Review Board Services and the investigators.

5.1.4.5 Statements of significant new findings provided to subjects.

5.1.4.6 Documentation of all determinations required by federal or state laws, regulations, guidance or Emmes policies.
5.1.4.7 For research reviewed via expedited review procedures, the justification for using expedited review procedures, and the action taken by the reviewer.

5.1.4.8 For research determined to be exempt, the justification for making the exempt determination.

5.2 Administrative Documents

5.2.1 The Prime Review Board Services Office maintains and retains all records regarding Prime Review Board Services administrative activities that affect review activities for least three (3) years, or three (3) years after completion of the research, including:

5.2.1.1 Current rosters of regular and alternate members of each Prime Review Board Services.

5.2.1.2 Rosters include the following information:

5.2.1.2.1 Member name;
5.2.1.2.2 Earned degrees;
5.2.1.2.3 Representative capacity;
5.2.1.2.4 Indications of experience sufficient to describe each regular and alternate member's chief anticipated contribution to the Prime Review Board Services's deliberations;
5.2.1.2.5 Affiliation status;
5.2.1.2.6 Alternate members, with an indication of the regular members for whom the alternate may substitute;
5.2.1.2.7 Scientific/non-scientific status.

5.2.1.3 An updated roster of Prime Review Board Services members will be submitted to OHRP and the FDA within 90 days after the changes are made by the Director, Prime Review Board Services.

5.2.1.4 Obsolete membership rosters.

5.2.1.5 Current and obsolete copies of the Standard Operating Policies and Procedures.

5.3 Maintenance of Prime Review Board Services Records

5.3.1 All Prime Review Board Services files, including studies cancelled without subject enrollment, will be kept for a minimum of 3 years after study
completion, withdrawal or termination in compliance with Emmes policy and regulatory requirements.

5.3.2 Actions related to HIPAA determinations will be retained for at least 6 years after study completion, withdrawal or termination.

6 MATERIALS

6.1 None

7 REFERENCES

45 CFR 46.103, 45 CFR 46.115
21 CFR 56.115
45 CFR 164
<table>
<thead>
<tr>
<th>Version 0.2</th>
<th>Name</th>
<th>Status (Pending, Reviewed, Approved)</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Written by</td>
<td>Karl Nelson</td>
<td></td>
<td>14-July-2017</td>
</tr>
<tr>
<td>Reviewed by</td>
<td>Jennifer Neal-Jimenez</td>
<td></td>
<td>6-January-2018</td>
</tr>
<tr>
<td>Approved by</td>
<td>Jennifer Neal-Jimenez</td>
<td>Approved</td>
<td>9-January-2018</td>
</tr>
</tbody>
</table>
1 PURPOSE

1.1 This procedure establishes the process to maintain Prime Review Board Services records.

1.2 The process begins when records are to be filed.

1.3 The process ends when records have been filed.

2 REVISIONS FROM PREVIOUS VERSION

2.1 None.

3 POLICY

3.1 Prime Review Board Services records are to include:

   3.1.1 Protocol files.
   3.1.2 Minutes of Prime Review Board Services meetings.
   3.1.3 Copies of all correspondence between the Prime Review Board Services and the investigators.
   3.1.4 Prime Review Board Services member rosters.
   3.1.5 Prime Review Board Services member files.
   3.1.6 Policies and procedures.

3.2 Protocol files are to include:

   3.2.1 All submitted materials.
   3.2.2 Protocols.
   3.2.3 Scientific evaluations.
   3.2.4 DHHS-approved sample consent document and protocol, when they exist.
   3.2.5 Progress reports submitted by investigators.
   3.2.6 Reports of injuries to subjects.
3.2.7 Records of continuing review activities.

3.2.8 Correspondence between the Prime Review Board Services and investigator related to the protocol.

3.2.9 Statements of significant new findings provided to subjects.

3.2.10 For initial and continuing review of research by the expedited procedure:
   3.2.10.1 The specific permissible category.
   3.2.10.2 Description of action taken by the reviewer.
   3.2.10.3 Any findings required under the regulations.

3.2.11 For exemption determinations the specific category of exemption.

3.2.12 Unless documented in the Prime Review Board Services minutes determinations required by the regulations and protocol-specific findings supporting those determinations for.
   3.2.12.1 Waiver or alteration of the consent process.
   3.2.12.2 Research involving pregnant women, fetuses, and neonates.
   3.2.12.3 Research involving prisoners.
   3.2.12.4 Research involving children.
   3.2.12.5 Significant/non-significant device determinations.

3.2.13 For each protocol’s initial and continuing review, the frequency for the next continuing review.

3.2.14 Correspondence between the Prime Review Board Services and the Veterans Administration (VA) Research and Development Committee.

3.2.15 Problems submitted to the Prime Review Board Services under the prompt reporting requirements including the adverse events and protocol violations that require prompt reporting to the Prime Review Board Services.

3.3 Protocol files are maintained in chronological order with the latest information in front.

3.4 Policies and procedures include:
   3.4.1 Checklists.
   3.4.2 Forms.
   3.4.3 SOPs.
   3.4.4 Template letters.
   3.4.5 Template minutes.
3.4.6 Worksheets.

3.5 Prime Review Board Services member files include a resume for each Prime Review Board Services member.

4 RESPONSIBILITIES

4.1 Prime Review Board Services staff members are responsible to carry out these procedures.

5 PROCEDURE

5.1 Protocol records:

5.1.1 Print a copy of the current protocol history.

5.1.2 Replace the previous protocol history with a copy of the current protocol history.

5.1.3 Print a copy of the current protocol action, place it on top of all other materials to be filed, place it on top of previous materials.

5.2 Minutes of Prime Review Board Services meetings: File in minutes binder.

5.3 Copies of all correspondence between the Prime Review Board Services and the investigators: File in investigator files.

5.4 Prime Review Board Services member rosters: File in Prime Review Board Services member roster binder.

5.5 Prime Review Board Services membership records: File in Prime Review Board Services member files.

5.6 Policies and procedures:

5.6.1 File current policies and procedures in polices and procedures binder.

5.6.2 File replaced policies and procedures in the policies and procedures history file.

5.7 Provide copies of Prime Review Board Services records to sponsors or federal agencies when requested for archiving.
6 MATERIALS

6.1 None.

7 REFERENCES

7.1 None.
<table>
<thead>
<tr>
<th>Version 0.2</th>
<th>Name</th>
<th>Status (Pending, Reviewed, Approved)</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Written by</td>
<td>Karl Nelson</td>
<td></td>
<td>14-July-2017</td>
</tr>
<tr>
<td>Reviewed</td>
<td>Jennifer Neal-Jimenez</td>
<td></td>
<td>6-January-2018</td>
</tr>
<tr>
<td>Approved</td>
<td>Jennifer Neal-Jimenez</td>
<td>Approved</td>
<td>9-January-2018</td>
</tr>
</tbody>
</table>
1 PURPOSE

1.1 This procedure establishes the process to create and update standard operating procedures and associated checklists and worksheets.

1.2 The process begins when the IRB manager or Organizational Official determines that a standard operating procedure needs to be created or modified.

1.3 The process ends when the new or revised standard operating procedure has been approved and filed.

2 REVISIONS FROM PREVIOUS VERSION

2.1 None.

3 POLICY

3.1 None.

4 RESPONSIBILITIES

4.1 The Director, Prime Review Board Services carries out these procedures.

5 PROCEDURE

5.1 For new standard operating procedure, assign a number.

5.2 Assign an author and approver.

5.3 Have the author create or update the standard operating procedure following the “TEMPLATE SOP” or update the associated checklist or worksheet.

5.4 Have the approver review and approve the document.

5.5 Once approved by the approver:

5.5.1 Update the approval date.
5.5.2 File the approved new or revised document in the standard operating procedure files.

5.5.3 Post the approved procedure on the Human Research Protection Program Web site.

5.5.4 File the old document, if any, in the standard operating procedure files.

5.6 Send an email to affected individuals informing them of the change.

6 MATERIALS

6.1 TEMPLATE SOP

7 REFERENCES

7.1 None.
<table>
<thead>
<tr>
<th>Version 0.2</th>
<th>Name</th>
<th>Status (Pending, Reviewed, Approved)</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Written by</td>
<td>Karl Nelson</td>
<td></td>
<td>14-July-2017</td>
</tr>
<tr>
<td>Reviewed by</td>
<td>Jennifer Neal-Jimenez</td>
<td></td>
<td>6-January-2018</td>
</tr>
<tr>
<td>Approved by</td>
<td>Jennifer Neal-Jimenez</td>
<td>Approved</td>
<td>9-January-2018</td>
</tr>
</tbody>
</table>
1 PURPOSE

1.1 This procedure establishes the process to retain Prime Review Board Services records.

1.2 The process begins each year in June.

1.3 The process ends when records that no longer need to be retained are destroyed.

2 REVISIONS FROM PREVIOUS VERSION

2.1 None.

3 POLICY

3.1 Protocol files are to be retained as long as required by law and then destroyed.\(^1\)

3.2 All records not in protocol files are retained indefinitely.

3.3 Protocols in which there was no subject enrollment or no research was conducted are to be retained the same as protocols where research was conducted.

3.4 All records for research conducted or funded by a Common Rule agency are to be accessible for inspection and copying by authorized representatives of that agency at reasonable times and in a reasonable manner.

3.5 All records for research subject to FDA regulations are to be accessible for inspection and copying by authorized representatives of FDA at reasonable times and in a reasonable manner.

3.6 All records are to be accessible for inspection and copying by the Veterans Administration (VA) Research and Development Committee at reasonable times and in a reasonable manner.

3.7 Veterans Administration (VA) IRB records are retained in accordance with VHA’s Records Control Schedule.\(^2\)

---

\(^1\) Revise if the organization’s policy is for longer retention.
4 RESPONSIBILITIES

4.1 The Prime Review Board Services staff members carry out these procedures.

5 PROCEDURE

5.1 Destroy protocol files for Veterans Administration (VA) research when approved by the National Archives and Records Administration.

5.2 Destroy all other protocol files when the protocol has been closed, withdrawn, or terminated more than three years ago.³

6 MATERIALS

6.1 None.

7 REFERENCES

7.1 None.

² This is a requirement of Veterans Administration (VA) facilities, but not a requirement of Veterans Administration (VA) affiliates.
³ This assumes that HIPAA records are maintained separately.
<table>
<thead>
<tr>
<th>Version 0.2</th>
<th>Name</th>
<th>Status (Pending, Reviewed, Approved)</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Written by:</td>
<td>Karl Nelson</td>
<td></td>
<td>14-July-2017</td>
</tr>
<tr>
<td>Reviewed by:</td>
<td>Jennifer Neal-Jimenez</td>
<td></td>
<td>6-January-2018</td>
</tr>
<tr>
<td>Approved by:</td>
<td>Jennifer Neal-Jimenez</td>
<td>Approved</td>
<td>9-January-2018</td>
</tr>
</tbody>
</table>
1. PURPOSE

1.1. To outline the courses of action the Prime Review Board Services may take when reviewing and approving research involving human subjects.

2. REVISIONS FROM PREVIOUS VERSION

2.1. None.

3. POLICY:

3.1. The Prime Review Board Services renders motions/determinations according to the federal regulations.

3.2. This document describes the determinations which are used by the Prime Review Board Services to indicate the results of their review, and includes the appropriate investigator response/s upon receipt of the written notification from the Prime Review Board Services. This document also describes how the Prime Review Board Services notifies investigators and the institution in writing of its determinations.

3.3. As a result of its review, the IRB may take any of the following courses of action including:

   3.3.1. to approve the proposed research activity,
   3.3.2. to approve the activity with revisions required (specified changes to the proposed research),
   3.3.3. to defer the action,
   3.3.4. to disapprove the proposed research activity, or
   3.3.5. to acknowledge receipt of non-material changes to previously approved research.

4. RESPONSIBILITIES

4.1. Director, Prime Review Board Services: Responsible for establishing processes and educating Analysts so they are knowledgeable in the processes for documentation of all IRB decisions; for ensuring that documentation of IRB determinations is forwarded to
the Investigator and that electronic copies of IRB meeting minutes are forwarded to the 
Institutional Official.

4.2. Chair, Prime Review Board Services: The Chair (or designee) is responsible for 
ensuring the appropriateness of all IRB decisions and actions.

4.1. Prime Review Board Services Analyst: The Prime Review Board Services Analyst is 
responsible for documenting the basis for all decisions in the minutes for convened 
meetings and/or in the Study Record for reviews conducted using Expedited or Exempt 
procedures.

5. PROCEDURE

5.1. Approved. An approval is granted if the research activity meets the criteria for 
approval as defined in 45 CFR 46.111 and no changes to the research application are 
recommended.

5.1.1. The date of approval is the date on which the Prime Review Board Services 
reaches an approval determination. Approval will begin the day the study is 
approved by an action of the convened IRB or the Chair or designee 
(reviewer).

5.1.2. The duration of the approval period is determined at the time of approval. For 
federally funded and FDA regulated research the approval period will not 
exceed one (1) year. For minimal risk research funded by other mechanisms and 
not subject to FDA regulation, the approval period will not be greater than three 
(3) years

5.1.3. The investigator will not begin research activities until he/she has received the 
written Prime Review Board Services notification of approval.

5.2. Approved Pending Review and Approval by the Chairperson or His/Her Designee. A 
status of pending is granted if the research activity would meet the criteria for approval 
as defined in 45 CFR 46.111 once the Principal Investigator has agreed to implement 
the modifications required by the Prime Review Board Services. The application is 
approved if, on review, the modifications have been made by the Principal Investigator 
and confirmed by the Chairperson or his/her Designee. If any modifications have not 
been made, or additional modifications have been made that were not requested, the 
Chairperson or his/her designee refers the study to full Prime Review Board Services, 
unless the Prime Review Board Services asked for factual errors.
5.2.1. The Prime Review Board Services may require the following as conditions of approval of research:

5.2.1.1. Confirmation of specific assumptions or understandings on the part of the IRB regarding how the research will be conducted (e.g., confirmation that the research excludes children) or other aspects of the research;

5.2.1.2. Submission of additional documentation (e.g., certificate of training);

5.2.1.3. Precise language changes to protocol, informed consent documents, or other study documentation;

5.2.1.4. Substantive changes to protocol or informed consent documents that do not affect or alter the regulatory criteria for approval, along with clearly stated parameters that the changes must satisfy.

5.2.2. In these cases, the investigator will be informed in writing of the required specific revisions and requested information, and must provide the Prime Review Board Services with the changes or information.

5.3. Deferred. A deferral is granted if the study does not meet the criteria for approval as defined in 45 CFR 46.111, or the Prime Review Board Services recommends substantial revisions to the submitted research rendering it unable to assess the risk/benefit ratio without the completed revisions.

5.3.1. This action applies to both research reviewed by a convened IRB and research reviewed using expedited procedures. If the risks of the research have been determined to be greater than minimal, the review of the requested modifications (e.g. application, protocol or consent form) must be performed at a convened meeting of the IRB. For research that is not greater than minimal risk, review may take place using expedited procedures.

5.3.2. The Prime Review Board Services will include in its written notification of deferral, a statement of the reasons for its decision and give the Investigator an opportunity to respond. Investigator deferral responses require review by the convened Prime Review Board Services.

5.3.3. Deferred New Application: The application may be revised and resubmitted for reconsideration by the Prime Review Board Services or the Investigator may provide justification to the Prime Review Board Services why the actions or changes are unnecessary.

5.3.3.1. The investigator will take the actions, make the requested changes, and/or justify in the deferral response why the actions or changes are
unnecessary before the Prime Review Board Services will reconsider the application.

5.3.3.1.1. The investigator will include a copy of any revised documents including protocol and consent form with their deferral response.

5.3.3.1.2. The investigator will not begin the research activities until he/she receives written notification of approval from the IRB.

5.3.3.1.3. The date of approval is the date on which the Prime Review Board Services reaches an approval determination.

5.3.4. Deferred Modification(s): The modification(s) cannot be implemented and the Prime Review Board Services expects the research will continue as previously approved.

5.3.4.1. The investigator will continue to conduct the research activities as previously approved by the Prime Review Board Services.

5.3.4.2. The investigator will take the actions, make the requested changes and/or justify in the deferral response why the actions and/or changes are unnecessary before the Prime Review Board Services will reconsider the application.

5.3.4.3. The investigator will include a copy of any revised documents including protocol and consent form with their deferral response.

5.3.4.4. The investigator will not implement proposed modifications until he/she receives written notification of approval from the Prime Review Board Services.

5.3.4.5. The date of approval is the date on which the Prime Review Board Services reaches an approval determination.

5.3.5. Deferred Continuing Review:

5.3.5.1. The investigator will take the actions, make the requested changes and/or justify why the changes are unnecessary before the Prime Review Board Services will reconsider the application.

5.3.5.1.1. If the Continuing Review has not been approved by the expiration date, Prime Review Board Services approval will expire and the Investigator must proceed in
accordance with Prime Review Board Services Procedure Expired PRIME IRB Approval.

5.3.5.2. The investigator will include a copy of any revised documents including protocol and consent form with their deferral response.

5.3.5.3. The investigator will not continue the research activities beyond the expiration date unless or until they have received the written notification of approval from the Prime Review Board Services.

5.3.5.4. The date of approval is the date on which the Prime Review Board Services reaches an approval determination.

5.4. Tabled. A study that lacks sufficient information to conduct an adequate review at the full Prime Review Board Services Committee review level may be tabled pending receipt of the requested information.

5.5. Tabled due to Lack of Time. A study that is unable to be reviewed at the Prime Review Board Services Committee meeting due to lack of time. The study is then placed first on the following month’s agenda.

5.6. Administrative Hold. The Prime Review Board Services Committee or Prime Review Board Services Chairperson or designated Committee member may request the Principal Investigator place some or all research activities on hold when more information is needed (See Prime IRB SOP 409: Suspension or Termination of Research). The determination may be made and lifted at the level of review for which the study qualifies.

5.7. Disapproved. The Prime Review Board Services has determined that the research activity, as submitted, does not meet the criteria for approval as defined in 45 CFR 46.111 (and 21 CFR 56.111 and/or 32 CFR 219.111, when applicable) and/or that the Prime Review Board Services requires substantial revisions to the application, informed consent document(s), or other relevant documents in order to assess the subject's risk/benefit ratio. The action to disapprove the research may only be taken by majority vote at a convened meeting of the IRB

5.7.1. If the Prime Review Board Services disapproves a research activity, it will include in its written notification a statement of the reasons for its decision and give the investigator an opportunity to respond in person or in writing, at the discretion of the Prime Review Board Services.

5.7.1.1. Disapproved New Application: The application may be reconsidered as a new submission after substantial changes have been made to the proposed study.
5.7.1.2. Disapproved Modification(s): The change cannot be implemented, and the Prime Review Board Services expects the research will continue as previously approved.

5.7.2. The investigator will not conduct any research activities that have been disapproved in writing by the Prime Review Board Services.

5.8. **Sponsor-Imposed Suspension.** A sponsor-imposed suspension is when the Prime Review Board Services receives written notification that the sponsor has suspended the research study. This will be acknowledged by the Prime Review Board Services Committee, Chairperson or his/her Designee when the appropriate level of review determines the suspension is appropriate. The Prime Review Board Services may impose additional criteria for suspension, if needed, to protect participants from potential harm.

5.9. **Suspension for Cause.** A currently approved study is suspended for cause when evidence of a possible increase in risk to participants or non-compliance by the Investigator has been determined by the Prime Review Board Services. Suspensions for cause are made under full Prime Review Board Services Committee review procedures.

5.10. **Expiration.** A currently approved study is expired when continuing review has not been conducted and approved prior to the study’s expiration date.

5.11. **Complete.** Research activity has been completed. This means no research data is being obtained through intervention or interaction with an individual or with his/her identifiable private information or an individual who was a participant in research, either as a recipient of the test article or as a control.

5.11.1. No subjects are currently being enrolled in this study; no subjects are undergoing any research procedures; no data from medical records or databases is being obtained and/or shared with other individuals or organizations; and no subjects are being contacted by telephone or mail for purposes of follow-up.

5.12. **Termination for Cause.** A currently approved study may be terminated if the study is not being conducted in accordance with the Prime Review Board Services policies, is not in compliance with Federal regulations, and/or has been associated unexpected serious harm to participants. Terminations for cause are made under convened Prime Review Board Services review procedures.

5.13. **Acknowledge Receipt:** Submission of non-material changes to previously approved research that do not influence the conduct of the research may be acknowledged by the IRB office.
6. **NOTIFICATIONS**

6.1. The Prime Review Board Services notifies investigators in writing of its determinations, including decisions to approve, disapprove, or defer an item under review. When the Prime Review Board Services defers an item under review, the investigator is notified of the required investigator actions and mechanism for requesting further consideration by the Prime Review Board Services. If the Prime Review Board Services disapproves an application, a statement of the reasons for the disapproval is provided and the investigator may request to respond in writing or in person.

6.2. Prime Review Board Services notifications are generated by authorized Prime Review Board Services Operations Office personnel and are issued through the electronic IRB system via electronic mail to the investigator and other study personnel designated by the investigator to receive the notifications.

6.3. Individual Prime Review Board Services notifications and the complete Prime Review Board Services record are available to the Institutional Official. The Prime Review Board Services procedure for reporting problems or events to the Institutional Official is described in *Prime IRB SOP 806: Reporting to the Appropriate Institutional Officials, and the Department or Agency Head(s)*.

7. **REFERENCES**

Prime IRB SOP 305: IRB Meeting Administration
Prime IRB SOP 800: Non-Compliance with Human Research Subjects.
21 CFR 56.109
21 CFR 56.111
21 CFR 56.113
45 CFR 46.109
45 CFR 46.111
45 CFR 46.113
<table>
<thead>
<tr>
<th>Version 0.2</th>
<th>Name</th>
<th>Status (Pending, Reviewed, Approved)</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Written by</td>
<td>Karl Nelson</td>
<td></td>
<td>14-July-2017</td>
</tr>
<tr>
<td>Reviewed by</td>
<td>Jennifer Neal-Jimenez</td>
<td></td>
<td>6-January-2018</td>
</tr>
<tr>
<td>Approved by</td>
<td>Jennifer Neal-Jimenez</td>
<td>Approved</td>
<td>9-January-2018</td>
</tr>
</tbody>
</table>
1 PURPOSE

1.1 To outline the criteria required for approval by the Prime IRB

2 REVISIONS FROM PREVIOUS VERSION

2.1 None.

3 POLICY

3.1 All research that involves human subjects must be approved by the IRB before the research activities commence. The research must meet certain criteria before study related procedures can be initiated. The criteria are based on the principles of justice, beneficence and autonomy as discussed in the Belmont Report and as specified in Federal regulation (45 CFR 46.111 and 21 CFR 56.111).

4 RESPONSIBILITIES

4.1 Director, Prime Review Board Services: Director, Prime Review Board Services and Analysts are responsible for ensuring that IRB reviewers have all the tools and resources needed to complete their research reviews

4.2 Chair, Prime Review Board Services: IRB Chairperson (or designee) is responsible for ensuring that the research satisfies the criteria for IRB approval.

5 PROCEDURE

5.1. **Minimal Criteria for Approval of Research:** In order for a research project to be approved, the Prime IRB must find that:

5.1.1. Risks to Subjects are Minimized

5.1.1.1. By using procedures that are consistent with sound research design and which do not unnecessarily expose subjects to risk, and

5.1.1.2. Whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.
5.1.2. Risk Assessment: Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may be expected to result.

5.1.2.1. In evaluating risks and benefits, the Prime IRB will consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies that subjects would receive even if not participating in the research). The Prime IRB should not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research benefits that fall within the purview of its responsibility.

5.1.3. Selection of Subjects is Equitable

5.1.3.1. In making this assessment, the Prime IRB should consider the purposes of the research and the setting in which the research will be conducted and should be particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, handicapped, or mentally disabled persons, or economically or educationally disadvantaged persons.

5.1.4. Informed consent will be sought from each prospective subject or the subject’s legally authorized representative, in accordance with, and to the extent required by federal and state regulations and institutional policies and procedures including the Prime IRB;

5.1.5. Informed Consent will be appropriately documented, in accordance with, and to the extent required by the Federal and State regulations and Institutional policies and procedures including the Prime IRB;

5.1.6. When appropriate, the research plan makes adequate provisions for monitoring the data collected to ensure the safety of subjects;

5.1.7. When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data;

5.1.8. There are adequate provisions to protect the rights and welfare of vulnerable populations from coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons. The Prime IRB Committee must determine if additional safeguards need to be included in the study to protect the rights and welfare of these subjects;
5.1.9. When appropriate, the need for ancillary care, additional monitoring, counseling, and social support are provided; and

5.1.10. When appropriate, the Informed Consent Document should include the additional elements of informed consent (See Prime IRB SOP 600: Required Elements of Consent and Documentation of Consent).

5.1.11. The full Prime IRB determines a review interval for the research as appropriate to the degree of risk, but not greater than one year from the last date of Prime IRB approval (See Prime IRB SOP 405: Continuing Review of Approved Research). The regulations make no provision for any grace period extending the conduct of research beyond the expiration date of Prime IRB approval. Therefore, continuing review and re-approval of the research occurs on or before the date when Prime IRB approval expires. The following factors are taken into consideration when determining the appropriate review interval, but are not limited to:

5.1.11.1. Involvement of vulnerable populations;

5.1.11.2. Use of waiver of informed consent procedures, (e.g. surrogate consent);

5.1.11.3. Research for which participants would be exposed to additional risks, e.g. breach of confidentiality, phase I studies, disproportionate number or severity of adverse events; and/or

5.1.11.4. Previous Administrative Holds or Suspensions of the research due to compliance, record-keeping or other concerns.

5.2. Other Criteria for Approval of Research

5.2.1. The Prime IRB may require verification of information submitted by an Investigator. The need to verify any information will be determined by the IRB at a convened meeting. The purpose of the verification will be to provide necessary protection to subjects when deemed appropriate by the Prime IRB.

5.2.2. Requiring independent verification may be based on the Prime IRB’s routine audit plan or any legitimate concern that may include, but is not limited to, the following:

5.2.2.1. Studies being conducted by Key Research Personnel who have previously failed to materially comply with regulations and Prime IRB policies, including non-responsiveness to requests for information;
5.2.2.2. Studies for which the Key Research Personnel’s conduct was suspect considering information provided during continuing review or audit;

5.2.2.3. Complaints from any participating institution or research subjects that appear not to be adequately addressed by the Key Research Personnel;

5.2.2.4. Studies in which the IRB discovers previously undisclosed information that should have been reported to the IRB;

5.2.2.5. Studies in which the Key Research Personnel has disclosed or failed to disclose significant conflict(s) of interest; or

5.2.2.6. Studies that exhibit high-risk profiles such as unexpected frequencies or severity of reported serious adverse events, high participant dropout rates or involving an unusual level or types of risks to subjects.

5.2.2.7. The Prime IRB may require that the Investigator attend the Prime IRB meeting.

5.3. Use of Consultants

5.3.1. The Prime IRB Chairperson can request individuals with expertise in matters under review to provide information to the Prime IRB relevant to consideration of the research in question.

6 MATERIALS

6.1 CHECKLIST: Approval Criteria

7 REFERENCES

45 CFR 46.111

21 CFR 56.108, 56.111

OHRP Guidance on Knowledge of Local Research Context: http://www.hhs.gov/ohrp/humansubjects/guidance/local.htm

Prime IRB SOP 405: Continuing Review of Approved Research
Prime IRB SOP 500: Vulnerable Subjects
Prime IRB SOP 501: Research Involving Pregnant Women, Fetuses and Neonates
Prime IRB SOP 503: Research Involving Children (Additional Protections)
Prime IRB SOP 504: Minors Who are Not Children in the Research Context
Prime IRB SOP 600: Required Elements of Consent and Documentation of Consent Documentation
Prime IRB SOP 605: Waiver of Elements of Consent and Waiver of HIPAA Authorization
Prime IRB SOP 606: Requirements for and Documentation of HIPAA Authorization in Research
Prime IRB SOP 701: Data and Safety Monitoring Plans

<table>
<thead>
<tr>
<th>Version &lt;xx&gt;</th>
<th>Name</th>
<th>Status (Pending, Reviewed, Approved)</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Written by:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reviewed by:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Approved by:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Version 0.2</td>
<td>Name</td>
<td>Status (Pending, Reviewed, Approved)</td>
<td>Date</td>
</tr>
<tr>
<td>------------</td>
<td>---------------------</td>
<td>--------------------------------------</td>
<td>-------------</td>
</tr>
<tr>
<td>Written by:</td>
<td>Karl Nelson</td>
<td></td>
<td>14-July-2017</td>
</tr>
<tr>
<td>Reviewed by:</td>
<td>Jennifer Neal-Jimenez</td>
<td></td>
<td>6-January-2018</td>
</tr>
<tr>
<td>Approved by:</td>
<td>Jennifer Neal-Jimenez</td>
<td>Approved</td>
<td>9-January-2018</td>
</tr>
</tbody>
</table>
**1 PURPOSE**

1.1 This procedure establishes the process to handle investigator submissions of modifications required to secure approval.

1.2 The process begins when modifications required to secure approval are received by the Prime IRB.

1.3 The process ends when the acceptance or rejection of the modifications is provided to the investigator.

**2 REVISIONS FROM PREVIOUS VERSION**

2.1 None.

**3 POLICY**

3.1 None.

**4 RESPONSIBILITIES**

4.1 Prime IRB staff members carry out these procedures.

**5 PROCEDURE**

5.1 If the investigator requests a review by the convened Prime IRB, place on the agenda for a convened Prime IRB meeting.

5.2 Otherwise follow “Prime IRB SOP 403: Expedited Review Procedures.”

**6 MATERIALS**

6.1 CHECKLIST: Expedited Review

6.2 CHECKLIST: Approval Criteria
7 REFERENCES

7.1 Prime IRB SOP 403: Expedited Review Procedures
<table>
<thead>
<tr>
<th>Version 0.2</th>
<th>Name</th>
<th>Status (Pending, Reviewed, Approved)</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Written by</td>
<td>Karl Nelson</td>
<td></td>
<td>14-July-2017</td>
</tr>
<tr>
<td>Reviewed by</td>
<td>Jennifer Neal-Jimenez</td>
<td></td>
<td>6-January-2018</td>
</tr>
<tr>
<td>Approved by</td>
<td>Jennifer Neal-Jimenez</td>
<td>Approved</td>
<td>9-January-2018</td>
</tr>
</tbody>
</table>
1 PURPOSE

1.1 To describe the process for using expedited review procedures.

2 REVISIONS FROM PREVIOUS VERSION

2.1 None.

3 POLICY

3.1 The IRB may approve research using expedited review procedures provided that the following criteria are met: the research activities (1) present no more than minimal risk to human subjects, and (2) if federally funded or FDA regulated, involve only procedures listed in one or more of the specific categories listed in the regulations at Federal Register 63: 29748, 1998, 21 CFR 56.110, and 45 CFR 46.110. The IRB may also use expedited procedures to review and approve minor changes to approved research. Non-material changes will be administratively reviewed.

4 RESPONSIBILITIES

4.1. Director, Prime Review Board Services: Responsible for triaging new submissions and determining eligibility for expedited review or delegating this authority to another qualified member of the IRB Office.

4.2. Chair, Prime Review Board Services: The Chair is responsible for reviewing submissions eligible for expedited review or selecting a designee.

4.3. Analyst, Prime IRB: Prime IRB Analyst is responsible for processing and assisting the Prime IRB member reviewer with studies eligible for expedited review and communicating results of the review with investigators.
5 PROCEDURE

5.1 Establishing Applicability of Expedited Review Procedures
Federal regulations (45 CFR 46.110, 38 CFR 16.110) allow the Prime IRB to review certain submissions on an expedited basis if they meet specified criteria. Expedited review procedures may be used when the research presents no more than minimal risk to human subjects, and when the procedures involved are limited to those in a listing of minimal risk procedures (Appendix 1: A and B; Appendix 2: A and B).

5.1.1 The expedited review procedure will not be used where identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.

5.1.2 The Prime IRB will apply the same requirements for informed consent, as well as for its waiver, alteration, or exception for research reviewed using expedited procedures as for research reviewed by the convened Prime IRB.

5.2 Expedited Review Procedures

5.2.1 Pre-review procedures to ensure completeness of the submission will be followed in accordance with Prime IRB SOP 104: IRB Review Process.

5.2.2 An expedited review will be performed by the Prime IRB Chair or by an experienced Prime IRB member designated by the Prime IRB Chair, i.e. a member with demonstrated knowledge and application of research ethics in human subject protections of at least one year.

5.2.3 The Prime IRB Chair may also conduct expedited review in such a manner as to notify and allow comments from all Prime IRB members prior to issuing a determination. This is done by email distribution of the submitted materials to the entire Prime IRB inviting their comments on the research. Prime IRB members will be given up to 48 hours to respond to the Chair’s request for their views before the Chair proceeds with review.

5.2.4 The Reviewer may also request review of the research by an expert consultant for issues which require expertise beyond, or in addition to, that available on the Prime IRB.

5.2.5 Materials to be Reviewed: Reviewers receive and review the same materials that the convened Prime IRB receives for protocols reviewed by the convened Prime IRB. The required materials for review are described in Prime IRB SOP 300: Research Submission Requirements. Research materials submitted
include sufficient detail for the Reviewer to determine the study meets criteria for approval [45 CFR 46.111].

The Chair or designee (the reviewer) will have access to all materials submitted in the eIRB system including but not limited to:

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

5.2.5.2 Proposed consent document(s).

5.2.5.3 Recruitment materials.

5.3. **Reviewer Responsibilities:**

5.3.1. The reviewer discloses conflicting interest with any submission forwarded for review. If there is a conflict of interest the review will be forwarded to another reviewer.

5.3.2. The reviewer evaluates the research using the criteria outlined in *Prime IRB SOP 401: Criteria for Approval*. The criteria for approval using the expedited procedure are the same as those for review by a convened Prime IRB.

5.3.3. The reviewer will make one of the following determinations regarding the application:

5.3.3.1. Approved

5.3.3.2. Revisions and/or additional information required.

5.3.3.3. Forward to Convened Prime IRB.

5.3.4. The reviewer exercises all of the authorities of the IRB, except that they may not disapprove the research. A research protocol may be disapproved only after review by a convened IRB.

5.3.5. The Reviewer determines a review interval for the research as appropriate to the degree of risk, but not greater than one year from the last date of Prime IRB approval (See *Prime IRB SOP 405: Continuing Review of Approved Research*).

5.3.6. Documentation of the review, action taken by the reviewer, and any specific findings required by federal regulations will be documented in the eIRB system.

5.3.6.1. If the study qualifies for expedited review, the Prime IRB Chairperson or designee will document his/her determination of the level of risk and the applicable expedited review category(ies).
5.3.6.2. The minutes will include documentation of the studies that were reviewed via expedited review and any issues resolved relating to questions that Prime IRB members had concerning the research reviewed.

5.3.7. In all cases the expedited reviewer reserves the authority to refer any study to the Convened Prime IRB for review.

5.3.8. Information obtained during the review of an amendment, adverse event, sponsor notification, or other pertinent information may possibly disqualify the study from being approved under an expedited review procedure. The study is forwarded to the Prime IRB for determination at a convened meeting.

5.3.9. Items approved using the expedited review procedure (initial review, modifications, and continuing review) are forwarded via the electronic Prime IRB system to a convened Prime IRB agenda for review.

5.4. **Post Review Procedures**

5.4.1. Expedited review actions will be reported in the agenda for the next convened meeting via the agendas in the Prime IRB electronic management system. This report will include actions taken by the reviewer. Members will have access to the complete submission and all review materials.

5.4.2. The IRB Analyst provides documentation for the Investigator regarding the IRB’s determinations in accordance with *Prime IRB SOP 104: IRB Review Process*.

5.5. **Appropriate Use of Expedited Review Procedures for Initial Review of Research:**

5.5.1. The Prime IRB may use an expedited procedure to conduct initial review of research provided all research activities do not fall under any of the general restrictions, present no more than minimal risk to human subjects, and involve procedures listed in Appendix 1: A and B; Appendix 2: A and B.

5.5.2. The activities listed should not be deemed to be of minimal risk simply because they are included on this list. Inclusion on this list merely means that the activity is eligible for review through the expedited review procedure when the specific circumstances of the proposed research involve no more than minimal risk to human subjects.

The Prime IRB may use an expedited procedure to conduct continuing review of research provided all research activities do not fall under any of the general restrictions, present no more than minimal risk to human subjects, and involve procedures listed in one or more of the following categories:

5.6.1. Research procedures that meet the criteria for initial review of research by an expedited procedure.

5.6.2. Continuing review of research previously approved by the Prime IRB at a convened meeting as follows:

5.6.2.1. Where the research is permanently closed to the enrollment of new subjects; all subjects have completed all research-related interventions; and the research remains active only for long-term follow-up of subjects; or

5.6.2.2. Where no subjects have ever been enrolled (at any performance site for which the Prime IRB is the IRB of record) and no additional risks have been identified; or

5.6.2.3. Where the remaining research activities are limited to data analysis.

5.6.2.4. Continuing review of research, not conducted under an investigational new drug application or investigational device exemption where the above categories do not apply but the Prime IRB has determined and documented at a convened Prime IRB meeting that the research involves no greater than minimal risk and no additional risks have been identified [45 CFR 46.110(f)(9)].

5.6.3. The regulations make no provision for any grace period extending the conduct of research beyond the expiration date of Prime IRB approval. Therefore, continuing review and re-approval of the research occurs on or before the date when Prime IRB approval expires. OHRP recognizes the logistical advantages of keeping the Prime IRB approval period constant from year to year throughout the life of each project. When continuing review occurs annually and the Prime IRB performs continuing review within 30 days before the Prime IRB approval period expires, the Prime IRB may retain the anniversary date as the date by which the continuing review must occur, if it so chooses.
5.7. **Appropriate Use of Expedited Review Procedures for Review of Modifications to Previously Approved Research:**

The Prime IRB may use an expedited procedure to conduct review of modifications to previously approved research provided the changes meet the following criteria. Reviewers evaluate whether modifications to previously approved research undergoing review meet these criteria.

5.7.1. Modifications do not pose an increased risk to subjects

5.7.2. The change does not adversely alter the overall risk/benefit ratio

5.7.3. The change will not potentially adversely affect the willingness of current participants to remain in the study or the willingness of potential participants to enroll in the study

5.7.4. The change will not diminish the scientific validity of the study

5.7.5. Any additional procedures fall within categories [listed in Appendix 1: A and B; Appendix 2: A and B] of research that may be reviewed using the expedited procedure

5.7.6. Modifications constitute a minor change to previously approved research

6 **MATERIALS**

6.1 CHECKLIST: Expedited Review

6.2 CHECKLIST: Approval Criteria

7 **REFERENCES**

45 CFR 46.110(b)(1)(2)

21 CFR 56.110(b)(1)(2)

OHRP Guidance for Expedited Review

http://www.hhs.gov/ohrp/humansubjects/guidance/expedited98.htm

http://www.hhs.gov/ohrp/humansubjects/guidance/exprev.htm

FDA Information Sheets: Continuing Review After Study Approval: (4) Process for reviewing ongoing changes

http://www.fda.gov/oc/ohrt/irbs/review.html
APPENDIX 1: Expedited Review Categories

Research activities involving "no more than minimal risk" and in which the only involvement of human subjects will be in one or more of the following categories may be reviewed using an expedited procedure by the Chairman of the Prime IRB or his designee(s). Each of the categories is quoted from the Federal regulations at 45 CFR 46, and followed by an explanatory paragraph.

Inclusion on this list indicates that the activity is eligible for review through the expedited review procedure when the specific circumstances of the proposed research involve no more than minimal risk to human subjects. The categories in this list apply regardless of the age of subjects, except as noted.

A. Research Categories Published in the Federal Register (Source: 63 FR 60364-60367, November 9, 1998) (for federally funded or FDA-regulated research)

(1) Clinical studies of drugs and medical devices only when condition (a) or (b) is met.
   
   (a) Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required. (Note: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for minimal risk review.)
   
   (b) Research on medical devices for which (i) an investigational device exemption application (21 CFR Part 812) is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.

This category is limited to drugs and devices that pose minimal risk to human subjects. Most of the activities eligible for review in this category will involve over-the-counter drugs and devices, pharmaco-economic studies of drugs and devices used in accordance with approved labeling, and “Phase 4” post-marketing studies of approved drugs and devices.

(2) Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:

   (a) From healthy, nonpregnant adults who weigh at least 110 pounds: For these subjects, the amounts drawn may not exceed 550 ml in an 8-week period and collection may not occur more frequently than 2 times per week; or
   
   (b) From other adults and children, considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount
drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8-week period and collection may not occur more frequently than 2 times per week.

This category allows minimal risk review of activities involving invasive blood draws from healthy normal subjects and from non-healthy, pregnant, and minor subjects, within certain limits. Unless the researcher can demonstrate that infants and other minors would undergo a blood draw as a part of a “routine” physical examination, blood draws from healthy minors will not be reviewed as minimal risk using the expedited procedure.

(3) Prospective collection of biological specimens for research purposes by noninvasive means.

Examples:

(a) Hair and nail clippings in a nondisfiguring manner;
(b) Deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction;
(c) Permanent teeth if routine patient care indicates a need for extraction;
(d) Excreta and external secretions (including sweat);
(e) Uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or by applying a dilute citric solution to the tongue;
(f) Placenta removed at delivery;
(g) Amniotic fluid obtained at the time of rupture of the membrane prior to or during labor;
(h) Supra- and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques;
(i) Mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings;
(j) Sputum collected after saline mist nebulization.

The examples listed are neither exclusive nor exhaustive. This category may be applied to research involving prospective collection of biological specimens for research purposes using non-invasive methods in addition to those listed as examples.

(4) Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and
effectiveness of the medical device are not generally eligible for minimal risk review, including studies of cleared medical devices for new indications.)

Examples:

(a) Physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject’s privacy;
(b) Weighing or testing sensory acuity;
(c) Magnetic resonance imaging;
(d) Electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroneutinography, ultrasound, diagnostic infrared imaging, Doppler blood flow, and echocardiography;
(e) Moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

The examples listed are neither exclusive nor exhaustive. This category may be applied to research involving prospective collection of data for research purposes using non-invasive methods in addition to those listed as examples.

(5) Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for nonresearch purposes (such as medical treatment or diagnosis). (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b) (4). This listing refers only to research that is not exempt.)

This category allows the prospective use of data collected for non-research purposes. Data include information from medical records, insurance claim data, educational testing data, and other non-public information in identifiable form. Data set linkages could be considered in this category. The researcher must demonstrate that sufficient measures will be used to protect the confidentiality of the data to minimize the risk to subjects of inadvertent disclosure.

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

Because recordings made of subjects are de facto identifiable, research involving these techniques, which would otherwise be exempt, are eligible for minimal risk review using the expedited procedures. Such studies will be approved if the researcher outlines appropriate mechanisms to minimize the risks of invasion of privacy and breach of confidentiality.
(7) Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies. (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b) (2) and (b) (3). This listing refers only to research that is not exempt.)

Much behavioral research that does not qualify for exemption may be reviewed as minimal risk using the expedited procedure. This category is designed to accommodate research activities that pose no more than minimal risk to subjects and that are not eligible for exemption. Please note that this category now includes minor subjects.

(8) Continuing review of research previously approved by the convened IRB as follows:

(a) Where (i) the research is permanently closed to the enrollment of new subjects; (ii) all subjects have completed all research-related interventions; and (iii) the research remains active only for long-term follow-up of subjects; or

(b) Where no subjects have been enrolled and no additional risks have been identified; or

(c) Where the remaining research activities are limited to data analysis.

Researchers who wish to have their applications for continuing review of projects previously reviewed by the full Prime IRB will have to demonstrate that the above conditions have been met.

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

This category applies to situations in which the full Prime IRB conducts a continuing review of a study and determines that the continuing activity poses only minimal risks.
B. Expanded Categories of Minimal Risk Research Procedures as Established by the Prime IRB (for research that is neither federally funded nor subject to FDA regulations)

1. Skin biopsy not requiring suturing.

2. Ionizing radiation exposure that does not exceed 100 mrem (1 mSv) per year.

3. Blood draws via an indwelling catheter, regardless of frequency.

4. Blood sampling (that meets the NIH policy) for children that is limited to no more than 5 mL/kg on a single day or 9.5 mL/kg over the course of 8 weeks and for adults to no more than 10.5 mL/kg or 550 mL, whichever is less, over the course of 8 weeks.

5. Obtaining additional blood, CSF or bone marrow at the time of a clinically indicated procedure.

6. Obtaining additional endoscopic biopsies, other than esophageal biopsies, during the course of a clinically indicated gastrointestinal endoscopy.

7. Bronchioalveolar lavage in individuals with an existing artificial airway.

8. Prolongation of clinically indicated sedation or general anesthesia.
APPENDIX 2: ADMINISTRATIVE AND MINOR MODIFICATIONS

A. Administrative Modifications

Non-material changes to research-related documentation, previously approved by the IRB, do not require IRB review and only require acknowledgment of receipt by the IRB. These changes will not affect the conduct of the research at CHOP. Examples of administrative modifications include, but are not limited to:

1. Research sponsor clarification and notification memos;
2. Protocol amendments that effect sites at other locations but do not modify the conduct of the research at CHOP;
3. DSMB or other reports with recommendations of no change to the research;
4. Typographical or editorial corrections to study documents, including consent forms, recruitment materials, protocols, etc.; and
5. Study closure notifications.

B. Minor Modifications

Proposed modifications (amendments) to research-related activities approved by the convened IRB may be considered to be minor changes provided that they are limited to one or more of the categories below. The reviewer will make the final determination whether the proposed change may be reviewed using expedited procedures as listed below.

1. Change in appropriately credentialed study personnel;
2. Change qualifying for exemption or expedited review;
3. Increase/decrease in subject number;
4. Changes to inclusion or exclusion criteria without increase in risk to subjects;
5. Changes in the dosage form (e.g., tablet to liquid) but not route of administration;
6. Changes in the number of study visits without increase in risk to subjects; and
7. Change in remuneration (i.e. payments and reimbursement) to subjects.
<table>
<thead>
<tr>
<th>Version 0.2</th>
<th>Name</th>
<th>Status (Pending, Reviewed, Approved)</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Written by:</td>
<td>Karl Nelson</td>
<td></td>
<td>17-July-2017</td>
</tr>
<tr>
<td>Reviewed by:</td>
<td>Jennifer Neal-Jimenez</td>
<td></td>
<td>6-January-2018</td>
</tr>
<tr>
<td>Approved by:</td>
<td>Jennifer Neal-Jimenez</td>
<td>Approved</td>
<td>9-January-2018</td>
</tr>
</tbody>
</table>
1 PURPOSE

1.1 The purpose of this standard operating procedure is to establish procedures for review and acknowledgment of modifications or changes to approved research.

2 REVISIONS FROM PREVIOUS VERSION

2.1 None.

3 POLICY

3.1 Investigators may not make any material changes in the research activity, except when necessary to eliminate apparent immediate hazards to the subject. Reports of significant information received by the investigator or IRB during the course of the approval period may constitute a change in the research and require modification of the research.

4 RESPONSIBILITIES

4.1 Director, Prime Review Board Services: The Director is responsible for establishing the processes for conducting ongoing reviews of research.

4.2 Chair, Prime Review Board Services: The Prime IRB Chair (or designee) is responsible for conducting expedited reviews of new reports during the approval period or assigning review to the full Board.

5 PROCEDURE

5.1 Amendments

5.1.1 Material changes in approved research may not be initiated without prior IRB review (full or expedited review, as appropriate) and approval, except where necessary to eliminate apparent immediate hazards to human subjects.
5.1.1.1. When an immediate hazard is present, investigators may take any action necessary to mitigate risk to study participants.

5.1.1.2. The investigators must promptly report to the IRB all actions taken and changes made in approved research without IRB approval.

5.1.1.3. The IRB will review the change to determine whether or not the action was consistent with ensuring the subject’s continued welfare.

5.1.2. Changes in the research activity which are anticipated, must be approved by the IRB prior to implementation; sponsor approval is necessary but not sufficient.

5.1.3. Investigators must submit the materials listed in Prime IRB SOP 300: Research Submission Requirements for IRB review of the proposed protocol amendment(s).

5.1.4. Upon receipt of the submission containing material changes, the Chair or designee will determine if the revision requires simple acknowledgment, meets the criteria for expedited review procedure or requires full Board review. Prime IRB SOP 403: Expedited Review Procedures enumerates those amendments eligible for review using expedited procedures.

5.1.5. All modifications to previously approved research will be available to all members in the eIRB system.

5.2. Reports of New Information During the Approval Period

The IRB Office may receive additional materials from the investigative team that constitute a change in the research activity. These materials will be reviewed in order to determine whether or not the materials impact the risk - benefit assessment or conduct of the research. These additional materials may include:

5.2.1. Reports generated from a Data and Safety Monitoring Board (DSMB) or study Steering Committees;

5.2.2. Reports in the current literature;

5.2.3. Updates to the Investigator’s Brochure; and

5.2.4. Complaints from research participants (or parents).
5.3 **Complaints:**

Complaints from participants may be reported to the investigator, to research staff, other personnel or directly to the IRB.”

5.3.1 When reported to the investigator, a description of the complaint, an assessment of the merits of the complaint and a summary of the actions taken by the investigator to address the issues raised including any modifications to the research will be submitted via the electronic IRB management system.

5.3.1 When the IRB receives a complaint, the following actions will take place:

5.3.1.1 The individual receiving the call will transfer the call to the Director, Prime Review Board Services or the Prime IRB Chair.

5.3.1.2 If neither the Director nor Chair is available, the Prime IRB staff member will record the study number, subject name and contact information and will obtain basic information related to the complaint. The subject/family will be contacted within 1 business day.

5.3.1.3 The Director or the Chair will discuss the events leading to the complaint with the subject/family and will provide follow up contact as necessary.

5.3.1.4 A comment will be logged in the eIRB system to document the contact and the complaint.

5.3.1.5 The Director or the Chair will discuss the complaint with the principal investigator or other representatives of the investigative team to determine the appropriate course of action.

5.4 **IRB Actions in Response to Reports of New Information**

5.4.1 Reports of new information submitted during the approval period will be reviewed using expedited procedures, as applicable. Based on the initial review, the Chair or designee may determine that the report should be forwarded to a convened IRB for review. The IRB will determine whether the new information should be communicated to research participants.

5.4.2 If the event meets the definition of an unanticipated problem, the study team will be required to report the event in the eIRB system in accordance with *Prime IRB SOP 408: Unanticipated Problems Involving Risks to Subjects.*
5.4.3. If the event represents non-compliance with the research plan, then the event will be managed in accordance with *Prime IRB SOP 800: Non-Compliance with Human Subjects Research Policies*.

6 MATERIALS

6.1 None

7 REFERENCES

45 CFR 46.103(b)(4), 110(b)
21CFR56.108(a), 110(b)
Prime IRB SOP 104: IRB Review Processes
Prime IRB SOP 300: Research Submission Requirements
Prime IRB SOP 400: Determinations and Motions
Prime IRB SOP 407: Unanticipated Problems Involving Risks to Subjects or Others
Prime IRB SOP 800: Non-Compliance with Human Subjects Research
<table>
<thead>
<tr>
<th>Version 0.2</th>
<th>Name</th>
<th>Status (Pending, Reviewed, Approved)</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Written by</td>
<td>Karl Nelson</td>
<td></td>
<td>17-July-2017</td>
</tr>
<tr>
<td>Reviewed by</td>
<td>Jennifer Neal-Jimenez</td>
<td></td>
<td>6-January-2018</td>
</tr>
<tr>
<td>Approved by</td>
<td>Jennifer Neal-Jimenez</td>
<td></td>
<td>9-January-2018</td>
</tr>
</tbody>
</table>
1 PURPOSE

1.1 The Prime Review Board Services (Prime IRB) must periodically review research activities at intervals appropriate to the degree of risk, but not less than once per year as required by the federal regulations.

1.2 The purpose of this SOP is to identify the requirements for investigators and the Prime IRB for the conduct of continuing review in accordance with the regulations and Prime IRB’s policies and procedures.

2 REVISIONS FROM PREVIOUS VERSION

2.1 None.

3 POLICY

3.1 The Prime IRB conducts continuing review of approved research at intervals appropriate to the degree of risk. Federally funded research and FDA regulated research must be reviewed at least annually. The Prime IRB must obtain and review sufficient information to conduct substantive continuing review of research.

4 RESPONSIBILITIES

4.1 Director, Prime Review Board Services: Is responsible for establishing and implementing processes for making research renewal decisions

4.2 Chair, Prime Review Board Services: The Chair (or designee) is responsible for educating the members to their role in reviewing submissions for continuing review and for conducting or delegating the expedited review of protocols.
5  PROCEDURE

5.1  Requirement for Submission of a Continuing Review

5.1.1  A complete Continuing Review Application should be submitted at least 30 days before the study approval period ends (expiration date) in order to provide sufficient time for review.

5.2  Approval Period

5.2.1  The Continuing Review submission must be reviewed and approved by the IRB prior to the expiration date in order for study-related activities involving human subjects to continue.

5.2.2  Extensions of approval cannot be granted; there is no grace period extending the conduct of the research beyond the expiration date of IRB approval.

5.2.3  If an investigator fails 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 human subjects research activities must stop, unless the IRB finds that it is in the best interest of individual subjects to continue participating in the research interventions or interactions.

5.2.3.1  Enrollment of new subjects, review of additional retrospective records or other human subjects’ activities cannot occur after the expiration of IRB approval.

5.2.3.2  No research data can be collected until the Continuing Review Submission is reviewed and approved by the IRB, unless determined otherwise by the IRB.

5.2.4  Approval period for research approved using expedited review procedures and not subject to either FDA regulations or funded by a federal grant:

5.2.4.1  The initial approval period will be for 1 year. Thereafter, the reviewer of the continuing review submission may extend the approval period based upon the nature of the research and the IRB’s experience with the individual investigator.

5.2.4.2  The maximum approval period will be 3 years.

5.3  Review Procedures

5.3.1  When considering whether or not to renew a study, the IRB reviews the study according to the same criteria used to grant initial approval, as listed in Prime IRB SOP 401: Criteria for Initial IRB Approval.
5.3.2 IRB Office and IRB Member Pre-review, Review, and Post-review procedures will be conducted as outlined in Prime IRB SOP 104: IRB Review Process.

5.3.3 The reviewer will have access to all of the study materials.

5.4 Submission Requirements

5.4.1 In order to determine the status of the study, the following will be available for the IRB members to review:

5.4.2 Materials maintained within the study workspace in the electronic IRB system including but not limited to:

5.4.2.1 Current and previous versions of IRB-approved consent document(s).

5.4.2.2 Current and previous versions of the IRB-approved protocol including any previously-approved amendments to the research.

5.4.2.3 All unanticipated problems related to the research involving risks to subjects or others including SAEs and major protocol deviations that required prompt reporting under Prime IRB SOP 407: Unanticipated Problems Involving Risks to Subjects within the last year.

5.4.2.4 All amendments to the study submitted within the last year.

5.4.2.5 A list of all current study personnel.

5.4.2.6 All relevant federal grants that provide funding for the research.

5.4.3 Continuing Review Submission and supporting documents.

5.5 Possible Outcomes of Continuing Review

As an outcome of continuing review, the IRB may take any of actions listed in Prime IRB SOP 400: Categories of Actions. Additionally, the IRB may also take any of the following actions:

5.5.1 Require revision of the protocol, consent or other approved materials consistent with the current status of the study and any change in regulatory requirements. (Comment: in eIRB, revisions must be submitted as a separate amendment).

5.5.2 Suspend or terminate approval of the research.

5.5.3 Impose special conditions or relax conditions previously imposed on the research protocol.
5.6 Expedited Review for Renewal

5.6.1 A protocol that was originally reviewed using the expedited review procedure may receive its continuing review using an expedited review procedure (Prime IRB SOP 403: Expedited Review Procedures).

5.6.2 Research, not conducted under an investigational new drug application or investigational device exemption, where expedited review Categories two (2) through eight (8) do not apply but the IRB determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified (expedited review Category 9).

5.6.3 Continuing review of research previously approved by the convened IRB as follows (expedited review Categories 8 (a)(b) or (c))

5.6.3.1 8(a) where the research is permanently closed to enrollment of new subjects and all subjects have completed all research-related interventions and the research remains active only for long-term follow-up of subjects;

5.6.3.2 8(b) where no subjects have been enrolled and no additional risk to subjects have been identified;

5.6.3.3 8(c) where the protocol remains open for data management (query resolution) or analysis.

5.6.4 When conducting research under an expedited review procedure, the IRB reviewer conducts the review using the same criteria used to grant initial approval, as listed in Prime IRB SOP 401: Criteria for Initial IRB Approval.

5.6.4.1 If the review indicates that there has been a change to either the risks or benefits, the study may be referred for full Board review.

5.7 Duration of Requirement for Continuing Review

Continuing IRB review is required as long as the research activity continues to meet the definition of human subjects’ research (see Prime IRB SOP 406: Study Completion for requirements for study completion).

6 MATERIALS

6.1 None.

7 REFERENCES

45 CFR 46.111
21CFR56.108, 56.111
OHRP Reports 95-01
Prime IRB SOP 104: IRB Review Processes
Prime IRB SOP 300: Research Submission Requirements
Prime IRB SOP 400: Determinations and Motions
Prime IRB SOP 401: Criteria for Initial IRB Approval
Prime IRB SOP 403: Expedited Review Procedures
Prime IRB SOP 406: Study Completion
Prime IRB SOP 407: Unanticipated Problems Involving Risks to Subjects
<table>
<thead>
<tr>
<th>Version 0.2</th>
<th>Name</th>
<th>Status (Pending, Reviewed, Approved)</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Written by</td>
<td>Karl Nelson</td>
<td></td>
<td>17-July-2017</td>
</tr>
<tr>
<td>Reviewed by</td>
<td>Jennifer Neal-Jimenez</td>
<td></td>
<td>6-January-2018</td>
</tr>
<tr>
<td>Approved by</td>
<td>Jennifer Neal-Jimenez</td>
<td>Approved</td>
<td>9-January-2018</td>
</tr>
</tbody>
</table>
1 PURPOSE

1.1 The purpose of this SOP is to outline the information required in order for the Prime IRB to conduct its review of completion of research. Although subjects will no longer be "at risk" as a result of participation in the study, the final report to the Prime IRB permits it to close the study files and provides information that may be used by the Prime IRB for the evaluation and approval of related studies.

2 REVISIONS FROM PREVIOUS VERSION

2.1 None.

3 POLICY

3.1 The completion of the study is considered a change in research activity and must be reported to the Prime IRB.

4 RESPONSIBILITIES

4.1 Director, Prime Review Board Services: The Director is responsible for establishing and implementing processes for making research completion decisions.

4.2 Prime IRB Analyst: The Prime IRB Analyst is responsible for ensuring all study completion documentation is complete prior acceptance of the report of study closure.

5 PROCEDURE

5.1 Determining When the Project Status May be Changed to “Complete.”

As long as human subjects research is ongoing, including analysis of the collected data that contains identifiable private information, the study must maintain Prime IRB approval. When individually identifiable data are no longer being collected, maintained for analysis or verified at the local site, and there is no further interaction or
interventions to collect data about subjects, the status of the study may be changed to “Complete” when the Investigator submits his/her Final Report to the Prime IRB.

5.1.1. Investigators must report study completion to the Prime IRB when either of the following conditions are met:

5.1.1.1. When individually identifiable data are no longer being collected and all identifiable private information has been removed from the data set that will be used for analysis purposes, the study may be closed.

5.1.1.2. When the investigator will not be involved in data management and analysis (e.g., multi-center clinical trials), when all data collection is completed at Emmes and the study sponsor has completed all closeout activities, the study may be considered complete even if there is research activity at other study sites.

5.2 Final Reports

5.2.1 A Final Report must be submitted to the Prime IRB. The final report should include study progress and must indicate that all human subjects research activity is complete and that all non-exempt research activities have ceased at the location(s) over which the Prime IRB has oversight.

5.2.2 Prime IRB staff will administratively review all final reports to ensure that the study may be closed. By submitting a Final Report, the Principal Investigator is formally attesting to the fact that all non-exempt human subjects research activities have concluded.

5.2.2.1 If any questions arise or submitted information is incomplete, additional information may be requested from the investigator by the Prime IRB staff.

5.2.2.2 Once it has been determined that human subjects research has ended the investigator will be notified of acceptance of study closure in writing and the study status is updated to reflect that the study is “Complete”.

5.2.3 Project closures are an administrative procedure conducted by the Prime IRB Operations Office on behalf of the Prime IRB. If the Prime IRB Operations Office has questions or concerns, they may refer project closure requests to the Prime IRB Chair or convened Prime IRB. The Principal Investigator will receive a letter notifying him/her that the study has been closed with the Prime IRB. Until this letter is received, Prime IRB oversight will be maintained.

5.2.4 A listing of closed studies will be included on the Prime IRB meeting agenda, and copies of the Final Report and supplementary information are made.
available to the Prime IRB members upon request. Alternatively, Prime IRB members may be made aware of the closure by cc on the letter sent to the Principal Investigator.

6 MATERIALS

6.1 None.

7 REFERENCES

21 CFR 56.103
21 CFR 56.108
21 CFR 56.109
45 CFR 46.103
45 CFR 46.108
45 CFR 46.109
<table>
<thead>
<tr>
<th>Version 0.2</th>
<th>Name</th>
<th>Status (Pending, Reviewed, Approved)</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Written by</td>
<td>Karl Nelson</td>
<td></td>
<td>17-July-2017</td>
</tr>
<tr>
<td>Reviewed by</td>
<td>Jennifer Neal-Jimenez</td>
<td></td>
<td>6-January-2018</td>
</tr>
<tr>
<td>Approved by</td>
<td>Jennifer Neal-Jimenez</td>
<td>Approved</td>
<td>9-January-2018</td>
</tr>
</tbody>
</table>
1 PURPOSE

1.1 To describe the procedures for processing reports of potential unanticipated problems involving risks to participants or others submitted to the Prime IRB.

1.2 The purpose of this policy is to define unanticipated problems establish the reporting process and timeline.

1.3 45 CFR 46.103(b)(5) and 21 CFR 56.108(b) require that Institutions engaged in human subjects’ research must have written procedures for ensuring prompt reporting to the Prime IRB, appropriate institutional officials, and any supporting department or agency head of any unanticipated problem involving risks to subjects or others.

2 REVISIONS FROM PREVIOUS VERSION

2.1 None.

3 POLICY

3.1 Principal Investigators are required to immediately submit to the Prime IRB any unanticipated problems involving risk to human subjects or others. The notification to the Prime IRB must occur no later than 2 weeks from the time of identification of the unanticipated problem.

4 RESPONSIBILITIES

4.1 Director, Prime Review Board Services: Director, Prime Review Board Services is responsible for establishing processes for Prime IRB staff to triage the review of unanticipated problems involving risks to subjects or others.

4.2 Chair, Prime Review Board Services: The Chair or Vice-Chair are responsible for initial review of possible unanticipated problems and for expedited review of
unanticipated problems that do not involve more than minimal risk to subjects or others.

4.3 Investigators: Investigators for Prime IRB approved research are responsible for reporting potential unanticipated problems involving risks to subjects or others as outlined in the Prime IRB SOP 700: Investigator Responsibilities and in the Investigator Responsibilities information sheet.

5 PROCEDURE

5.1 Assessment of Potential Unanticipated Problems

If the investigator determines that the incident, experience, or outcome represents an unanticipated problem, the investigator must report it promptly to the Prime IRB.

5.1.1 Assessments of adverse events are described in Section 5.2;
5.1.2 Assessments of unanticipated problems that are not adverse events are described in Section 5.3.

Some of the AEs experienced by subjects enrolled in research studies will meet the criteria for unanticipated problems involving risks to subjects or others and so must be reported promptly to the Prime IRB. However, the vast majority of adverse events, both SAEs and non-serious AEs, occurring in the context of research, are expected considering the known toxicities and side effects of the research procedures or are expected due to the natural history of subjects’ underlying diseases and conditions. Thus, most individual AEs do not represent unanticipated problems subject to the reporting requirements outlined in the federal regulations at 45 CFR 46.103(b)(5) and 21 CFR 56.108(b)(1).

5.2 Potential Unanticipated Problems: Adverse Events

In order for an adverse event to meet the definition of an unanticipated problem involving risk to subjects or others the adverse event must meet the following conditions. It must be unexpected, it must be related to the research, and it must suggest that subjects are at greater risk than was previously known or recognized. The investigator must determine that these conditions are met before reporting the event to the Prime IRB.

5.2.1 Assessment of whether an adverse event is unexpected
5.2.2 Assessment of whether an unanticipated problem is related to the research.
5.2.2.1 Unanticipated problems and adverse events may be caused by one or more of the following: (1) the procedures involved in the research; (2) an underlying disease, disorder, or condition of the subject; or (3) other circumstances unrelated to either the research or any underlying disease, disorder, or condition of the subject.

5.2.2.2 Unanticipated problems and adverse events that are determined to be at least partially caused by one or more procedures involved in the research activity are considered related to participation in the research, whereas adverse events determined to be solely caused by a subject’s underlying disease or other circumstances unrelated to the research are considered unrelated to participation in the research.

5.3 Unanticipated Events that are not Adverse Events and Require Reporting

Events that expose research subjects or others to a risk of physical, social or psychological harm, which is greater than the risk to subjects that was previously known or recognized, should be promptly reported when they warrant a change in the research protocol, the informed consent process, the informed consent document or other protective action is required to protect the rights and welfare of research participants or others.

Examples of unanticipated problems that are not adverse events that require reporting to the Prime IRB due to their serious nature and relatedness to the research include:

5.3.1 Breach of privacy or confidentiality, including lost or stolen confidential information that might involve risk to that individual or others;

5.3.2 Receipt of the wrong dose of a study medication without evidence of harm;

5.3.3 Contaminated study drug (put subjects at risk of harm);

5.3.4 Publication in the literature, safety monitoring report, including a Data and Safety Monitoring Report, interim result, or other finding that indicates an unexpected change to the risk - benefit assessment;

5.3.5 Accidental or unintentional change to the Prime IRB-approved protocol that involves risks or has the potential to recur;

5.3.6 Complaint from a subject or family member that indicates an unanticipated problem;

5.3.7 Laboratory or medication errors that may involve risk to that individual or others
5.3.8 Change in FDA labeling because of adverse consequences or withdrawal from marketing of a drug, device, or biologic used in a research protocol;

5.3.9 Disqualification or suspension of an investigator;

5.3.10 Sponsor imposed suspension of the study or study enrollment for risk;

5.3.11 Change in the status of a subject that might affect their eligibility to remain in the study, require their withdrawal from the study or require the Prime IRB to re-review the research to make determinations that adequate protections are in place to protect vulnerable populations. Examples include:

5.3.11.1 Incarceration within a penal institution or detention facility;

5.3.11.2 Pregnancy at any time during participation in a research study;

5.3.11.3 Transfer of a child from their parents/guardians to foster care (ward of the state).

5.3.12 Other events that are unanticipated and indicate the potential for increased risk of harm to subjects or others.

5.3.13 Potential non-compliance with Prime IRB research policies, federal research regulations or State laws controlling the conduct of research must be reported in accordance with the Prime IRB’s Non-Compliance Policy (Prime IRB SOP 800: Non-Compliance with Human Subjects Research Policy.)

5.4 Reporting Unanticipated Problems Involving Risks to Subjects or Others to the Prime IRB

5.4.1 All internal (at Prime IRB) unanticipated problems that are both serious (including SAEs) and related (at least possibly related) to the research procedures must be reported promptly to the Prime IRB. Investigators must report these events in accordance with the following timeline:

5.4.1.1 Those events that are either life-threatening or which result in death must be reported to the Prime IRB via telephone, fax or email, within one business day of discovery. The full report must be submitted to the Prime IRB within 48 hours of initial notification.

5.4.1.2 Events that are not life-threatening and do not result in death, must be reported to the Prime IRB within 7 business days of discovery.

5.4.2 A full report comprises the following materials and must be completed and submitted in accordance with the time requirements listed above:

5.4.2.1 SAE report pathway in the eIRB electronic IRB management system
5.4.2.1.1 Information such as a summary of the event, the cooperating center, or drug company reports should be attached and submitted when applicable.

5.4.2.1.2 The information included in the SAE report can be abbreviated when supplemental materials (below) are available.

5.4.2.2 The case-report form pages prepared for the study sponsor must be attached (when applicable);

5.4.2.3 MedWatch or CIOMS form must be attached (when available);

5.4.3 In addition to their reporting responsibilities to the Prime IRB, investigators must meet the reporting requirements of the study sponsor, the monitoring entity, coordinating center, applicable regulatory agencies (NIH, FDA, etc.) and those of the CTRC (if applicable).

5.4.4 All reports of external (at sites other than Prime IRB) unanticipated problems including SAE reports that are both serious and related to the research procedures must be reported to the Prime IRB within 7 days of receipt of the report from the study sponsor. External reports that do not meet the criteria for an unanticipated problem do not need to be forwarded to the Prime IRB.

5.5 Investigation and Evaluation of Reports of Unanticipated Problems

Once a report of a potential unanticipated problem is received in the Prime IRB Office the following actions will occur:

5.5.1 The report will be screened by the Director, Prime Review Board Services or designee to determine:

5.5.1.1 Whether the events are possibly unanticipated problems and are related to the research and increase risks to subjects or others. If there are questions regarding the classification of the event, the Chair or designee will be contacted.

5.5.1.2 Whether the currently enrolled or prospective subjects in the trial may be subject to immediate increased harm to their health, safety, or welfare. If a concern arises, the Chair or designee will be promptly contacted and if necessary, the protocol be suspended or terminated in accordance with Prime IRB SOP 409: Suspensions and Terminations of Research.

5.5.2 Reports that do not meet these reporting criteria will be acknowledged and will be retained in the eIRB electronic management system.
5.5.3 The investigator will receive notification, acknowledging receipt, and whether additional information, action, or reporting is required.

5.6 Prime IRB Review and Determinations

When the Director, Prime Review Board Services determines that a reported event possibly constitutes an unanticipated problem involving risks to subjects or others, the event will be triaged to the Chair or Vice-Chair, Prime Review Board Services for review. All materials submitted in the eIRB system will be available for review.

5.6.1 Chair or Vice-Chair may make a final determination as to whether the event meets the criteria for an unanticipated problem involving risks to subjects or others or forward the report to the convened Prime IRB.

5.6.2 Those events that do not meet the criteria will be acknowledged and filed.

5.6.3 For events meeting the criteria for an unanticipated problem, the Prime IRB, Chair or Vice-Chair may make multiple determinations. These include but are not limited to the following:

5.6.3.1 Additional information is required to clarify the events or circumstances;

5.6.3.2 No further Prime IRB action is required;

5.6.3.3 Recommend modification of the protocol including inclusion and exclusion criteria, the consent process, the consent document(s), the monitoring frequency, or other aspects of the safety management and reporting plan;

5.6.3.4 Determine that the protocol should be suspended or terminated (Prime IRB SOP 409: Suspensions and Terminations of Research);

5.6.3.5 Refer the report to the Office of Research Compliance and Regulatory Affairs for an internal investigation (audit) of the study.

5.6.3.6 Require notification of participants;

5.6.3.7 Require that enrolled subjects be provided with additional information (e.g., verbal information, written addendum, revised consent document). This will be required whenever the information may relate to the participants’ willingness to continue participating;

5.6.3.8 Determine that the incident may involve serious or continuing noncompliance (Prime IRB SOP 800: Non-Compliance with Human Subjects Research Policy);
5.6.3.9 Require notification of investigators at other sites;
5.6.3.10 Observe the process of informed consent
5.6.3.11 Refer concerns or findings to other parts of the organization that administer other policies, laws, and regulations.

5.6.4 The Prime IRB, Chair or Vice-Chair will determine whether the research still meets the criteria for approval, whether risks to subjects have been minimized and are reasonable in relation to anticipated benefits, if any, to the subjects and the importance of the knowledge that may reasonably be expected to result and whether additional action may be warranted by the Prime IRB in order to protect current and prospective participants.

5.6.5 Applicable unanticipated problems involving risks to subjects or others will be reported in accordance with Prime IRB SOP 806: Reporting to Regulatory Agencies and Sponsors.

5.7 Additional Investigator Responsibilities

5.7.1 Any proposed changes to the research study in response to an unanticipated problem must be reviewed and approved by the Prime IRB before being implemented, except when necessary to eliminate apparent immediate hazard to subjects (Prime IRB SOP 700: Investigator Responsibilities).

6 MATERIALS

6.1 None.

7 REFERENCES

21 CFR 312.32
21 CFR 56.109, 21 CFR 56.113
21 CFR 812.50
45 CFR 46.109, 45 CFR 46.113
Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events. OHRP January 15, 2007
<table>
<thead>
<tr>
<th>Version 0.2</th>
<th>Name</th>
<th>Status (Pending, Reviewed, Approved)</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Written by</td>
<td>Karl Nelson</td>
<td></td>
<td>17-July-2017</td>
</tr>
<tr>
<td>Reviewed by</td>
<td>Jennifer Neal-Jimenez</td>
<td></td>
<td>7-January-2018</td>
</tr>
<tr>
<td>Approved by</td>
<td>Jennifer Neal-Jimenez</td>
<td>Approved</td>
<td>9-January-2018</td>
</tr>
</tbody>
</table>
1 PURPOSE

1.1 The purpose of this Standard Operating Procedure is to delineate when an investigator must obtain an Investigational New Drug (IND) or Investigational Device Exemption (IDE) Submission prior to IRB approval of proposed research.

2 REVISIONS FROM PREVIOUS VERSION

2.1 None.

3 POLICY

3.1 The U.S. Food and Drug Administration (FDA) regulates the marketing of new drugs, biologics or devices. FDA’s regulations specify the circumstances under which either an IND (21 CFR 312) or an IDE (21 CFR 812) are required prior to conducting a clinical investigation. When a marketed drug or device is the subject of proposed research, investigators are required to submit their determination that the research meets the requirements for exemption from these requirements. They must also submit supporting documentation to allow the IRB to concur or disagree with their determination that an IND or IDE is not required for that use. If uncertainty exists, the IRB may resolve the matter by requesting that the investigator consult with FDA.

4 RESPONSIBILITIES

4.1 Director, Prime Review Board Services: Responsible for reviewing incoming submissions and conducting preliminary review for either IND or IDE requirement.

4.2 Chair, Prime Review Board Services: Responsible for making sure IRB committee deliberations consider whether an IND or IDE is required and confirming the validity of IND or IDE numbers, or delegating confirmation to designated committee member(s).

4.3 Designee: Responsible for making sure IRB committee deliberations consider whether an IND or IDE is required and confirming the validity of IND or IDE numbers.
5 PROCEDURE

5.1 Investigational New Drug

When use of an investigational drug is proposed, an IND Submission to the FDA is required. Confirmation of the FDA-distributed IND number is required for final IRB approval of a protocol to be granted.

To document a valid IND number, investigators are required to submit the notification of the IND number assigned from the FDA, a letter from the sponsor, or the commercially or NIH-sponsored protocol containing the IND number. The IRB will confirm the validity of the IND number.

5.2 Research Involving an FDA-Approved Drug for an Unapproved Use

The clinical investigation of a marketed drug or biologic does not require submission of an IND provided that one of the following Exemptions is met:

5.2.1 §312.2(b) Exemption 1: All six conditions specified in 21 CFR 312.2(b)(1) are met:

5.2.1.1 The study is not intended to be reported to FDA in support of a new indication for use or to support any other significant change in the labeling for the drug;

5.2.1.2 The study is not intended to support a significant change in the advertising for the product;

5.2.1.3 The study does not involve a route of administration or dosage level, use in a subject population, or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product;

5.2.1.4 The study is conducted in compliance with the requirements for IRB review and informed consent [21 CFR parts 56 and 50, respectively];

5.2.1.5 The study is conducted in compliance with the requirements concerning the promotion and sale of drugs [21 CFR 312.7]; and

5.2.1.6 The study does not intend to invoke 21 CFR 50.24.

5.2.2 §312.2(b) Exemption 2:

5.2.2.1 A clinical investigation is for an in vitro diagnostic biological product that involves one or more of the following:
5.2.2.1 Blood grouping serum
5.2.2.1.2 Reagent red blood cells
5.2.2.1.3 Anti-human globulin

5.2.2.2 The diagnostic test is intended to be used in a diagnostic procedure that confirms the diagnosis made by another, medically established, diagnostic product or procedure; and

5.2.2.3 The diagnostic test is shipped in compliance with 21 CFR 312.160.

5.2.3 §312.2(b) Exemption 4: A clinical investigation involving use of a placebo if the investigation does not otherwise require submission of an IND.

5.3 Investigator’s Responsibilities

FDA Guidance assigns the responsibility to the investigator to ensure that the above requirements are met.

5.3.1. The IRB will review the information provided by the investigator.

5.3.2. If the IRB concurs with the investigators determination, then an IND is not required.

5.3.3. If the IRB does not concur, the investigator must either submit a request for an exemption from the FDA or obtain an IND.

5.3.1.1 If the FDA issues an exemption, an IND is not required.

5.3.1.2 If the FDA disagrees that the investigation meets the criteria for exemption, the investigator must obtain an IND for the proposed investigational use of the drug/biologic.

5.4 Investigational Devices

The Investigational Device Exemptions (IDE) regulation (21 CFR 812) describes three types of device studies: significant risk (SR), non-significant risk (NSR), and exempt studies. Sponsors are responsible for making the initial risk determination and should provide the IRB with their risk assessment and the rationale used in making its SR or NSR determination.

To document a valid IDE number, investigators are required to submit the notification of the IDE number assigned from the FDA, a letter from the sponsor, or the commercially or NIH-sponsored protocol containing the IDE number. The Chair, CPHS or designee will confirm the validity of the IDE number.

5.4.1 Significant Risk Devices
5.4.1.1 If the Sponsor or the FDA has already determined that the device is a significant risk device, the investigator must present evidence of an FDA-approved IDE.

5.4.2 Non-Significant Risk Devices

5.4.2.1 An IDE is not required prior to IRB review and/or approval of a study of a NSR device, however the IRB must make a determination that the device meets the criteria for an NSR device.

5.4.2.1.1 In order to make a determination, the IRB will review the relevant information provided by the sponsor and investigator at a convened meeting. The required information includes a description of the device, reports of prior investigations conducted with the device, the proposed investigational plan, and subject selection criteria.

5.4.2.1.2 The IRB may agree or disagree with the sponsor’s initial NSR assessment.

5.4.2.2 If the IRB determines the device is NSR, the IRB may approve the study using the criteria at 21 CFR 56.111. The study may begin without submission of an IDE application to FDA. The approved NSR device must meet comply with the abbreviated IDE requirements defined below:

5.4.2.2.1. The device is not a banned device.

5.4.2.2.2. The sponsor labels the device in accordance with 21 CFR §812.5.

5.4.2.2.3. The sponsor obtains IRB approval of the investigation after presenting the reviewing IRB with a brief explanation of why the device is not a significant risk device, and maintains such approval.

5.4.2.2.4. The sponsor ensures that each investigator participating in an investigation of the device obtains, from each subject under the investigator’s care, consent under 21 CFR §50 and documents it, unless documentation is waived.

5.4.2.2.5. The sponsor complies with the requirements of 21 CFR §812.46 with respect to monitoring investigations;

5.4.2.2.6. The sponsor maintains the records required under 21 CFR
CFR §812.140(b)(4) and (5) and makes the reports required under 21 CFR §812.150(b) (1) through (3) and (5) through (10);

5.4.2.2.7. The sponsor ensures that participating investigators maintain the records required by 21 CFR §812.140(a)(3)(i) and make the reports required under §812.150(a) (1), (2), (5), and (7); and

5.4.2.2.8. The sponsor complies with the prohibitions in 21 CFR §812.7 against promotion and other practices.

5.4.2.3. If an IRB determines that an investigation, presented for approval under 812.2(b)(1)(ii), involves a significant risk device, it shall so notify the investigator and, where appropriate, the sponsor. The study may not be approved until the investigator presents evidence of an FDA-approved IDE or the FDA makes a final determination that the device is NSR.

5.4.3. Devices that Qualify for an Exemption

In accordance with 21 CFR 812.2(b), sponsors and investigators of certain studies are exempt from the requirements of 21 CFR Part 812 (with the exception of §812.119, disqualification of a clinical investigator). Examples of exempt studies are consumer preference testing, testing of a device modification, or testing of two or more devices in commercial distribution if the testing does not collect safety or effectiveness data, or put subjects at risk. These studies include:

5.4.3.1. Studies of an already cleared medical device in which the device is used or investigated in accordance with the indications in the cleared labeling are exempt from Part 812.

5.4.3.1.1. Studies of a cleared device for a new use must comply with the human subject protection (informed consent and additional safeguards for children in research), IRB, and IDE regulations.

5.4.3.1.2. Studies of a PMA approved device are exempt from the IDE requirements if the device is being studied for the indications in the approved labeling.

5.4.3.2. Diagnostic device studies (e.g., in vitro diagnostic studies) are exempt from the requirements of 21 CFR Part 812 under certain circumstances.
5.4.3.2.1. If the sponsor complies with the requirements at 21 CFR 809.10(c) for labeling; and

5.4.3.2.2. If the testing: (i) is noninvasive; (ii) does not require an invasive sampling procedure that presents significant risk; (iii) does not by design or intention introduce energy into a subject; and (iv) is not used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure (21 CFR 812.2(c)(3)).

5.4.3.3. A custom device, as defined in 21 CFR §812.3(b), unless the device is being used to determine safety or effectiveness for commercial distribution.

6 MATERIALS

6.1 None.

7 REFERENCES

45 CFR 46.108, 45 CFR 46.111
21CFR312, 21 CFR 314.21
21 CFR 56.108, 21 CFR 56.111
CFR 812

Humanitarian Device Exemption (HDE) Regulation: Questions and Answers; Final Guidance for Industry (CDRH, July 2001)


Information Sheet Guidance for IRB’s, Clinical Investigators and Sponsors. Significant Risk and Nonsignificant Risk Medical Device Studies (FDA, January 2006)

Prime IRB SOP 300: Research Submission Requirements

Prime IRB SOP 401: Criteria for Approval

Prime IRB SOP 700: Investigator Responsibilities
<table>
<thead>
<tr>
<th>Version 0.2</th>
<th>Name</th>
<th>Status (Pending, Reviewed, Approved)</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Written by</td>
<td>Karl Nelson</td>
<td></td>
<td>17-July-2017</td>
</tr>
<tr>
<td>Reviewed by</td>
<td>Jennifer Neal-Jimenez</td>
<td></td>
<td>7-January-2018</td>
</tr>
<tr>
<td>Approved by</td>
<td>Jennifer Neal-Jimenez</td>
<td>Approved</td>
<td>9-January-2018</td>
</tr>
</tbody>
</table>
1 PURPOSE

1.1 The purpose of this policy is to define the procedures the Prime IRB will follow when suspending or terminating Prime IRB approved human subjects research.

2 REVISIONS FROM PREVIOUS VERSION

2.1 None.

3 POLICY

3.1 This policy is established to comply with the regulatory requirement in 45 CFR 46.103(b)(5)(ii) and 21 CFR 56.108(b)(3) requiring IRBs to have written procedures ensuring prompt reporting to the IRB, appropriate Institutional Officials, Office for Human Research Protections, and, when applicable, the Food and Drug Administration (FDA), any suspension or termination of IRB approval.

3.2 Consistent with federal regulations, the Prime IRB has the authority to suspend or terminate approval of research that is not being conducted in accordance with the requirements or determinations of the Prime IRB or that has been associated with unexpected serious harm to subjects, or where suspension or termination has been initiated by a sponsor or other outside entity.

3.3 Any suspension or termination of Prime IRB approval of research for cause shall be reported promptly to the Principal Investigator, the Relying Institution, the Institutional Official, and to the Office for Human Research Protection (OHRP) and other federal agencies as appropriate.

3.4 All currently approved research is subject to modification or change in approval status, as deemed necessary by the Prime IRB. The Prime IRB may ask the Principal Investigator to place research on administrative hold to gather information or the Prime IRB may suspend or terminate research due to cause for the research not being conducted in accordance with the Prime IRB’s requirements or the Federal regulations or if it has been associated with unexpected serious harm to participants.
3.5 An administrative hold does not apply to interruptions of research related to concerns regarding the safety, rights, or welfare of human research participants, research investigators, research staff, or others. If there is an unanticipated problem involving risks to participants or others, the study is not eligible for an administrative hold.

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

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

4 RESPONSIBILITIES

4.1 Director, Prime Review Board Services: Responsible for notifying the research community of investigator responsibilities regarding suspensions and terminations.

4.2 Chair, Prime Review Board Services: Responsible for making sure the IRB adheres to their responsibilities regarding suspensions and terminations.

4.3 Investigator: Responsible for adhering to their responsibilities noted in this SOP pertaining to suspensions and terminations.

   The Principal Investigator will:

   4.3.1 Cease research activities as specified in the Prime IRB notification until notified that the Prime IRB has granted approval for resumption of the research activities, or in the case of termination, cease all research activities.

   4.3.2 Notify subjects of the suspension or termination as directed by the Prime IRB.

   4.3.3 Report to the Prime IRB any unanticipated problems involving risk to subjects or others that occur while the research activities are suspended.

   4.3.4 Comply with all corrective action(s) as directed by the Prime IRB.

   4.3.5 Consider actions to protect the rights and welfare of study subjects.

4.4 The Prime IRB in convened meeting will:

   4.4.1 Review any suspension or termination initiated by the sponsor or other outside entity.

   4.4.2 Notify the Principal Investigator and Relying Institution that research activities have been suspended or terminated and provide the rationale for their action.

   4.4.3 Direct the Principal Investigator and Relying Institution to undertake corrective action as appropriate. See Prime IRB SOP 800: Investigating Any Non-
Compliance, Serious or Continuing Non-Compliance for a list of possible actions.

4.4.4 Direct the Principal Investigator and Relying Institution to notify subjects of the suspension or termination as appropriate.

4.4.5 Review reports of unanticipated problems involving risks to subjects or others during the time in which research is suspended for cause.

4.4.6 Report any suspension for cause or termination for cause to the Institutional Official, to the Relying Institution, and to regulatory agencies as appropriate. See Prime IRB SOP 806: Reporting to the Appropriate Institutional Officials, and the Department or Agency Head(s).

4.4.7 Consider actions to protect the rights and welfare of study subjects.

5 PROCEDURE

5.1 Investigator Initiated Holds

The investigator may choose to initiate an Administrative Hold either at the request of the multi-center study leadership (e.g., the study sponsor or data coordinating center) or on his/her own initiative. An Administrative Hold may be used to correct a study-wide or site-specific issue that has potential for resulting in harm to subjects (e.g., problem with drug supply, faulty instructions for drug administration).

5.1.1 The investigator must report the administrative hold to the IRB, along with the rationale for the hold and the corrective action plan.

5.1.2 If subjects are currently receiving a study intervention, the investigator must request that the IRB permit subjects to continue on treatment. The basis for the IRB’s determination will be as outlined below in Section 5.5 of this SOP.

5.1.3 In order to reactivate IRB approval for enrollment of new subjects, an amendment must be submitted outlining the changes in the research that have been made to mitigate risk to subjects.

5.2 Administrative Hold.

5.2.1 The Prime IRB may ask the Principal Investigator to place some or all research activities on hold until additional information can be obtained in order to determine if a change in the risk-potential benefit profile has occurred, if a change in the rights or welfare of the participants has occurred or if potential areas of non-compliance exist in a currently approved research protocol. This may occur through various sources including:
5.2.1.1 A complaint received by the Prime IRB (See Prime IRB SOP 806: Reporting to the Appropriate Institutional Officials, and the Department or Agency Head(s));

5.2.1.2 An allegation of noncompliance made to the Prime IRB (See Prime IRB SOP 800: Investigating Any Non-Compliance, Serious or Continuing Non-Compliance);

5.2.1.3 A discovery by the Principal Investigator of potential additional risks; or

5.2.1.4 Prime IRB deliberations.

5.2.2 The Prime IRB notifies the Principal Investigator in writing or by phone of the Prime IRB’s request for “Administrative Hold,” the time-frame for responding, and the specific requested activities to be placed on hold.

5.2.3 If the Principal Investigator does not respond within the Prime IRB’s requested time-frame, the study is suspended and reporting occurs in accordance with the Prime IRB policy on reporting to institutional officials (See Prime IRB SOP 806: Reporting to the Appropriate Institutional Officials, and the Department or Agency Head(s));

5.2.4 At any point, the Prime IRB may request or make recommendations for additional education and/or compliance interventions for the Principal Investigator and his/her staff through the Prime IRB Chair.

5.2.5 If the additional information is evaluated and it is determined that no change to the risk- potential benefit profile has occurred, rights or welfare of participants has not been compromised and the issue of non-compliance has been ruled out, the Prime IRB notifies the Principal Investigator that the study may return to active status. Otherwise, the matter is referred to the convened Prime IRB.

5.3 Sponsor-Imposed Suspensions.

5.3.1 Notification of suspension by sponsor unrelated to risk is submitted to the Prime IRB for review and approval as a modification to previously approved research. Such modifications are considered minor and may be reviewed by the expedited procedure (See Prime IRB SOP 404: Amendments and Reports of New Findings).

5.3.2 Notification of suspension by sponsor possibly related to risk is submitted to the Prime IRB for review by the full Prime IRB for evaluation as a potential unanticipated problem(s) involving risk to participants or others (See Prime IRB SOP 700: Informing Obligations for Investigators), and as a review of a modification to previously approved research.
5.4 Study Expiration.

5.4.1 If the Principal Investigator has failed to provide continuing review information to the Prime IRB or the Prime IRB has not reviewed and approved a research study by the specified continuing review expiration date, the study expires. Enrollment of new participants cannot occur after the expiration of Prime IRB approval and all research activities must stop.

5.4.2 The Prime IRB notifies the Principal Investigator in writing of the Study Expiration.

5.4.2.1 The letter indicates that after the expiration date:

5.4.2.1.1 Enrollment of new participants must stop;
5.4.2.1.2 All research activities must stop; and
5.4.2.1.3 Any continuation of research activity is a violation of federal regulations.

5.4.2.1.4 It is acceptable to the Prime IRB to continue study-related intervention with any subjects currently enrolled to the extent necessary for their safety and well-being.

5.4.3 Studies not submitted for continuation within ninety (90) days of the notification of Expiration are administratively closed by the Prime IRB. Reinstatement of the research requires submission of a research protocol for initial review.

5.5 IRB Suspension or Termination of Research

5.5.1 The convened IRB may suspend or terminate previously approved research as the result of the following circumstances:

5.5.1.1 Serious or continuing non-compliance (Prime IRB SOP 800: Non-Compliance with Human Subjects Research Policy);

5.5.1.2 Evidence that the research intervention or monitoring procedures present undue risk of harm to participants (Prime IRB SOP 407: Unanticipated Problems Involving Risks to Subjects);

5.5.1.3 Evidence of serious issues with study conduct discovered during the review of the research (Prime IRB SOP 405: Continuing Review of Approved Research);

5.5.1.4 New report of an unmanageable financial Conflict of Interest related to the research (Prime IRB SOP 804: Handling Investigators and Team Members Conflict-of-Interest Issues).
5.5.1.5 Disqualification of the Principal Investigator by OHRP, the FDA, the study sponsor, the Emmes Corporation’s Office of Compliance and Regulatory Affairs or other offices or bodies providing oversight of human subjects’ research activities.

5.5.2 The Chair, Prime IRB (or Vice-Chair) may also suspend or terminate research on an urgent basis, as deemed necessary, to protect the rights and welfare of participants. If the Chair Prime IRB exercises the authority to suspend or terminate approval, the convened IRB will be informed of this action and will determine the appropriate course of action going forward.

5.5.3 The Prime IRB reports in writing, all suspensions due to cause, promptly to the Principal Investigator and the Relying Institution. The letter:

5.5.3.1 Includes a statement of the reasons for the Prime IRB's action;

5.5.3.2 Describes requirements of the Prime IRB for orderly suspension or termination of the research which may include

5.5.3.2.1 a request for the Principal Investigator to submit to the Prime IRB proposed procedures for withdrawal of currently enrolled subjects that considers their rights and welfare;

5.5.3.2.2 a request for the Principal Investigator to provide the Prime IRB with draft materials (e.g. a script, letter, or similar) to notify current subjects who are affected by the suspension or termination; or

5.5.3.2.3 a request that the Principal Investigator report any events to the Prime IRB or sponsor that would have required reporting had the former subjects continued to be enrolled in the research.

5.5.4 Principal Investigators receiving repetitive suspensions or terminations due to cause may necessitate review for potential serious and continuing non-compliance (See Prime IRB SOP 407: Review of Adverse Events, Serious Adverse Events and Unanticipated Problems Involving Risk to Participants or Others).

5.5.5 All suspensions and terminations will be reported according to Prime IRB Policy (See Prime IRB SOP 806: Reporting to the Appropriate Institutional Officials, and the Department or Agency Head(s)).

5.3. Subject Withdrawal and Notification Procedures
For interventional studies that are suspended or terminated by the IRB, the IRB Chair or convened IRB considers and determines whether subjects currently on active treatment must be withdrawn from the study; will be placed at risk of harm by withdrawing them from the study; or must continue to be followed for safety reasons. For non-interventional studies, the IRB Chair or convened IRB will determine whether or not participants must be withdrawn from the study or notified by the investigator.

5.3.1. Early Withdrawal of Subjects: When the suspension or termination involves withdrawal of subjects from an interventional study, the IRB considers and determines what, if any, termination procedures are required for the safety and welfare of those subjects. Termination procedures may include, but are not limited to the following:

5.3.1.2. tapering of the study drug;
5.3.1.3. having a final study visit at which a physical exam and/or laboratory or other tests will be performed; or
5.3.1.4. making arrangements for subjects to receive medical care by their primary care physician or specialist or through referrals to other healthcare providers.

5.3.2. Subjects who are at Risk of Harm: If the IRB determines that the suspension or termination will place subjects at risk of harm, the IRB must consider and determine what subjects are to be told and the manner in which they are to be notified, e.g., in writing, in person, or by telephone.

5.3.3. Subject Follow-Up: When the IRB requires or approves subject follow-up for safety reasons, the investigator is subject to continuing review and is required to promptly report any unanticipated problems involving risks to subjects or others, including adverse events, to the IRB and, when applicable, the sponsor in accordance with Prime IRB SOP 404: Amendments and Reports of New Findings and Prime IRB SOP 407: Review of Adverse Events, Serious Adverse Events and Unanticipated Problems Involving Risk to Participants or Others.

5.3.4. Subject Notification: Depending upon the reasons for the suspension or termination and the design of the protocol, the IRB may require that the following subjects be notified of the suspension or termination:

5.3.4.2. all subjects who have been or are enrolled;
5.3.4.3. subjects currently on protocol; or
5.3.4.4. subjects who participated in a certain aspect of the protocol.
5.4. Communication with Principal Investigator and Relying Institution

5.4.1. Results of a “For Cause Review” that results in Suspension or Termination by the Prime IRB will promptly be sent to the Principal Investigator, and Relying Institution in writing. All for Cause Suspensions or Terminations will be reported to regulatory agencies and institutional officials in accordance with the Prime IRB’s external reporting policy (See Prime IRB SOP 806: Reporting to the Appropriate Institutional Officials, and the Department or Agency Head(s)).

5.4.2. If the Investigator’s research privilege or subject enrollment in the research study (or any other research studies) has been suspended by the Prime IRB, the letter will outline the conditions or timeframe for lifting the suspension.

5.4.3. The Investigator must acknowledge receipt of the letter and respond to any instructions included in the letter within ten (10) working days of receipt of a “For Cause Review” that results in Suspension or Termination. Any response from the Investigator related to the Prime IRB’s investigation, findings, or instructions will be brought before the full Prime IRB.

5.5. Reporting to the Institutional Official, Human Protections Administrator, Regulatory Agencies, and Sponsors

5.5.1. Whenever the Prime IRB suspends or terminates a research study involving human subjects, the IRB Director, the CPHS Chair or designee shall be responsible for submitting a written report to the Institutional Official. The Institutional Official will report applicable suspensions and termination following Prime IRB SOP 806: Reporting to Regulatory Agencies & Sponsors.

5.5.2. If the Prime IRB determines that under applicable regulations or under the terms of the Relying Institution’s FWA a report is required to a regulatory agency (e.g., OHRP, FDA), and/or other oversight authority of a For Cause Suspension or Termination, the Prime IRB will communicate this action according to Prime IRB SOP 806: Reporting to Regulatory Agencies & Sponsors.

6 MATERIALS

6.1 None.

7 REFERENCES

21 CFR Part 56.108(b)(3)
21 CFR Part 56.113
45 CFR Part 46.113
45 CFR Part 46103(b)(ii)

Prime IRB SOP 404: Modifications to Previously Approved Research and New Information
Prime IRB SOP 405: Continuing Review of Approved Research
Prime IRB SOP 407: Unanticipated Problems Involving Risks to Subjects
Prime IRB SOP 800: Non-Compliance with Human Subjects Research Policies
<table>
<thead>
<tr>
<th>Version 0.3</th>
<th>Name</th>
<th>Status (Pending, Reviewed, Approved)</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Written by:</td>
<td>Karl Nelson</td>
<td></td>
<td>26-March-2018</td>
</tr>
<tr>
<td>Reviewed by</td>
<td>Jennifer Neal-Jimenez</td>
<td></td>
<td>26-March-2018</td>
</tr>
<tr>
<td>Approved by</td>
<td>Jennifer Neal-Jimenez</td>
<td>Approved</td>
<td>26-March-2018</td>
</tr>
</tbody>
</table>
1 PURPOSE

1.1 The purpose of this operating procedure is to address the review of research involving individuals or groups that could be potentially vulnerable to coercion or undue influence because of neurological or psychiatric disorders; educational disadvantages; medical, social, or economic conditions; or other circumstances that might restrict the individual’s capacity to provide informed consent or to protect their own interests.

2 REVISIONS FROM PREVIOUS VERSION

2.1 None.

3 POLICY

3.1 Certain populations may be prone to be vulnerable to the consequences of participation in a research study. This vulnerability may be either through limited self-determination capacity or through exposure to external undue influence. The extent of protection afforded should depend upon the risk of harm, the likelihood of benefit, and the ability of the individual to make reasoned decisions. The judgment that any individual lacks autonomy should be periodically reevaluated and will vary in different situations.

3.2 The IRB will assure that additional protections are implemented, as necessary, to protect vulnerable research subjects. The extent of additional protection afforded should depend upon the risk of harm and the likelihood of benefit.

4 RESPONSIBILITIES

4.1 Director, Prime Review Board Services: Responsible for making sure appropriate representatives are present during review of research involving vulnerable subjects.

4.2 Chair, Prime Review Board Services: Responsible for making sure meetings are conducted adhering to regulations outlined in Subpart B, C, and D.
5 PROCEDURE

5.1 Review, Revision, Approval of Research Involving Vulnerable Subjects

5.1.1 When there is a reasonable expectation that prisoners will participate in the research, or that subjects who participate have a reasonable likelihood of being incarcerated at some time point during the study, the procedures outlined in *Prime IRB SOP 502: Research Involving Prisoners* will be followed.

5.1.2 When pregnant women, fetuses, neonates who are either non-viable or of uncertain viability will participate in the research, or when the research will involve fetal materials or products of conception, the procedures outlined in *Prime IRB SOP 501: Research Involving Pregnant Women, Fetuses, and Neonates* will be followed.

5.1.3 When children will participate in the research, the procedures outlined in *Prime IRB SOP 503: Research Involving Children* will be followed.

5.1.4 When minors who do not meet the definition of “children” will participate in the research, the procedures outlined in *Prime IRB SOP 504: Minors Who Are Not Children in the Research Context* will be followed.

5.1.5 When there is a reasonable possibility that Wards and Foster Children will participate in the research, the procedures outlined in *Prime IRB SOP 503: Research Involving Children* will be followed.

5.1.6 When adults with limited capacity for self-determination are identified for recruitment, the IRB will determine whether or not it is appropriate to enroll them into the research.

5.1.6.1 The decision will be based on the objectives and the potential risks of the research.

5.1.6.2 When adults with limited capacity for self-determination are permitted to enroll, the IRB will determine whether or not additional protections are required and whether or not there are adequate procedures for ensuring that an appropriate assessment of capacity is performed and valid consent (subject or subject’s legally authorized representative) will be obtained.

5.1.7 When there is a reasonable possibility that non-English speaking individuals will participate in the research, the procedures outlined in *Prime IRB SOP 600: Required Elements of Consent and Documentation of Consent* will be followed to ensure that adequate procedures are in place to obtain valid consent (unless a waiver of consent is issued).
5.1.8 Employees who are under the supervision of the investigator(s), hospital volunteers and the non-adult immediate families of the investigators, are potentially vulnerable in the research context. Potential vulnerability is due to the possibility that refusal to participate might adversely affect the prospective subject’s position, performance evaluation or future employment status. Pressures to participate may be real or perceived.

5.1.8.1 Employees, volunteers, and non-traditional personnel may not participate in a research study conducted by investigators to whom they report, unless it is a therapeutic or treatment study (i.e. a study for which the IRB has determined that there is a prospect for direct benefit).

5.1.8.1.1 A waiver may be granted by the Chair, Prime IRB or his/her designee for studies in which employees are by design the subject of the research (e.g. educational interventions directed at physicians, nurses or other health care providers). The decision will be based on the objectives, potential benefits and the potential risks of the research.

5.1.8.2 Non-adult immediate families of investigators may not participate in research studies conducted by investigators, unless it is a therapeutic or treatment study (i.e. a study for which the IRB has determined that there is a prospect for direct benefit), and a physician unaffiliated with the study has confirmed that it is the best therapeutic option available for the child.

5.1.9 When the proposed research may involve subjects that are potentially vulnerable, the IRB may choose to apply additional protections to ensure that the subjects’ rights and welfare are adequately protected. Examples of additional protections include having a third party observe the consent process, having a subject advocate assist the subject, engaging consultant reviewers or requiring additional monitoring of the research.

5.2 Prime IRB Review and Approval of Research Involving Cognitively Impaired Participants.

5.2.1 Cognitively Impaired Subjects include those individuals having a psychiatric disorder (e.g., psychosis, neurosis, personality or behavior disorders), an organic impairment (e.g., 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. Although there are no federal regulations specifically written to address the needs of this vulnerable group, the IRB will generally follow the recommendations governing the conduct of research in children and of specific recommendations made by the National Commission.

5.2.2 **Selection of Subjects:** Because cognitively impaired individuals may have diminished autonomy that may limit their capacity to provide consent or their ability to withdraw, research involving cognitively impaired participants should be reviewed and approved through consideration of the **PRIME IRB** policies and the special considerations as determined by the *Belmont Report*, Federal and State regulations, and guidance documents.

5.2.2.1 Research involving individuals with diminished capacity to consent should have a direct relationship to their illness or condition. Particular attention should be paid to institutionalized individuals, as issues of dependence and coercion may be factors that may compromise the voluntary nature of their participation in research. For this reason, subjects should be recruited from among non-institutionalized populations whenever possible.

5.2.3 The Prime IRB must review all research in which cognitively impaired individuals will be considered as participants to assure that the Investigator has provided additional safeguards to protect the rights and welfare of this vulnerable population.

5.2.4 **Risk Determination:** The Prime IRB must consider the degree of cognitive impairment of the participant, the level of risk, and the prospect of benefit to the individual participant. Generally, the IRB will follow the recommendations of the National Commission when determining the degree of risk and its impact on the approvability of a research protocol in cognitively impaired subjects as follows:

5.2.4.1 A minor increase over minimal risk may be permitted in research involving those institutionalized as mentally disabled, but only where the research is designed to evaluate an intervention of foreseeable benefit to their care.

5.2.4.2 For research that does not involve beneficial interventions and that presents more than minimal risk, the anticipated knowledge sought
should be of vital importance for understanding or eventually alleviating the subject's disorder or condition.

5.2.5 **Limiting Risks** Investigators should include a description of appropriate psychological or medical screening criteria to prevent or reduce the chances of adverse reactions to the therapeutic and research procedures. When appropriate, IRBs might want to require that other health care providers be consulted to ensure that proposed research procedures will not be detrimental to ongoing therapeutic regimens. Specific diagnostic, symptomatic, and demographic criteria for subject recruitment should be described in the research proposal.

5.2.5.1 Any plan to hospitalize subjects or extend hospitalization for research purposes should be justified by the investigator. The effects of separation from supportive family or friends, of disruption in schooling or employment, and the question of responsibility for bearing any additional costs should be carefully considered. Methods for assuring adequate protections for the privacy of the subjects and the confidentiality of the information gathered should also be described by the investigator.

5.3 **Requirements for Evaluating Decision-Making Capacity for Cognitively Impaired Participants.**

5.3.1 **General Assumption of Competence** As a general rule, all adults, regardless of their diagnosis or condition, should be presumed competent to consent unless there is evidence of serious mental disability that would impair reasoning or judgment. Even those who do have a diagnosed mental disorder may be perfectly able to understand the matter of being a research volunteer, and quite capable of consenting to or refusing participation. Mental disability alone should not disqualify a person from consenting to participate in research; rather, there should be specific evidence of individuals' incapacity to understand and to make a choice before they are deemed unable to consent.

5.3.2 **Evaluation of Mental Status of Subjects** In the case of research involving subjects who may be cognitively impaired, the investigator must propose adequate procedures for evaluating the mental status of prospective subjects to determine whether they are capable of consenting. Determination of capacity to consent or inability to withdraw may be made through a standardized measure and/or consultation with another qualified professional in accordance with the level of risk and the prospect of benefit. When appropriate, the patient's physician or other health care provider may be consulted. The
investigator must explain and the IRB must determine whether procedures for evaluating the mental status of subjects are appropriate both to the subject population and the nature of the proposed research.

5.4 Informed Consent

5.4.1 The Prime IRB must find that appropriate provisions are made for determining the participant’s ability to provide consent or their ability to withdraw, through evidence of one or more of the following pertaining to the individual:

5.4.1.1 The ability to make a choice;
5.4.1.2 The ability to understand relevant information;
5.4.1.3 The ability to appreciate the situation and its likely consequences; and
5.4.1.4 The ability to manipulate information rationally.

5.4.2 The determination of capacity to consent or ability to withdraw may be made through a standardized measure or consultation with another qualified professional. The Prime IRB must approve the process for making such a determination.

5.4.3 Because the capacity to consent or the ability to withdraw may fluctuate, the Prime IRB must evaluate the process for continued verification of understanding and willingness to participate.

5.4.3.1 The consent procedures should describe a plan for protecting individuals who may lose their capacity to provide consent or their ability to withdraw while participating in research activities (e.g., use of an ombudsman).

5.4.3.2 The Prime IRB may require that an outside witness observe and confirm the consenting process.

5.4.4 For participants who lack decision-making capacity, the permission of the individual’s legally authorized representative is required and assent should be obtained from the participant (See Prime IRB SOP 600: Required Elements of Consent and Documentation of Consent).

5.4.4.1 In research situations where there is the potential for direct benefit to the participant, the Prime IRB may waive the requirement to obtain assent. However, permission from the legally authorized representative must be obtained.

5.4.4.2 Even where the Prime IRB determines that the individuals are capable of consenting or withdrawing, the Prime IRB may still waive the consent requirements under the circumstances described...
in the Prime IRB informed consent policy (See Prime IRB SOP 600: Required Elements of Consent and Documentation of Consent).

5.4.5 The Prime IRB must also review and approve the appropriate consent documents with the required elements of consent written in a language understandable to the participant.

5.5 Appropriate Provisions for Legally Authorized Representative Consent.

5.5.1 When it is determined by the Investigator that the participant lacks decision-making capacity, the Prime IRB must find that appropriate provisions are made for soliciting the permission of each individual’s legally authorized representative unless the criteria are met to approve a waiver of informed consent (See Prime IRB SOP 600: Required Elements of Consent and Documentation of Consent).

5.6 Institutionalized Participants.

5.6.1 The Prime IRB must consider the rationale and justification for involvement of institutionalized participants, including an explanation as to why non-institutionalized individuals could not be used.

5.6.2 Regardless of financial support or funding, the Prime IRB must assure that all performance sites “engaged” in research have approval from the IRB of Record for the proposed research to be conducted at the site.

5.6.3 When performance sites are "not engaged" in research and have an established IRB/IEC, the Investigator must obtain approval to conduct the research at the "not engaged" site from the site’s Prime IRB/IEC or provide documentation that the site’s IRB/IEC has determined that approval is not necessary for Aultman to conduct the proposed research at the site.

5.6.4 When performance sites are "not engaged" in research and the "not engaged" site does not have an established IRB/IEC, a letter of cooperation must be obtained demonstrating that the appropriate institutional officials are permitting the research to be conducted at the performance site.

5.7 Composition of Prime IRB when Cognitively Impaired Participants are Involved in Research.

5.7.1 When reviewing research involving cognitively impaired participants, the Prime IRB Committee will include into its composition one or more individuals who are knowledgeable about and experienced in working with the cognitively impaired.
5.7.2 When the study requires review by the full Prime IRB Committee, it must meet the special composition requirements when conducting reviews for initial review, continuing review, protocol amendments, and reports of adverse events or unanticipated problems when the research involves cognitively impaired individuals.

6 MATERIALS
6.1 None.

7 REFERENCES
21 CFR 56 Subpart D
21 CFR 56.111(b)
45 CFR 46 Subpart B,
45 CFR 46 Subpart C,
45 CFR 46 Subpart D
45 CFR 46.107
45 CFR 46.107, 45 CFR 46.111(b),
Prime IRB SOP 501: Research Involving Pregnant Women, Fetuses, and Neonates
Prime IRB SOP 503: Research Involving Children
Prime IRB SOP 504: Minors Who Are Not Children in the Research Context
Prime IRB SOP 600: Required Elements of Consent and Documentation of Consent
The Office of Human Subjects Research (OHSR), National Institutes of Health, Information Sheet #7, “Research Involving Cognitively Impaired Subjects: A Review of Some Ethical Considerations”
<table>
<thead>
<tr>
<th>Version 0.2</th>
<th>Name</th>
<th>Status (Pending, Reviewed, Approved)</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Written by:</td>
<td>Karl Nelson</td>
<td></td>
<td>17-July-2017</td>
</tr>
<tr>
<td>Reviewed by:</td>
<td>Jennifer Neal-Jimenez</td>
<td></td>
<td>7-January-2018</td>
</tr>
<tr>
<td>Approved by:</td>
<td>Jennifer Neal-Jimenez</td>
<td>Approved</td>
<td>9-January-2018</td>
</tr>
</tbody>
</table>
1 PURPOSE

1.1 The regulations governing federally funded research, 45 CFR 46 Subpart B provide for special considerations and protections to be afforded to pregnant women and fetuses for their participation research. Some state law severely restricts research on the fetus. It is illegal under these state laws for any person to perform "non-therapeutic experimentation" upon any unborn child/fetus or upon any child born alive during the course of an abortion.

1.2 Pregnant women, fetuses and neonates are considered to be potentially vulnerable in the research context. They may be under constraints because of their status, which could affect their ability to make truly voluntary, uncoerced decisions. It is the purpose of this standard operating procedure to confirm that the Prime IRB provides all required additional safeguards for the protection of these populations.

1.3 The Prime IRB follows written policies and procedures for determining the risks to vulnerable populations, in particular pregnant women, fetuses and neonates of uncertain viability and non-viable neonates, as defined in applicable federal and state regulations.

2 REVISIONS FROM PREVIOUS VERSION

2.1 None.

3 POLICY

3.1 It is the policy of the Prime IRB that federally funded research involving pregnant women, human fetuses, or neonates (those with uncertain viability or non-viable neonates) must comply with the special protection considerations described under 45 CFR 46 Subpart B, and in this policy, to receive and maintain Prime IRB approval. The Prime IRB will document the determinations required by the regulations along with protocol specific findings justifying those determinations.

3.2 For studies without federal funding, where the applicable research procedures are not greater than minimal risk, 45 CFR Part 46, Subpart B will be used as a guide, but
determinations of approval for inclusion of pregnant women will predominantly be made by assuring that risks to the fetus are not greater than minimal and that all criteria for approval (§46.111 or §56.111) are met. The Prime IRB may require additional protocol-specific safeguards based on the potential risks to the woman or the fetus.

4 RESPONSIBILITIES

4.1 Director, Prime Review Board Services: Responsible for ensuring that the applicable Subpart B Checklist is completed prior to the IRB making a determination regarding research involving pregnant women, fetuses and neonates (non-viable and uncertain viability) and fetal materials and the products of conception.

4.1.1 The IRB reviews the proposed research according to all applicable IRB policies and procedures, taking into consideration the additional requirements for involvement of pregnant women, fetuses, or neonates as outlined in this policy and the criteria set forth in IRB document IRB Initial Approval of Research, and confirms that the investigator has provided approval from the appropriate research committees.

4.1.2 The IRB documents in its determination that additional protections necessary for the subject population are adequate

4.2 Chair, Prime Review Board Services: Responsible for ensuring the IRB applies the appropriate regulations and makes the required determinations regarding pregnant women, fetuses and neonates (non-viable and uncertain viability) and fetal materials and the products of conception.

4.3 Investigator:

4.3.1 The Investigator obtains review and approval from the appropriate institutional research committee(s) responsible for the oversight of the subject population(s) prior to IRB review.

4.3.2 The Investigator describes the population for the research and provides justification for inclusion of any of the following potential subjects: pregnant women, fetuses, or neonates in the IRB application.

4.3.3 Following IRB review and approval, the Investigator obtains informed consent from the mother and father as determined by the IRB.
5 PROCEDURE

Research involving women who are or may become pregnant should receive special attention from the Prime IRB because of women's additional health concerns during pregnancy and because of the need to avoid unnecessary risk to the fetus. Further, in the case of a pregnant woman, the Prime IRB must determine when informed consent of the father is required for research. Special attention is justified because of the involvement of a third party (the fetus) who may be affected but cannot give consent and because of the need to prevent harm or injury to future members of society. Procedural protections beyond the basic requirements for protecting human participants are prescribed in the Federal regulations for research involving pregnant women.

5.1 §46.204: Research Involving Pregnant Women and Fetuses

Pregnant women or fetuses may be involved in research if all of the following conditions are met:

5.1.1 Where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies, including studies on nonpregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses; and

5.1.2 The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus; or if there is no such prospect of benefit, the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge which cannot be obtained by any other means; and

5.1.3 Any risk is the least possible for achieving the objectives of the research; and

5.1.4 If the research holds out the prospect of direct benefit to the pregnant woman, the prospect of a direct benefit both to the pregnant woman and the fetus, or no prospect of benefit for the woman nor the fetus when risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means, her consent is obtained in accord with the informed consent provisions of 45 CFR 46 Subpart A; and

5.1.5 If the research holds out the prospect of direct benefit solely to the fetus then the consent of the pregnant woman and the father is obtained in accord with the informed consent provisions of 45 CFR 46 Subpart A, except that the father’s consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity or the pregnancy resulted from rape or incest; and
5.1.6 Each individual providing consent under (d) or (e) above, is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate; and

5.1.7 For children as defined in 45 CFR 46.402(a) who are pregnant, assent and permission are obtained in accord with the provisions of 45 CFR 46 Subpart D (See Prime IRB SOP 503: Research Involving Children); and

5.1.8 No inducements, monetary or otherwise, will be offered to terminate a pregnancy; and

5.1.9 Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy; and

5.1.10 Individuals engaged in the research will have no part in determining the viability of a neonate.

5.2 §46.205: Research Involving Non-Viable Neonates or those of Uncertain Viability

5.2.1 Neonates of uncertain viability and nonviable neonates may be involved in research if all of the following conditions are met:

5.2.1.1 Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates; and

5.2.1.2 Each individual providing consent under §5.2.2.2 or §5.2.3.5 of this section is fully informed regarding the reasonably foreseeable impact of the research on the neonate; and

5.2.1.3 Individuals engaged in the research will have no part in determining the viability of the neonate; and

5.2.1.4 The requirements of §5.2.2 or §5.2.3 of this section have been met as applicable.

5.2.2 Neonates of uncertain viability. Until it has been ascertained whether or not a neonate is viable, a neonate may not be involved in research covered by this policy unless the following additional conditions have been met:

5.2.2.1 The Prime IRB must determine that:

5.2.2.1.1 The research holds out the prospect of enhancing the probability of survival of the neonate to the point of viability, and any risk is the least possible for achieving that objective; or
5.2.2.1.2 The purpose of the research is the development of important biomedical knowledge which cannot be obtained by other means and there will be no added risk to the neonate resulting from the research; and

5.2.2.2 The legally effective informed consent of either parent of the neonate, or if neither parent is able to consent because of unavailability, incompetence, or temporary incapacity, the legally effective informed consent of either parent’s legally authorized representative is obtained in accord with 45 CFR 46 Subpart A, except that the consent of the father or his legally authorized representative need not be obtained if the pregnancy resulted from rape or incest.

5.2.3 Nonviable neonates. After delivery a nonviable neonate may not be involved in research covered by this policy unless all of the following additional conditions are met:

5.2.3.1 Vital functions of the neonate will not be artificially maintained; and

5.2.3.2 The research will not terminate the heartbeat or respiration of the neonate; and

5.2.3.3 There will be no added risk to the neonate resulting from the research; and

5.2.3.4 The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means; and

5.2.3.5 The legally effective informed consent of both parents of the neonate is obtained in accord with 45 CFR 46 Subpart A, except that the waiver alteration provisions of 45 CFR 46.116(c) and (d) do not apply. However, if either parent is unable to consent because of unavailability, incompetence, or temporary incapacity, the informed consent of one parent of a nonviable neonate will suffice to meet the requirements of this paragraph, except that the consent of the father need not be obtained if the pregnancy resulted from rape or incest. The consent of a legally authorized representative of either or both of the parents of a nonviable neonate will not suffice to meet the requirements of this paragraph.

5.2.4 Viable neonates. If a neonate is judged viable (i.e. likely to survive to the point of sustaining life independently, given the benefit of available medical therapy), it is then called an infant and should be treated as a child for purpose of research participation. A neonate, after delivery, that has been determined
to be viable may be included in research only to the extent permitted by and in accord with the requirements of 45 CFR 46 Subparts A and D.

5.3 §46.206: Research Involving, After Delivery, the Placenta, the Dead Fetus, or Fetal Material

5.3.1 Research involving, after delivery, the placenta; the dead fetus; macerated fetal material; or cells, tissue, or organs excised from a dead fetus, shall be conducted only in accord with any applicable Federal, State, or local laws and regulations regarding such activities.

5.3.1.1 For example, some state law makes it unlawful for any person or entity to engage in the following activities without the prior knowledge and consent of the mother:

5.3.1.1.1 medical experiments,
5.3.1.1.2 research, or
5.3.1.1.3 taking of photographs upon an aborted fetus.

5.3.1.1.4 Additionally, no person or entity may offer or accept money or anything of value for an aborted fetus. Violations of these provisions are punishable as a Class E felony.

5.3.2 If information associated with material described in §5.3.1 of this section is recorded for research purposes in a manner that living individuals can be identified, directly or through identifiers linked to those individuals, those individuals are research subjects and all pertinent subparts of the regulations are applicable.

5.4 Studies in Which Pregnancy is Coincidental to Subject Selection.

5.4.1 Any study in which women of childbearing potential are possible subjects may inadvertently include pregnant women. Federal regulations require that, when appropriate, subjects be provided a statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable as part of the informed consent process.

5.4.1.1 Women of childbearing potential will be included in all study populations unless the investigator provides clear, sound rationale for excluding this population group. If exclusion of pregnant women, nursing women, or women who wish to start a pregnancy is
justified, the protocol and informed consent document should explain the reasons for the exclusion.

5.4.1.2 The Prime IRB must judge whether the mother's participation would pose any risk to the fetus or nursing infant. In some studies, the Prime IRB may need to assure that nonpregnant subjects are advised to avoid pregnancy or nursing for a time during or following the research. Furthermore, where appropriate, subjects should be advised to notify the Investigator immediately should they become pregnant. In some instances, there may be potential risk sufficient to justify requiring that pregnant women either be specifically excluded from the research or studied separately.

5.4.1.3 If the research study poses known risks and/or lack of knowledge relative to the risks to a pregnant woman and/or fetus, the eligibility screening will include a pregnancy test; pregnancy tests will be performed throughout the woman's participation as appropriate.

5.4.1.4 As appropriate, the informed consent will include statements regarding:

- 5.4.1.4.1 the need for pregnancy testing before and during the study,
- 5.4.1.4.2 the recommended contraceptive methods based on the known risks,
- 5.4.1.4.3 the need to notify the Principal Investigator immediately if pregnancy occurs and
- 5.4.1.4.4 the possibility of unforeseen risks to the subject and/or fetus.

5.5 **Exemption from Review.**

5.5.1 Note that with the revision of Subpart B on November 13, 2001, the exemptions from Prime IRB review listed at 45 CFR 46.101(b) may now be applied to research involving pregnant women, human fetuses, and neonates in accordance with 45 CFR 46.201(b).
5.6 Research on Transplantation of Fetal Tissue.

The Prime IRB must assure that the following provisions have been met before approving such research activities:

5.6.1 Research involving the transplantation of human fetal tissue for therapeutic purposes may be conducted only if the woman providing the tissue makes a statement, in writing and signed by the woman, declaring that:

5.6.1.1 The woman donates the fetal tissue for research; and
5.6.1.2 The donation is made without any restriction regarding the identity of individuals who may be the recipients of transplantations of the tissue; and
5.6.1.3 The woman has not been informed of the identity of any such individuals.

5.6.2 Research involving the transplantation of human fetal tissue for therapeutic purposes may be conducted only if the attending physician with respect to obtaining the tissue from the woman involved makes a statement, in writing and signed by the attending physician, declaring that:

5.6.2.1 In the case of tissue obtained pursuant to an induced abortion:

5.6.2.1.1 The consent of the woman for the abortion was obtained prior to requesting or obtaining consent for a donation of the tissue for use in such research; and
5.6.2.1.2 No alteration of the timing, method, or procedures used to terminate the pregnancy was made solely for the purposes of obtaining the tissue; and
5.6.2.1.3 The abortion was performed in accordance with applicable State law; and

5.6.2.2 The tissue has been donated by the woman in accordance with § 5.6.1 of this section; and

5.6.2.3 Full disclosure has been provided to the woman with regard to:

5.6.2.3.1 Such physicians interest, if any, in the research to be conducted with the tissue; and
5.6.2.3.2 any known medical risks to the woman or risks to her privacy that might be associated with the donation of the tissue and that are in addition to risks of such type that are associated with the woman’s medical care.
5.6.3 Research involving transplantation of human fetal tissue for therapeutic purposes may be conducted only if the Principal Investigator makes a statement in writing and signed by the Principal Investigator, declaring that the Principal Investigator:

5.6.3.1 Is aware that:

5.6.3.1.1 The tissue is human fetal tissue; and

5.6.3.1.2 The tissue may have been obtained pursuant to a spontaneous or induced abortion or pursuant to a stillbirth; and

5.6.3.1.3 The tissue was donated for research purposes; and

5.6.3.2 The Principal Investigator has provided such information to other individuals with responsibilities regarding the research; and

5.6.3.3 The Principal Investigator will require, prior to obtaining the consent of an individual to be a recipient of a transplantation of the tissue, written acknowledgment of receipt of such information by such recipient; and

5.6.3.4 The Principal Investigator has had no part in any decisions as to the timing, method, or procedures used to terminate the pregnancy made solely for the purpose of the research.

5.6.4 Research involving transplantation of human fetal tissue for therapeutic purposes may be conducted only if the head of the agency or other entity conducting the research involved certifies to the Secretary of the Department of Human Services (DHHS) that the statements required under §5.6.2 and §5.6.3 of this section will be available for audit by the Secretary.

5.6.5 Research involving transplantation of human fetal tissue for therapeutic purposes may be conducted only if it is conducted in accordance with applicable Federal, State and local laws and institutional policies and procedures.

6 MATERIALS

6.1 None.
7 REFERENCES

21 CFR 56.204
21 CFR 56.205
21 CFR 56.206
45 CFR 46.204
45 CFR 46.205
45 CFR 46.206
<table>
<thead>
<tr>
<th>Version 0.2</th>
<th>Name</th>
<th>Status (Pending, Reviewed, Approved)</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Written by:</td>
<td>Karl Nelson</td>
<td></td>
<td>17-July-2017</td>
</tr>
<tr>
<td>Reviewed by:</td>
<td>Jennifer Neal-Jimenez</td>
<td></td>
<td>7-January-2018</td>
</tr>
<tr>
<td>Approved by:</td>
<td>Jennifer Neal-Jimenez</td>
<td>Approved</td>
<td>9-January-2018</td>
</tr>
</tbody>
</table>
1 PURPOSE

1.1 The purpose of this standard operating procedure is to describe the special regulatory requirements that the researcher and the Prime IRB must take into consideration when a proposed research study involves children, a vulnerable population, to provide additional protection for children involved in research.

2 REVISIONS FROM PREVIOUS VERSION

2.1 None.

3 POLICY

3.1 When reviewing research with children as subjects, in addition to ensuring adherence to the general regulatory requirements of 45 CFR part 46 (§46), Subpart A or 21 CFR 50 and 56 (§50 or §56), the Prime IRB must determine which of four categories of research apply to that study, based on the degree of risk and benefit to the individual subjects (pursuant to Subpart D of §46 or §50 [Subpart D]). The Prime IRB must also determine that there are adequate provision for soliciting the assent of the children and the permission of their parents or guardians. Special protections apply if children who are wards are to be included in the research.

4 RESPONSIBILITIES

4.1 Prime IRB Reviewer: Responsible for reviewing the submitted materials including the protocol and application and to document their findings on the Prime IRB Review Form or its equivalent.

4.2 Prime IRB Analyst: The Prime IRB Analyst is responsible for documenting the Prime IRB’s findings in the meeting minutes and in the appropriate correspondence with the investigator.

4.3 Investigator: Responsible for providing sufficient information to allow the Prime IRB to make a risk – benefit determination as required under Subpart D.
5 PROCEDURE

5.1 Prime IRB Review and Approval of Research Involving Children.

5.1.1 Research involving persons below the legal age of consent is important for the health and well-being of all children, and may be conducted provided the Prime IRB (and where applicable, those of its affiliated institutions where such research will be performed), has determined that:

5.1.1.1 studies, where appropriate, have been conducted first on animals, adult humans, then on older children, before involving infants;

5.1.1.2 risks are minimized by using the safest procedures consistent with sound research design; and

5.1.1.3 adequate provisions are made to protect the privacy of subjects and their families, and to maintain confidentiality of data.

5.1.2 The special vulnerability of children makes consideration of involving them as research subjects particularly important. To safeguard their interests and to protect them from harm, special ethical and regulatory considerations apply for reviewing research involving children. The Prime IRB may approve research involving children only if special provisions are met. The Prime IRB must classify research involving children into one of four categories and document their discussions of the risks and benefits of the research study. The four categories of research involving children that may be approved by the Prime IRB are based on degree of risk and benefit to individual subjects.

5.2 Categories of Research Involving Children.

During initial review, the Prime IRB determines and documents which of four categories of research, (below) applies to the particular study, based on the degree of risk and benefit to individual subjects. At the time of continuing review, amendment review or new information review the Prime IRB may determine that the category has changed.

5.2.1 Research Not Involving Greater than Minimal Risk to Children (45 CFR 46.404). When the Prime IRB finds that no greater than minimal risk to children is present, the Prime IRB may approve the proposal only if the Prime IRB finds that adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians, as set forth below in Section 5.3.
5.2.2 Research Involving Greater than Minimal Risk but Presenting the Prospect of Direct Benefit to the Individual Child (45 CFR 46.405). If the Prime IRB finds that more than minimal risk to children is presented by an intervention or procedure but that the intervention or procedure holds out the prospect of direct benefit for the individual subject, or by a monitoring procedure that is likely to contribute to the subject's well-being, the Prime IRB may approve the research only if the Prime IRB finds that:

5.2.2.1 The risk is justified by the anticipated benefit to the children;

5.2.2.2 The relation of the anticipated benefit to the risk is at least as favorable to the children as that presented by available alternative approaches; and

5.2.2.3 Adequate provisions are made for soliciting the assent of the children and permission of their parents or legal guardians, as set forth below in Section 5.3. 4

5.2.3 Research Involving Greater than Minimal Risk and No Prospect of Direct Benefit to the Individual Child, but Likely to Yield Generalizable Knowledge about the Child’s Disorder or Condition. (45 CFR 46.406). If the Prime IRB finds that more than minimal risk to children is presented by an intervention or procedure that does not hold out the prospect of direct benefit for the individual child, by a monitoring procedure which is not likely to contribute to the well-being of the child, the Prime IRB may approve the research only if the Prime IRB finds that:

5.2.3.1 The risk represents a minor increase over minimal risk;

5.2.3.2 The intervention or procedure presents experiences to participants that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations;

5.2.3.3 The intervention or procedure is likely to yield generalizable knowledge about the participants’ disorder or condition which is of vital importance for the understanding or amelioration of the participants’ disorder or condition; and

5.2.3.4 Adequate provisions are made for soliciting assent of the children and permission of their parents or legal guardians, as set forth below in §5.3.5
5.2.4 **Research Not Otherwise Approvable, which Presents an Opportunity to Understand, Prevent, or Alleviate a Serious Problem Affecting the Health or Welfare of Children** *(45 CFR 46.407)*. If the Prime IRB finds the research does not meet the requirements set forth in categories 46.404, 46.405 or 46.406 as described above, the Prime IRB may approve the research only if:

5.2.4.1 The Prime IRB finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children; and

5.2.4.2 If Federally funded, the Secretary of the Department of Health and Human Services (DHHS), after consultation with a panel of experts in pertinent disciplines (for example: science, medicine, education, ethics, law) and following opportunity for public review and comment, has determined either:

5.2.4.2.1 That the research in fact satisfies the conditions of categories 46.404, 46.405, or 46.406; or

5.2.4.2.2 The following:

5.2.4.2.3 The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children;

5.2.4.2.4 The research will be conducted in accordance with sound ethical principles; and

5.2.4.2.5 Adequate provisions are made for soliciting the assent of children and the permission of their parents or legal guardians, as set forth below in §5.3.6.
5.3 Requirements for Permission by Parents or Legal Guardians and for Assent by Children.

5.3.1 Adequate Provisions for Child’s Assent. The Prime IRB must find that adequate provisions are made for soliciting the assent of child participants when in the judgment of the Prime IRB the children are capable of providing assent. 7

5.3.1.1 "Assent" in this context means the child's affirmative agreement to participate, not merely the absence of his or her objection, after adequate explanation. Mere failure to object should not, absent affirmative agreement, be construed as assent.8 This differs from the term "consent," which indicates voluntary participation by a person of legal age and competency that is able to exercise free power of choice based on complete information. Assent must be obtained from any child who might reasonably be expected to comprehend the nature of his or her involvement in the research, regardless of age but at least by seven years. Research protocols should include forms for documentation of assent of subject children. Simplified written forms are recommended for children of seven years and over, and forms documenting oral assent for those under seven years of age or otherwise incapable of utilizing written forms.

5.3.1.2 In determining whether children are capable of assenting, the Prime IRB shall consider the ages, maturity, and psychological state of the children involved. This judgment may be made for all children to be involved in research under a particular protocol, or for each child, as the Prime IRB deems appropriate.9 The child should be given an explanation of the proposed research procedures in a language that is appropriate to the child's age, experience, maturity, and condition.10

5.3.1.3 Waiver of Assent. If the Prime IRB determines either of the following to be true, then the assent of the children is not a necessary condition for proceeding with the research:

5.3.1.3.1 The capability of some or all of the children is so limited that they cannot reasonably be consulted; or

5.3.1.3.2 The intervention or procedure involved in the research holds out a prospect of direct benefit that is important to
the health or well-being of the children and is available only in the context of the research.  

5.3.1.3.2.1 Therefore, when the research offers the child the possibility of a direct benefit that is important to the health or well-being of the child and is available only in the context of the research, the Prime IRB may determine that the assent of the child is not necessary. 

5.3.1.3.3 Additionally, in such circumstances, a child's dissent which normally should be respected, may be overruled by the child's parents at the Prime IRB's discretion. When research involves the provision of experimental therapies for life-threatening diseases such as cancer; however, the Prime IRB should be sensitive to the fact that parents may wish to try anything, even when the likelihood of success is marginal and the probability of extreme discomfort is high. Should the child not wish to undertake such experimental therapy, difficult decisions may have to be made. In general, if the child is a mature adolescent and death is imminent, the child's wishes should be respected.

5.3.1.3.4 Finally, even where the Prime IRB determines that the child participants are capable of assenting, the Prime IRB may still waive the assent requirement under circumstances in which consent may be waived for adults in accordance with Prime IRB SOP 600: Legally Effective and Prospectively Obtained Informed Consent regarding waiver or alteration of informed consent generally.
5.3.2 Adequate Provisions for Parents’ or Legal Guardians’ Permission. The Prime IRB must find that adequate provisions are made for soliciting the permission of each child's parents or legally authorized representative.\(^{15}\)

If a child is to participate in a clinical trial that the Prime IRB determines presents more than minimal risk, consent must be obtained from both parents unless one parent is deceased, unknown, incompetent, or not reasonably available, or unless one parent has legal responsibility for the care and custody of the child. When possible, consent by a parent or guardian should be accompanied by the consent and voluntary participation of the child. A refusal to participate by the subject (adult or child) or the subject’s parent/guardian is to be taken as a final decision.

5.3.2.1 Research not involving greater than minimal risk to children. Where parental permission is to be obtained, the Prime IRB may find that the permission of one parent is sufficient for research not involving greater than minimal risk when the provisions of Section 2.a above are met.

5.3.2.2 Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual child. Where parental permission is to be obtained, the Prime IRB may find that the permission of one parent is sufficient for research involving greater than minimal risk but presenting the prospect of direct benefit to the individual participants when the provisions of Section 2.b above are met.

5.3.2.3 Research involving greater than minimal risk and no prospect of direct benefit to the individual child, but likely to yield generalizable knowledge about the child's disorder or condition. When the research is approved under §5.2.3 above, and permission is to be obtained from parents, both parents must give their permission unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.

5.3.2.4 Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children. When the research is approved under §5.2.4 above and permission is to be obtained from parents, both parents must give their permission unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.
5.3.3 When parents of research subjects are under the legal age of consent, their consent alone may be considered sufficient where they are "emancipated minors," i.e., where they are maintaining their own residence and exercising primary economic and social control of their own and the child's life. When the parents of the child are dependent upon others for support, then consent of those exercising ultimate economic and social control of the child's life must also be obtained.

5.3.4 Waiver of Parental or Legal Guardian Permission. If the Prime IRB determines that a research protocol is designed for conditions or for a participant population for which parental or legally authorized representative permission is not a reasonable requirement to protect the participants (for example, neglected or abused children), it may waive the consent requirements described above, provided both:

5.3.4.1 An appropriate mechanism for protecting the children who will participate as subjects in the research is substituted; and

5.3.4.2 The waiver is not inconsistent with Federal, State, or local law. The choice of an appropriate mechanism would depend upon the nature and purpose of the activities described in the protocol, the risk and anticipated benefit to the research participants, and their age, maturity, status, and condition. 16

5.3.4.3 The Prime IRB may waive the requirement for consent of parents or guardians when a research protocol is designed for conditions where such permission is not a reasonable requirement, provided an appropriate mechanism for protecting the subjects is substituted.

Examples might include some research involving abused or neglected children, or high school and college students engaged as subjects in classroom projects involving minimal risk. One alternative that may be used under these circumstances is the appointment of a social worker, physician, nurse, school authority, or other individual to act as surrogate parent. A person so appointed would be expected to participate not only in the process of solicitation of the child's assent, but also in the conduct of the research, in order to provide reassurance for the subject and to intervene or support the child's desire to withdraw if participation becomes too stressful.
5.3.5 Documentation.

5.3.5.1 Permission by parents or legal guardians shall be documented in the same manner as required for participants under Prime IRB SOP 600: Legally Effective and Prospectively Obtained Informed Consent.¹⁷

5.3.5.2 When the Prime IRB determines that assent of a child is required, it shall also determine whether and how assent must be documented.¹⁸

5.3.6 Wards of the State or Other Agency. Children who are wards of the state or any other agency, institution, or entity can be included in research approved under §5.2.2 and §5.2.3 only if the Prime IRB finds and documents that such research is:

5.3.6.1 Related to their status as wards; or

5.3.6.2 Conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as participants are not wards.¹⁹

5.3.7 If the research is approved under §5.2.4 of this policy, the Prime IRB must require appointment of an advocate for each child who is a ward, in addition to any other individual acting on behalf of the child as guardian or in loco parentis. One individual may serve as advocate for more than one child. The advocate shall be an individual who has the background and experience to act in, and agrees to act in, the best interests of the child for the duration of the child's participation in the research and who is not associated in any way (except in the role as advocate or member of the Prime IRB) with the research, the Investigators, or the guardian organization.²⁰

5.3.8 Pediatric Expertise on Prime IRB Committee. An Prime IRB Committee considering a protocol involving children as participants should:

5.3.8.1 Assess its needs for pediatric expertise among the Prime IRB voting membership to assure that it possesses the professional competence necessary to review the specific research activities; and

5.3.8.2 Consider inclusion of one or more individuals who are knowledgeable about and experienced in working with children.²¹ To fulfill this requirement, the Prime IRB Committee may invite nonvoting individuals to assist in the review of issues which require expertise beyond, or in addition to, that available among voting Prime IRB members.²²
6 MATERIALS

6.1 None.

7 REFERENCES

45 CFR 46, Subpart D
21 CFR 50, Subpart D
Prime IRB SOP 601: Assent and Parental Permission
Prime IRB SOP 504: Minors Who Are Not Children in the Research Context
Age of majority is 18 years of age. The age of majority in Nebraska is 19. The age of majority in Alabama for research conducted by universities.

Title 45 CFR Part 46, Subpart D provides for "Additional Protections for Children Involved as Subjects of Research."

45 CFR 46.404.
45 CFR 46.405.
45 CFR 46.406.
45 CFR 46.407.
45 CFR 46.408(a).
45 CFR 46.402(b).
45 CFR 46.408(a).

OHRP Institutional Review Board Guidebook, Chapter 6, Section C, Children and Minors.
45 CFR 46.408(a).
45 CFR 46.408(a).

OHRP Institutional Review Board Guidebook, Chapter 6, Section C, Children and Minors.
45 CFR 46.408(a); 45 CFR '46.116.
45 CFR 46.408(b).
45 CFR 46.408(c).
45 CFR 46.408(d).
45 CFR 46.408(e).
45 CFR 46.409(a).
45 CFR '46.409(b).
1 PURPOSE

1.1 This standard operating procedure is intended to define which minors do not meet the definition of children for the purposes of adhering to applicable Federal regulations and State law.

1.2 The Office of Human Research Protections OHRP has clarified on its website when minors may provide their own informed consent.

1.2.1 “HHS regulations at 45 CFR 46.402(a) define “children” as “persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted.” If research on a specific treatment involves solely treatments or procedures for which minors can give consent outside the research context (under applicable state and local laws, for example, research on sexually transmitted diseases or pregnancy), such individuals would not meet the definition of children as defined at 45 CFR 46.402(a). Thus, subpart D would not apply to the research and parental permission (or waiver thereof) is not a consideration for these minors. Under these circumstances, minors may provide their own informed consent.”

1.3 Under certain circumstances, state law allows a minor (an individual under age eighteen) to consent to treatments or procedures. These minors are therefore not “children” under the Federal Regulations. When research is conducted in these states, the applicable state laws are followed.

1.4 In determining who is a “child” or “guardian” when conducting research, the applicable state laws will be applied. When necessary, Emmes Legal Counsel will be consulted.

2 REVISIONS FROM PREVIOUS VERSION

2.1 None.
3 POLICY

3.1 Minors who are permitted under state law and hospital policy to consent to treatment will be permitted to provide their own consent for research. To participate in the research, the minor must be (1) competent to understand the research, including, but not limited to, the purpose of the research, the nature of the procedures and the risks and benefits and (2) the research procedures must be limited in scope to treatments or procedures for which the minor can consent outside the research context.

4 RESPONSIBILITIES

4.1 Director; Prime Review Board Services: The Director is responsible for consulting with hospital legal counsel in cases where clarifications are required regarding state law and right to consent to treatment.

4.2 Chair; Prime Review Board Services: The Chair is responsible for assuring that research that involves minors who are not children is limited to the condition(s) for which they are receiving treatment.

4.3 Investigator: The investigator is responsible for ensuring the rights and welfare for minors who are not children. They must ensure that the minor has both the right to consent and the capacity to consent.

5 PROCEDURE

5.1 Determining When a Minor May Consent to Participate in Research

The Investigator submits to the IRB the protocol and supplementary material with an explanation of the following:

5.1.1 The criteria that will be used to determine whether or not the minor has the legal right to consent (e.g., they are seeking diagnosis, counseling or treatment for a sexually transmitted disease);

5.1.2 The procedures to be employed to assure the minor possesses the ability to comprehend all of the elements of informed consent as delineated in Prime IRB SOP 600: Required Elements of Consent and Documentation of Consent (Sections V.D. and V.E.);

5.2 Consent for Participation Research When a Minor Consents for Treatment

The Prime IRB determines the consent requirements when the consent of the minor is considered valid for diagnosis, treatment or counseling.
5.3 Protections for Minors who are Not Children

5.3.1 The Prime IRB does not consider subpart D protections when reviewing research involving minors who are not children. When a determination has been made that a minor is not a “child”, the following are not considered applicable:

5.3.1.1 *Prime IRB SOP 500: Vulnerable Subjects* and *Prime IRB 503: Research Involving Children*

5.3.1.2 45 CFR 46, Subpart D and 21 CFR 50, Subpart D

The Prime IRB may apply additional protections for minors who can consent for themselves. The Prime IRB considers the ability of minors to understand the nature of the research, likelihood of direct benefit, the availability of alternatives outside of the research context, the risks and benefits, and other factors that might be of importance prior to approval of the research.

6 MATERIALS

6.1 None.

7 REFERENCES

21 CFR 50.50 – 54

45 CFR 46.401 - 409

OHRP FAQs: Children: Question 13 (Answer 1016): If a child can consent to treatment, can they also participate in treatment-related research?

Prime IRB SOP 503: Research Involving Children

Prime IRB SOP 500: Vulnerable Subjects
<table>
<thead>
<tr>
<th>Version 0.2</th>
<th>Name</th>
<th>Status (Pending, Reviewed, Approved)</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Written by:</td>
<td>Karl Nelson</td>
<td></td>
<td>17-July-2017</td>
</tr>
<tr>
<td>Reviewed by:</td>
<td>Jennifer Neal-Jimenez</td>
<td></td>
<td>7-January-2018</td>
</tr>
<tr>
<td>Approved by:</td>
<td>Jennifer Neal-Jimenez</td>
<td>Approved</td>
<td>9-January-2018</td>
</tr>
</tbody>
</table>
1. PURPOSE

1.1. The purpose of this standard operating procedure is to describe the required elements of consent and the general requirements for documentation of informed consent.

2. REVISIONS FROM PREVIOUS VERSION

2.1. Addition of addendum regarding non-English speaking subjects.

3. POLICY

3.1. It is the policy of the Prime Review Board Services (Prime IRB) that investigators will not involve human beings as subjects in research unless the investigator has obtained the legally effective informed consent of the subject or the subject’s legally authorized representative. Exception to this policy requires that the IRB grant a waiver of the informed consent requirement.

3.2. Unless waived by the IRB, consent will be documented using an approved, written consent form. The form will be signed and dated (including the time) by the prospective subject or the prospective subject’s legally authorized representative. Note: research personnel may not fill in the date and time.

3.3. The consent document will include the basic elements of informed consent as specified in 45 CFR 46.116 - General Requirements for Informed Consent and 21 CFR 50.25 - Elements of Informed Consent.

3.4. An investigator will seek informed consent only under circumstances that provide the prospective subject or, when approved by the IRB, the subject's legally authorized representative sufficient opportunity to understand and consider whether to participate and that minimize the possibility of coercion or undue influence.

3.5. The information that is given to the subject or the representative will be in language understandable to the subject or the representative.
3.6. No informed consent, whether oral or written, will include any exculpatory language through which the subject or their legally authorized representative is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution or its agents from liability for negligence

4. RESPONSIBILITIES

4.1. Director, Prime Review Board Services: Responsible for establishing and periodically reviewing and modifying (as appropriate) IRB standard operating policies and procedures involving the consent process.

4.2. Chair, Prime Review Board Services: Responsible for establishing and periodically reviewing and modifying (as appropriate) IRB and Investigator responsibilities pertaining to obtaining and documenting consent.

4.3. Investigator: Responsible for obtaining consent from research subjects, their parent/guardian(s) or the legally authorized representative of the subject as required by this SOP.

4.4. Prime IRB Staff: Responsible for ensuring that all informed consent documents include the required elements.

4.5. Prime IRB Reviewer: Responsible for ensuring that all informed consent documents include the required and applicable optional elements and for ensuring that the documents comply with the requirements of this policy.

5. PROCEDURE

5.1. Review of the Informed Consent Document

5.1.1. The Investigator submits informed consent documents or requests an alteration in the consent process for review by the Prime IRB (Prime IRB SOP 605: Waiver of Elements of Consent).

5.1.2. The IRB reviews the description of the proposed consent process and documentation to ensure that:

5.1.2.1. The informed consent document is consistent with the protocol and the investigator’s brochure regarding the purpose, risks, and benefits of the research;

5.1.2.2. The document contains all the required elements of informed consent as defined by applicable federal regulations unless waived
by the Prime IRB (*Prime IRB SOP 605: Waiver of Elements of Consent and Waiver of HIPAA Authorization*);

5.1.2.3. All additional elements are appropriate to the research and are incorporated into the document;

5.1.2.4. The document minimizes the use of scientific language, and contains the appropriate statements regarding safety and effectiveness for FDA regulated research.

5.1.2.5. The circumstances of the consent process minimize the possibility of coercion or undue influence;

5.1.2.6. The information must be presented to the subject or the legally authorized representative in language understandable to the subject or the representative;

5.1.2.7. The information being communicated during the consent process will not include exculpatory language through which the subject or the representative is made to waive or appear to waive any of the subject’s legal rights, or release or appears to release the investigator, the sponsor, the institution or its agents from liability for negligence.

5.1.3. When the consent document includes a written authorization (a combined consent/authorization), the Prime IRB ensures that the document satisfies the requirements of HIPAA at 45 CFR 164.508(c)(1) - (2) (*Prime IRB SOP 606: Requirements for and Documentation of HIPAA Authorization*).

5.1.4. The Investigator documents the consent and authorization as required by the Prime IRB.

### 5.2. Required Elements of Consent

5.2.1. The Investigator and IRB ensure that all the following elements are included as part of the informed consent document unless a waiver or alteration is granted by the IRB.

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

5.2.1.2. A description of any reasonably foreseeable risks or discomforts to the subject or others.
5.2.1.3. A description of any potential benefits to either the subject or others. The description within the consent process or document must also be clear if no direct benefit is expected.

5.2.1.4. A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous or affect the subject’s willingness to participate in the research.

5.2.1.5. A statement describing the extent to which, if any, the confidentiality of records identifying the subject will be maintained and that notes the possibility that representatives of the institution (such as the IRB) or any of the federal regulatory agencies may inspect the records.

5.2.1.6. For research involving more than minimal risk, an explanation as to whether any compensation or medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained. The informed consent document must not contain any exculpatory language and must not waive or appear to waive the rights of the participant or release or appear to release those conducting the study from liability for negligence.

5.2.1.7. An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject.

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

5.2.1.9. For FDA-regulated research, the following statement must be included as part of the consent document:

   A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.
5.3. **Additional Elements**

5.3.1. The IRB will ensure that, when appropriate, one or more of the following elements of information shall also be provided to each subject:

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

5.3.1.2. Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent.

5.3.1.3. Any additional costs to the subject that may result from participation in the research.

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

5.3.1.5. A statement that 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.

5.3.1.6. The approximate number of subjects involved in the study.

5.4. **The Informed Consent Process:**

Because informed consent is not simply a document, but a process, the following should be considered when consenting a subject to a research study:

5.4.1. Giving the subject adequate information concerning the research in language that is as nontechnical as possible (eighth grade language or lower if more appropriate for subject population).

5.4.2. Providing sufficient time and opportunity for the subject to ask questions about the research project and to decide whether to participate in the research, as well as to consider other available options, if any.

5.4.3. Responding to subject’s questions to his/her satisfaction.

5.4.4. Obtaining the subject’s voluntary consent.

5.4.5. Documenting that the process has occurred.

5.4.6. All Key Research Personnel including the Investigator(s) are responsible for continuing the informed consent process throughout the subject’s participation in the study.
5.5. Who May Obtain Informed Consent

5.5.1. If permitted by the sponsor and IRB of record, the Principal Investigator may delegate the duty of obtaining informed consent to appropriate members of the research team (“designee”). The Principal Investigator is responsible for assuring that any such designee is knowledgeable about the specific research study and the process of informed consent. Because the IRB of record needs to be aware of who will be obtaining consent from subjects, this designee, as well as any member of the research team interacting with subjects as part of the informed consent process, should be listed as Key Research Personnel and pass required human subjects’ protection training.

5.5.2. For more than minimal risk studies, the person conducting the consent process must sign the informed consent document as well as obtain the signature of the subject, unless the IRB of record has approved a Waiver of Documentation of Informed Consent or alternative process. Ongoing studies that are not currently meeting this standard have until the next continuing review to initiate this process.

5.6. Informed Consent Procedures When the Subject is a Minor:

5.6.1. If the potential subject is a minor, he/she may not be capable of giving legally valid consent, but may be able to assent or dissent from participation. The assent process requires that Key Research Personnel discuss with the child what participation in the research study will involve as well as the possible risks and benefits. Federal regulations require that assent be obtained from all subjects capable of assenting unless certain conditions are met. When determining if minors can give assent, factors such as age, maturity, psychological state and medical condition of potential subjects must be considered. If the condition is life threatening and the research presents the prospect of benefit, the IRB may vote that assent be waived. If the study may involve minors, an assessment must be made of the expected level of understanding of the study so that an appropriate level assent be developed and approved by the IRB of record. In addition, parental consent must be obtained and documented per federal and state laws and local policies.

5.7. Informed Consent Procedures Adult Subject is Cognitively Impaired:

5.7.1. If the potential subject is unable to consent, or lacks the decisional capacity to consent, informed consent must be obtained by the potential subject’s guardian, spouse, or legally authorized representative.
5.8. **Informed Consent Procedures When the Subject is Unable to Read or Understand the Consent Document:**

5.8.1. If written consent is required and the subject is unable to read, the IRB-approved consent document must be read in its entirety in the presence of a witness. This should be documented directly onto the consent document by obtaining both the subject and witness signatures.

5.8.2. If the potential subject is unable to understand the IRB-approved written informed consent document because of the language in which it is written, the Principal Investigator must obtain IRB approval for a written informed consent written in a language that the potential subject can understand. During the consent process using a non-English consent form (and in a language which the potential subject understands), a certified translator must be present. Involvement of a certified translator must be documented. Another option is to obtain an IRB-approved short form of the informed consent with verbal certified translator (see 45 CRF 46.117(b) and 21 CFR 50.27(b)(2) for more information). Certified translators or sign language interpreters should be part of the ongoing communication throughout the research study and may be used to assist with verbal and written translation.

5.8.3. Use of family members or friends as interpreters or translators during the consenting process is not allowed.

5.9. **Required Informed Consent Document Signatures:**

5.9.1. Written consent must be signed and dated by the subject and if the study is more than minimal risk it also needs to be signed and dated by the person who conducts the informed consent discussion. Other signatures must be provided as required by the sponsor, institution, and/or IRB of record.

5.9.2. The person who conducts the informed consent process with the potential subject (explains the necessary parts of the protocol, reviews the consent document, answers questions) must sign the consent document for studies that are more than minimal risk studies. This signature confirms that the consent process was properly conducted, not that he/she just witnessed the subject sign the consent document.
5.10. Methods of Documenting Consent

During the review of the research the IRB considers the requirements for documentation of consent that may include any of the following

5.10.1. **Written consent document** that embodies the elements of informed consent and the required elements of HIPAA authorization (or a separate HIPAA Authorization is used);

   5.10.1.1. This form may be read to the subject.
   5.10.1.2. The investigator shall give the subject adequate opportunity to read the document before it is signed.
   5.10.1.3. The form must be signed and dated by the subject or the subject’s legally authorized representative.
   5.10.1.4. Each participant shall be provided a copy of the consent document.
   5.10.1.5. When the informed consent is combined with a written authorization, the subject must be provided a signed copy of the consent/authorization.

5.10.2. **Short form written consent document** may be used in combination with an oral presentation of the informed consent information.

   5.10.2.1. When this method is used, there shall be an impartial witness to the oral presentation.

   5.10.2.1.1. The witness must attest to the adequacy of the consent process and the subject’s voluntary consent.
   5.10.2.1.2. For participants who do not speak English, the witness shall be conversant in both English and the language of the participant.

   5.10.2.2. The written summary must embody the basic elements and required additional elements of informed consent, unless an alternation of consent is approved by the IRB (**Prime IRB SOP 605: Waiver of Elements of Consent and Waiver of HIPAA Authorization**). The summary can either be

   5.10.2.2.1. The approved consent form that includes the appropriate signature pages for the investigator and the witness; or
5.10.2.2. A written summary of what will be said to the subject. When a study summary document is used the content must be consistent with the information contained in the IRB-approved English version of informed consent form.

5.10.2.3. The subject and the witness both sign (and date if required by sponsor) the short form.

5.10.2.4. The witness and the investigative team member both sign and date a copy of the consent form or summary document.

5.10.2.5. A copy of the consent form/summary document shall be provided to the subject in addition to a copy of the short form.

5.10.2.6. The interpreter for the Short Form Consent process can include the following:

5.10.2.6.1. A trained medical interpreter subject to the following requirements and limitations:

5.10.2.6.1.1. Patients should never be used to interpret for their parents in substantive medical encounters.

5.10.2.6.1.2. Family members, friends, children or other individuals should not be used to interpret for a patient and/or patient representative in substantive medical encounters.

5.10.2.6.1.3. If a patient and/or patient representative chooses to use a family member or friend as an interpreter in substantive medical encounters after being informed of free interpreter services, staff are encouraged to involve a Trained Medical Interpreter (in person or by telephone) during the encounters in order to provide staff with information regarding the accuracy of Interpretation.

5.10.2.6.2. A bilingual staff member, who is obtaining consent. In this case, a second individual must serve as the witness...
5.10.3. **Waiver of Documentation of Consent**

5.10.3.1. An IRB may waive the requirement for the investigator to obtain a signed consent form from some or all subjects if it finds either:

5.10.3.1.1. That the only record linking the subject and the research would be the consent document, the principal risk would be potential harm resulting from a breach of confidentiality, and the research is not regulated by the FDA. In this case, each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern; or

5.10.3.1.2. That 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.

5.10.3.2. 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.

5.10.3.3. The waiver of written documentation does not change the requirement for including the required and applicable additional elements of informed consent in the consent process.

5.10.3.4. The subject’s agreement to participate can be either captured on the consent form or in the study records. When consent is waived under 46.117 (c)(i) there will be no documentation.

5.11. **Obtaining New Consent and/or Notifying Subjects of Major Changes to any component of the Informed Consent Document:**

5.11.1. At the time of continuing review, the Principal Investigator must submit appropriate informed consent document(s) to the IRB(s) of record. This newly approved consent document becomes the “current” consent document for the study and must be the version to be signed by all future subjects until such time that a revision to it is approved by the IRB of record. The IRB of record should state in their approval letter whether or not previously consented subjects need to sign the newly reapproved consent document. If it is not stated, the Principal Investigator or designee should clarify this with the IRB of record. In situations where the IRB does not require re-consenting, it may be appropriate to send a letter to subjects to notify them of a change: Examples of
when a letter may be appropriate instead of re-consenting include the following:

5.11.1.1. the principal investigator has changed;

5.11.1.2. the study contacts have been changed and/or the contact telephone numbers have been changed;

5.11.1.3. the information is such that learning it would not materially affect the subject’s decision to continue participation or follow-up.

5.12. REVIEW OF “E-CONSENT” (ELECTRONIC CONSENT)

5.12.1. Prime IRB reviews e-consent technologies during development and in their final form to ensure that they meet the regulatory requirements for the elements and documentation of consent. This section provides some simple best practices on how to prepare an informed consent Prime IRB submission so that it is suitable for use in an electronic consent tool.

5.12.2. e-Consent Submission Timing

5.12.2.1. Principal Investigators considering e-Consent may wish to obtain Prime IRB approval of the consent document text prior to developing the electronic consent tool. Revisions based on Prime IRB feedback are easier to implement before e-consent programming and animation has begun.

5.12.3. e-Consent Submission Items

5.12.3.1. For a typical e-consent Prime IRB submission, the Principal Investigator and e-consent vendor will jointly prepare the Prime IRB submission of materials. Typical submissions include:

5.12.3.1.1. scripts for any video or audio files;

5.12.3.1.2. storyboards for any planned video creation; and

5.12.3.1.3. content for any screens on the e-consent tool that will be viewed by the participant.

5.12.4. Prime IRB Review of e-Consent Process and Documentation

5.12.4.1. The information presented to the subject, the process used for obtaining informed consent, and documentation of the informed
consent must meet the requirements set forth in 45 CFR 46. The Prime IRB must ensure that regulatory elements are present.

5.12.4.2. The Prime IRB will review the process by which consent is obtained (in-house or remotely); process by which the signer is provided with a copy of the signed consent document (electronic or paper); and plans to verify the “electronic signature” is:

5.12.4.2.1. Unique to the signer;
5.12.4.2.2. Capable of being verified;
5.12.4.2.3. Under the signer’s sole control;
5.12.4.2.4. Linked to the record in a way that it can be determined if anything in the document was changed after the signature was applied; and
5.12.4.2.5. Created by a reliable method for the purpose in which the signature was used.

5.12.5. Conditional and Final Approval

5.12.5.1. The Prime IRB’s decision to conditionally approve versus defer will depend on the extent to which the draft version reflects the content of the final electronic version. If the bulk of the electronic process has been provided in draft text or in story boards, then the Prime IRB can conditionally approve the consent document.

5.12.5.2. However, if there is still substantial content to be developed, then the Prime IRB must defer the consent document for future board review. Principal Investigators must determine how much time and resources they want to commit to developing an electronic consent before seeking an Prime IRB decision. The most optimal process is for the Principal Investigator to provide in writing to the Prime IRB a complete description of the electronic consent process, with story boards for videos if applicable. Then the Prime IRB will likely be able to provide conditional approval and have a single individual review the final product. If the final step is solely the transfer of the Prime IRB approved consent document to the tablet, without any modification of the text wording, the Prime IRB does not have to conditionally approve the consent document and does not have to review the final version of the consent document on the tablet. The Prime IRB can issue a final approval of the consent document. If
there are photos or audio materials to add to the final version, then the Prime IRB should review the final electronic version.

5.12.6. Use of Electronic Signatures

5.12.6.1. Unless the Prime IRB waives the requirement for a signed consent document, a written consent document must be given to and signed and dated by the subject or the subject’s legally authorized representative. An electronic signature on a consent document may be used of the procedures for obtaining an electronic signature are approved by the Prime IRB.

5.12.6.2. Electronic signatures may be used for documenting consent, but they must meet the electronic signature requirements in the jurisdiction where the research is conducted. Two laws that address electronic signature on the consent document include the Federal Electronic Signatures on Global and National Commerce Act (eSIGN) and the states adoption of the Uniform Electronic Transaction Act (UETA).

5.12.6.3. The participant must agree to use the electronic format by clicking an “I Agree” icon and there must be a clear statement of the participant’s rights with respect to the electronic document. These include the right to obtain a copy of the consent document in a non-electronic form and the description of any procedures that must be followed to withdraw the subject’s agreement to use an electronic consent document.

5.13. Other General Requirements:

5.13.1. Written in language understandable to the subject: For consent to be valid, the subject must be able to comprehend the information presented in the consent document. When possible, the target grade level should be written in the subject’s native language at a 6 – 8th grade level.

5.13.2. FDA-Regulated Test Articles: For all research involving test articles regulated by the U.S. Food and Drug Administration (FDA), informed consent documents must include a statement that the purpose of the study includes evaluation, whether for safety and/or effectiveness of the test article. The consent form must also include a statement that the FDA has access to the subject’s medical records.

5.13.3. Other Sponsor or Funder Requirements: When the funding agency requires additional language, this will be included in the consent document.
5.14. Special Considerations

5.14.1. Non-English-Speaking Subjects

5.14.1.1. Investigators indicate in the research submission when potential subjects may not be able to understand English. The submission includes the Investigator’s plans for the enrollment of this potentially vulnerable population.

5.14.1.2. Consent forms must be written in a language understandable to the participant or the participant's parent/guardian(s).

5.14.1.2.1. The investigator may submit the IRB-approved English version of the consent to a certified translation service or a colleague who is fluent in the native language for translation.

5.14.1.2.1.1. The Investigator submits the translated document to the IRB for review and approval and a statement by the translator indicating that the translation is a true representation of the English version and the qualifications of the person providing the translation.

5.14.1.2.1.2. The Investigator engages an interpreter who is fluent in English and the subject's native language during the consent interview.

5.14.1.2.2. Short Form Consent is another option available to Investigators when few non-English subjects are expected to enroll in the research.

5.14.1.2.2.1. The Investigator uses a short form consent form that will be presented orally to the subject or legally authorized representative.

5.14.1.2.2.2. The IRB maintains an English version of the Short Form as well as certified translations for other languages.

5.14.1.2.2.3. Certified translations in languages other than those available on the IRB website may be submitted to the IRB for approval.
5.14.1.2.2.4. The Investigator also uses the consent form or study summary document as described in §5.10.2.2.

5.14.1.2.2.5. The Investigator engages an interpreter who is fluent in English and the subject's native language during the consent interview.

5.14.1.2.3. For research where the IRB requires written consent, the non-English speaking subject’s and the witness/interpreter’s signature are required on a Translated Consent or Short Form Consent document (as described above).

5.14.1.2.4. When the IRB has approved a waiver of documentation of consent, the investigator may propose and the IRB may permit non-English speaking subjects to consent with waiver of documentation from either or both the subject and the interpreter/witness.

5.14.1.3. The IRB determines if the Investigator’s plan for the enrollment of subjects who do not speak English provides sufficient protections.

5.14.2. Illiterate Subjects

5.14.2.1. Investigators indicate in the research submission when potential subjects may be illiterate. The submission includes the Investigator’s plans for the enrollment of this potentially vulnerable population.

5.14.2.1.1. Before asking a subject to review and sign an informed consent form, the Investigator ensures that the potential research subject can read the form. (Children under a certain age are presumed to be unable to read; this policy is not intended for this population.)

5.14.2.1.2. Investigators do not assume that subjects are able to read and, when appropriate, inquire in a sensitive way whether the subject is able to do so. If a subject is not able to read the investigator makes special arrangements without causing embarrassment to the subject.
5.14.2.1.3. Illiterate subjects are not to be excluded from the research because they are unable to read unless there is an overriding scientific or safety concern.

5.14.2.1.4. If illiterate (in whatever the language of the consent process) but cognitively competent, the Investigator may plan for the consent process to proceed as usual. The informed consent will be read to the subject and the subject should be encouraged to ask questions.

5.14.2.1.5. This process must be conducted with a witness present. In this case, the witness is to observe the consent process.

5.14.2.1.6. If able, the subject will affix a signature to or make an "X" on the consent document.

5.14.2.1.7. The witness is to sign and date the consent document, and is to document, in writing, that the process took place and that the subject voluntarily consented to participate.

5.14.2.2. The IRB determines if the Investigator’s plan for the enrollment of subjects who are not able to read provides sufficient protections.

6. MATERIALS

TEMPLATE: Consent Template


7. REFERENCES

45 CFR 46.117
21 CFR 56.117
45 CFR 46.111
21 CFR 56.109
45 CFR 46.116
21 CFR 50.25
45 CFR 164.508

Prime IRB SOP 601: Assent and Parental Permission
ADDENDUM

Until this SOP is revised, no later than 31 December 2019, the following modification will be adopted as best practices, amending Section 5.8. Informed Consent Procedures When the Subject is Unable to Read or Understand the Consent Document: 5.8.2:

**Use of a Qualified Translator**

Section 5.8.2 specifies the use of a “certified” translator. This addendum replaces the word “certified” with “qualified,” thereby expanding the criteria to allow other acceptable qualified translators to participate in the consent process. The term "qualified" provides researchers with flexibility with respect to translation. The IRB will make a case by case determination as to whether the qualifications of the translator/verifier are sufficient based on the study and the specific study documents. Each site enrolling non-English speaking subjects must provide documentation of the translator’s qualifications (i.e., expertise in the foreign language, such as certified translator, native speaker or other evidence of fluency, and an appropriate scientific or medical background).
<table>
<thead>
<tr>
<th>Version 1.1</th>
<th>Name</th>
<th>Status (Pending, Reviewed, Approved)</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Written by:</td>
<td>Michelle Cook</td>
<td></td>
<td>1 February 2019</td>
</tr>
<tr>
<td>Reviewed by:</td>
<td>Toby Schonfeld</td>
<td></td>
<td>1 February 2019</td>
</tr>
<tr>
<td>Approved by:</td>
<td>Toby Schonfeld</td>
<td>Approved</td>
<td>1 February 2019</td>
</tr>
</tbody>
</table>
1. PURPOSE

1.1. The purpose of this standard operating procedure is to describe the requirements for assent and parental permission for research involving children.

1.2. The principle of respect for persons requires that the choice of an autonomous person be respected. Under the usual conditions of clinical research, this is accomplished by soliciting the informed consent of the prospective research subject. However, as children are generally unable to consent for themselves, researchers must seek the permission of parent(s) or guardian and the assent of the child.

2. REVISIONS FROM PREVIOUS VERSION

2.1. None.

3. POLICY

3.1. It is the policy to comply with all federal and state regulations that pertain to informed consent, parental permission, and assent. Assent and parental/guardian permission must be obtained in accordance with Prime IRB determinations for research involving children.

3.2. When a child who was enrolled in research with parental or guardian permission subsequently reaches the legal age of consent to the procedures involved in the ongoing research (in most instances 18 years of age), the subject’s participation in the research is no longer regulated by the requirements regarding parental or guardian permission and subject assent.

3. RESPONSIBILITIES

3.1. Director, Prime Review Board Services: Responsible for establishing and periodically reviewing and modifying (as appropriate) the consent form template.

3.2. Chair, Prime Review Board Services: Responsible for periodically reviewing the consent form template and requesting modifications (as appropriate).
5. PROCEDURE

5.1. ASSENT

5.1.1. The Investigator submits research involving children following Prime IRB SOP 300: Research Submission Requirements, and must provide the Prime IRB with either a detailed description of how assent will be obtained and documented, or requests consideration of a waiver of assent.

5.1.2. The Prime IRB reviews the submitted research following Prime IRB SOP 104: IRB Review Process and determines whether adequate provisions are made for soliciting the assent of a child when, in the judgment of the Prime IRB, the child is capable of providing assent.

5.1.2.1. When determining whether children are capable of assenting, the Prime IRB considers the ages, maturity, condition, and psychological state of the children involved. The Prime IRB has the discretion to judge children’s capacity to assent for all of the children to be involved in a proposed research activity, or on an individual basis.

5.1.2.2. The default age at which solicitation of assent will be 7 years of age but younger or older limits may be chosen based on the nature of the study and the expected capacity for the prospective subject(s) to understand the purpose of the research, the nature of the procedures and the ability to express their voluntary approval or disapproval to participate.

5.1.3. The Prime IRB may determine that children’s assent is not required in any of the following three types of circumstances:

5.1.3.1. The capability of some or all of the children is so limited that they cannot reasonably be consulted;

5.1.3.2. The intervention or procedure involved in the research holds out a prospect of direct benefit to the health or well-being of the children and is available only in the context of the research.

5.1.3.3. The Prime IRB grants a waiver of assent when the research meets the same conditions as those for waiver or alteration of informed consent in research involving adults, as specified in the regulations at either 45 CFR 46.116(c) or 45 CFR 46.116(d). See Prime IRB SOP 605: Waiver of Elements of Consent and Waiver of HIPAA Authorization.
5.1.4. When the Prime IRB determines that a child’s assent is required:

5.1.4.1. The child shall be given an explanation of the proposed research procedures in language that is appropriate to the child’s age, experience, maturity, and condition; and

5.1.4.2. The Prime IRB shall determine whether and how assent must be documented.

5.1.5. A child's dissent to participation in a study, which should normally be respected, may be overruled by the child's parents as specifically approved by the Prime IRB if the Prime IRB determines that the capability of some or all of the children is so limited that they cannot reasonably be consulted, or that the intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the children and is available only in the context of the research.

5.2. PARENTAL PERMISSION

5.2.1. The Investigator submits research involving children following Prime IRB SOP 300: Research Submission Requirements and provides the Prime IRB with either a detailed description of how permission will be obtained and documented, or requests consideration of a waiver of permission.

5.2.1.7. Documentation of permission from the child’s parent(s) or guardian(s) is provided by their signature and date on the Informed Consent document.

5.2.1.8. All the requirements for informed consent apply to obtaining parental/guardian permission and all the appropriate informed consent elements must be included in a written consent document unless otherwise waived by the Prime IRB.

5.2.1.9. Permission must be obtained before the initiation of any screening processes performed solely for the purpose of research.

5.2.2. If children who are Wards (or foster children) are to be included as research subjects (See, Prime IRB SOP 503: Research Involving Children), the investigator provides the Prime IRB with detailed information about the proposed permission/assent process, as well as the identity and authority of the individuals who will provide permission for the Ward subjects. A foster parent can never give valid permission for a Ward.
5.2.3. If a person other than a parent signs an Informed Consent/Permission Document, the investigator obtains documentation from that individual that he or she is legally authorized to consent for the child, or in the case of Wards, that a governmental agency or public official has guardianship of the child.

5.2.4. The Prime IRB reviews the research submission following Prime IRB SOP 104: IRB Review Process and determines, to the extent that consent is required, that adequate provisions are made for soliciting the permission of parents or guardians of each child involved in a research study.

5.2.5. The Prime IRB makes the following additional determinations, which will be documented in the Prime IRB meeting minutes for full Board determinations and in the Prime IRB Correspondence for determinations made using expedited review procedures:

5.2.5.1. Whether the permission of both parents is required;

5.2.5.2. Whether the permission of one parent is sufficient;

5.2.5.3. Whether the parental permission process is waived because the research is not subject to FDA regulations and meets the requirements of 45 CFR 46.116(c), 45 CFR 46.116 (d), or 45 CFR 46.408(c).

5.2.6. The Prime IRB may find that the permission of one parent is sufficient for research to be conducted under §46.404 (§50.51) or §46.405 (§50.52). When research is to be conducted under §46.406 (§50.53) and §46.407 (§50.54) permission must be obtained from both parents, unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.

5.2.7. The Prime IRB may alter or waive the requirement for obtaining parental or guardian permission if it determines that:

5.2.7.1. The research meets the same conditions as those for waiver or alteration of informed consent in research involving adults, as specified in the regulations at either 45 CFR 46.116(c) or 45 CFR 46.116(d); or

5.2.7.2. The relevant research protocol is designed to study conditions or a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects (for example, neglected or abused children); provided that an appropriate mechanism is in place to protect the children, provided that the
research is not FDA-regulated, and provided that the waiver is not inconsistent with federal, state, or local law, or 45 CFR 46.408(c); or

5.2.7.3. The research satisfies all the requirements for an Exception to the General Requirements (for informed consent) as specified in 21 CFR 50.23 including:

5.2.7.3.1. the prospective subject is confronted with a life-threatening situation necessitating the use of a test article;

5.2.7.3.2. informed consent (parental permission) cannot be obtained because of inability to communicate or unavailability of the parent/guardian;

5.2.7.3.3. time is insufficient to obtain consent from the subject’s legal representative; and

5.2.7.3.4. there is no available alternative method of approved or generally recognized therapy that provides an equal or greater likelihood of saving the life of the subject.

5.3. **Children Who Reach the Legal Age of Consent While Enrolled in a Study**

5.3.1. When a child who was enrolled in research with parental or guardian permission subsequently reaches the legal age of consent the Investigator seeks and obtains the legally effective informed consent for the now-adult subject for any ongoing interactions or interventions with the subjects.

5.3.2. The Prime IRB considers, if appropriate, a waiver under 45 CFR 46.116(d) of the requirements for obtaining informed consent in order for the subjects to continue their participation in the research.

5.4. **Signatures**

5.4.1. The Prime IRB provides the consent form template with an assent section at the end of the document. This section is to be completed by the individual obtaining assent. If subjects are ages 12-17 years, their signature may be obtained on the form, but their signature is optional. Children who voluntarily choose to sign the consent document are permitted to do so.

6. **MATERIALS**

6.1 None]
7. REFERENCES

21 CFR 50 Subpart B
21 CFR 50 Subpart D
21 CFR 56.116
21 CFR 56.408,
45 CFR 46 Subpart D
45 CFR 46.116
45CFR46.408,
Prime IRB SOP 503: Research Involving Children
Prime IRB SOP 504: Minors Who Are Not Children in the Research Context
<table>
<thead>
<tr>
<th>Version 0.2</th>
<th>Name</th>
<th>Status (Pending, Reviewed, Approved)</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Written by</td>
<td>Karl Nelson</td>
<td></td>
<td>17-July-2017</td>
</tr>
<tr>
<td>Reviewed by</td>
<td>Jennifer Neal-Jimenez</td>
<td></td>
<td>7-January-2018</td>
</tr>
<tr>
<td>Approved by</td>
<td>Jennifer Neal-Jimenez</td>
<td>Approved</td>
<td>9-January-2018</td>
</tr>
</tbody>
</table>
1 PURPOSE

1.1 This policy establishes legal council’s opinion of which individuals meet the following DHHS and FDA definitions when the research is conducted in Maryland:

   1.1.1 Legally authorized representative
   1.1.2 Children
   1.1.3 Guardian

2 REVISIONS FROM PREVIOUS VERSION

2.1 None

3 POLICY

3.1 Under DHHS and FDA regulations a “legally authorized representative” means an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject’s participation in the procedure(s) involved in the research. Unless the IRB has waived the requirement to obtain consent, when research involves adults unable to provide consent, permission must be obtained from a legally authorized representative. When research is conducted in Maryland the following individuals meet this definition:

   3.1.1 For medical research and minimal risk non-medical research:
      3.1.1.1 A “health care agent” as defined in Maryland State Law.
      3.1.1.2 A “guardian” as defined in Maryland State Law. (“Individual, organization or agency, if any that has been appointed legal guardian of the person found to be incompetent by a court of competent jurisdiction.”)
      3.1.1.3 A “responsible party” as defined in Maryland State Law.

   3.1.2 For all other research, legal counsel has to determine that the individuals proposed to serve as legally authorized representatives meet the federal definition of “legally authorized representative.”
3.2 For research outside Maryland, a determination of who meets the DHHS and FDA definitions of “legally authorized representative” is to be made with consultation from legal counsel.

3.3 Under DHHS and FDA regulations “children” are persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted. Subpart D of the DHHS must be applied if and only if an individual involved in the research meet this definition. When research is conducted in Maryland all individuals under the age of 18 years meet this definition with the following exceptions:

3.3.1 Emancipated minors, defined as individuals who meet one of the following criteria, do not meet the DHHS and FDA definition of “children”: (Maryland State Law)

- 3.3.1.1 Married/widowed/divorced;
- 3.3.1.2 A parent;
- 3.3.1.3 A member of the armed forces;
- 3.3.1.4 Living apart from parents and managing his or her own finances; or
- 3.3.1.5 In the case of a female pregnant or believes herself to be pregnant, unless the procedures involved in the research include abortion as described below.

3.3.2 Individuals under the age of 18 when the research procedures are limited to:

- 3.3.2.1 Diseases dangerous to the public health;
- 3.3.2.2 Drug dependency (but not alcohol dependency).
- 3.3.2.3 Pregnancy, unless the procedures involved in the research include abortion as described below.

3.3.3 Exception: If the research procedures involve abortion, a female under the age of 18 who is not and has never been married meets meet the DHHS and FDA definition of “children.” (Maryland State Law)

3.4 For research outside Maryland, a determination of who meets the DHHS and FDA definitions of “children” is to be made with consultation from legal counsel.

3.5 Under DHHS and FDA regulations a “guardian” means an individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care. When research involves children and parental permission is required, consent may only be obtained from parents (biologic or adoptive) or a guardian as defined by DHHS and FDA regulations. When research is conducted in any jurisdiction and permission for a child to
participate in research is to be obtained from an individual other than biological or adoptive parents, the individual providing such permission must provide written documentation of the legal ability to consent to the child’s general medical care. A copy of this documentation is to be kept with the consent document in the investigator’s files.

4 RESPONSIBILITIES

4.1 Investigators are to follow this policy when obtaining permission for adults unable to consent or children to take part in research.

5 PROCEDURE

5.1 Investigator Responsibilities.

5.1.1 Prime IRB Approval.

5.1.1.1 New studies. The Investigator must indicate in the Prime IRB application that the protocol will utilize consent of a Health Care Decision-Maker and submit the Health Care Decision-Maker consent rider.

5.1.1.2 Ongoing studies. If the Investigator later decides to utilize consent of a Health Care Decision-Maker, an amendment must be submitted requesting the use of surrogate consent along with a revised informed consent document that incorporates the surrogate consent rider.

5.1.2 Identifying the Health Care Decision-Maker (HCDM).

5.1.2.1 The HCDM identified to make health care decisions on the patient’s behalf is generally the individual who should make decisions regarding the patient’s participation in Prime IRB-approved clinical research studies.

5.1.2.2 In the case of adult patients who are incompetent or lack decision-making capacity, AND who do not have a valid Durable Power of Attorney for Healthcare (“DPOA”) or a court-appointed guardian or conservator, the Health Care Decision-Maker should be an adult who has exhibited special care and concern for the patient, who is familiar with the patient’s personal values, and who is reasonably available.

5.1.2.3 Consideration shall be given, if possible, in order of descending preference for service as a Health Care Decision-Maker to:

5.1.2.3.1 The patient’s guardian
5.1.2.3.2 The patient’s spouse;
5.1.2.3.3 The patient’s adult child;
5.1.2.3.4 The patient’s parent;
5.1.2.3.5 The patient’s adult sibling;
5.1.2.3.6 Any other adult relative of the patient; or
5.1.2.3.7 If none of these individuals are available a guardianship may be created by application to the probate court.

5.1.2.4 Health Care Decisions made by an HCDM must be made in accordance with the patient’s individual health care instructions, if any, and other wishes, if known to the HCDM. If the patient has not given individual health care instructions, and the patient’s specific wishes are not known, decisions are to be made in accordance with the HCDM’s determination of the patient’s desires or best interests in light of the patient’s personal values and beliefs to the extent they are known.

5.1.3 No Appropriate Health Care Decision-Maker Available.

5.1.3.1 If none of the individuals eligible to act as a Health Care Decision-Maker under 5.1.2.2 or 5.1.2.3 above is reasonably available, the patient’s treating physician may make health care decisions for the patient after the treating physician either:

5.1.3.1.1 Consults with and obtains the recommendations of the Clinical Ethics Consultation Service; OR
5.1.3.1.2 Consults with a second physician who:

5.1.3.1.2.1 Is not directly involved in the patient’s healthcare; AND
5.1.3.1.2.2 Who either:

5.1.3.1.2.2.1 Does not serve in a capacity of decision-making, influence, or responsibility over the treating physician; OR
5.1.3.1.2.2.2 For whom the treating physician does not exert decision-making, influence, or responsibility over the treating physician; AND
5.1.3.1.2.2.3 Concurs with the treating physician’s decision.
5.1.3.2 In the event that the patient’s treating physician is acting in the role of Health Care Decision-Maker and is also the Principal Investigator in a proposed clinical research study, before enrolling the patient in a clinical research study, the physician must do one of the following so that there is an independent determination of the appropriateness of enrolling the patient in the research study. The physician must either:

5.1.3.2.1 Withdraw as treating physician and transfer the patient’s care to another treating physician; OR
5.1.3.2.2 Allow the decisions regarding whether to enroll and continue the patient in the study to be made by either:

5.1.3.2.2.1 Consulting with and obtaining the recommendations of the Clinical Ethics Consultation Service; OR
5.1.3.2.2.2 Consulting with a second physician who:

5.1.3.2.2.2.1 Is not directly involved in the patient’s health care; AND
5.1.3.2.2.2.2 Who either: Does not serve in a capacity of decision-making, influence, or responsibility over the treating physician; OR For whom the treating physician does not exert decision-making, influence, or responsibility; AND Concurs with the treating physician’s decision.

5.1.3.3 A Clinical Ethics Consult should be obtained in all situations where the physician is acting as Health Care Decision-Maker and the patient is being considered for enrollment in a clinical research study. The recommendations(s) of the Clinical Ethics Consultation Service and/or the consulting physician shall be documented as to the appropriateness of enrolling the patient in the clinical research study, and this recommendation shall be determinative as to whether or not the patient should be enrolled.

5.1.4 Required Documentation. In all cases involving adult patients who are incompetent or lacks decision-making capacity for healthcare decisions and consent of a Health Care Decision-Maker is utilized, the treating physician, the
consulting physician(s) and other involved members of the healthcare team shall document in the medical record:

5.1.4.1 The basis for their determination that the patient lacks decision-making capacity;

5.1.4.2 The identity of the HCDM and the rationale for the selection of the individual as HCDM, which shall be documented on the Healthcare Decision-Maker Identification Documentation Form (a copy shall be maintained in the research records);

5.1.4.3 The process by which a treating physician is determined to be the HCDM if no other appropriate individuals are identified, as well as the recommendations of the Clinical Ethics Consult Service and/or consulting physician when the treating physician is identified as the HCDM, if applicable; and

5.1.4.4 The process by which the patient was enrolled or declined to be enrolled in the clinical research.

5.2 Prime IRB Committee Responsibilities.

5.2.1 The Prime IRB Committee, the Chairperson, or his/her designee will review the informed consent documents with the attached Health Care Decision-Maker consent rider in accordance with *Prime IRB SOP 600: Required Elements of Consent and Documentation of Consent*.

5.2.2 The Prime IRB Committee, the Chairperson or his/her designee will review the Investigator’s rationale for the need to utilize consent by a Health Care Decision-Maker assuring:

5.2.2.1 There are appropriate safeguards in place for cognitively impaired participants;

5.2.2.2 The Investigator has a thorough understanding of the appropriate use of consent of a Health Care Decision-Maker in clinical research; and

5.2.2.3 The Investigator has detailed how reconsenting will take place when and if an individual becomes competent to consent for oneself.

5.2.3 The Prime IRB should consider whether and when to require a reassessment of decision-making capacity. Additionally, after taking into account the study’s anticipated length and the condition of the individuals to be included, whether and when periodic reconsenting of the HCDM should be required to assure that a participant’s continued involvement is voluntary.
5.3 Prime IRB Staff Responsibilities.

5.3.1 The Prime IRB staff will conduct a pre-review of the informed consent document with the Health Care Decision-Maker consent rider submitted with a new study application to determine that the correct forms have been submitted for the targeted population, assess the readability of the document, and verify all required elements are present for adequate informed consent, including if any additional elements are appropriate.

5.3.2 If additional information regarding the informed consent process or documentation is needed, the Prime IRB staff will contact the Investigator and request the additional information.

5.3.3 The Prime IRB staff will assure that the Prime IRB database is updated appropriately to reflect Prime IRB approval for the use of consent of a Health Care Decision-Maker for the research.

5.3.4 The Prime IRB staff will draft all approval letters for signature by the Chair or his/her designee.

6 MATERIALS

6.1 Healthcare Decision-Maker Identification Documentation

7 REFERENCES

7.1 45 CFR §46.102, 45 CFR §46.402

7.2 21 CFR §50.3
Healthcare Decision-Maker/Surrogate Identification Documentation

I. Category of Potential Health Care Decision Maker/Surrogate: Please circle the category that best describes the capacity in which the individual is serving as a Healthcare Decision-Maker for the patient (A, B, C or D).

| A | Court-appointed Conservator or Guardian of the individual with authority to make health care decisions for the patient. | [Attach a copy of the court order to this Documentation.]* |
| B | Person named in the patient’s Durable Power of Attorney for Health Care. | [Attach a copy of the Durable Power to this Documentation.]* |
| C | Family Member or Friend (check one) | Complete Section III on next page |
|   | □ Spouse |
|   | □ Adult Child |
|   | □ Parent |
|   | □ Adult Sibling |
|   | □ Other Adult relative or Friend: Specify _________________________ |
| D | None of the above is available to serve. |

II. For A, B, or C above, complete the following information for the Health care decision-maker/surrogate’s contact information:

Name: ____________________________________________
Address: _________________________________________
Home Phone: ( ) ___________________________________
Work Phone: ( ) ___________________________________
Cell Phone: ( ) ___________________________________
Pager: ( ) _______________________________________
E-mail: _________________________________________
Other: ___________________________________________

*Attach copy of Court-Order or DPOA if either A or B is selected.
III. **Justification for Selecting Category C (Surrogate):**

If the patient does NOT have a Court-appointed guardian or conservator, AND does NOT have a person authorized to act under a Durable Power of Attorney for Health Care, then both of the following must be TRUE for the individual identified under Category C above (friend or family) to serve as the Surrogate healthcare decision-maker for this patient. Check if True:

☐ The person identified above is:

1. an adult
2. who has exhibited special care and concern for the patient,
3. who is familiar with the patient’s personal values, AND
4. who is reasonably available to serve as a surrogate.

☐ It appears as though the person can make health care decisions for the patient in accordance with the patient’s individual health care instructions, if any, and other wishes, if known to the HCDM. If the patient has not given individual health care instructions, and the patient’s specific wishes are not known, the HCDM can make a determination of the patient’s desires or best interests in light of the patient’s personal values and beliefs to the extent they are known.

If available, provide additional information evidencing the person’s qualification to serve as a surrogate for this patient:

☐ The person has lived/lives with the patient for _______ years.

☐ The person has known the patient for _______ years.

☐ The person sees the patient on a daily/weekly/monthly basis.

☐ Other evidence of the appropriateness of the selected Surrogate:  (please describe):

__________________________________________________________________
__________________________________________________________________
__________________________________________________________________
__________________________________________________________________
__________________________________________________________________
__________________________________________________________________
__________________________________________________________________
__________________________________________________________________
__________________________________________________________________
__________________________________________________________________
__________________________________________________________________
__________________________________________________________________
__________________________________________________________________
__________________________________________________________________
<table>
<thead>
<tr>
<th>Version 0.2</th>
<th>Name</th>
<th>Status (Pending, Reviewed, Approved)</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Written by :</td>
<td>Karl Nelson</td>
<td></td>
<td>17-July-2017</td>
</tr>
<tr>
<td>Reviewed by:</td>
<td>Jennifer Neal-Jimenez</td>
<td></td>
<td>7-January-2018</td>
</tr>
<tr>
<td>Approved by:</td>
<td>Jennifer Neal-Jimenez</td>
<td>Approved</td>
<td>9-January-2018</td>
</tr>
</tbody>
</table>
1 PURPOSE

1.1 The purpose of this standard operating procedure is to document the mechanism for Prime IRB review and approval of research study recruitment methods and materials of non-exempt human subjects’ research.

2 REVISIONS FROM PREVIOUS VERSION

2.1 None

3 POLICY

3.1 Recruitment materials (including, but not limited to: advertisements, flyers, phone scripts, newspaper ads, radio and television announcements, bulletin board tear-offs, and posters) are part of the informed consent process and the subject selection process. As such, the Prime IRB must review and approve all recruitment materials prior to their use by an investigator.

3.2 The Prime IRB is responsible for ensuring fair and equitable selection of subjects; this responsibility includes ensuring that the content of recruitment materials accurately reflect the study, and do not unduly induce potential subjects to participate. To fulfill this responsibility, the Prime IRB reviews participant recruitment methods, advertising materials and participation payment arrangements, and approves them when fair, honest and appropriate.

Recruitment methods, including advertisements, and participant payment arrangements affect the equitable selection of subjects and are therefore important components of the Prime IRB’s review and approval process. Advertisements, whether in print media, broadcast media, Web sites or other formats, often provide the prospective participant with their first exposure to study information. For this reason, recruitment materials are considered part of the process of informed consent.

Payment arrangements among sponsors, organizations, investigators and those referring research subjects may place subjects at risk of coercion or undue influence or cause inequitable selection. Paying finders’ fees is a violation of the AMA Code of Ethics E- 6.03, and is not permitted by the Prime IRB.
3.2. **Content of Recruitment Materials**

Generally, the information included in recruitment materials should be limited to the information the prospective participants need to determine their eligibility and interest such as:

3.2.1. The name and address of the investigator, the research facility and/or the institution conducting the study;

3.2.2. The condition under study and/or the purpose of the research;

3.2.3. In summary form, the criteria that will be used to determine eligibility for the study;

3.2.4. A brief description of what is involved in study participation (i.e., number of visits, length of participation, general study procedures);

3.2.5. The location where the research will take place and the person or office to contact for further information; and

3.2.6. If reimbursement for expenses or payment for time and effort will be provided, these can be stated but the amount and terms should not be specifically stated unless the Prime IRB determines such statements are appropriate and do not entice subjects. Nothing in this recruitment precludes the amount of compensation from being disclosed as part of in-person or telephone recruitment conversations (even if the conversation adheres to a written script).

3.3. **Recruitment materials must NOT include any of the following:**

3.3.1. Any direct or implied claim that the purpose of the research is to treat the condition or that the test article, if any, is safe and effective, or equal or superior to an existing treatment; or

3.3.2. Any express or implied claim that the research will improve the participant’s medical condition; or

3.3.3. A statement that promises “free medical treatment;” or

3.3.4. The term “new” unless modified (e.g., “new research medication” or “new investigational medication”); or

3.3.5. Use of terms such as “new treatment,” “new medication,” or “new drug” without explaining that the test article/test procedure is investigational; or Exculpatory language.

3.3.6. Emphasized payment/compensation amount (e.g., larger or bold type).
4 RESPONSIBILITIES

4.1 Principal Investigator: Responsible for submitting draft and final versions of all recruitment materials to the Prime IRB for approval prior to implementation and use.

4.2 Prime IRB Reviewer: Responsible for reviewing the content of all recruitment materials submitted for Prime IRB review

5 PROCEDURE

5.1 When to Submit Recruitment Materials to the Prime IRB

5.1.1 Advertising for research subjects is considered part of the informed consent process. As such, recruitment materials must be submitted to the Prime IRB with the research protocol for initial review.

5.1.2 If the investigator decides at a later date to use recruitment materials or to change currently approved materials, the new/modified materials must be submitted to the Prime IRB for review as a modification to the approved research.

5.2 Format and Use of Recruitment Materials

5.2.1 Recruitment materials are evaluated for visual impact (e.g. size, type face, size of print, graphics), context, and use. Materials should be submitted to the Prime IRB in their final format and be accompanied by a description of how the materials will be used (i.e. clinic staff will hand flyer to patients, advertisement will be published in local newspaper, flyers will be placed in the waiting room).

5.2.2 For recruitment materials that are to be recorded for broadcast, transcripts must be submitted for review and approval. The final recorded message may be approved via expedited procedure.

5.2.3 Recruitment materials may be subject to approval from other Relying Institution departments, such as Advertising and Marketing Communications and/or the specific areas in which recruitment materials may be posted. It is the responsibility of the Principal Investigator to obtain all necessary approvals for recruitment materials.

5.3 Content Restrictions

5.3.1 Recruitment material may not unduly influence potential subjects.

5.3.2 Recruitment material may not promise a cure or other benefits beyond what is set forth in the informed consent document and the research protocol.

5.3.3 If an investigational drug, device or service (“test article”) is used in the research, this must be disclosed. No claims may be made (explicitly or implicitly) that the
test article is safe or effective for the purposes under investigation, or that it is known to be equivalent or superior to any other drug, device or service.

5.3.4 Recruitment materials may not use the terms "new treatment," "new medication," or "new drug" without explaining that the test article is investigational, i.e. not approved by the FDA.

5.3.5 Recruitment materials may not promise "free medical treatment" without also disclosing if there may be costs to the subjects.

5.3.6 Recruitment materials may state that subjects will be compensated or reimbursed, but specific dollar amounts should not be a major feature of the advertisement.

5.4 **Items that Must Be Included in Recruiting Materials**

5.4.1 A description of the type of research (i.e. clinical trial) and purpose of the research. The word "research" must be included in this description.

5.4.2 Contact information for the person and/or office to contact for additional information.

5.4.3 The Prime IRB research study number.

5.4.4 The name of the institution responsible for the research.

5.5 **Information that Should be Included in Recruiting Materials**

5.5.1 The title of the research

5.5.2 The sponsor of the research

5.5.3 Where the research is being performed (specific location) (i.e. Prime Cancer Center).

5.5.4 In summary form, the criteria that will be used to determine eligibility for participation in the research.

5.5.5 A brief description of the time commitment and duration of the subjects' participation.

5.5.6 A brief description of the benefits of the research to the subjects, if any (e.g., smoking cessation).

5.5.7 The Principal Investigator's name and contact information.

5.5.8 The compensation/reimbursement that may be provided.

5.6 **Electronic Medical Records (EMR) Use for Identifying Prospective Study Subjects:**

The EMR(s) may be used to help identify prospective patients for research studies, provided such use is consistent with the 1996 Health Insurance Portability and
Accountability Act (HIPAA) and applicable Relying Institution policies governing protected health information (PHI).

5.6.1 Upon approval of the study by the Prime IRB, the inclusion and exclusion criteria for the study will be programmed into the EMR.

5.6.2 During the course of providing medical care, the appropriate caregiver (provider or nurse depending on the nature of the study) will be notified electronically if the patient potentially could qualify for the study.

5.6.3 The caregiver may, at their medical or nursing discretion, discuss the opportunity to participate in the trial with the patient.

5.6.4 The patient’s decision, on whether to receive further information or not, will be relayed to the research coordinator for that research study.

5.6.5 If the patient agrees to be contacted to receive more information on the study, the research coordinator will arrange a time to meet with the patient and begin the recruitment/consenting process.

5.6.6 If the patient does not wish to learn more about the study or declines to participate in the study, the research coordinator will update the patient’s record so that future caregivers will not receive the notification as described above in (b).

5.7 **Recruitment Methods Involving Identification of Potential Research Participants from Medical Records Indicating a Specific Medical Diagnosis**

5.7.1 The investigator will ensure that potential subjects and their families are protected from undue psychological distress or harm, in accordance with the ethical principles specified in the Belmont Report.

5.7.2 The investigator will ensure that the association of a diagnosis with a potential research subject is accurate, and that the subject is alive prior to attempting to contact the individual. Family members of a deceased person may not be contacted for the purpose of research without Prime IRB approval.

5.7.3 The methods for identifying potential subjects with a specific diagnosis, for confirming the accuracy of the information, and for confirming that the individual is alive must be specified in the protocol.

5.7.4 The methods for identifying potential deceased subjects with a specific diagnosis for the purpose of contacting family members must include methods for confirming the association of the individual with the diagnosis and that the potential participant is deceased.

5.7.5 The Prime IRB recommends that study protocols intending to use EMR will have the following, or similar, language inserted in the recruitment section of the protocols.
5.7.5.1 “The EMR will be used to identify prospective patients for this study. Patients who could potentially qualify for this study will be identified and their physician or nurse will be notified. A member of the Hospital workforce may ask a patient if he/she is interested in being contacted by study personnel to learn more about a research project and to possibly participate in the study. The patient’s preferences will be relayed to the research coordinator who will either contact the patient if the patient is interested in participating, or indicate in the chart that the patient does not wish to participate.”

5.8 What Does Not Require Prime IRB Review

5.8.1 Medical society newsletters.

5.8.2 News stories (i.e. public service announcements).

5.8.3 Publicity intended for other audiences, such as financial page advertisements directed towards prospective investors.

5.9 Investigator Responsibilities

5.9.1 All recruitment materials, as defined above, must be submitted to the Prime IRB for review and approval in accordance with Prime IRB SOP 300: Research Submission Requirements. These materials must meet the standards established in §3.2. and §3.3. (above) and must be submitted to the Prime IRB at the time of initial submission of the protocol or at a subsequent time as a modification to the protocol.

5.9.1.1 Recruiting materials developed or revised after the initial Prime IRB approval must be submitted to the Prime IRB as a protocol amendment prior to use.

5.9.2 A change in any of the following during the course of the research is considered a protocol amendment and must be presented to the Prime IRB for review and approval:

5.9.2.1 Recruitment methods; or

5.9.2.2 Revised or newly developed recruiting materials.

5.9.3 Investigators who get referrals from other physicians should use one of the following procedures to ensure that the prospective participant’s permission to be contacted:

5.9.3.1 The referring physician can obtain the individual’s permission to be contacted; or
5.9.3.2 The investigator may send a letter inviting the individual to participate and the prospective participant can then contact the investigator; or

5.9.3.3 The investigator can notify the prospective participant (e.g., by mail) that they will be contacted unless they opt-out and the individual can exercise the option to opt-out from further contact if they do not wish to take part.

5.10 **Prime IRB Review of Recruitment Material Content**

5.10.1 The Prime IRB will review:

5.10.1.1 The information contained in the advertisement;

5.10.1.2 The mode of its communication;

5.10.2 The final copy of printed advertisements.

5.10.2.1 Screen shots of website advertisements;

5.10.2.2 The final audio or video for broadcast advertisements.

5.10.3 If the material is included as part of the initial submission, the Prime IRB will review the material as part of its review, using the principles described above.

5.10.4 If the material is submitted as a modification to the protocol, the Chair, Prime IRB or his/her designee will review the material using the principles described above to make sure the content is appropriate and does not pose any undue influence or coercion to potential research participants.

5.10.5 Once the material is approved, the Prime IRB approval and Prime IRB approved material will be made available to the investigator and study team.

5.10.6 If the recruitment material needs to be formatted/recorded into the final version that potential participants will see/hear, the investigator will submit the Prime IRB approved text and Prime IRB approval letter to the entity responsible for creating the final format material.

5.11 **Final Format Recruitment Material Creation and Review**

In addition to ensuring that the content of final versions of recruitment materials has not been altered without its approval, the Prime IRB will review and approve the final version of all materials.

Regardless of which agent prepares the recruitment materials the following steps will be taken to ensure that the materials still meet the requirements for final approval.

5.11.1 The investigator will submit and the Prime IRB will review the final version of all recruitment materials. The Prime IRB will review the materials for grammar/syntax changes, for changes in emphasis due to layout or typographical
5.11.2 Once the final versions of the recruitment materials are approved, the Prime IRB will communicate the approval to the investigator and study team in writing. (Note: it might not be feasible for final versions of some materials, such as copies of websites, radio or television ads to reside within the electronic Prime IRB management system.)

5.11.3 The Prime IRB and the investigator will each maintain a copy of the approved materials.

6 MATERIALS

6.1 Review of Recruitment Advertisement

7 REFERENCES

21 CFR 50.20,
21 CFR 56.111(a)(3)
45 CFR 46.111(a)(3)
45 CFR 46.116
REVIEW OF RECRUITMENT ADVERTISEMENT

PROJECT IDENTIFICATION
Prime IRB Protocol
Number: $$PROTOCOL NUMBER$$
PI: $$FIRST NAME$$ $$LAST NAME$$, $$DEGREE$$
Sponsor: $$SPONSOR$$ $$SPONSOR PROTOCOL NUMBER$$
Title: $$TITLE$$

Type of Advertisement
☐ Flyer
☐ Letter
☐ TV
☐ Radio
☐ Internet
☐ Newspaper
☐ Referral Letter (if it will be read by the subject)

Please check below to confirm that the ACCOMPANYING advertisement(s) includes:
☐ The name and location of the investigator and/or research facility/institution conducting the research
☐ Condition being studied and/or purpose of the research with a statement that this is a research study
☐ Summary of the eligibility criteria used to admit subjects into the study.
☐ A straightforward and truthful description of the benefits (e.g., a no-cost health examination) to the subject from participation in the study.
☐ A brief list of procedures involved
☐ Time or other commitment required (number of visits, total duration including follow-up visits, etc.)
☐ The name and phone # of the person or office to contact for further information
☐ If participants are to be paid monies or given goods, you may only state "Compensation/Remuneration Available". Stating the amount of money is not permissible.
☐ Approved by Expedited Review; reported to full Prime IRB at Meeting.
   Approval Date ______________
   Meeting Date: ______________

______________________________
Signature of Prime IRB Member Conducting Expedited Review:

☐ Approved by Prime IRB at Convened Meeting.
   Meeting Date: ______________
<table>
<thead>
<tr>
<th>Version 0.2</th>
<th>Name</th>
<th>Status (Pending, Reviewed, Approved)</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Written by:</td>
<td>Karl Nelson</td>
<td></td>
<td>17-July-2017</td>
</tr>
<tr>
<td>Reviewed by:</td>
<td>Jennifer Neal-Jimenez</td>
<td></td>
<td>7-January-2018</td>
</tr>
<tr>
<td>Approved by:</td>
<td>Jennifer Neal-Jimenez</td>
<td>Approved</td>
<td>9-January-2018</td>
</tr>
</tbody>
</table>
1 PURPOSE

1.1 Participant payment arrangements may affect the equitable selection of participants and may also unduly influence subject decision-making during the informed consent process. The purpose of this standard operating procedure is to define the types of payments made to subjects, and to provide guidance as to acceptable practices.

2 REVISIONS FROM PREVIOUS VERSION

2.1 None

3 POLICY

3.1 The IRB is responsible for review and approval of participant payment arrangements offered to a subject or family, as part of a research protocol. The IRB will permit reimbursement to families for expenses related to travel, time or inconvenience and will permit compensation for study participation when the compensation is considered fair, honest and appropriate. For studies that involve greater than minimal risk, the IRB will apply a “Wage” model for determining fair and appropriate compensation.

4 RESPONSIBILITIES

4.1 Director, Prime Review Board Services: Responsible for establishing and periodically reviewing and modifying (as appropriate) the IRB policy on payment to subjects

4.2 Chair, Prime Review Board Services: Responsible for establishing and periodically reviewing and modifying (as appropriate) the IRB policy on payment to subjects

4.3 Principal Investigator: Responsible for submitting a payment plan to the IRB for approval prior to implementation.

4.4 Prime IRB Reviewer: Responsible for reviewing compensation plan for adherence to IRB policy on wording in recruitment materials and amount of payment.
5 PROCEDURE

5.1 Permissible Forms of Payment

5.1.1 Payment to compensate for time, effort and inconvenience of research participation is permissible, provided that it does not represent an undue inducement.

5.1.2 Payment for adults should be based on a wage-model, calibrated to the least well off amongst anticipated study participants.

5.1.3 Payment to children 9 years and older should be based on a wage-model, with the wage scaled to those that children can earn for common jobs such as baby-sitting or shoveling snow.

5.1.4 Payments for children younger than 9 years should either be non-monetary or based on tokens of appreciation.

5.2 Non-Permissible Forms of Payment or Compensation

5.2.1 The IRB does not permit any of the following forms of payment/compensation or financial arrangements unless the IRB grants a waiver (e.g. when the impact of payments on subject recruitment or retention is the object of the study):

5.2.2 Lottery or prize drawings for individuals who participate in research.

5.2.3 Use of finders’ fees, recruitment bonuses or incentives, other than referral payments to participants as outlined in the Appendix: ‘Bonus Payments in Clinical Research’.

5.2.4 A coupon good for a discount on the purchase price of the product once it has been approved for marketing

5.3 Investigator Responsibilities

5.3.1 The investigator must include information describing when and how the proposed payments will be made to a participant in either the protocol or in the IRB application. The informed consent document, must fully disclose to whom payments are due, the type of payment (reimbursement or compensation or token of appreciation) and the amount of each type of payment.

5.3.2 A change in the amount or terms of compensation during the course of the research is considered a protocol modification, and must be submitted to the IRB for review and approval.
5.4 **IRB Review**

5.4.1 When reviewing the protocol and IRB application, the IRB will ensure that the following conditions are met:

5.4.1.1 The protocol or IRB application should disclose the amount, form of payment, timing and purpose of the payment. The IRB will review the documentation and determine if the amount of payment is appropriate for the procedures, time, effort and inconvenience involved.

5.4.1.2 Either the IRB application or the protocol must state who will receive the payment.

5.4.1.3 The payments are insufficient to unduly induce subjects to participate and thereby assume risks that they would not otherwise agree to.

5.4.2 When reviewing the consent form, the IRB will ensure that the following conditions are met:

5.4.2.1 The consent form does not include payment as a benefit;

5.4.2.2 The purpose, timing, form and amount of payments have been specified;

5.4.2.3 Payments to subjects as specified above, are listed separately from payments to parents/guardians;

5.4.2.4 When payment or reimbursement will be made with bankcards, the consent form will include information that the bank will have access to identifiable information but not to any medical information;

5.4.2.5 Payment to subjects and families are not conditioned upon completion of the research; if a subject withdraws from a study, they must be offered payment for the portion of the study completed.

- For studies lasting only a few days, a single payment date at the end of the study, even to participants who had withdrawn before that date, is acceptable.

- It is permitted to withhold payment until the time specified in the consent form.

5.4.3 When payment to an individual could exceed $600 in a calendar year, the IRB will inform the study team in writing that they must verbally disclose to subjects that the sponsor will be required to issue IRS Form 1099 to the participant.

### 6 MATERIALS

6.1 None
7 REFERENCES

21 CFR 50.20,
21 CFR 56.111(a)(3)
45 CFR 46.111(a)(3),
45 CFR 46.116

Prime IRB SOP 104: IRB Review Processes
Prime IRB SOP 300: Research Submission Requirements
Prime IRB SOP 401: Criteria for Approval
Prime IRB SOP 600: Required Elements of Consent and Documentation of Consent
Prime IRB SOP 603: Review of Recruitment Materials

   https://www.fda.gov/RegulatoryInformation/Guidances/ucm126429.htm


AMA Council on Ethical and Judicial Affairs: Finders Fees
**Question on Investigator Payment Incentives** (12/30/2012)
https://firstclinical.com/fda-gcp/?show=2013/RE%20Question%20on%20Investigator%20Payment%20Incentives

**Question 1:**
I would like to know if it is acceptable for Sponsors to allow for a "bonus" payment to investigators participating in clinical research.

The intent is for this bonus payment to be delineated in the Clinical Trial Agreement so that if a particular site reaches the agreed upon recruitment of "x" number of subjects within the agreed upon timeframe, it would be entitled to a supplemental research grant of "x" dollars to be deposited into the PI's research fund as all other payments are.

**Answer 1:**

FDA's regulations do not specifically address your question of whether it is acceptable for a sponsor to pay investigators a bonus payment for meeting recruitment parameters within a specified timeframe. From the limited information provided, it appears that the sponsor is paying the investigator a “bonus” for actually meeting the agreed upon recruitment parameters specified in the Clinical Trial Agreement. It is also not clear what constitutes a “supplemental research grant of "x" dollars to be deposited into the PI's research fund”. FDA has regulations addressing the reporting to FDA of certain financial interests and relationships of clinical investigators, see 21 CFR 54, Financial Disclosure by Clinical Investigators found at
www.accessdata.fda.gov/scripts/cdrh/cfdocs/cf/cfr/CFRSearch.cfm?CFRPart=54. FDA also has draft guidance on financial disclosure by clinical investigators that can be found at www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM256525.pdf. I recommend that you determine whether this bonus payment is a significant payment of other sorts as described in the financial disclosure regulations at 21 CFR 54.2(f). You may also want to reference section IV., question C.4 in the draft guidance document mentioned above.

That being said, there are also concerns that financial relationships and interests in clinical trials may affect the rights and welfare of human subjects. The guidance titled, “Financial Relationships and Interests in Research Involving Human Subjects: Guidance for Human Subject Protection” found at www.hhs.gov/ohrp/policy/fguid.pdf, discusses financial relationships in research and points to consider to ensure that financial interests do not compromise the protection of research subjects. It is also very important to be familiar with any policy requirements regarding bonus payments that an investigator or their institution must follow. For example, there are a number of institutions and IRBs that by policy, do not allow investigators to accept bonus payments from sponsors for activities such as recruitment or enrollment, as they think this may create a potential conflict of interest. Specifically, the institution or IRB may prohibit such bonus payments out of concern that the
investigator may be motivated by financial interest to refer a patient when such referral might not be of any benefit to, or in the best interest of the subject.

Some sponsors actually have policies that do not allow clinical study incentives such as enrollment bonuses, finder's fees, awards, or gift certificates that are designed to reward the achievement of subject enrollment goals within a specified time period. If you are offering the recruitment bonus, or are in the position of being offered a recruitment bonus, you will want to be sure that you check with your company, institution, IRB, and any other appropriate oversight entities about whether there are any prohibitions.
Payment for Referral/Recruitment of Subjects in Human Research (Finder’s Fees and Bonus Payments)

Bonus payments for subject recruitment and finder’s fees for subject referral may compromise the integrity of a research study by giving an appearance of affecting the judgment of the investigator/research team and in some cases, may violate federal law. Ethical conduct of research requires that the participation of all human volunteers be completely voluntary. Particularly in a health care setting where relationships are hierarchical, it is important that there be no suggestion of subtle encouragement for any person’s participation in a research study by someone who will receive a finder’s fee or bonus payment if that person is enrolled as a subject.

The American Medical Association, and RhPHARMA have issued guidelines suggesting that finder’s fees and bonus payments may represent real or perceived cases of fee-splitting, a well-recognized and unethical behavior. Individuals participating in the conduct of research should be reimbursed only for activities directly related to performance of the research and at a rate not exceeding the fair-market value for the level of activity performed. Federal Medicare anti-kickback laws may also prohibit finder’s fees and bonus payments if there is real or apparent billing of standard of care costs as part of the research activity.

In addition, the Prime IRB believes that finder’s fees and bonus payments to investigators and study staff create a potential conflict of interest. Specifically, the investigator may be motivated by financial interest to refer a patient when such referral might not be of any benefit to, or in the best interest of the subject. Finder’s fees to physicians or nurses may diminish the patient’s free choice in deciding whether to volunteer for a clinical study. Specifically, the patient may rely unduly on the physician’s or nurse’s recommendation to enroll, against his/her own better judgment.

Finally, the Prime IRB believes that there does need to be guidance for investigators who wish to recruit subjects for research activity and where outside third parties need to be reimbursed for their activities in such manner as to avoid the appearance of fee splitting.

GUIDANCE:
Payment of Finder’s Fees and Bonus Payments to Relying Institution Physicians, Investigators or Study Staff by External Sponsors

The Prime IRB does not approve of finder’s fees being paid to Relying Institution investigators, physicians, nurses, and others who have a treating and/or counseling relationship to a subject being referred for enrollment in a clinical trial. The Prime IRB does not approve of finder’s fees being paid to any house staff or Relying Institution Health System or Relying Institution employee for referring or recruiting prospective subjects. The Prime IRB may review and approve small, nominal value gifts to staff organizations as long as such gifts are not based on any indicator of trial enrollment.
All payments for the conduct of a research project must be negotiated at the beginning of the study and not provide for additional payments based on either number or rate of subject enrollment. Payments tied to the number or rate of subject enrollment are considered to be bonus payments and are not permissible. Supplemental payments, or additional compensation, payments, or other incentives beyond nominal (less than $100 in value) must be negotiated as part of an addendum to the clinical agreement and reported to the Prime IRB. The investigator, physicians and staff must be aware of the existing reporting requirements under the Relying Institution Policy on Conflicts of Interest should there be any change in their financial relationship with any sponsor during the performance of a research study.

**Payment of Finder’s Fees to Referring Physicians or Others Outside the Relying Institution or Relying Institution Health System**

Finder’s fees include any payment or gift to an individual who identifies or assists in the recruitment of prospective subjects.

The use of finder’s fees to elicit recruitment of research subjects from outside the Relying Institution or Relying Institution Health System is discouraged. In some cases, it may be acceptable for investigators to offer a nominal incentive if the Prime IRB can be assured that the person who receives that incentive will in no way encourage subjects to enroll in a study and that applicable laws are not violated. Each case must be considered individually. The use of any compensation (payment, gift, etc.) must be reviewed and approved by the Prime IRB prior to being initiated. Payment to physicians outside of the Relying Institution Health System should be structured as a contract with the referring physician(s) and provide reimbursement for actual services rendered by the physician or their staff for the recruitment purposes.

If an investigator wishes to consult the Prime IRB regarding this issue, the following questions must be answered as part of the protocol submission:

- What compensation will be offered (for example, money, textbook, dinner, movie pass)?
- Who will obtain consent or HIPAA authorization (if applicable) from the subject?
- To whom is the compensation being offered and what is the person being asked to do?
- Could the compensation provided be coercive or appear to be linked to successful enrollment in the study?
- Will the subject or their insurance be charged for any study-related activity?
- If a person is enrolled in the study, will there be a change in the responsibility for patient care? For example, will the study investigators now provide primary treatment for a problem?

The Prime IRB requires that the role of a person not directly involved in the study who is identifying potential subjects be limited to asking the potential subject if he/she would be willing to talk to a researcher about a relevant study. If the potential subject is not interested, no further encouragement should occur.
Compensation to the person assisting in identifying potential subjects should be made whether or not the potential subject enrolls in the study.
<table>
<thead>
<tr>
<th>Version 0.2</th>
<th>Name</th>
<th>Status (Pending, Reviewed, Approved)</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Written by:</td>
<td>Karl Nelson</td>
<td></td>
<td>18-July-2017</td>
</tr>
<tr>
<td>Reviewed by:</td>
<td>Jennifer Neal-Jimenez</td>
<td></td>
<td>7-January-2018</td>
</tr>
<tr>
<td>Approved by:</td>
<td>Jennifer Neal-Jimenez</td>
<td>Approved</td>
<td>9-January-2018</td>
</tr>
</tbody>
</table>
1 PURPOSE

1.1 This policy describes the requirements for waiver of some or all elements of informed consent. It also describes the requirements for waiver or partial waiver of subject authorization for use and/or disclosure of protected health information (PHI) pursuant to section 45 CFR 164.512 of the Privacy Rule (HIPAA).

2 REVISIONS FROM PREVIOUS VERSION

2.1 None

3 POLICY

3.1 The Prime IRB may waive some or all the required elements for informed consent under 45 CFR 46.116(d). Under 45 CFR 164.512, the Prime IRB may waive, alter or partially waive the requirements for prospective authorization for use of PHI in research. Before the Prime IRB can waive these requirements, it must assure that all the conditions in the regulations are met and that its decisions are documented.

3.2 When following DHHS and FDA regulations, the following policy on waivers or alterations to consent is applicable:

3.2.1 Waiver of Parental Permission – Public Demonstration Project
- The research is conducted by or subject to the approval of state or local government officials.
- The research or demonstration protocol is designed to study, evaluate, or otherwise examine:
  - Public benefit or service programs.
  - Procedures for obtaining benefits or services under those programs.
  - Possible changes in or alternatives to those programs or procedures.
  - Possible changes in methods or levels of payment for benefits or services under those programs.
- The research cannot practicably be carried out without the waiver or alteration.

3.2.2 Waiver of Consent Process – Permission is not a reasonable requirement
- The research is designed for conditions or for a participant population for which parental or guardian permission is not a reasonable requirement to protect the participants.
• An appropriate mechanism for protecting the children who will participate as participants in the research is substituted.

3.2.3 Waiver of Documentation of the Consent Process – Based on Harm
• The only record linking the participant and the research is the consent document.
• The principal risk is potential harm resulting from a breach of confidentiality.
• Each participant will be asked whether he or she wants documentation linking the participant with the research, and the participant’s wishes will govern.

3.2.4 Waiver of Consent Process
• The research or clinical investigation involves no more than minimal risk to the participants.
• The waiver or alteration did not adversely affect the rights and welfare of the participants.
• The research cannot practicably be carried out without the waiver or alteration.
• When appropriate, the participants will be provided with additional pertinent information after participation.

4 RESPONSIBILITIES

4.1 Director, Prime Review Board Services: Responsible for establishing and periodically reviewing and modifying (as appropriate) Prime IRB SOPs regarding waiver or alteration of informed consent and HIPAA authorization

4.2 Chair, Prime Review Board Services: Responsible for ensuring that the Prime IRB appropriately applies the criteria for waiver or alteration of elements of consent and for waiver or partial waiver of required components of HIPAA authorization. Responsible for ensuring reviewers appropriately document their findings
5 PROCEDURE

5.1 Waiver or Alteration of Consent Procedure (45 CFR 46.116(d))

The Prime IRB may approve a consent procedure that does not include, or that alters, some or all the elements of informed consent or that waives the requirement to obtain informed consent provided the research is not regulated by the FDA and the Prime IRB finds and documents the following:

5.1.1 The research involves no more than minimal risk to the subjects; and
5.1.2 The waiver or alteration will not adversely affect the rights and welfare of the subjects; and
5.1.3 The research could not practicably be carried out without the waiver or alteration; and
5.1.4 Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

5.2 Waiver of Written Authorization for Use and/or Disclosure of Protected Health Information under the Privacy Rule

5.2.1 Researchers may use and/or disclose protected health information of one or more of the covered entities for research purposes without prospective written authorization provided that they provide a request for such waiver or partial waiver and the Prime IRB agrees that the request satisfies the criteria at §164.512(i)(2)(ii) as listed below.

5.2.1.1 The use or disclosure of the protected health information involves no more than minimal risk to the privacy of individuals based on:

5.2.1.1.1 The provision of an adequate plan to protect the identifiers from improper use and disclosure; and
5.2.1.1.2 The provision of an adequate plan to destroy the identifiers at the earliest possible opportunity consistent with the conduct of the research, unless there is a health or research justification for retaining the identifiers or such retention is otherwise required by law; and
5.2.1.1.3 The provision of adequate written assurances that the protected health information will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research project, or for other research for which the use...
or disclosure of protected health information would be permitted by law; and

5.2.1.2 The research could not be practicably conducted without the waiver or alteration; and

5.2.1.3 The research could not be practicably conducted without access to and use of the protected health information.

5.2.2 Provided the requirements of §5.2.1 are met, the Prime IRB may grant an alteration or partial waiver of the Privacy Rule requirements. The purposes for waiver or alteration include:

5.2.2.1 Waiver or alteration of one or more of the required elements of authorization

5.2.2.2 Waiver of the requirement to obtain authorization in writing such as when PHI is collected over the phone, fax, internet or email from study participants;

5.2.2.3 Waiver is requested to disclose PHI from one covered entity to another for the purposes of contacting and recruiting individuals into a study.

5.2.3 Documentation of Waiver of HIPAA Authorization

When the Prime IRB grants a waiver or partial waiver of Written Authorization under §5.2.2 above, it will provide documentation of its determinations as required by 45 CFR 164.512(ii):

5.2.3.1 Identification that the waiver was granted by the Prime IRB, and the date on which the alteration or waiver was approved; and

5.2.3.2 A statement that the Prime IRB determined that the alteration or waiver of Written Authorization, in whole or in part, satisfied the criteria of §5.2.2 of this policy; and

5.2.3.3 A brief description of the protected health information for which use or access was determined to be necessary by the Prime IRB; and

5.2.3.4 A statement that the alteration or waiver of HIPAA Authorization was reviewed and approved under expedited review procedures or at a convened meeting of the Prime IRB.
6 MATERIALS

6.1 Waiver of Consent Supplement
6.2 HIPAA Supplement and Waiver of Authorization
6.3 Partial Waiver of Consent for Screening/Recruitment Purposes
6.4 Partial Waiver of Authorization for Screening/Recruitment Purposes

7 REFERENCES

21 CFR 56.116
45 CFR 164.512(i)(2)(ii)
45 CFR 46.116
Prime IRB SOP 600: Required Elements of Consent and Documentation of Consent
Prime IRB SOP 606: Requirements for and Documentation of HIPAA Authorization
Waiver of Consent
Supplement
Clinical Investigation

1. Is this study regulated by the FDA (operating under an IND/IDE), or will data be used in supporting the commercialization of an FDA-regulated product?
   - No
   - Yes

   **Note**: A waiver or alteration of consent is generally not allowed for FDA regulated research.

2. What aspects of the study are you requesting the waiver or alteration of consent?
   - Full Waiver for all aspects of the research
   - Partial Waiver for certain aspects of the research → Explain: (e.g., screening for eligibility, minors who reach the age to consent for themselves)

   The patient's records will be reviewed to determine whether the patient is eligible for this clinical investigation. Limited information about the potential subject, i.e., the minimum necessary to establish whether or not the patient is eligible for the study will be recorded.

   **Note**: If you are accessing individual private information (e.g., medical records for screening) without authorization please also complete a **HIPAA Supplement and Waiver of Authorization**.
3. Please describe why the research, or aspects of the research, involves no more than minimal physical; psychological; social; economic risk to subjects:

**Physical Risk**
- This research study is limited to accessing, collecting and analyzing existing medical record information. There are no physical or psychological risks to the human subjects (i.e., the respective patients) associated with the conduct of this research study.
- The research involves minimal risk, as the review of the subjects’ medical records is for limited information, the data is not sensitive, and the data are derived from clinically indicated procedures
  - Other: _____

**Psychological Risk**
- This research study is limited to accessing, collecting and analyzing existing medical record information. There are no physical or psychological risks to the human subjects (i.e., the respective patients) associated with the conduct of this research study.
- Contacting subjects for Authorization/Consent could be considered an invasion of privacy and cause subjects undue anxiety.
  - Other: _____

**Social Risk**
- The data are not sensitive in nature
- The data are sensitive in nature. The precautions taken to limit the record review to specified data and the double coding of data further minimize the major risk, which is a breach of confidentiality.

**Economic Risk**
- There is an extremely low probability of harm to subjects’ status, employment, or insurability.
  - Other: _____

4. Please describe why the waiver of informed consent will not adversely affect the rights and welfare of the subjects:

**IF INVESTIGATOR HAS TREATMENT RELATIONSHIP WITH SUBJECTS:** Consistent with this waiver request, access to and the recording and use of identifiable medical record information for the purpose of this research study will be limited to an investigator(s) who is (are) also involved directly in the care of the respective patients. The medical record information that will be accessed, recorded and used by this (these) investigator(s) will be limited to that information which is related to the investigator's (investigators') area of medical practice. Since this (these) investigator(s) would already have knowledge of and access to
such identifiable medical record information for his/her (their) patient care responsibilities, granting of this waiver will not adversely affect the privacy of the involved patients or the confidentiality of their medical record information.

5. Please describe why the research could not practicably be carried out without the waiver:

- It is not possible to conduct this research study without access to and the use of the patients’ medical record information. In accordance with the Federal Policy regulations governing human subject protections, the process of accessing identifiable medical record information for the purpose of identifying eligible patients for this research study so as to permit the subsequent obtaining of their informed consent, itself, requires the prior informed consent of the involved patients. The patients, whose protected health information will be accessed under this waiver request, have not previously provided informed consent for this research activity. Thus, obtaining the informed consent of these patients for the collection and use of their identifiable medical record information for the purpose of this research study is impractical. In the absence of obtaining the informed consent of the patients for the use of their identifiable medical record information for research, the Prime IRB recommends the involvement of an honest broker system/process to perform an independent (i.e., independent of the research investigators) collection of the requisite medical record information and its subsequent de-identification prior to providing the information to the research investigators. Such involvement of an independent honest broker system/process is cumbersome and adds expense to the study, but is typically necessary so as to avoid a violation of the patients’ privacy and medical record confidentiality by the research investigators. However consistent with this waiver request, the research investigator(s) who will access and use the patients’ identifiable medical record information is (are) also involved directly in the care of the patients, thus obviating the privacy and confidentiality concerns.

In summary, this research study could not practically be conducted without a waiver of the informed consent requirement.

6. Please describe, if appropriate, whether subjects will be provided with additional pertinent information after participation:

- Should the analysis of the medical record information collected for the purpose of this research study reveal a situation that may impact on the health of a patient, the investigator(s), who is (are) also involved in the care of the respective patient, will promptly notify the patient and offer the availability of care.
7. If you are requesting waiver of consent under 45 CFR 46.116(c) or for *in vitro*
diagnostic device studies using leftover human specimens that are not individually
identifiable, please contact the Prime IRB and attach supporting documentation if
appropriate.
This document facilitates the submission and review of a request to use or disclose protected health information (PHI) for research purposes under a waiver or alteration by the Prime IRB. The Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule requires an Authorization that includes all core elements and required statements in order to use or disclose an individual’s PHI, unless a permissible exception applies. Research is a permissible exception allowing use or disclosure of PHI without a HIPAA Authorization where it is impractical or impossible to obtain a HIPAA Authorization from every individual research participant and the Prime IRB approves a waiver or alteration of an Authorization.

Based on the information provided in this Application, the Prime IRB will determine whether a full or partial waiver of a HIPAA Authorization or an alteration of the HIPAA Authorization is appropriate in a particular research project in accordance with the HIPAA Privacy Rule. It is important that all questions are answered thoroughly and completely and that all required documents are provided as requested to avoid any delays in the review process.

HIPAA regulations allow the Prime IRB to approve access to and use of protected health information (PHI) through the waiver of the requirement for a HIPAA authorization under certain circumstances. The criteria for obtaining a Waiver of HIPAA Authorization are similar (but not identical) to those used to obtain a waiver of consent for research. This form should be completed to determine whether your study is eligible for a waiver of HIPAA authorization.

**PHI is defined under HIPAA as health information transmitted or maintained in any form or medium that:**
1. identifies or could be used to identify an individual;
2. is created or received by a healthcare provider, health plan, employer or healthcare clearinghouse; and
3. relates to the past, present or future physical or mental health or condition of an individual; the provision of health care to an individual; or the past, present or future payment for the provision of healthcare to an individual.

**Health-related information is considered PHI if (any of the following are true):**
1. the researcher obtains it directly from a provider, health plan, health clearinghouse or employer (other than records relating solely to employment status);
2. the records were created by any of the entities in “1” and the researcher obtains the records from an intermediate source which is NOT a school record or an employer record related solely to employment status; OR
3. The researcher obtains it directly from the study subject in the course of providing treatment to the subject.
Note: If you access PHI under a waiver of HIPAA authorization, you must “account” for those disclosures of PHI by a covered entity. This accounting must include a specific listing of the PHI, the date of the access, and the purpose for the access. If access to the PHI is through the electronic medical record (EMR) system at the Relying Institution you may be able to work with EMR and/or HIPAA compliance staff at The Relying Institution to establish a mutually convenient method to “account” for the disclosures.
Please respond to the following:

1. **Use of Limited Data Set**: A “limited data set” is PHI containing no names, addresses, social security numbers, medical record numbers or other identifiers. Admission, discharge and service dates, birth date and geographical data such as state and zip code can be included in a “limited data set.” When access to PHI is through clinical databases or electronic medical record systems, this does not constitute a “limited data set”. For more information about whether your study might involve the use of a “limited data set”, please contact the Prime Review Board Services. If you are accessing or using a “limited data set”, you may be required by the HIPAA covered entity to obtain authorized Prime IRB approval of a data use agreement in a form acceptable to the covered entity releasing the PHI for use in the study.

Are you accessing, recording, analyzing or removing protected health information (“PHI”) from a HIPAA-covered entity beyond a “limited data set” without a signed HIPAA authorization?

- [ ] No No further action required on this form.
- [x] Yes You will be required to obtain an Prime IRB approved Waiver of HIPAA Authorization.

2. Type of waiver requested:

- [ ] **Full Waiver of HIPAA Authorization**
  
  Please complete questions 3 – 4 and FW01-FW12.
**Partial Waiver for Recruitment Purposes.** This type of waiver is typically used to access medical records solely for purposes of ascertaining potential subject eligibility prior to initial contact for recruitment.

Please complete questions 3 – 4 and PW01-PW06.

3. What type of record/chart/database will be reviewed for research (check all that apply)?

- [x] Medical Record/Chart Review (paper record)
- [ ] Outpatient Clinic Records
- [x] Drug and alcohol treatment records
- [x] Computer/database (electronic record)
- [x] History & Physical Exams
- [ ] HIV Test Results
- [x] Quality Improvement Records
- [x] Consultation
- [ ] Mental Health Records
- [x] The Relying Institution Administrative Billing Records
- [ ] Dental Records
- [ ] Psychotherapy Notes
- [x] Laboratory Reports
- [x] Operative Reports
- [x] Data previously collected for research purposes
- [x] Pathology Reports
- [x] EKG
- [x] Other types of records/schedules (specify): *Office visit and procedure schedules*
- [x] Diagnostic Imaging Reports
- [x] Progress Notes
- [x] Radiology Reports
- [x] Discharge Summary
- [x] Radiologic & MR Scans
4. Will you collect any of the following identifiers regarding a study subject, a subject’s relative, household member, or employee along with the PHI? (HIPAA Identifiers under 164.514(b)(2)(i) and (ii)[* indicates identifiers permitted in a Limited Data Set]

- Account Numbers
- Admission/Discharge Date*
- Age 90 or over
- Biometric identifiers, including finger and voice prints
- Certificate/license number
- Date of Birth*
- Dates of Services*
- Device identifiers and serial numbers
- E-mail address
- Fax number
- Full-face photo
- Health plan beneficiary number
- Internet Protocol (IP) address
- Medical record number
- Patient Address--State *
- Patient Address--Street
- Patient Address—Zip Code *
- Patient Geocode
- Patient’s Relatives, Employees, or Household Members Names
- Patients Name
- Social Security Number
- Telephone Numbers
- Vehicle identifiers or serial number
- Web Universal Resource Locators (URLs)
- Year of Death
- Any other unique identifying number/name: E-mail address
Full Waiver of HIPAA Authorization

Justification for Information Requested

The Waiver of Authorization will not adversely affect the rights and welfare of the participants.

☐ The PHI collected will not affect patient care.

☐ Participation in the study presents the possibility of benefit to the individual.

☐ The patient’s care team will be informed of the patient’s eligibility for a study. A member of the care team will make the initial contact with the potential subject.

☐ Other [Please use separate page to explain]

Plan to Minimize Risk to the Subjects’ Privacy

The use or disclosure of protected health information involves no more than minimal risk to the privacy of individuals, based on, at least, the presence of the following criteria:

FW01 Federal regulations require investigators to only obtain the minimum necessary data in order to achieve the goals of the research. Please explain why the data you are obtaining is necessary to achieve the goals of the research.

Provide a brief description of the “Minimum Necessary” PHI required for the purpose of this research or recruitment. (Note: “Minimum Necessary” is a HIPAA Privacy Rule standard requiring that when PHI is used or disclosed for research, only the information that is needed for the immediate use or disclosure should be made available by the health care provider or other covered entity.)

FW02 Does the use or disclosure of Protected Health Information (PHI) involve more than a minimal risk to the privacy of individuals?

☐ Access to and the use of PHI is requested by investigator(s) who is (are) directly involved in the care of respective subjects involves no more than a minimal risk to the privacy since these investigator(s) already has (have) knowledge of and access to the patients’ PHI for his/her (their) patient care responsibilities. Granting of this waiver will not adversely affect the privacy of the involved patients or the confidentiality of their medical record information.

☐ Subjects cannot be identified by re-identifying the data collected. Protected health information will be assigned a research code number and any obvious patient identifiers (name, social security number, hospital record number) will be removed and not collected or recorded in the research record. [See Coded Data/Samples]

☐ Investigators will only have access to de-identified information and cannot reasonably identify subjects from the data used in this study

☐ Other:
FW03 Describe the plan to protect the identifiers from improper use/disclosure, including physical and electronic measures.

☐ Using only de-identified data. All 18 HIPAA identifiers have been removed prior to the start of the project and it is not possible to use remaining information alone or in combination with other information readily available to identify the subject. [All identifiers in #4 are blank]

☐ Recording only de-identified data. Information is recorded by the investigator in such a way that the patients cannot be identified (i.e., by the investigator or others) either directly, or indirectly via linkage codes assigned to the data. As a consequence, the resulting research data set is completely anonymous. Once the information has been extracted from the medical record, it will not be possible for the investigator to go back to the medical record and add other patient-specific information to this research dataset. [All identifiers in #4 are blank]

☐ Identifiers will be destroyed at the earliest opportunity consistent with the conduct of the research and contractual obligations (absent a patient care or legal reason to retain them). [See FW05]

☐ Identifiable health information will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research study, or for other permitted research purposes.

☐ Securing all PHI in locked desks or file cabinets in an access-controlled office.

☐ Electronic data will be password protected on access-controlled computers.

☐ All identifiers will be limited in access to the research team only.

☐ Removable media (CDs, diskettes, USB keys, etc.) are kept in secure location and encrypted.

FW04 Will data be stored, used or transmitted to portable electronic devices (laptop, CDs, flash/USB drives, etc.)?

☐ No

☐ Yes If yes, what security measures are being taken to ensure security of data/devices?

FW05 Describe the plan to destroy the identifiers at the earliest opportunity consistent with the conduct of the research. If there is a health or research justification for retaining identifiers or if such retention is required by law, please provide this information as well.

The information linking the research code numbers to the patients’ identities and the anonymized health information will be destroyed:

☐ Upon completion of data collection

☐ Upon completion of data analysis

☐ Immediately after a determination has been made to not publish the respective research study
At 5 years following the publication of the respective research study

Other [Specify]:

Identifiers will be retained indefinitely because:

☐ This is a longitudinal study

☐ Of federal requirements [Specify]:

☐ Other [Specify]:

Coded Data/Samples

☐ N/A (Instructions: If no code is maintained, check N/A and skip this section.)

FW06 Explain how the code is derived, i.e. Research team on this project has a log of the medical record number and assigned study number or if the code is unknown or unavailable to anyone on the research team make a statement to that effect.

FW07 Describe the access/ability/possibility for anyone involved with the project to, in any way, link the code to a specific individual.

☐ Data will be coded prior to any disclosure outside of the research team. A Code Access Agreement will be in place prior to the release of data to an individual outside of the research team or to another organization. The PI will retain the Master List.

The protected health information collected for the purpose of this research study will be assigned a research code number and any obvious patient identifiers (name, social security number, hospital record number) will be removed from this information. Both the anonymized health information and the information linking the research code numbers to the patients’ identities will be stored in a secure manner (e.g., locked file cabinet, password protected database) accessible only to the research study investigator(s). The information linking the research code numbers to the patients’ identities will be stored separate from the anonymized health information.

☐ Research team members will sign a Confidentiality Agreement.

FW08 Check the mechanism(s) in place to minimize the chance of the code being linked to an individual.

☐ Key to decipher code is destroyed. Indicate time point of code destruction:

☐ Investigator(s) and key holder have entered into a written agreement prohibiting the release of the key. Instructions: Include a copy of the agreement.
There are other legal requirements preventing the release of the key to research team.

**The Research Could Not Practically Be Conducted Without Access to and Use of the Protected Health Information**

You must specify and provide justification for the PHI that will be used or disclosed and why that particular PHI is essential to the study. In situations where a waiver of authorization is requested, such as retrospective medical record research, you will need to give careful thought to what PHI is relevant to the hypothesis under study.

FW09 Provide a detailed explanation as to why your research could not practicably be conducted without access to and use of the PHI you are requesting.

**The Research Cannot Be Practically Conducted Without the Waiver or Alteration**

FW10 Explain why the research or recruitment activity could not be practicably conducted without the alteration or waiver. Why is it not practicable to conduct this research without the alteration or waiver of authorization? What barriers are there to acquiring authorization from your potential subject pool?

It is not possible to conduct this research study without access to and the use of the patients’ medical record information. In accordance with the Federal Policy regulations governing human subject protections, the process of accessing identifiable medical record information for the purpose of identifying eligible patients for this research study so as to permit the subsequent obtaining of their informed consent, itself, requires the prior informed consent of the involved patients. The patients, whose protected health information will be accessed under this waiver request, have not previously provided informed consent for this research activity. Thus, obtaining the informed consent of these patients for the collection and use of their identifiable medical record information for the purpose of this research study is impractical. In the absence of obtaining the informed consent of the patients for the use of their identifiable medical record information for research, the Prime IRB and the Relying Institution recommend the involvement of an honest broker system/process to perform an independent (i.e., independent of the research investigators) collection of the requisite medical record information and its subsequent de-identification prior to providing the information to the research investigators. Such involvement of an independent honest broker system/process is cumbersome and adds expense to the study, but is typically necessary so as to avoid a violation of the patients’ privacy and medical record confidentiality by the research investigators. However consistent with this waiver request, the research investigator(s) who will access and use the patients’ identifiable medical record information is (are) also involved directly in the care of the patients, thus obviating the privacy and confidentiality concerns.

In summary, this research study could not practically be conducted without a waiver of the informed consent requirement.
FW11 Please check any and all of the criteria outlined below which you believe make it impossible and/or impractical for you to obtain a written, signed Authorization from every individual research participant. Below each criterion that is checked, provide a detailed explanation as to how that criterion applies to this research and adds to the conclusion that the research could not practicably be conducted without the waiver or alteration.

☐ The number of research subjects.

☐ Difficulty of obtaining individual written authorizations, including, but not limited to, cost and necessary resources.

☐ Subjects are deceased making it impossible to determine who the personal representatives are or how to locate them; subjects are inactive military, and current contact information is unavailable in the system making it impossible to contact them.

☐ Time since last contact with the individuals whose PHI will be used or disclosed (i.e., a long time has lapsed since last contact with the individual making it difficult to locate the individual to request the authorization.).

☐ Whether obtaining a written authorization for the use of PHI unnecessarily burdens or poses a new risk to the individual from whom the PHI was collected.

☐ Whether informing practitioners or individuals from whom the PHI was collected could alter their behavior and, thus, bias the results of the study.

☐ Explain any other criteria not listed above making it impossible or impractical for you to obtain written authorizations.
**Written Assurance**

**FW12** Provide adequate written assurances that the protected health information will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research study, or for other research for which the use or disclosure of protected health information would be permitted this subpart;

By signing below, I attest that:

- The PHI for which I seek access is necessary in order to perform the research project indicated above.
- The requested information constitutes the minimum necessary data to accomplish these research goals.
- The protected health information will not be reused or disclosed to (shared with) any other person or entity, except as required by law, for authorized oversight of the research study, or for other research for which the use or disclosure of protected health information would be permitted under the Privacy Rule.
- I understand data **cannot be reused** for any other studies or inquires into possible studies, i.e. cannot be data mined, without submitting a research protocol to the Prime IRB indicating a desire to use the data for other research projects and/or request for use of PHI in Activities Preparatory to Research.
- If there are any changes to the information and/or methods in which I will be collecting, recording, using, or disclosing the information described herein, I will seek an amendment to the protocol alerting the IRB to those changes prior to implementing the changes.
- I understand that any suspected or actual breach of physical or electronic security of the data will immediately be reported to the Relying Institution’s Privacy Officer.

---

**Principal Investigator (Signature and Date)**
Partial Waiver for Recruitment Purposes

Justification for Information Requested

The Waiver of Authorization will not adversely affect the rights and welfare of the participants.

- The PHI collected will not affect patient care.
- Participation in the study presents the possibility of benefit to the individual.
- The patient’s care team will be informed of the patient’s eligibility for a study. A member of the care team will make the initial contact with the potential subject.
- Other [Please use separate page to explain]

Plan to Minimize Risk to the Subjects’ Privacy

PW01 Federal regulations require investigators to only obtain the minimum necessary data in order to achieve the goals of the research. Please indicate why the data you are obtaining is necessary to achieve the goals of the research. Provide a brief description of the “Minimum Necessary” PHI required for the purpose of this research or recruitment. (Note: “Minimum Necessary” is a HIPAA Privacy Rule standard requiring that when PHI is used or disclosed for research, only the information that is needed for the immediate use or disclosure should be made available by the health care provider or other covered entity.)

- Partial Waiver for Recruitment Purposes: Will access medical records to verify eligibility for research study, i.e., the patient meets the inclusion and exclusion criteria.

PW02 Does the use or disclosure of Protected Health Information (PHI) involve more than a minimal risk to the privacy of individuals? Describe the plan to protect the identifiers from improper use/disclosure.

- The use of PHI for identifying eligibility and contacting potential subjects will not involve more than minimal risk to the individual’s privacy.
- Access to and the use of PHI is requested by investigator(s) who is (are) directly involved in the care of respective subjects involves no more than a minimal risk to the privacy since these investigator(s) already has (have) knowledge of and access to the patients’ PHI for his/her (their) patient care responsibilities. Granting of this waiver will not adversely affect the privacy of the involved patients or the confidentiality of their medical record information.
- The sharing of the patient’s/potential subject’s contact information (linked to medical diagnosis or condition) between the health care provider and the researchers involves no more than a minimal risk to the privacy of the patient since the health care provider, who introduces the research study to his/her patient, will obtain and appropriately document the verbal permission of the patients to provide the patient’s contact information to the researchers.
☐ Subjects cannot be identified by re-identifying the data collected. Protected health information will be assigned a research code number and any obvious patient identifiers (name, social security number, hospital record number) will be removed and not collected or recorded in the research record.

☐ Investigators will only have access to de-identified information and cannot reasonably identify subjects from the data used in this study.

☐ The PHI being reviewed is not sensitive in nature and will not affect an individual’s insurability, employability, financial standing or reputation.

☒ Access to the PHI is limited to only research team members who are trained to protect the individual’s privacy.

☒ The individual has received the Notice of Privacy Practices which explains that The Relying Institution is a research institution and that they may be approached to participate in a study

☐ Other [Please use separate page to explain]

To further ensure that the risk to the privacy of the involved patients remains minimal, screening data [the patient’s/potential subject’s recorded contact information] will be:

☒ Stored by the researchers in a secure manner (e.g., locked file cabinet, password protected database) accessible only to the researcher who was provided this information and other members of the research team involved in the conduct of the research study (studies) for which this information was originally provided)

☒ Destroyed immediately after the researchers have contacted the patient to discuss the research study (studies) for which this information was originally provided; unless, upon such contact, the patient/potential subject indicates a further interest in study participation.

☒ For patients/potential subjects who indicate a further interest in study participation, the patient will be engaged in an informed consent process to further determine research study eligibility and/or study interest. The patient’s recorded contact information will be destroyed immediately after ascertaining that the patient is not eligible for or declines participation in the research study (studies).
PW03 Describe the plan to destroy the identifiers at the earliest opportunity consistent with the conduct of the research. If there is a health or research justification for retaining identifiers or if such retention is required by law, please provide this information as well.

The information linking the research code numbers to the patients’ identities and the anonymized health information will be destroyed:

- [ ] Upon completion of data collection
- [ ] Upon completion of data analysis
- [ ] Immediately after a determination has been made to not publish the respective research study
- [ ] At 5 years following the publication of the respective research study
- [x] Other [Specify]: In accordance with local, federal, sponsor contractual obligations

Identifiers will be retained indefinitely because:

- [ ] This is a longitudinal study
- [ ] Of federal requirements [Specify]: ______
- [ ] Other [Specify]: ______

**The Research Could Not Practically Be Conducted Without Access to and Use of the Protected Health Information**

PW04 Explain why the research or recruitment activity could not be conducted without access to and use of the PHI.

- [x] Recruitment cannot practicably be conducted without the participant’s PHI.
- [x] Health information is required to determine eligibility and identifiers are necessary to contact the individual for participation.
- [x] It is not possible to conduct this research study unless we are able to identify and recruit potential research subjects. To avoid “cold-calling” it is recommended by the Prime IRB that the research study first be introduced to patients/potential subjects by an individual (e.g., a referring health care provider) involved directly in their health care. If a patient is interested in study participation, his/her contact information (linked to medical diagnosis or condition) must be provided by the referring health care provider to the researchers in order to provide an effective mechanism to follow up on this interest and to recruit subjects into this research study.
The Research Cannot Be Practically Conducted Without the Waiver or Alteration

PW05 Explain why the research or recruitment activity could not be practicably conducted without the alteration or waiver.

- Recruitment cannot be practicably carried out without the Partial Waiver of Authorization.
- The PI is unable to recruit subjects by the other recruitment methods because historically, colleague assistance has been minimal, producing sub-par accrual.
- The targeted study population will not be exposed to information about the trial in a timely fashion, permitting them to seek access to the trial.
- It is not possible to conduct this research study unless we are able to identify and recruit potential research subjects. To avoid “cold-calling” it is recommended by the Prime IRB that the research study be first introduced to patients/potential subjects by an individual involved directly in their health care (i.e., referring health care provider). If the patient/potential subject is interest in study participation, s/he can be given the contact information for the researchers and asked to contact the researchers directly. However, this approach has been routinely shown to result in a very low rate of patient/potential subject follow up. A much more effective alternative is for the health care provider, who introduced the research study to the patient, to obtain the permission of the patient/potential subject to provide the patient’s contact information to the researchers. While it may be possible for this permission to be documented in the form of a valid written HIPAA Authorization, such is reasonably practical only in those situations wherein the respective health care provider and patient interaction occurs face-to-face (e.g., during a clinic visit). It is not reasonably practical to obtain a valid written HIPAA Authorization if the research study is introduced to the patient/potential subject via a letter from the patient’s health care provider or via a telephone interaction between the patient and health care provider. Even in the situation where the respective health care provider and patient interaction occurs face-to-face, the requirement for the patient to sign a valid (at minimum 2 page) HIPAA Authorization to document the patient’s permission to simply provider his/her contact information to the researchers is considered to be excessive by both the involved health care providers and the patients/potential subjects; thus impacting substantially on the willingness of these individuals to participate in this research subject recruitment activity.

In summary, this research activity (i.e., the sharing of the patient’s interest in research study participation and the patient’s contact information [linked to medical diagnosis or condition] between referring health care providers and the researchers) could not practically be conducted without a waiver of the HIPAA authorization requirement.
**Written Assurance**

PW06  Provide adequate written assurances that the protected health information will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research study, or for other research for which the use or disclosure of protected health information would be permitted this subpart;

By signing below, I attest that:

- The PHI for which I seek access is necessary in order to perform the research project indicated above.
- The requested information constitutes the minimum necessary data to accomplish these research goals.
- The protected health information will not be reused or disclosed to (shared with) any other person or entity, except as required by law, for authorized oversight of the research study, or for other research for which the use or disclosure of protected health information would be permitted under the Privacy Rule.
- I understand data **cannot be reused** for any other studies or inquiries into possible studies, i.e. cannot be data mined, without submitting a research protocol to the Prime IRB indicating a desire to use the data for other research projects and/or request for use of PHI in Activities Preparatory to Research.
- If there are any changes to the information and/or methods in which I will be collecting, recording, using, or disclosing the information described herein, I will seek an amendment to the protocol alerting the IRB to those changes prior to implementing the changes.
- I understand that any suspected or actual breach of physical or electronic security of the data will immediately be reported to the Privacy Officer.

---

**Principal Investigator (Signature and Date)**
Partial Waiver of Consent For Screening/Recruitment Purposes

Prime Review Board Services
The EMMES Corporation
Suite 700
401 N Washington Street
Rockville, MD 20850

PROJECT IDENTIFICATION
PI: $$FIRST NAME$$ $$LAST NAME$$, $$DEGREE$$
SPONSOR: $$SPONSOR$$ $$SPONSOR PROTOCOL NUMBER$$
PROJECT TITLE: $$TITLE$$

1. The Prime Review Board Services approved the Partial Waiver of Consent for Screening/Recruitment Purposes on $$INITIAL REVIEW DATE$$.

2. The Prime Review Board Services is an Institutional Review Board (IRB), established in accordance with 21 CFR 56.107 and 45 CFR 46.107. [IRB Registration Number $$IRB REGISTRATION NUMBER$$]

3. The Prime Review Board Services has made the following determinations:
   (a) The research is not FDA-regulated;
   (b) The research does not involve non-viable neonates;
   (c) The research is not conducted or funded by the Department of Defense (DoD);
   (d) The research activity [review of medical records to identify potential subjects] involves no more than minimal risk to the subjects;
   (e) The waiver or alteration will not adversely affect the rights and welfare of the subjects;
   (f) The research could not practicably be carried without the waiver or alteration; and
   (g) Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

4. The protected health information for which use or access has been determined to be necessary by the Prime Review Board Services is as follows:
   Physician/clinic records;
   Hospital/medical records; and
   Lab, pathology and/or radiology results

5. The waiver of consent has been reviewed and approved under:
   ☒ Normal review procedures
   • The Prime Review Board Services has followed the requirements of the Common Rule for the normal review procedures
   • The Prime Review Board Services has reviewed the request for a Partial Waiver of Consent For Screening/Recruitment Purposes at a
convened meeting at which a majority of the Prime Review Board Services members were present, including at least one member who is not affiliated with the <<Relying Institution>>, not affiliated with any entity conducting or sponsoring the research, and not related to any person who is affiliated with any of such entities.

- The majority of the Prime Review Board Services members present at the meeting approved the Partial Waiver of Consent for Screening/Recruitment Purposes through normal review.

Expeditied review procedures
- The Prime Review Board Services has followed the requirements of the Common Rule for the expedited review procedures.
- The Prime Review Board Services used an expedited review procedure because the research involves no more than minimal risk to the privacy of the individuals who are the subject of the protected health information for which use or disclosure is being sought. The Chair of the Prime Review Board Services carried out the review and approval of the Partial Waiver of Consent for Screening/Recruitment Purposes.

Karl M. Nelson, Ph.D.  Date:  $$GENERATED DATE$$
Chairman, Prime Review Board Services


8. The Prime Review Board Services has made the following determinations:
   (a) That the use or disclosure of protected health information for recruitment/screening purposes involves no more than minimal risk to the privacy of individuals based on at least, the presence of the following elements:
      (i) An adequate plan to protect the identifiers from improper use and disclosure;
      (ii) An adequate plan to destroy the identifiers at the earliest opportunity consistent with conduct of the research, unless there is a health or research justification for retaining the identifiers, or such retention is otherwise required by law; and
      (iii) Adequate written assurances that the protected health information will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research project, or for other research for which the use or disclosure of protected health information would be permitted under the law.
   (b) That the recruitment for this research project cannot practicably be conducted without the Partial Waiver of Authorization for Screening/Recruitment Purposes.
   (c) That the recruitment for this research project research cannot practicably be conducted without access to and use of the protected health information.

9. The protected health information for which use or access has been determined to be necessary by the Prime Review Board Services is as follows:
Physician/clinic records; Hospital/medical records; and Lab, pathology and/or radiology results

10. The waiver of authorization has been reviewed and approved under:

☐ Normal review procedures
  • The Prime Review Board Services has followed the requirements of the Common Rule for the normal review procedures
  • The Prime Review Board Services has reviewed the proposed research at a convened meeting at which a majority of the Prime Review Board Services members were present, including at least one member who is not affiliated with the <<Relying Institution>>, not affiliated with any entity conducting or sponsoring the research, and not related to any person who is affiliated with any of such entities.
  • The majority of the Prime Review Board Services members present at the meeting approved the Waiver of Authorization through normal review.

☒ Expedited review procedures
  • The Prime Review Board Services has followed the requirements of the Common Rule for the expedited review procedures.
  • The Prime Review Board Services used an expedited review procedure because the research involves no more than minimal risk to the privacy of the individuals who are the subject of the protected health information for which use or disclosure is being sought. The Chair of the Prime Review Board Services carried out the review and approval of the Partial Waiver of Authorization for Screening/Recruitment Purposes.

Karl M. Nelson, Ph.D.                                      Date: $$GENERATED DATE$$
Chairman, Prime Review Board Services
1 PURPOSE

1.1 Under the Federal Health Insurance Portability and Accountability Act of 1996 (HIPAA) Security and Privacy Rule, researchers must meet certain requirements before using or disclosing individually identifiable health information for research. The purpose of this policy is to describe confidential protections required when Protected Health Information is used for research purposes.

1.2 The purpose of this standard operating procedure is to describe the general requirements for documentation of HIPAA authorization and to enumerate the situations where an authorization or waiver is required.

2 REVISIONS FROM PREVIOUS VERSION

2.1 None

3 POLICY

3.1 A covered entity and its employees may not use or disclose individually identifiable health information (called "protected health information", or "PHI") for research, except in one of the following circumstances:

3.1.1 The patient/participant has signed a written authorization containing all the elements specified in the Privacy Rule, or

3.1.2 An IRB has waived or altered the requirement for HIPAA authorization, or

3.1.3 The covered entity and its employees have "de-identified" the data prior to its use and disclosure for research, or

3.1.4 The data are in the form of a "limited data set" and the investigator/recipient of the data has signed a data use agreement

3.2 Investigators must obtain written Authorization from all participants in the research study prior to the use or disclosure of protected health information (PHI) for any research-related purpose unless the Prime IRB has issued a waiver or alteration (Prime IRB SOP 605: Waiver of Elements of Consent and Waiver of HIPAA Authorization) or the limited situations where the Privacy Rule does not require authorization or waiver.
3.3 In the environment of research, it is essential to ensure the confidentiality of data and to protect the subjects’ privacy. Since certain types of research require use and disclosure of Protected Health Information (PHI) and since the nature of the research may preclude the obtaining of Authorization from the research subject to use or disclose such information, it may be necessary to proceed with such research without an Authorization.

3.4 The Prime IRB, if acting as the Privacy Board for an entity other than Emmes, shall review, and if appropriate approve, revise or reject, all submissions of HIPAA Authorizations, and requests for HIPAA Authorization waivers in accordance with that entity's HIPAA policies and procedures.

3.5 Researchers relying on the Prime IRB must use a PRIMNE IRB-approved HIPAA Authorization template unless the Prime IRB has approved use of another form. This approval can be given by the Director, Prime Review Board Services, on behalf of the Prime IRB.

3.6 When it is not feasible to obtain a signed HIPAA Authorization, certain exceptions may allow a researcher to use or receive PHI without a may apply depending on whether the researcher is internal or external. These exceptions, are:

3.6.1 Purposes preparatory to research

3.6.2 Waiver of Authorization by a Privacy Board or an Institutional Review Board (IRB) acting as a Privacy Board.

3.6.3 Research involving only Decedents

3.6.4 “Grandfathered” Authorizations

3.7 All research disclosures are considered “accountable disclosures” under the patient accounting right, except those made pursuant to a HIPAA Authorization.

3.8 Researchers may also request for de-identified information or PHI in a limited data set.

4 RESPONSIBILITIES

4.1 Director, Prime Review Board Services: Responsible for establishing and periodically reviewing and modifying (as appropriate) IRB standard operating policies and procedures involving the consent process.

4.2 Chair, Prime Review Board Services: Responsible for establishing and periodically reviewing and modifying (as appropriate) IRB and Investigator responsibilities pertaining to ensuring that HIPAA authorization when combined with written consent meets the requirements of HIPAA.
4.3 Principal Investigator: Responsible for obtaining written authorization from research subjects, their parent/guardian(s) or the legally authorized representative of the subject as required by this SOP unless waived by the IRB.

4.4 Prime IRB Reviewer: Responsible for pre-reviewing all stand-alone and combined consent/authorization documents to ensure that the required elements and required statements of HIPAA Authorization are present.

5 PROCEDURE

5.1 Use or Disclosure of PHI in Research with Authorization

5.1.1 A written Authorization must be signed by an individual who is authorized under law to provide consent or permission to participation in the research.

5.1.2 The requirement for written authorization applies to all uses and disclosures of PHI for research purposes unless the investigator:

5.1.2.1 Obtains a waiver or alteration of the requirement as described in Prime IRB SOP 605: Waiver of Elements of Consent and Waiver of HIPAA Authorization;

5.1.2.2 Receives a limited dataset from a provider under the provisions of a duly executed data use agreement in accordance with Prime IRB Policies; or

5.1.2.3 Provides the IRB with an attestation for use and disclosure of PHI without authorization or waiver for work preparatory to research or research involving decedents in accordance with Prime IRB Policies.

5.1.3 Stand-Alone Authorization. The investigator is responsible for the content and format of the stand-alone written Authorization and for ensuring that it meets the requirements listed in §5.2.

5.1.3.1 The investigator is required to submit a copy of stand-alone authorization to the IRB to complete the study file.

5.1.3.2 The IRB will review the authorization for accuracy and completeness and may provide suggested edits.

5.1.3.3 The IRB does not approve stand-alone authorizations; the ultimate responsibility for compliance with HIPAA requirements rests with the investigator.
5.1.4 **Combined Consent/Authorization.** When a combined consent/authorization will be
used, the investigator must submit the consent/authorization to the Prime IRB for
review and approval prior to use.

5.1.5 An additional, separate Authorization will be required if the research involves the
use or disclosure of Psychotherapy Notes

5.2 **Authorization Document Requirements**

An Authorization for use and disclosure of PHI for research must be written in plain
language and contain all of the core elements and required statements unless one or more
are waived (*Prime IRB SOP 605: Waiver of Elements of Consent and Waiver of HIPAA
Authorization*).

5.2.1 **Core Elements**

5.2.1.1 A specific and meaningful description of the information to be used or
disclosed;

5.2.1.2 The name or identification of the persons or class of persons authorized
to make disclosures of PHI and to use the PHI for research-related
purposes;

5.2.1.3 The name or identification of the persons or class of persons authorized
to receive disclosures of the PHI and to use the PHI for research-related
purposes;

5.2.1.4 A description of the purpose of each use or disclosure;

5.2.1.5 An expiration date or event, or a statement “end of research study” or
“none” when appropriate (e.g., for a research database).

5.2.2 **Required Statements**

5.2.2.1 A statement that the individual may revoke the Authorization if done in
writing to the investigator (member of the Research Workforce); however, the investigator may continue to use and disclose, for research
integrity and reporting purposes, any PHI collected from the individual
pursuant to such Authorization before it was revoked;

5.2.2.2 A statement that an individual’s clinical treatment may not be
conditioned upon whether or not the individual signed the
Authorization; however, participation in research may be conditioned on
a signed Authorization,
5.2.2.3 A statement that information disclosed under the Authorization could potentially be re-disclosed by the recipient and would no longer be protected under HIPAA.

5.2.2.4 The individual's signature (or that of his/her legally authorized representative) and date.

5.2.3 An authorization for the use or disclosure of PHI for a research study may be combined with any other type of written permission for the same research study (including the consent form).

5.2.4 A signed copy of an authorization for the use or disclosure of PHI may be received by facsimile or electronically transmitted.

5.3 Procedures for Reviewing Combined Consent/Authorization Documents

Whenever the investigator combines a written Authorization with an informed consent document, the IRB will review the document and approve it prior to use.

5.3.1 The reviewer will assure that the combined form meets the requirements for informed consent as enumerated under Prime IRB SOP 600: Required Elements of Consent and Documentation of Consent.

5.3.2 The reviewer will also ensure that the document contains all of the required elements of written authorization enumerated in §5.2.1 and §B5.2.2 (above), unless the Prime IRB has provided a waiver of alteration of one or more elements. See Prime IRB SOP 605: Waiver of Elements of Consent and Waiver of HIPAA Authorization.

5.4 Protocols Approved Prior to April 3, 2003

5.4.1 The Research Workforce may use and/or disclose PHI for research protocols approved prior to 13-April-2003 that have not been amended. Such use and/or disclosure is limited to that outlined in the original approved protocol and informed consent.

5.4.2 Protocols initially approved prior to 13-April-2003 which have been amended since that date require the application of the HIPAA privacy requirements as outlined in this policy as it pertains to use and disclosure of PHI.

5.5 Prime IRB Procedures for Receipt and Acknowledgement of Reviews Preparatory to Research and Research on Decedents’ Information

Under the Privacy Rule, investigators may use or disclose PHI for research purposes without IRB approval for reviews preparatory to research and research on decedents information provided that they meet the requirements below and adhere to Prime IRB
5.5.1 Reviews preparatory to research provided that the Prime IRB obtains from the investigator representation that:

5.5.1.1 The use or disclosure is sought solely to review protected health information as necessary to prepare a research protocol or for similar purposes preparatory to research;

5.5.1.2 No PHI will be removed from the covered entity or disclosed external to the covered entity by the researcher in the course of the review; and

5.5.1.3 The PHI for which use or access is sought is necessary for the research purposes.

5.5.1.4 When accessing PHI for activities preparatory to research, the investigator must make reasonable efforts to limit use and recording of PHI to the minimum necessary to accomplish the intended purpose of the use.

5.5.1.5 Prime IRB approval is required prior to the analysis of the PHI abstracted from Review Preparatory to Research activities. If there is not an IRB approved protocol submitted following the Review Preparatory to Research, then the abstracted data cannot be analyzed or disseminated in any form.

5.5.2 Research on decedents’ information (decedents are not considered human subjects under the Common Rule but use of their information is subject to the requirements of the Privacy Rule) provide that the IRB obtains representation from the researcher that:

5.5.2.1 The use or disclosure sought is solely for research on PHI of decedents; and

5.5.2.2 The PHI for which use or disclosure is sought is necessary for the research purposes.

5.5.2.3 Investigators can submit reviews preparatory to research and research on decedents’ information to the IRB through the electronic IRB Management system. The IRB will check the certifications for accuracy and acknowledge receipt.

5.6 Research Use or Disclosure of a Limited Data Set

5.6.1 An investigator may use or disclose a Limited Data Set for research purposes without an authorization or waiver of authorization, if a Data Use Agreement is
completed. For example, a Data Use Agreement is used when an investigator wants to share a Limited Data Set of research data with a colleague at another institution or with a private registry not involved in the study.

5.6.2 When uses or disclosures of a Limited Data Set are made pursuant to a Data Use Agreement, the investigator must make reasonable efforts to limit PHI to the minimum necessary to accomplish the intended purpose of the use or disclosure.

5.6.3 A Limited Data Set excludes direct identifiers of the individual or of relatives, employers, or household members of the individual as defined in the De-identification of Protected Health Information and Limited Data Set Policy. A Limited Data Set may include:

5.6.3.1 Study identification number, subject ID, or any other unique identifying number, characteristic, or code related to or derived from an existing direct identifier.

5.6.3.2 Dates: all elements of dates [month, day, and year] directly related to an individual, e.g. date of birth, death, or diagnosis, etc.

5.6.3.3 City, county, precinct, zip code, and their equivalent geocodes

5.7 Research Use or Disclosure of "De-Identified" Health Information

5.7.1 De-identified health information is exempt from HIPAA regulations and may be used or disclosed for research purposes without an authorization or IRB waiver of authorization.

5.7.2 De-identified health information is health information that has been stripped of all 18 direct identifiers as defined by the De-identification of Protected Health Information and Limited Data Set Policy.

5.7.3 De-identified information may be assigned a code or other means of record identification to allow de-identified information to be re-identified, provided that the key to such a code is not accessible to the investigator requesting to use or disclose the de-identified health information, the code is not derived from or related to information about the individual, and the code is not capable of being translated so as to identify the individual.

5.8 Participant's Access to Research Information

5.8.1 An individual who participates in research generally has a right to access his/her own PHI that is maintained in a Designated Record Set. However, an individual's access to PHI created or obtained in the course of research that involves treatment may be temporarily suspended for as long as the research is in progress, provided
that the individual has agreed to the denial of access when consenting to participate in the research study, and the investigator has informed the individual that the right of access is to be reinstated upon completion of the research.

5.9 **Participant’s Request to Revoke Research Authorization**

5.9.1 An individual may revoke his or her authorization at any time, provided that the revocation is in writing, except to the extent that the investigator has taken action in reliance on the authorization. The investigator may continue to use and disclose any PHI collected pursuant to a valid authorization before it was revoked, for study integrity and reporting purposes.

6 **MATERIALS**

6.1 Authorization to Use and/or Disclose (Release) Individually Identifiable Health Information for Research Purposes

7 **REFERENCES**

45 CFR 164.508
45 CFR 164.512(i)(2)(ii)
Prime IRB SOP 600: Required Elements of Consent and Documentation of Consent
Prime IRB SOP 605: Waiver of Elements of Consent and Waiver of Written Authorization
<table>
<thead>
<tr>
<th>Version 0.2</th>
<th>Name</th>
<th>Status (Pending, Reviewed, Approved)</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Written by:</td>
<td>Karl Nelson</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reviewed by</td>
<td>Jennifer Neal-Jimenez</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Approved by</td>
<td>Jennifer Neal-Jimenez</td>
<td>Approved</td>
<td></td>
</tr>
</tbody>
</table>

Written by: Karl Nelson, 18-July-2017
Reviewed by: Jennifer Neal-Jimenez, 7-January-2018
Approved by: Jennifer Neal-Jimenez, Approved 9-January-2018
Authorization to Use and/or Disclose (Release)
Individually Identifiable Health Information for Research Purposes

1. Protocol Information

Sponsor:
Protocol Number:
Protocol Version Date:
Protocol Title:
Principal Investigator (PI):
Principal Investigator’s Mailing Address:
Principal Investigator’s Phone Number:

You have rights regarding the privacy of your medical information collected prior to and in the course of this research study. These rights are protected by a federal law that requires the <<Relying Institution>> and its affiliated hospitals and clinics, researchers, health care providers and physicians (collectively, “<<Institution>>”) to protect the privacy of information that identifies you and relates to your past, present, and future physical and mental health and conditions (“protected health information”).

Before researchers use or share any health information about you as part of this study, <<Institution>> is required to obtain your authorization. This Authorization helps explain to you how this information will be used or shared with others involved in the study.

- The <<Relying Institution>> and its hospitals, clinics, health-care providers and researchers are required to protect the privacy of your health information.
- You should have received a Notice of Privacy Practices when you received health care services here. If not, let us know and a copy will be given to you. Please carefully review this information. Ask if you have any questions or do not understand any parts of this notice.
- If you agree to take part in this study your health information will be used and shared with others involved in this study. Also, any new health information about you that comes from tests or other parts of this study will be shared with those involved in this study.
- Health information about you that will be used or shared with others involved in this study may include your research record and any health care records at <<Institution>>. For example, this may include your medical records, x-ray or laboratory results. Psychotherapy notes in your health records (if any) will not, however, be shared or used. Use of these notes requires a separate, signed authorization.
- If you decide to participate in this research study, your protected health information will be used and shared with others as explained below.
2. Purpose of Use and/or Disclosure of Health Information

By signing this form, you are giving permission to <<Relying Institution>>, <<Institution>> Hospital, <<Institution>> Clinical Trials, and all other <<Relying Institution>> affiliated health care provider organizations to use and/or disclose your health information that individually identifies you for the purposes of the research study ("Study") listed above.
By signing this form, you are giving permission to <<Institution>> Clinical Trials to add your contact information and medical information to the Clinical Trials Participant Database.

3. What Health Information May be Used and/or Disclosed?

To do this research study, we need your permission to collect and use some of your health information, or you cannot be in the study. This information may come from questions we ask, forms we ask you to fill out, or your medical record, as described below. We will only collect and use information needed for the study.

<<Institution>>iv may use and/or disclose your past, present and future records and information as described in the study protocol approved by the Human Research Review Board which may include:

- Lab test results (which may include genetic tests, HIV/AIDS tests and/or tests for other communicable diseases if part of my records)
- Procedure reports
- Hospitalization records
- Operative reports
- Outpatient/Office visits, exams, consultations, phone call records and notes
- Radiology/x-ray images and/or reports
- Registration and billing information
- Emergency room reports
- Medication information including chemotherapy, and other drugs, vitamins, and herbal remedies
- Questionnaires and diaries
- Pathology reports
- Other (describe):

4. Why will protected health information [PHI] about me be used or shared with others?v

The main reasons include:

- To conduct and oversee the research described in the consent document and for all purposes necessary to conduct and ensure the integrity of the study.
- To ensure the research meets legal, institutional, and accreditation requirements; and
- To conduct public health activities (including reporting of adverse events or situations where you or others may be at risk of harm).

Other reasons may include for treatment, payment or health care operations. For example, some medical information produced by this study may become part of your hospital medical record because the information may be necessary for your medical care.
5. Who will use or share protected health information about me at the <<Relying Institution>>\textsuperscript{vi}

Those who oversee the study will have access to your information, including:

- Researchers and staff at <<Institution>> will use, share and receive your personal health information for this research study. They will make every reasonable effort to protect the information and keep it confidential.

- The only <<Institution>> Hospital employees allowed to handle your health information are those on the study team, and those on the <<Institution>> Human Research Review Board, the committee that oversees research at <<Institution>>, and <<Institution>> officials who review the research plan and check the research activities to make sure the hospital’s rules are followed.

- Authorized <<Institution>> staff not involved in the study may be aware that you are participating in a research study and have access to your information. If this study is related to your medical care, your study-related information may be placed in your permanent hospital, clinic or physician’s office records. As a result, this research information may be seen by authorized members of the <<Institution>> workforce who need to access your medical record in the performance of their duties (for example, to provide treatment, to ensure integrity of the research, accounting or billing matters, etc.)

6. Will my protected health information be shared with people outside the <<Relying Institution>>?\textsuperscript{vii}

We may share your information with people who do not work at <<Institution>> Hospital because they planned this study, pay for this study, or work with us on this study. The federal Privacy Rule may no longer protect your health information once it leaves <<Institution>> Hospital.\textsuperscript{viii} Once your health information has been disclosed, the information may no longer be protected under the laws and regulations that apply to <<Institution>>. The recipients may share the information with others without your permission, if permitted by laws governing them.

There are organizations that may inspect your records for quality assurance and data analysis. These organizations are required to make sure your information is kept private, unless required by law to provide information. For this study, we plan to share information with those doctors, researchers or government representatives working with us on this study at the institutions or companies listed here:

Your health information may also be shared with federal and state agencies that have oversight of the study or to whom access is required under the law. These may include:

**If the research involves an FDA-regulated drug, device or biologic, add:**

- The Food and Drug Administration (FDA);

Or

- Federal and state agencies (for example, the Department of Health and Human Services, the Food and Drug Administration, the National Institutes of Health and/or the Office for...
Human Research Protections), or other domestic or foreign government bodies if required by law and/or necessary for oversight purposes.

These researchers, companies and/or organization(s) outside of <<Institution>> may also use, share and receive your health information in connection with this study:

If NCI National Clinical Trials Network study, add:
- The (name of National Clinical Trials Network study group);
- The (name of National Clinical Trials Network study group) Operations Center;
- The (name of National Clinical Trials Network study group) Biostatistical Center;
- Other people or organizations assisting with (name of National Clinical Trials Network study group) research efforts. This may include drug manufacturers or drug companies that may provide partial support for the study, drug distributors, and/or their designees (e.g., drug companies associated with protocol); and
- Designated central laboratories, central review centers, and central reviewers. The central laboratories and review agencies may also give your health information to those groups listed above.

If a Clinical Trials Support Unit (CTSU) study, add:
- The Cancer Trials Support Unit (CTSU) or designee, a research group sponsored by the National Cancer Institute that supports the research of (name of cooperative study group)

For trials where the NCI CIRB is the IRB of record, add:
- The NCI Central Institutional Review Board (CIRB)

If the <<Relying Institution>> is expecting third party payers to pay for clinical procedures performed in the course of the research, add:
- Your health insurance company;

If the research is sponsored, add:
Your PHI may also be shared with:
- The research sponsor [Name of Sponsor], the manufacturer of <insert name of drug(s)>, including its agents and contractors and companies owned or connected with the sponsor;
- Private laboratories and other persons and organizations that analyze your health information in connection with this study: [insert name(s) of organizations that analyze lab results or data or any collaborative groups that will have access to the data or delete];
- [Name of CRO, if applicable] which has been hired by the sponsor to coordinate the study; and whose job is to review and correct any mistakes before the results are given to the sponsor; and a
• [If applicable]. The Data Safety Monitoring Board (DSMB) for this study. The DSMB is an independent group of experts that will be reviewing the data from this research throughout the study.

7. What are the risks of sharing this health information?

One risk of taking part in a research study is that more people will handle your personal health information collected for this study. While the study team makes every effort to keep the information confidential, an unauthorized person might see it. Depending on the kind of information being collected, it might be used in a way that could embarrass you or affect your ability to get insurance. If you have questions, you can talk to the study doctor about whether this could apply to you.

8. How long will protected health information about me be used or shared with others? ix

If you sign this form, we plan to keep your information for 10 years after the research study ends in case we need to check it again for this study.

We will not use your health information for a different study without your permission, or the permission of the <<Institution>> Human Research Review Board. Once all personal identification is removed, the information might be used or released for other purposes without asking you.

9. May I have access to my medical information that results from my participation in this research study? x

In accordance with the <<Relying Institution>> Notices of Privacy Practices document that you have been provided, you are permitted access to information (including information resulting from your participation in this research study) contained within your medical records filed with your health care provider.

During your participation in this study, you will have access to your medical record and any study information that is part of that record.

If information is withheld from the subject, e.g., the study is blinded or other studies where access will be denied, add: xi

During your participation in this study, you will not be able to access your medical records. This will be done to prevent the knowledge of any study results from affecting the reliability of the study.

OR

Information obtained in the course of the research that will not be shared with you is [insert details of the information to be withheld].

By signing this authorization, you are temporarily waiving your right to see this research-related information while the research is going on. You will be able to see this information if you wish after the research is completed. Your PHI will be available should an emergency arise that would require your treating physician to know this information.
10. Statement of Privacy Rights\[xii\]

If you change your and later and do not want us to collect or share your health information, you need to send a letter to the Principal Investigator at the mailing address on the first page. The letter must say that you have changed your mind and do not want the researcher to collect and share your health information. If you change your mind and revoke the authorization, you will not be allowed to continue to participate in the Study.

If you revoke this authorization, <<Institution>> may not continue to use and/or disclose your health information for this Study, except that\[xiii\]:

- Your health information that has already been disclosed before you revoked this Authorization cannot be taken back; and
- <<Institution>> and the recipients may continue to use and disclose your health information already collected for this research Study for the purposes of maintaining the integrity of the Study, and for regulatory compliance.

You have the right to limit the use and sharing of your PHI, and you have the right to see your medical records and know who else is seeing them.

You have the right to refuse to sign this authorization. You do not have to give this permission for use of your PHI.\[xiv\] If you decide not to provide permission, you will not be able to participate in this research study.\[xv\] Your health care outside of the study, payment for your health care, and your health care benefits will not be affected if you choose not to sign this form.

10. SIGNING THE AUTHORIZATION

I am the subject or am legally authorized to act on behalf of the subject. I have read this form (or someone has read it to me). I have been able to ask questions. All of my questions about this form have been answered to my satisfaction. By signing below, I permit the Principal Investigator and the others listed on this form to use and share my personal health information for this study. I will receive a copy of this authorization after it is signed.\[xvi\]

<table>
<thead>
<tr>
<th>Signature of research subject (or legal representative*)</th>
<th>Date</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Printed name of research subject</th>
</tr>
</thead>
</table>
*Printed name of legal representative (if applicable)*

*Please explain the legal representative’s authority to act on behalf of subject:*\[xvii\]
ENDNOTES

i  **PLAIN LANGUAGE REQUIREMENT**—The authorization must be written in plain language [45 CFR 164.508(c)(3)]

ii **CORE AUTHORIZATION ELEMENT: Purpose of the use or disclosure**—A description of each purpose of the requested use or disclosure.

   45 CFR 164.508(c)(1)(iv) A description of each purpose of the requested use or disclosure. The statement “at the request of the individual” is a sufficient description of the purpose when an individual initiates the authorization and does not, or elects not to, provide a statement of the purpose.

iii **CORE AUTHORIZATION ELEMENT: The information**—Specific and meaningful description of what will be used or disclosed.

   45 CFR 164.508(c)(1)(i) A description of the information to be used or disclosed that identifies the information in a specific and meaningful fashion.

iv **CORE AUTHORIZATION ELEMENT: Who may use or disclose the information**—The name or other specific identification of the person, or class of persons, authorized to make the use or disclosure.

   45 CFR 164.508(c)(1)(ii) The name or other specific identification of the person(s), or class of persons, authorized to make the requested use or disclosure.

v **CORE AUTHORIZATION ELEMENT: Purpose of the use or disclosure**—A description of each purpose of the requested use or disclosure.

   45 CFR 164.508(c)(1)(iv) A description of each purpose of the requested use or disclosure. The statement “at the request of the individual” is a sufficient description of the purpose when an individual initiates the authorization and does not, or elects not to, provide a statement of the purpose.

vi **CORE AUTHORIZATION ELEMENT: To whom the information will be disclosed**—The name or other specific identification of the person, or class of persons, to whom the covered entity may make the requested use or disclosure.

vii **CORE AUTHORIZATION ELEMENT: To whom the information will be disclosed**—The name or other specific identification of the person, or class of persons, to whom the covered entity may make the requested use or disclosure.

   45 CFR 164.508(c)(1)(iii) The name or other specific identification of the person(s), or class of persons, to whom the covered entity may make the requested use or disclosure.

viii **REQUIRED AUTHORIZATION STATEMENTS: Re-disclosure**—Information may be disclosed to others not subject to the Privacy Rule (cannot promise the information will definitely be protected.

   45 CFR 164.508(c)(2)(iii) The potential for information disclosed pursuant to the authorization to be subject to redisclosure by the recipient and no longer be protected by this subpart.
CORE AUTHORIZATION ELEMENT: Expiration date or expiration event--An expiration date/expiration event that relates to the individual or the purpose of the use or disclosure.

45 CFR 164.508(c)(1)(v) An expiration date or an expiration event that relates to the individual or the purpose of the use or disclosure. The statement “end of the research study,” “none,” or similar language is sufficient if the authorization is for a use or disclosure of protected health information for research, including for the creation and maintenance of a research database or research repository.

Document Retention: <<Institution>> has to keep the signed Authorization for six years after it was last in effect. If the “expiration date” is “without any end-date,” then <<Institution>> needs to keep the Authorization forever.

45 CFR 164.508(b)(6) Documentation. A covered entity must document and retain any signed authorization under this section as required by §164.530(j)(2)

45 CFR 164.530(j)(2) Implementation specifications: Retention period. A covered entity must retain the documentation required by paragraph (j)(1) of this section for six years from the date of its creation or the date when it last was in effect, whichever is later.

ADDITIONAL ELEMENTS: Right of Access

45 CFR 164.524(a)(1) Access of individuals to protected health information.

(a) Standard: Access to protected health information.

(1) Right of access. Except as otherwise provided in paragraph (a)(2) or (a)(3) of this section, an individual has a right of access to inspect and obtain a copy of protected health information about the individual in a designated record set, for as long as the protected health information is maintained in the designated record set, except for:

(i) Psychotherapy notes;

(ii) Information compiled in reasonable anticipation of, or for use in, a civil, criminal, or administrative action or proceeding; and

(iii) Protected health information maintained by a covered entity that is:

(A) Subject to the Clinical Laboratory Improvements Amendments of 1988, 42 U.S.C. 263a, to the extent the provision of access to the individual would be prohibited by law;

(B) Exempt from the Clinical Laboratory Improvements Amendments of 1988, pursuant to 42 CFR 493.3(a)(2).

ADDITIONAL ELEMENTS: Temporary Denial of Access

45 CFR 164.524(a)(2)(iii) An individual’s access to protected health information created or obtained by a covered health care provider in the course of research that includes treatment may be temporarily suspended for as long as the research is in progress, provided that the individual has agreed to the denial of access when consenting to participate in the research that includes treatment, and the covered health care provider has informed the individual that the right of access will be reinstated upon completion of the research.

REQUIRED AUTHORIZATION STATEMENTS: Right to revoke authorization—Outline the right for the individual to revoke their authorization in writing.

45 CFR 164.508(b)(5) Revocation of authorizations. An individual may revoke an authorization provided under this section at any time, provided that the revocation is in writing, except to the extent that:

(i) The covered entity has taken action in reliance thereon; or
(ii) If the authorization was obtained as a condition of obtaining insurance coverage, other law provides the insurer with the right to contest a claim under the policy or the policy itself.

45 CFR 164.508(c)(2)(i) The individual’s right to revoke the authorization in writing, and either:
(A) The exceptions to the right to revoke and a description of how the individual may revoke the authorization; or
(B) To the extent that the information in paragraph (c)(2)(i)(A) of this section is included in the notice required by §164.520, a reference to the covered entity’s notice.

ADDITIONAL ELEMENT: Action in Reliance—Written revocation of authorization, with withdrawal of existing research data, is permitted except when the investigator has relied on the data during the conduct of the study. Examples of reliance include having sent the data to the sponsor or assessing an adverse event.

45 CFR 164.508(b)(5)(i): Revocation of authorizations. An individual may revoke an authorization provided under this section at any time, provided that the revocation is in writing, except to the extent that:
(i) The covered entity has taken action in reliance thereon;

ADVERSE EVENT REPORTING [45 CFR 164.512(B)(1)(iii)(A)]

§164.512 Uses and disclosures for which an authorization or opportunity to agree or object is not required.
A covered entity may use or disclose protected health information without the written authorization of the individual, as described in §164.508, or the opportunity for the individual to agree or object as described in §164.510, in the situations covered by this section, subject to the applicable requirements of this section. When the covered entity is required by this section to inform the individual of, or when the individual may agree to, a use or disclosure permitted by this section, the covered entity's information and the individual's agreement may be given orally.

(b) Standard: Uses and disclosures for public health activities.
(1) Permitted uses and disclosures. A covered entity may use or disclose protected health information for the public health activities and purposes described in this paragraph to:
(iii) A person subject to the jurisdiction of the Food and Drug Administration (FDA) with respect to an FDA-regulated product or activity for which that person has responsibility, for the purpose of activities related to the quality, safety or effectiveness of such FDA-regulated product or activity. Such purposes include:
(A) To collect or report adverse events (or similar activities with respect to food or dietary supplements), product defects or problems (including problems with the use or labeling of a product), or biological product deviations;

REQUIRED AUTHORIZATION STATEMENT: Right to refuse to sign authorization.

45 CFR 164.508(c)(2)(ii) The ability or inability to condition treatment, payment, enrollment or eligibility for benefits on the authorization, by stating either:
(A) The covered entity may not condition treatment, payment, enrollment or eligibility for benefits on whether the individual signs the authorization when the prohibition on conditioning of authorizations in paragraph (b)(4) of this section applies; or
(B) The consequences to the individual of a refusal to sign the authorization when, in accordance with paragraph (b)(4) of this section, the covered entity can condition treatment, enrollment in the health plan, or eligibility for benefits on failure to obtain such authorization.

**REQUIRED AUTHORIZATION STATEMENT: Conditional terms**—ability or inability to condition treatment, payment, enrollment or eligibility for benefits on the authorization.

45 CFR 164.508(b)(4)(i) **Prohibition on conditioning of authorizations.** A covered entity may not condition the provision to an individual of treatment, payment, enrollment in the health plan, or eligibility for benefits on the provision of an authorization, except: A covered health care provider may condition the provision of research-related treatment on provision of an authorization for the use or disclosure of protected health information for such research under this section;

45 CFR 164.508(c)(2)(ii) The ability or inability to condition treatment, payment, enrollment or eligibility for benefits on the authorization, by stating either:

(A) The covered entity may not condition treatment, payment, enrollment or eligibility for benefits on whether the individual signs the authorization when the prohibition on conditioning of authorizations in paragraph (b)(4) of this section applies; or

(B) The consequences to the individual of a refusal to sign the authorization when, in accordance with paragraph (b)(4) of this section, the covered entity can condition treatment, enrollment in the health plan, or eligibility for benefits on failure to obtain such authorization.

**COPY TO THE INDIVIDUAL**—The covered entity must provide a copy of the signed authorization form to the individual.

45 CFR 164.508(c)(4) If a covered entity seeks an authorization from an individual for a use or disclosure of protected health information, the covered entity must provide the individual with a copy of the signed authorization.

**CORE AUTHORIZATION ELEMENT: Individual’s signature and date**—If the authorization is signed by a personal representative, a description of the representative’s authority must be provided.

45 CFR 164.508(c)(1)(vi) Signature of the individual and date. If the authorization is signed by a personal representative of the individual, a description of such representative’s authority to act for the individual must also be provided.
1 PURPOSE

1.1 The purpose of this standard operating procedure is to outline the general responsibilities of Investigators who conduct research involving human subjects.

2 REVISIONS FROM PREVIOUS VERSION

2.1 None

3 POLICY

3.1 Investigators conducting Human Subjects Research must understand, accept, and fulfill their responsibilities related to the protection of human subjects:

4 RESPONSIBILITIES

4.1 Director, Prime Review Board Services: Reviewing submissions and reports submitted by Investigators and Staff.

4.2 Chair, Prime Review Board Services: Reviewing submissions and reports submitted by Investigators and Staff.

4.3 Principal Investigator: Ensuring compliance with this SOP.

4.4 Prime IRB Reviewer: Reviewing submissions and reports submitted by Investigators and Staff.

5 PROCEDURE

5.1 Fulfilling Ethical Obligations

Investigators conducting Human Subjects Research will ensure that they fulfill their ethical obligations to protect the research participant via the following:

5.1.1 Obtaining the review and approval of the Prime IRB prior to initiating Human Subject Research in accordance with Prime IRB SOP 105: Research That Must Be Reviewed by The Prime IRB;
5.1.2 Obtaining the necessary training, accepting their responsibilities for protecting the rights and welfare of human subjects, and complying with all applicable provisions of Prime IRB policies and procedures, and with federal regulations and guidelines;

5.1.3 Overseeing the conduct of the research, including recruitment, obtaining consent and protocol procedures, managing data collection, storage, security and backup, and ensuring accurate analysis of data;

5.1.4 Ensuring that the research is conducted in accordance with an Prime IRB-approved protocol, and any conditions that are set in order to receive Prime IRB approval in accordance with Prime IRB SOP 401: Criteria for Approval;

5.1.5 Reporting to the Prime IRB all actions or processes that deviate from the protocol procedures approved by the Prime IRB;

5.1.6 Obtaining and documenting informed consent in accordance with the regulatory requirements and Prime IRB SOPs (Prime IRB SOP 600: Required Elements of Consent and Documentation of Consent and Prime IRB SOP 601: Assent and Parental Permission), unless waived by the Prime IRB.

5.1.7 Delegating responsibilities to qualified study team members that are commensurate with their training and qualification;

5.1.8 Ensuring that there are adequate resources available to safely conduct the research and to ensure the safety of research participants. (21 CFR 312.60).

5.1.9 Ensuring that all members of the study team have a) been trained to conduct the study in accordance with the approved protocol, b) completed mandatory Human Subjects Protection training as required by the Research Education department, and c) completed all required financial disclosures in accordance with the policies on “Conflicts of Interest” and “Conflicts of Interest in the Research Setting.”

5.1.10 Providing continuing review information to the Prime IRB in accordance with relevant federal regulations and Prime IRB SOP 405: Continuing Review of Approved Research.

5.2 Ensuring Appropriate Documentation and Communications

Investigators conducting Human Subjects Research will ensure that the following research activities are properly documented and reported to the Prime IRB as necessary:

5.2.1 Maintaining documentation for each study that contains, at a minimum, the following:

5.2.1.1 Prime IRB-approved protocol;

5.2.1.2 Prime IRB-approved approved informed consent documents;

5.2.1.3 Prime IRB-approved recruitment materials;
5.2.1.4 Prime IRB-approved study materials (e.g., surveys, questionnaires);
5.2.1.5 Pertinent correspondence with the Prime IRB, the sponsor (if applicable) and regulatory authorities (if applicable);
5.2.1.6 Additional Drug and Device Research-specific documentation as described in the Relying Institution Research Policy Manual Policies, “Administering, Storing, and Handling Investigational Drugs,” and “Administering, Storing, and Handling Investigational Devices.”

5.2.2 Reporting the following to the Prime IRB

5.2.2.1 Any proposed changes to the research activity including amendments to the previously approved protocol or proposed changes to study documents or procedures, in accordance with Prime IRB SOP 404: Amendments and Reports of New Findings to Approved Research.

5.2.2.2 Study progress, in accordance with relevant regulations and Prime IRB SOP 405: Continuing Review of Approved Research (at least annually for federally funded research and research involving more than minimal risk).

5.2.2.3 All unanticipated problems related to research, in accordance with relevant regulations and Prime IRB SOP 407: Unanticipated Problems Involving Risks to Subjects.

5.2.2.4 Copies of all external monitoring reports received by the investigator; DSMB reports and updates; and FDA reviews, if applicable, in accordance with Prime IRB SOP 404: Amendments and Reports of New Findings to Approved Research and Prime IRB SOP 407: Unanticipated Problems Involving Risks to Subjects.

5.2.2.5 Any noncompliance with regulations or Hospital policies and procedures in accordance with the Prime IRB SOP 800: Noncompliance with Human Subjects Research Policies.

5.3 Addressing Concerns That Arise During Research

Investigators conducting Human Subjects Research are responsible for addressing any concerns arising during research, including the following:

5.3.1 Any concern or question raised by a research subject before, during, or after the conduct of a research study.

5.3.2 Any concerns raised by any member of their research team. This responsibility includes the following:

5.3.2.1 Investigators should meet regularly with their research teams for
the purpose of reviewing the progress of the research, and to encourage discussion of any concerns about the research in general, or about a specific research subject.

5.3.2.2 Investigators should inform each member of the research team, individually, of his or her responsibility to voice any concerns he or she may have, without fear of repercussions.

5.3.2.3 Investigators must take seriously any concern raised. Investigators should investigate each expressed concern, and report back to the individual who raised it. No concern should be dismissed.

5.3.2.4 Investigators may not punish an individual who brings a concern to their attention.

5.3.2.5 Investigators are responsible for reporting to the Prime IRB any expressed concerns that result in findings regarding subject safety or potential breaches to the rights and welfare of a research subject, compliance with the research protocol, informed consent violations, or the integrity of the research data.

5.3.3 Acting to eliminate any immediate apparent hazard to subjects, even if this deviates from the approved protocol, as permitted by relevant regulations and in Prime IRB SOP 407: Unanticipated Problems Involving Risks to Subjects. A report of a deviation to eliminate such a hazard should be made promptly to the Prime IRB in accordance with Prime IRB SOP 407: Unanticipated Problems Involving Risks to Subjects

6 MATERIALS

6.1 FDA Regulatory Binder and PI Responsibility Requirements Checklist

7 REFERENCES

21 CFR 312.64
21 CFR 812.150
21 CFR 312.66

Prime IRB SOP 401: Criteria for Approval
Prime IRB SOP 404: Modifications to Previously Approved Research and New Information
Prime IRB SOP 405: Continuing Review of Approved Research
Prime IRB SOP 600: Required Elements of Consent and Documentation of Consent
Prime IRB SOP 601: Assent and Parental Permission
Prime IRB SOP 800: Noncompliance with Human Subjects Research Policies
Prime Review Board Services Human Research Protections Program Fact Sheet: Supervisory Responsibilities of Investigators

FDA Guidance for Industry: Investigator Responsibilities — Protecting the Rights, Safety, and Welfare of Study Subjects (October 2009)
<table>
<thead>
<tr>
<th>Version 0.2</th>
<th>Name</th>
<th>Status (Pending, Reviewed, Approved)</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Written by:</td>
<td>Karl Nelson</td>
<td></td>
<td>18-July-2017</td>
</tr>
<tr>
<td>Reviewed by:</td>
<td>Jennifer Neal-Jimenez</td>
<td></td>
<td>7-January-2018</td>
</tr>
<tr>
<td>Approved by:</td>
<td>Jennifer Neal-Jimenez</td>
<td>Approved</td>
<td>9-January-2018</td>
</tr>
</tbody>
</table>
1 PURPOSE

1.1 The purpose of this operating procedure is to outline the requirements for monitoring research data to ensure the safety of participants, and to describe when such plans are necessary. All research involving human subjects requires a plan calibrated to the anticipated risks associated with the research. Ensuring the integrity of the data collected and monitoring the study for emerging safety concerns ensures that the benefits derived from the research are maximized and the risk of harm to subjects and society are minimized.

2 REVISIONS FROM PREVIOUS VERSION

2.1 None

3 POLICY

3.1 In order to ensure the safety of research participants and the integrity of research, the Prime IRB will ensure that each study includes a plan for data and safety monitoring appropriate to the risks presented by the research.

4 RESPONSIBILITIES

4.1 Principal Investigator: The investigator is responsible for developing a Data Safety and Monitoring Plan (DSMP) appropriate to the risks inherent in the research.

4.2 Prime IRB Reviewer: The reviewer is responsible for reviewing the DSMP and making a recommendation to the Prime IRB regarding the appropriateness of the plan.

5 PROCEDURE

5.1 Description and Objectives of the Data Safety and Monitoring Plan (DSMP)

Investigators are required to develop a DSMP appropriate in scope to the anticipated risks of the research. The DSMP should at a minimum address the following issues.

5.1.1 A description of the plan to insure the integrity of the data including:

5.1.1.1 A description of the systems for storing and backing up the data;
5.1.2 Procedures for communication from the data monitor to the Prime IRB and other sites;

5.1.3 Protection of the rights and welfare of subjects during the recruitment, consenting process and study participation;

5.1.4 Protection of subject privacy and confidentiality;

5.1.5 A description of the mechanisms for detecting, reviewing and reporting unanticipated problems involving risks to subjects or others by the investigative team at a frequency and intensity sufficient to ensure the safety of participants. (Prime IRB SOP 407: Unanticipated Problems Involving Risks to Subjects);

5.1.5.1 If there are external reporting responsibilities, the plan should describe the processes and oversight the investigator has in place to report unanticipated problems and SAEs to the following as applicable: OHRP, the FDA and the study sponsor;

5.1.6 Assurance that research responsibilities delegated by the principal investigator to investigative team members are carried out in accordance with the protocol, federal regulations, federal, state and local laws and institutional policies and procedures. (Prime IRB SOP 700: Investigator Responsibilities Related to Human Subject Protections)

5.2 Assignment of Responsibility for Data and Safety Monitoring

The complexity of the study, the number of sites, the seriousness of the disease or condition and the risks inherent in the study intervention determine whether a single individual, several individuals or an independent group of individuals should take responsibility for execution of the DSMP. The responsibility may be shared by several individuals or groups of individuals. For example, the Principal Investigator, the study Sponsor and an Independent Data Monitoring Committee (DMC) may all play a role in the DSMP.
In reviewing the DSMP, the Prime IRB may consider a range of options as appropriate, including but not limited to the following:

5.2.1. The principal investigator will have sole responsibility for monitoring; or
5.2.2. A group of designated Prime IRB faculty/staff will have responsibility for monitoring; or
5.2.3. An independent individual or group of non-Prime IRB individuals will have responsibility for monitoring; or
5.2.4. A combination of Prime IRB faculty/staff and non-Prime IRB individuals will share responsibility; or
5.2.5. A designated medical monitor, or group of monitors, for commercially funded or for not-for-profit sponsored studies will have responsibility for monitoring; or
5.2.6. A formal Internal or Independent DMC will have responsibility for monitoring.

5.3. Independent Data Monitoring Committee (DMC)

The Prime IRB will make a determination for when to require a formal DMC to provide data and safety monitoring oversight.

5.3.1. An Independent DMC is generally not required for:
   5.3.1.1. Early phase studies which involve the investigative use of an open-label intervention, test article or device; or
   5.3.1.2. When the study involves non-serious conditions or when the outcomes are limited to symptom relief.

5.3.2. An Independent DMC is required for controlled trial of any size that will compare rates of mortality or major morbidity, or that involve a study population that is at increased risk for morbidity or mortality, or where the risks of the study intervention places subjects at risk of morbidity or mortality.

   5.3.2.1. Names of specific members of a DMC need not be provided to the Prime IRB provided the description of the DMC contains sufficient information about the criteria for selecting the individuals who will serve on the DMC.

5.2.1. Description of the DMC (Internal or Independent)
   5.2.1.1. DMC membership and their qualifications (if available);
   5.2.1.2. The frequency of DMC review of data;
   5.2.1.3. Description of data to be reviewed;
5.2.1.4. Plans for interim analysis that might impact continuation of the protocol; and

5.2.1.5. Any pertinent stopping rules.

5.2.2. Scope of the DMC responsibilities including:

5.2.2.1. Reviewing the research protocol, informed consent documents and plans for data and safety analysis;

5.2.2.2. Role in evaluating the progress of the intervention, including periodic assessment of data quality and timeliness, participant recruitment, accrual and retention and other factors that affect study outcome;

5.2.2.3. Considering factors external to the study when relevant, such as scientific or therapeutic developments that may have an impact on the safety of the subjects or the ethics of the trial;

5.2.2.4. Reporting on the safety and scientific progress of the trial;

5.2.2.5. Making recommendations to the PI and/or the sponsor, and, if required, to the FDA concerning continuation, termination or modification of the trial based on observed beneficial or adverse effects;

5.2.2.6. If appropriate, conducting interim analyses of efficacy in accordance with pre-specified stopping rules;

5.2.2.7. Ensuring the confidentiality of the trial data and the results of monitoring.

5.2.3. Prime IRB Review of the DSMP

As part of its review process, the convened Prime IRB will review the information contained in the protocol to ensure that plans for data and safety monitoring have been developed in accordance with the guidelines above, and are adequate for the protocol under review.

The Prime IRB’s decision regarding the adequacy of the plan will be recorded in the Prime IRB meeting minutes.

6 MATERIALS

6.1 None

7 REFERENCES

45 CFR 46.111(a)(6)

21 CFR 56.111(a)(6)
FDA Guidance for Clinical Trial Sponsors: Establishment and Operation of Clinical Trial Data Monitoring Committees (March 2006)


NIH Guide: Further Guidance on Data and Safety Monitoring for Phase I and Phase II Trials

NIH Guide: NIH Policy for Data and Safety Monitoring

Prime IRB SOP 700: Investigator Responsibilities Related to Human Subject Protections
<table>
<thead>
<tr>
<th>Version 0.2</th>
<th>Name</th>
<th>Status (Pending, Reviewed, Approved)</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Written by</td>
<td>Karl Nelson</td>
<td></td>
<td>18-July-2017</td>
</tr>
<tr>
<td>Reviewed by</td>
<td>Jennifer Neal-Jimenez</td>
<td></td>
<td>7-January-2018</td>
</tr>
<tr>
<td>Approved by</td>
<td>Jennifer Neal-Jimenez</td>
<td></td>
<td>9-January-2018</td>
</tr>
</tbody>
</table>
Data and Safety Monitoring Plan Guidelines

Purpose

To provide investigators and research teams with guidelines on how to develop a Data and Safety Monitoring Plan (DSMP).

For greater than minimal risk research, the Prime IRB requires the investigator to have a Data and Safety Monitoring Plan in place that protects the safety of subjects, the validity of the data, and the integrity of the research study. The Prime IRB reviews the plan and determines if the plan has adequate provisions in place for monitoring the data collected to ensure the safety of participants.

Guidelines

What is a Data and Safety Monitoring Plan?

Data and safety monitoring provides a clinical investigation with a system for appropriate oversight and attention to the protection of human subjects by the investigator, research team, or an independent reviewer. A Data and Safety Monitoring Plan is a quality assurance plan for a research study.

A written Data and Safety Monitoring Plan (DSMP) prospectively identifies and documents monitoring activities intended to protect the safety of the subjects, the validity of the data and the integrity of the research study. The DSMP may also identify when to terminate a subject’s participation (i.e. individual stopping rules) and/or the appropriate termination of a study (i.e. study stopping rules).

What is considered when developing a Data and Safety Monitoring Plan?

Consider the following DSMP elements and their relevance to the research protocol. The nature, size, risk, and complexity of the study will determine whether and how to address the following seven elements within your plan:

- Subject Safety – monitoring is conducted to avoid or minimize risks (i.e. physical, psychological or social).
- Data Integrity – monitoring is conducted to assure data is accurate and complete. Monitoring of data assures adherence to the approved clinical study.
- Subject Privacy – monitoring is conducted to assure individual’s rights are protected.
- Data Confidentiality – monitoring is conducted to assure data is secured.
- Product Accountability – monitoring is conducted to assure drug(s) or device(s) are tracked and accounted for.
- Study Documentation – monitoring is conducted to assure that required documentation and reports are on file, accurate, and complete.
• Study Coordination – monitoring is conducted to assure that investigator delegation and communication with the research team is planned and systematic.

What are the options for developing a Data and Safety Monitoring Plan?

A data and safety monitoring plan may be incorporated within the protocol, documented within the Prime IRB application, or attached to the Prime IRB application. The DSMP may be developed using the template provided by the Prime IRB, or developed using an outline format or narrative summary as preferred by the investigator.

When is a Data and Safety Monitoring Plan Needed?

The criteria for approval of research states that when the research involves more than minimal risk, the research plan makes adequate provision to monitor the data collected to ensure the safety of subjects, and that adequate provisions to protect the privacy of subjects and the confidentiality of the data are maintained (45 CFR 46.111).

The Prime IRB expects all studies that involve administration of an experimental agent or use of an experimental device, or use of an approved agent or device that has the potential for mortality or major morbidity will have a written Data and Safety Monitoring Plan. A Data and Safety Monitoring Board may also be required studies that have a high expected rate of morbidity or mortality in the study population.

If the research is considered minimal risk, then the development of a data and safety monitoring plan may be helpful, but its development is not required by the Prime IRB unless, the Prime IRB determines a data and safety monitoring plan is needed for the oversight of the study.

The National Institutes of Health (NIH) states that “oversight and monitoring of all intervention studies to ensure the safety of participants and the validity and integrity of the data” is required. NIH policy states that "monitoring should be commensurate with risks and with the size and complexity of the trials". NIH also emphasizes “the elements of the monitoring plan may vary depending upon the potential risks, complexity, and nature of the trial”. References: http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-038.html (release date June 5, 2000) and http://grants.nih.gov/grants/guide/notice-files/not98-084.html (release date June 10, 1998).
The **Office for Human Research Protection (OHRP)** Code of Federal regulations (45 CFR 46.111) states: “When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of the subjects”. Reference: http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html.

The **U.S. Food and Drug Administration (FDA)** states: "Existing requirements for sponsors of clinical investigations involving new drugs for human (including biological products for human use) and medical devices under 21 CFR Parts 312 and 812 respectively, require that a sponsor monitor the progress of a clinical investigation. The monitoring functions may be delegated to a contract research organization as defined in 21 CFR 312.3. Proper monitoring is necessary to assure adequate protection of the rights of human subjects and the safety of all subjects involved in clinical investigations and the quality and integrity of the resulting data submitted to the Food and Drug Administration (FDA)". Reference: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM269919.pdf

When following the **Department of Defense** regulations and requirements, the Prime IRB considers, when appropriate, the appointment of a research monitor for research involving greater than minimal risk. The research monitor is appointed by name and must be independent of the study team conducting the research. The monitor may be an ombudsman or a member of the data and safety monitoring board. The duties of the research monitor are determined on the basis of specific risks or concerns about the research (Reference: DoD Instruction 3216.02 http://www.dtic.mil/whs/directives/corres/pdf/321602p.pdf).

**Preparing the Data and Safety Monitoring Plan**

Consider the following seven Human Subject Protection elements when using the DSMP template form, developing a DSMP outline, or constructing a narrative summary for a DSMP. Select the DSMP components (as identified in the table below) depending on the level of risk and the nature of the research study.

<table>
<thead>
<tr>
<th>Protection Element</th>
<th>DSMP Component</th>
<th>Examples of monitoring activities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subject safety</td>
<td>Specific subject safety parameters</td>
<td>Vital signs, weight, safety blood tests, cardiac status, anxiety, depression scores, etc.</td>
</tr>
<tr>
<td></td>
<td>Frequency of subject safety observations</td>
<td>Weekly telephone follow-up, monthly appointments, observations of subject while in the clinical setting, etc.</td>
</tr>
</tbody>
</table>

---
<table>
<thead>
<tr>
<th>Protection Element</th>
<th>DSMP Component</th>
<th>Examples of monitoring activities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Individual responsible for safety monitoring</td>
<td>Principal investigator, study coordinator, safety monitor, independent monitor, or Data/Safety Monitoring Board, etc.</td>
<td></td>
</tr>
<tr>
<td>Subject stopping rules - under what conditions will a subject be removed from study participation and who will make the decision?</td>
<td>Exclusion criteria, including adverse response to study procedures, pregnancy, stroke, cardiac irregularity, non-compliance with medication, etc. Include procedures for analysis and interpretation of data, etc.</td>
<td></td>
</tr>
<tr>
<td>Study stopping rules - under what conditions will the study be modified or stopped and who will make the decision?</td>
<td>Unanticipated problems involving risks to subjects or others (UPIRTSOs), unexplained adverse outcomes, life threatening adverse event, etc.</td>
<td></td>
</tr>
<tr>
<td>Reporting mechanisms (i.e. deviations, adverse events, UPIRTSOs)</td>
<td>Reporting mechanisms to Prime IRB, FDA, Sponsor, Data/Safety Monitoring Board, etc.</td>
<td></td>
</tr>
<tr>
<td>Data integrity</td>
<td>Specific data elements to be reviewed</td>
<td>Subject inclusion criteria being met, transcription of data is accurate and complete, units of measure are recorded appropriately, calculations are standardized and performed accurately, etc.</td>
</tr>
<tr>
<td></td>
<td>Frequency of monitoring data, points in time, or after specific number of subjects</td>
<td>First 3 subjects and every 20th subject, monthly, quarterly, or annually, etc.</td>
</tr>
<tr>
<td></td>
<td>Individual responsible for data monitoring</td>
<td>Principal investigator, study coordinator, safety monitor, independent monitor, etc.</td>
</tr>
</tbody>
</table>
| Subject privacy | Under what conditions (time and place) will a subject be consented, interviewed, or telephoned? | Observations of consenting process, interviewing, or clinical visit performed quarterly on 3 subjects. Request input from 5
<table>
<thead>
<tr>
<th>Protection Element</th>
<th>DSMP Component</th>
<th>Examples of monitoring activities</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>subjects related to their experiences regarding privacy expectations, etc.</td>
</tr>
<tr>
<td>Data confidentiality</td>
<td>What are the conditions that will protect the confidentiality of the data?</td>
<td>Check for locked file cabinets, secure electronic records, secure location where protected health information is stored, etc.</td>
</tr>
<tr>
<td>Product accountability</td>
<td>Who is responsible for obtaining, storing, preparing, administering, or disposing of the study drug or study device? Who is responsible for overseeing product accountability?</td>
<td>Research Pharmacy, Principal Investigator, Central Pharmacy, Research Laboratory, Nursing, etc.</td>
</tr>
<tr>
<td>Study documentation</td>
<td>Study file management</td>
<td>Study File Management guidelines and checklists for monitoring (sampling of study files annually), etc.</td>
</tr>
<tr>
<td>Study Coordination</td>
<td>Roles and responsibilities are clarified, education needs are addressed, planned meetings or communications with documented meeting notes/minutes</td>
<td>Annual debriefing to determine if expectations are clear and if educational needs exist. Scheduled meetings are on calendar, and meeting outcomes are noted and available to staff, etc.</td>
</tr>
</tbody>
</table>
1 PURPOSE

1.1 This policy establishes the definitions followed by the human research protection program.

2 REVISIONS FROM PREVIOUS VERSION

2.1 None

3 OVERVIEW

3.1 All human subject research must be conducted in full compliance with the applicable regulations, state laws and institutional policies. The provisions refer to various sections of the final rule, instead of repeating all the requirements of those sections, and state that those sections are attached to the policies and procedures. An important function of an institution’s policies and procedures on non-compliance is to inform the research members of the institution on the institution’s policies and procedures for responding to allegations of non-compliance.

3.2 The Emmes Corporation has granted the responsibility for review of all human subjects’ research to the Prime Human Research Protection Program (HRPP). The investigators are responsible for conducting the approved research in accordance with the IRB’s requirements, as well as in accordance with all ethical standards, project policies, and federal or state laws or regulations applicable to the research study. It is the obligation of the investigators and staff to submit a written report to the HRPP if serious non-compliance occurs during the conduct of the research. It is the responsibility of the IRB to determine whether each incidence of non-compliance is serious non-compliance or continuing non-compliance.

4 POLICY

4.1 Definitions:

4.1.1 Non-compliance is defined by the Prime HRPP to be: Any situation, incident, or process during the conduct of human subject research that is inconsistent with any of the following: ethical standards, project policies, and federal or state laws or regulations applicable to the research study.

4.1.2 Serious non-compliance is defined by the JCHR to be:

(1) failure on the part of the investigators, any member of the staff, or any other individual involved in research’s review or oversight to follow the terms of the Prime IRB’s approval when that failure actually or potentially increases
risk to participants or adversely affects the rights and welfare of the participants;
(2) failure to comply with laws or regulations, organization policies, or the requirements or determinations of the HRPP when that failure potentially increases risk to participants or adversely affects the rights and welfare of the participants. A single instance of non-compliance may be determined by the HRPP to be serious non-compliance.
(3) a pattern of behavior or minor non-compliance issues that, if unaddressed, may compromise the integrity of human research protections applicable to the study.
(4) at the discretion of the Director of the HRPP.
Serious non-compliance poses an increase in the risk to participants, adversely affects the welfare, rights, and safety of the research participants, or negatively influences the scientific study integrity. Willful violations of federal regulations and/or policies may also be indications of serious non-compliance.

4.1.3 Continuing Non-compliance is defined by the JCHR to be: A pattern of repeated non-compliance which continues after initial discovery and approval of a corrective action plan that suggests that non-compliance will continue if there is no intervention; or if continued, could significantly increase risk to, or jeopardize the safety, welfare, and/or rights of subject(s) or others; or if continued, could decrease potential benefits.

4.2 Confidentiality: To the extent allowed by law, we shall maintain the identity of respondents and complainants securely and confidentially and shall not disclose any identifying information, except to:
(1) those who need to know in order to carry out a thorough, competent, objective and fair serious non-compliance proceeding;
(2) the Prime IRB members; and
(3) OHRP/FDA as it conducts its review of the serious non-compliance proceeding and any subsequent proceedings.
To the extent allowed by law, any information obtained during the serious non-compliance proceeding that might identify the subjects of research shall be maintained securely and confidentially and shall not be disclosed, except to those who need to know in order to carry out the research misconduct proceeding.

5 RESPONSIBILITIES

5.1 Individuals writing policies and procedures are to indicate terms defined in this policy with a double underline.

5.2 Individuals using policies and procedures are to consult this policy for the definitions of double underlined terms.
6 PROCEEDURES RELATED WITH CRITERIA, REPORTS, AND TIME LIMITATIONS

6.1 Non-Compliance: Allegations of non-compliance may originate from a lead investigator, site investigator, project staff, monitoring staff, site staff, other Organization staff or offices, sponsors/funding agency, or collaborators. All initial allegations, regardless of origin, will be reviewed by the Principal Investigator. If the allegation involves the Principal Investigator, it will be reviewed by the Director of the HRPP. The allegation reviewer must determine whether there is non-compliance, and if so, whether the non-compliance could be designated as serious and/or continuing. The allegation reviewer will be responsible for managing non-compliance determined to be neither serious nor continuing non-compliance. If serious and/or continuing non-compliance is alleged, a written report to the Director of the HRPP must be submitted within seven (7) days of the determination.

6.2 Serious Non-Compliance and Continuing Non-Compliance:

6.2.1 Written reports of serious non-compliance and/or continuing non-compliance may originate from a lead investigator, site investigator, project staff, monitoring staff, site staff, other Organization staff or offices, sponsors, or collaborators. All written reports, regardless of origin, will be reviewed by the Director of the HRPP.

6.2.2 The Director of the HRPP will review written reports of non-compliance or allegations of non-compliance that have a basis in fact. The Director of HRPP is authorized to collect additional information before making a determination. The Director of the HRPP may collect information using a variety of methods, such as, but not limited to, communicating directly with the investigators and staff, and determining whether or not a meeting with the investigators and project staff is required.

6.2.3 Promptly after receiving an allegation of serious non-compliance and/or continuing non-compliance, defined as a disclosure of possible serious non-compliance and/or continuing non-compliance through any means of communication, we shall assess the allegation to determine whether:
(1) it meets the organization’s definition of serious non-compliance and/or continuing non-compliance
(2) it involves either federal or non-federal supported research
(3) the allegation is sufficiently credible and specific so that potential evidence of serious non-compliance and/or continuing non-compliance may be identified.

6.2.4 If it is determined that an inquiry is warranted (i.e., an initial review of the evidence to determine if the criteria for conducting an investigation have been met), we shall complete the inquiry, including preparation of the inquiry report and giving the respondent a reasonable opportunity to comment on it, within 60 calendar days of its initiation, unless the circumstances warrant a longer period. If the inquiry takes longer than 60 days to complete, we shall include documentation of the reasons for the delay in the inquiry record. The inquiry report shall contain the following information:
(1) The name and position of the respondent(s);
(2) A description of the allegations of serious non-compliance and/or continuing non-compliance;
(3) The basis for recommending that the alleged actions warrant an investigation; and
(4) Any memo on the report by the respondent or the complainant.

6.2.5 The Director of the HRPP will make a written determination of whether an investigation is warranted. If the inquiry results in a determination that an investigation is warranted, we shall begin the investigation within 30 calendar days of that determination and, on or before the date on which the investigation begins, send the inquiry report and the written determination to the Prime IRB. We shall use our best efforts to complete the investigation within 120 calendar days of the date on which it began, including conducting the investigation, preparing the report of findings, providing the draft report for comment, and sending the final report to the Prime IRB.

6.2.6 If it becomes apparent that we cannot complete the investigation within that period, we shall promptly request an extension in writing from the Prime IRB. This time period does not apply to separate termination hearings.

6.2.7 In conducting all investigations, we shall:
(1) Use diligent efforts to ensure that the investigation is thorough and sufficiently documented and includes examination of all research records and evidence relevant to reaching a decision on the merits of the allegations;
(2) Interview each respondent, complainant, and any other available person who has been reasonably identified as having information regarding any relevant aspects of the investigation, including witnesses identified by the respondent, and record or transcribe each interview, provide the recording or transcript to the interviewee for correction, and include the recording or transcript in the record of investigation;
(3) Pursue diligently all significant issues and leads discovered that are determined relevant to the investigation, including any evidence of additional instances of possible serious non-compliance, and continue the investigation to completion; and
(4) Otherwise comply with the OHRP/FDA requirements.

6.2.8 In accordance with 45 CFR 46.109(d), we shall prepare the draft and final institutional investigation reports in writing and provide the draft report to the respondent(s) for comment as provided elsewhere in these policies and procedures. Comments are due 30 days after the respondent(s) receive the draft investigation report. The final investigation report shall:
(1) Describe the nature of the allegations of serious non-compliance and/or continuing non-compliance;
(2) Describe and document the federal or non-federal support involved, including, for example, grant numbers, grant applications, contracts, and publications listing;
(3) Describe the specific allegations of serious non-compliance and/or continuing non-compliance considered in the investigation;
(4) Include the institutional policies and procedures under which the investigation was conducted;
(5) Identify and summarize the research records and evidence reviewed, and identify any evidence taken into custody, but not reviewed. The report should also describe any relevant records and evidence not taken into custody and explain why.
(6) Provide a finding as to whether serious non-compliance and/or continuing non-compliance did or did not occur for each separate allegation of serious non-compliance identified during the investigation, and if the criteria was found, (i) identify it as intentional, knowing, or in reckless disregard, (ii) summarize the facts and the analysis supporting the conclusion and consider the merits of any reasonable explanation by the respondent and any evidence that rebuts the respondent’s explanations.
(7) Include and consider any comments made by the respondent and complainant on the draft investigation report.

6.2.9 We shall maintain and provide to the IRB upon request all relevant research records and records of our serious non-compliance and continuing non-compliance proceeding, including results of all interviews and the transcripts or recordings of such interviews. As a result of reviewing an incident of serious non-compliance and/or continuing non-compliance, possible research misconduct may also be uncovered.

7 PROCEDURES RELATED WITH NOTIFYING THE IRB OF THE DECISION TO OPEN AN INVESTIGATION AND OF INSTITUTIONAL FINDINGS AND CATIONS FOLLOWING THE INVESTIGATION

7.1 On or before the date on which the investigation begins (the investigation must begin within 30 calendar days of our finding that an investigation is warranted), we shall provide to the Prime IRB with the written finding by the Director of the HRPP. A copy of the report will be distributed among the President and the Chief Operating Officer (no later than 30 calendar days from the recognition of a reportable case).

7.2 Upon a request from the Prime IRB we shall promptly send them:
(1) a copy of our institutional policies and procedures under which the inquiry was conducted;
(2) the research records and evidence reviewed, transcripts or recordings of any interviews, and copies of all relevant documents; and
(3) the charges for the investigation to consider.

7.3 After the investigation we shall promptly provide to the JCHR IRB:
(1) A copy of the investigation report and all attachments;
(2) A statement of whether the institution found serious non-compliance and/or continuing non-compliance and, if so, who committed it;
(3) A statement of whether the institution accepts the findings in the investigation report; and
(4) A description of any pending or completed administrative actions against the respondent.
8 PROCEDURES RELATED WITH IRB DECISION AND ACTIONS

8.1 Once the Prime IRB Office receives the report from the Director of the HRPP, the report will be discussed at the next Prime IRB convened meeting providing a printed copy to each participating IRB member. Based on the report submitted by the Director of the HRPP, the Prime IRB members will make the final determination on whether the non-compliance is serious non-compliance or continuing non-compliance and what steps must be taken, if any, to protect enrolled participants. The Prime IRB will determine the elements of a corrective action plan including a timeframe to address the serious non-compliance and/or continuing non-compliance and to prevent recurrence of such an event. To ensure that the safety and well-being of subjects related to allegations of this level of non-compliance are addressed promptly, the timeframe will not exceed 30 calendar days. The Prime IRB may impose one or more of the following actions in the case of serious or continuing non-compliance:

1. Modify the study protocol
2. Modify information that must be disclosed in a consent document
3. Provide information about the non-compliance to current study participants, when such information may affect willingness to continue participation
4. Require re-consent of all participants
5. Modify the continuing review schedule
6. Monitor the research activities
7. Monitor the consent process
8. Suspend the conduct of research until corrective actions are implemented
9. Terminate the research.

8.2 The respondent will be informed of the IRB’s decision as well as information regarding the option to appeal the decision. An appeal should be filed in writing with the Director of the HRPP within 10 calendar days, and the investigator may request a meeting to discuss the appeal. The HRPP staff will inform the investigator of the outcome of the review of the appeal.

9 PROCEDURES RELATED WITH NOTIFICATION TO OHRP AND FDA

9.1 The Prime IRB will provide notification to the Food and Drug Administration and the Office of Human Research Protection as and when appropriate during the course of the inquiry and any subsequent investigation.

9.2 If the research study was reviewed by the IRB under ICH-GCP guidance (E6), the PI must promptly notify the sponsor and provide the sponsor with the IRB suspension or termination notification (see, 4.12.3 at http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm073122.pdf).

9.3 We will cooperate with and assist the OHRP and/or the FDA, as needed, to carry out any administrative actions any of them may impose as a result of a final finding of serious non-compliance and/or continuing non-compliance.
10 PROCEDURES RELATED WITH MAINTENANCE AND CUSTODY OF RESEARCH RECORDS AND EVIDENCE

10.1 We shall take the following specific steps to obtain, secure, and maintain the research records and evidence pertinent to the serious non-compliance and continuing non-compliance proceeding:

10.1.1 Either before or when we notify the respondent of the allegation, we shall promptly take all reasonable and practical steps to obtain custody of all research records and evidence needed to conduct the serious non-compliance and continuing non-compliance proceeding, inventory those materials, and sequester them in a secure manner, except in those cases where the research records or evidence encompass scientific instruments shared by a number of users, custody may be limited to copies of the data or evidence on such instruments, so long as those copies are substantially equivalent to the evidentiary value of the instruments.

10.1.2 Where appropriate, give the respondent copies of, or reasonable, supervised access to the research records.

10.1.3 Undertake all reasonable and practical efforts to take custody of additional research records and evidence discovered during the course of the serious non-compliance proceeding, including at the inquiry and investigation stages, or if new allegations arise, subject to the exception for scientific instruments in (1) above.

10.1.4 We shall maintain all records of the serious non-compliance and continuing non-compliance proceeding for 7 years after completion of the proceeding, or any OHRP/FDA proceeding, whichever is later, unless we have transferred custody of the records and evidence to OHRP/FDA.

11 MATERIALS

11.1 None

12 REFERENCES

12.1 45 CFR §46.103(b)(5)(i).
12.2 OHRP Guidance on Reporting to Incidents to OHRP (June 20, 2011)
12.3 21 CFR §56.108(b)(2)
12.4 21 CFR 56.113
<table>
<thead>
<tr>
<th>Version 0.1</th>
<th>Name</th>
<th>Status (Pending, Reviewed, Approved)</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Written by:</td>
<td>Jennifer Neal-Jimenez</td>
<td></td>
<td>4-January-2018</td>
</tr>
<tr>
<td>Reviewed by:</td>
<td>Laura Covington</td>
<td></td>
<td>7-January-2018</td>
</tr>
<tr>
<td>Approved by:</td>
<td>Laura Covington</td>
<td>Approved</td>
<td>9-January-2018</td>
</tr>
</tbody>
</table>