Policies & Standard Operating Procedures

August 2018

SPRINGFIELD COMMITTEE FOR RESEARCH INVOLVING HUMAN SUBJECTS (SCRIHS)

For more information about SCRIHS Policies and Procedures, visit:
http://www.siumed.edu/adrfa/scrihs.html

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IRB OPERATIONS AND TRAINING

DETERMINING WHICH RESEARCH ACTIVITIES NEED IRB REVIEW

EFFECTIVE DATE: June 8, 2011

REVISION DATE: November 11, 2015

OBJECTIVE

To describe policies and procedures for determining the types of activities that qualify as human subjects research or clinical investigations and thus require review and approval by the Institutional Review Board (IRB), also known as the Springfield Committee for Research Involving Human Subjects (SCRIHS), prior to implementation.

GENERAL DESCRIPTION OF POLICY

In accordance with federal regulations and institutional policy, research studies that involve humans as subjects require IRB review and approval prior to study implementation. . This includes research studies that are : (1) sponsored by Southern Illinois University School of Medicine (SIU-SOM); (2) conducted in SIU-SOM facilities; or (3) conducted by SIU-SOM faculty, staff, residents or medical students. Research to be performed by a community-based investigator and/or research to be conducted in any SIU-SOM affiliated hospitals or sites may also be reviewed by SCRIHS with the appropriate authorization agreements.

The federal regulations include specific definitions of "research" (45 CFR 46.102(d)) and "human subject" (45 CFR 46.102(f). If an investigator is unsure whether or not their project meets criteria as human subjects research, he/she is encouraged to submit a Non-Human Subjects Research Determination to SCRIHS through the IRB electronic system. In general, SCRIHS does not provide formal written determination for a project completed prior to submission. Requests for written determination for completed projects will be considered on a case-by-case basis by the SCRIHS Chair or designee.

Definitions

Department of Health and Human Safety (DHHS)/Common Rules

"Research"[45 CFR 46.102(d)] : A systematic investigation designed to develop or contribute to generalizable knowledge. Activities which meet this definition constitute research, whether or not they are conducted or supported under a program which is considered research for other purposes. For example, some demonstration and service programs may include research activities. Some research development or testing and evaluation procedures also meet this definition.

"Human subjects" [45 CFR 46.102(f)]: A living individual about whom an investigator conducting research obtains either (1) data through ***intervention*** or ***interaction*** with the individual or (2) identifiable ***private information***.

(1) ***Intervention****:* This includes 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.

(2) ***Interaction***: This includes communication or interpersonal contact between investigator(s) and a subject.

Private information. This includes information about the subject that occurs in a context in which the individual can reasonably expect that no observation and video or voice recording is taking place as well as information that has been provided for specific purposes by an individual (for example, a medical record) with the expectation that the information will not be made public. Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects.

Food and Drug Administration (FDA)

Clinical investigation: Involves use of a test article (specifically, drug, device, food substance, or biologic) and one or more human subjects. The investigation must meet requirements for prior submission to the FDA (when the study involves FDA approved drugs or medical devices which are being used for purposes other than those specifically stated upon initial approval by the FDA) or when study results are intended to be part of an application for research or a marketing permit.

When activities involve use of an FDA regulated test article (specifically, drug, device, food substance, or biologic under the purview of the FDA), SIU-SOM applies the FDA definitions of "human subjects."

Human subjects (FDA guidelines for drug, food, or biologic): A healthy individual or patient who is or becomes a participant in research either as a control or as a recipient of a test article or as an individual on whose specimen a device is used. A subject may be either a healthy individual or a patient [21 CFR 56.102(e)] .

Human subjects (FDA guidelines for medical devices): An individual who participates in an investigation, either as a control or a subject on whom or on whose specimen an investigational device is used. A subject may be in normal health or may have a medical condition or disease [21 CFR 812.3(p)] (Medical Devices). This definition includes the use of tissue specimens even if they are unidentified.

If the research involves any of the following, FDA regulations, 21 CFR 50 & 56 apply and require IRB approval prior to implementation:

- Any use of a drug in research other than the use of an FDA approved drug in the course of medical practice; or
- Any use of a medical device in studies where the purpose is to determine the safety or effectiveness of the device; or
- Data will be submitted to or held for inspection by the FDA as part of a marketing permit.

Principal Investigator

A *principal investigator* may be a SIU-SOM employee or employee at any site with which SIU-SOM has signed an IRB Authorization or Individual Investigator Agreement.

PROCEDURES

1. It is the responsibility of the principal investigator to seek IRB review and approval of a protocol prior to initiating any clinical research or investigation that involves human subjects.

2. The principal investigator is responsible for making a preliminary decision regarding whether his/her activities meet either (a) the Department of Health and Human Services (DHHS) definitions of both "research" and "human subjects" or (b) the FDA definitions of both "clinical investigations" and "human subjects." ***The PI is responsible for following individual publisher policies regarding IRB documentation that is to accompany works submitted for publication.***

3. If an authoritative decision and/or advice on the application of the federal regulations and IRB policy is needed, the principal investigator/study personnel may contact IRB staff or the IRB Chair/Vice Chairs for guidance, or submit a Non-Human Subjects Research Determination through the electronic IRB system.

4. IRB staff or the IRB may request the principal investigator/study personnel to complete and submit a research application to the IRB for a decision. IRB staff, along with the IRB Chair or his/her designee, make the final determination whether the activities meet the federal definitions. The IRB or IRB staff may require the principal investigator to contact applicable regulatory agencies to assist in making the determination.

5. IRB staff communicates the IRB's decision to the principal investigator/study personnel via e-mail or letter.

REFERENCES

21 CFR 56.102
45 CFR 46.102

MEMBERSHIP OF IRB

EFFECTIVE DATE: May 11, 2011

REVISION DATE: February 8, 2012; August 14, 2013; April 8, 2015

OBJECTIVE

To define policies and procedures for appointing Institutional Review Board (IRB) members, also known as the Springfield Committee for Research Involving Human Subjects (SCRIHS), and for maintaining the IRB membership roster that must be submitted to the Office for Human Research Protections (OHRP)/Food and Drug Administration (FDA)

GENERAL DESCRIPTION OF POLICY

The Institutional Review Board (IRB) at Southern Illinois University School of Medicine (SIU-SOM) shall have a minimum of five voting members sufficiently qualified through experience and expertise to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects. The membership includes regular members who may have designated alternates with qualifications comparable to the regular member. Administrative representatives may also attend meetings but do not vote and do not count towards quorum.

IRB membership shall comply with federal requirements outlined in 45 CFR 46.107 and 21 CFR 56.107 to ensure appropriate diversity of the members through consideration of multiple professions/disciplines, ethnicities and cultural backgrounds, gender, and sensitivity to such issues as community attitudes. In addition, the IRB includes members who can determine the acceptability of proposed research in terms of institutional commitments and regulations, applicable law, and standards of professional conduct and practice. If the IRB regularly reviews research involving a vulnerable category of subjects, the IRB membership includes individuals who are knowledgeable about and experienced in working with those subjects.

The IRB includes at least one member with each of the following primary affiliations: nonscientific, scientific, nonaffiliated (i.e., not affiliated with SIU-SOM and not part of the immediate family of a person affiliated with SIU-SOM), and a physician. The IRB includes at least one member from each affiliated hospital (St. John's Hospital and Memorial Medical Center).

In addition, the IRB invites individuals 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.

PROCEDURES

Appointment Procedures/Terms of Membership

1. Approximately once a year, the IRB Chair or designee is responsible for soliciting IRB membership recommendations, to fill vacancies or necessary areas of expertise, from sources that include SIU-SOM Faculty Council, SIU-SOM affiliated hospitals and other community members. Other SIU-SOM administrative units may also submit nominations for membership. IRB staff or Chair will ensure that the Federal requirements for IRB membership are met and submit the recommendations to the Dean and Provost.

2. IRB staff or Chair provides the Dean and Provost or designee and the IRB Chair with a copy of the recommendations. The Dean and Provost will make all final IRB membership appointments, including the IRB Chair and Vice-Chairs.

3. Appointments for the IRB Chair are for a one year term. Vice Chairs and IRB members (including alternates) are for three-year terms beginning with fiscal year. SIU-SOM has no limit on the number of terms IRB Chairs, Vice Chairs, members, and alternates may serve on the IRB. The Dean and Provost, or designee, can annually reappoint administrative representatives when there is no change in the individual's status regarding conflict of interest.

4. Individuals under consideration for appointment as an IRB Chair must meet the following requirements: completion of human research protections training; recent experience as a voting IRB member (or comparable experience) for at least one year prior to nomination as IRB Chair; display of adequate knowledge of ethical principles, professional standards, federal regulations, and other applicable law, through IRB meeting attendance and participation; and demonstration of professional competence necessary to review specific research activities. (IRB Chair Responsibilities are outlined in more detail in the IRB Chair Position Description). The IRB Chair shall have voting privileges and other authorities and responsibilities of members including the responsibility to review, make motions, participate in discussions and vote on approval/disapproval of studies.

5. IRB Vice Chair(s) fulfill the responsibility of the IRB Chair in his/her absence. IRB Vice Chair(s) may also assume responsibilities delegated by the IRB Chair.

6. IRB Chair, Vice Chairs, members, and alternates are responsible for providing IRB staff with curriculum vitae to document each member's expertise, degrees, and/or license number. IRB staff maintains vitae in the files for each member throughout his/her term on the IRB and periodically requests updates, as appropriate.

7. Alternate IRB members replace regular IRB members who are unable to attend convened meetings of the IRB. Alternate members must have qualifications comparable to the applicable regular member and may be alternates for more than one IRB member. IRB staff maintains the list of alternate members on the official membership list approved by OHRP. The OHRP list specifies which members the alternate is qualified to replace. Terms of appointment, length of service, and duties are identical to those for regular IRB members.

8. Alternates attending a meeting or conducting a protocol review have all the authority of regular IRB members and receive the same training and protocol review application materials as the regular members. If the regular member and his/her alternate attend the same convened meeting, only one individual may vote.

9. Administrative representatives do not vote and serve as administrators to ensure coordination among other SIU-SOM affiliated research units. Examples include but are not limited to: Associate Dean for Research and Faculty Affairs; Compliance Officer; Representatives from the Office of General Counsel.

10. IRB staff may recruit *ad hoc* consultants with competence in special areas to assist in the review of issues that require expertise beyond or in addition to that available on the IRB. These *ad hoc* consultants do not vote with the IRB and do not count toward a quorum at a convened meeting. *Ad hoc* consultants may provide comments or recommendations in writing to the IRB prior to the meeting or attend the convened meeting to participate in the review. See the Initial Full Board Review SOP for procedures for contacting consultants.

11. When the IRB reviews research that involves prisoners, a majority of the IRB (exclusive of the prisoner representative) must have no association with the prison involved, apart from their relationship on the IRB.

12. For IRB review of research on prisoners, at least one voting member at the IRB meeting must be a prisoner or a prisoner representative with appropriate background and experience to serve in that capacity.

Filling Appointments Due to Resignations During the Year

1. IRB Staff or the IRB Chair solicits recommendations from a variety of sources, recruits potential members, and makes recommendations for replacement of members who resign during the year. IRB staff sends a copy of the recommendations to the Dean and Provost and the IRB Chair. The Dean and Provost or designee makes all final appointments.

OHRP/FDA IRB Registration/IRB Membership Roster

1. IRB staff or designee completes the OHRP/FDA IRB registration forms in accordance with OHRP and FDA registration requirements and updates the registration in a timely manner when the IRB membership changes. The OHRP registration form serves as the IRB roster and denotes in which scientific capacity, if any, each member serves.

2. IRB staff or designee maintains membership records. A membership list is used to determine who may attend IRB meetings and count toward the quorum. It includes a list of regular members and their designated alternates. IRB staff ensures the membership list is kept updated and maintained on the SCRIHS website.

3. To meet OHRP/FDA registration requirements and in order to hold convened meetings, the scientist and nonscientist member designations are as follows:
   - Nonscientific: members who have had little or no scientific or medical training or who do not currently hold positions which involve scientific research or clinical practice (e.g., administrative positions).
   - Scientific: members who hold M.D., Ph.D., Pharm.D., D.O., or other advanced degrees who are actively engaged in research in the physical, educational, social, behavioral, or biological sciences and disciplines and/or hold regular faculty appointments.

REFERENCES

21 CFR 56.107
21 CFR 56.115(a)(5) & 56.106
45 CFR 46.103(b)(3) & 115(a)(5)
45 CFR 46.107
45 CFR 46 Subpart E

IRB MEMBER AND CONSULTANT CONFLICT OF INTEREST

EFFECTIVE DATE: August 10, 2011

REVISION DATE: June 19, 2013; March 25, 2016

OBJECTIVE

To describe policies and procedures for identifying and managing Institutional Review Board (IRB) member and ad hoc consultant conflict of interest in any type of review (e.g., initial, continuation, modification, noncompliance, unanticipated problem/adverse event, protocol violation, exemption certification)

GENERAL DESCRIPTION

In the environment of research, transparency and honesty are indicators of integrity and responsibility. These are characteristics that promote quality research and can only strengthen the research process. This policy helps ensure that personal and financial interests do not compromise the rights and welfare of human research subjects. The IRB excuses all IRB members' and consultants' with a conflict of interest (see definition below) prior to conducting IRB reviews.

Definitions

A *conflict of interest* involves any situation in which an IRB member or consultant has a significant personal or financial interest in the proposed research or clinical investigation or study sponsor.

Significant personal interest includes but is not limited to:

- An interest that the IRB member or consultant believes conflicts with his/her ability to objectively review a protocol including interests of the individual or immediate family member (spouse and dependent children) involved in the design, conduct, or reporting of the research protocol.

Examples of a conflicting interest are if the IRB member or consultant is any of the following:

- Principal investigator (PI);
- Co-investigator;
- Study staff;
- Study personnel receiving funding from the study;
- Supervisory over the PI of the study (e.g., graduate advisor);
- Family member of PI.

Significant financial interest is anything of monetary value, including, but not limited to:

- Salary or other payments for services (e.g., consulting fees or honoraria);
- Equity interests (e.g., stocks, stock options, or other ownership interests);
- A proprietary interest in the research such as a patent, trademark, copyright, or licensing agreements including royalties from such rights;
- A financial interest in the sponsor, product or service being tested;
- A position as an executive director or director of the agency or company sponsoring the research regardless of the amount of compensation;
- Any compensation that could be affected by the outcome of the research regardless of the amount of compensation.

Significant financial interest does NOT include:

- Salary, royalties, or other remuneration from the University;
- Income from seminars, lectures, or teaching engagements sponsored by public or non-profit entities with proper approval, as applicable;
- Income from service on advisory committees or review panels for public sector or non-profit entities;
- An equity or financial interest that when aggregated for the IRB member or consultant and the IRB member's or consultant's spouse and dependent children meets both of the following tests: does not exceed $5,000 in value as determined through reference to public prices or other reasonable measures of fair market value and does not represent more than a 5% ownership interest in any single entity;
- Salary, royalties or other payments that when aggregated for IRB member or consultant and the IRB member's or consultant's spouse and dependent children over the next 12 months are not expected to exceed $5,000.

PROCEDURES

1. At scheduled IRB meetings, SCRIHS staff provide all new IRB members with a *Confidentiality Statement* and *Conflict of Interest Statement*. Each IRB member completes and returns the signed statements to SCRIHS staff. Each IRB member is responsible for notifying SCRIHS staff of any changes to the *Conflict of Interest Statement* during their appointed term.

2. No regular or alternate member may participate in review of any research project in which the member has a conflict of interest, except to provide information as requested. Such review includes, without limitation, initial, continuation, exempt, modification, unanticipated problems involving risk to participants or others, protocol violation, and noncompliance reviews using expedited or convened procedures.

3. It is the responsibility of each voting member or alternate member of the IRB to disclose any conflict of interest when conducting a review and to excuse him or herself from deliberations and voting. The IRB Chair, other IRB members, or IRB staff may also identify any conflict of interest of voting members or alternate members and request such member excuse him or herself from deliberations and voting. If, after such request is made, the member does not excuse him or herself, the matter may be brought to the IRB for its deliberation and decision on the matter.

4. The procedure for excusing an IRB member, including the IRB Chair, from deliberating/voting on all full review protocols for which there is a conflict of interest is detailed in the Conduct of IRB Meetings SOP. SCRIHS staff documents all conflict of interest disclosures in the IRB meeting minutes.

5. A consultant may not participate in the review of any research project in which the consultant has a conflict of interest. Such review includes, without limitation, initial, continuation, exempt, modification, unanticipated problems involving risk to participants or others, protocol violation, and noncompliance reviews using expedited or convened procedures.

6. When contacting an individual to serve as a consultant, SCRIHS staff initially determine that no conflict of interest exists. Once SCRIHS staff has made this determination, they distribute the *Certification of Confidentiality* agreement to the consultant for confirmation and signature.

REFERENCES

45 CFR 46.103, 107
21 CFR 56.107
21 CFR 54 (as reference)
42 CFR 50 Subpart F
OHRP May 2004 Financial Relationships and Interests in Research Involving Human Subjects: Guidance for Human Subject Protection

HUMAN SUBJECTS PROTECTION TRAINING

EFFECTIVE DATE: December 14, 2011

REVISION DATE: June 12, 2013; March 11, 2015; May 13, 2015; October 4, 2016

OBJECTIVE

To describe the institution's program for ensuring that all persons engaged in human subjects research, including SCRIHS members and SCRIHS staff, are appropriately educated about the regulatory requirements and ethical considerations for the protection of human subjects involved in research

GENERAL DESCRIPTION

The foundation for the effective implementation of all facets of human subjects research compliance at Southern Illinois University School of Medicine (SIU-SOM) and its affiliated research institutions, and for efforts to promote compliance with these requirements, lies in a comprehensive, mandatory education program for all applicable research personnel, including, without limitation, IRB members and research support staff in SCRIHS. SIU-SOM has a multifaceted human subjects' protection education program which is designed to provide essential training on ethics and regulations of research and local IRB policies/procedures as explained below.

PROCEDURES

Initial Education for Authorized Study Personnel (ASP)

1. All ASP are required to complete human subjects research training prior to engaging in human subjects research. Instructions for accessing the training modules can be found on the SCRIHS website and within the electronic IRB system.

2. Completion certificates will be available to ASP after completing their assigned modules. These certificates should be printed and retained by the Principal Investigator/Research Coordination team for reference.

3. SCRIHS has access to user completion certificates. It is not necessary to submit completion certificates to the SCRIHS office.

4. SCRIHS can accept successful completion of prior human subjects protection training from other institutions. This is reviewed on a case-by-case basis. The decision to accept outside training is based on review of the curriculum and the completion date. Please contact the SCRIHS office for further guidance.

Continuing Education for ASP

1. SCRIHS requires ASP to re-certify human subjects protection training every three (3) years. This is accomplished by retaking all assigned human subjects protection training curriculum.

Initial Education for IRB Members

Following appointment to membership on the IRB and prior to serving as reviewers, IRB members, *administrative representatives*, and alternate members receive the following training:

1. New IRB members must successfully complete all human subjects protection training curriculum prior to being assigned to complete reviews.

2. New IRB members are required to attend at least one (1) convened IRB meeting to observe the process prior to being assigned to complete reviews.

3. SCRIHS staff offers to assign new IRB members to a mentor who is an experienced IRB member who guides the new member in his/her reviews of protocols, IRB policies and procedures, and federal, state, and institutional regulations.

4. In addition to the above training, members receive the following educational materials:
    - SCRIHS consent form templates ;
    - Code of Federal Regulations;
    - University of Rochester Manual, "Protecting Study Volunteers in Research";
    - Link to HIPAA guidance;
    - Link to OHRP regulations;
    - Link to FDA regulations;
    - SCRIHS website and contact information.

Continuing Education of IRB Members

SCRIHS staff offers the following continuing education opportunities to current members of the IRB.

1. On-going Protocol Specific Training: SCRIHS staff disseminates materials containing ethical and regulatory guidance for the review of protocols involving a specialized area, (i.e., gene therapy or tissue banking) or selected vulnerable subject populations (i.e., prisoners) to each IRB member. In the agenda, SCRIHS staff refers IRB reviewers to pertinent materials (e.g., if a research project involves children, SCRIHS staff refers the reviewers to the materials on children). Resource materials come from a variety of sources, including but not limited to: *OPRR Guidebook*, 1993; *OPRR Reports*; *FDA Information Sheets*; *OHRP/FDA regulations;* handout materials prepared by SCRIHS; journal articles.

2. IRB Members E-mail Lists: SCRIHS maintains e-mail mailing lists which are used on an on-going basis to send IRB members a variety of materials such as copies of pertinent articles, regulatory updates, web references to resource materials or government reports, or communication about a specific protocol review. If an IRB member does not have e-mail, paper copies will be provided.

3. Presentations: Upon request or as appropriate, SCRIHS presents training on selected topics or invites a specialist in a specific area to address the IRB.

4. Dissemination of Articles or Educational Materials Collected at Professional Meetings or from Scientific Literature: Periodically, SCRIHS staff includes copies of these materials in the IRB

agenda. Also, the SCRIHS staff sends correspondence to the IRB members periodically informing them that the materials are available upon request.

5. Webinars: Periodically, SCRIHS staff invites and encourages IRB members to attend relevant webinars related to human subjects protections.

6. IRB members are required to re-certify human subjects' protection training every three (3) years. This is accomplished by retaking assigned human subjects protection training curriculum.

7. SCRIHS encourages and periodically requires the Chair and/or Vice-Chairs to attend university, city, state, national, or regional IRB teleconferences, webinars, workshops, or lectures.

Initial Education for New SCRIHS Staff

1. New SCRIHS staff receive the following educational materials or website links:
   - 45CFR46: Protection of Human Subjects (OHRP);
   - 21CFR50: Protection of Human Subjects (FDA);
   - 21CFR56: Institutional Review Boards (FDA);
   - FDA Information Sheets;
   - All SCRIHS required human subjects protection training curriculum.
   - HIPAA educational materials.

2. SCRIHS supervisory staff establishes and implement a training plan for each new SCRIHS staff member, which includes direct hands-on training by designated experienced staff members.

3. New SCRIHS staff members must read all existing SCRIHS/IRB standard operating procedures.

4. SIU-SOM requires that all SCRIHS staff be trained in the protection of human subjects. SCRIHS staff may meet this requirement by successful completion of human subjects protection training curriculum.

5. SCRIHS staff completes the on-line Office for Human Research Protections (OHRP) Assurance Module.

Continuing Education of SCRIHS Staff

1. SCRIHS encourages and periodically requires its staff members to attend university, city, state, national, or regional IRB teleconferences, webinars, workshops, or lectures.

2. SCRIHS staff receives all of the materials distributed to IRB members. Also, staff receive copies of selected compliance information/materials (e.g., OHRP publications, copies of innovative materials used by other IRBs/institutions, Food and Drug Administration (FDA) and OHRP correspondence, training materials developed by external groups, Public Responsibility in Medicine & Research (PRIM&R) Board educational e-mails).

3. If, during the year, designated SCRIHS staff revise Standard Operating Procedures (SOPs) or add information to an SOP, and the SOP is subsequently approved/signed by the SCRIHS Chair (and when applicable, other individuals, e.g., SOPs for coordination between units), SCRIHS staff are

notified by the designated SCRIHS staff upon implementation of the approved/signed revised SOP. For additional details, see the Generation, Use, and Revision of Standard Operating Procedures SOP.

4. SCRIHS staff is required to re-certify human subjects' protection training every three (3) years. This is accomplished be retaking assigned human subjects protection training curriculum.

Expired Human Subjects Protection Training

1. If ASP human subjects protection training expires, that ASP is not able to participate in any human subjects research until training requirements are successfully fulfilled.
2. If the Principal Investigator's training expires, subject enrollment in all of that Investigator's protocols must cease until the Investigator successfully completes the required human subjects protection training curriculum.
3. If IRB member human subjects protection training expires, the IRB member will be notified directly by SCRIHS staff and given two weeks to complete the appropriate training. The IRB member cannot conduct reviews until training requirements are successfully fulfilled.

REFERENCES

Generation, Use, and Revision of Standard Operating Procedures SOP

GENERATION, USE, REVISION AND ARCHIVING OF STANDARD OPERATING PROCEDURES

EFFECTIVE DATE: May 11, 2011

REVISION DATE: October 9, 2013; May 13, 2015

OBJECTIVE

To describe the policies and procedures for developing, reviewing, revising, distributing and archiving standard operating procedures (SOPs) for the Institutional Review Board (IRB), also known as the Springfield Committee for Research Involving Human Subjects (SCRIHS), and the IRB office.

GENERAL DESCRIPTION OF POLICY

Southern Illinois University School of Medicine (SIU-SOM) IRB office maintains standard operating procedures to ensure effective functioning of the IRB and IRB office operations. SCRIHS documents when procedures are initiated, revised, and disseminated to staff, IRB members, investigators, and study personnel. Further, it is necessary to document the procedures for staff training regarding SOPs and maintenance of training records.

PROCEDURES

Procedure for Developing Standard Operating Procedures

1. IRB staff, with recommendation from the IRB Chair, Vice Chairs, IRB members and/or investigators, determines when a new SOP needs to be established and initiates production of the draft document including background or reference material.

2. The development of the SOP is performed by IRB staff in collaboration with a consulting team (i.e. legal counsel, IRB Advisory Panel or other advisors) as appropriate.

3. All SOPs are in compliance with federal, state, and institutional regulations and developed by IRB staff.

4. If the SOP involves approval from another University administrative office, IRB staff coordinate communications, review and approval with that administrative office.

5. The IRB Advisory Panel approves or recommends changes to the draft SOP. The draft SOP is then sent to the full board IRB for review and approval. The SOP becomes officially approved upon the IRB Chair signature.

Distribution of Approved Standard Operating Procedures

1. IRB staff disseminate or notify all other IRB staff, the IRB Chair, Vice Chairs, and/or IRB members when a new SOP is approved.

2. All IRB staff are responsible for reviewing each approved SOP within 10 business days of the IRB Chair approval.

3. The IRB office maintains the most recent versions of all approved SOPs on the SCRIHS website. IRB staff provide information on the availability of the SOPs through a variety of educational initiatives [e.g., *mass emails, newsletters, presentations*].

4. It is the responsibility of the IRB office to provide access to its investigators and research staff the SOPs which are relevant to conducting human research. The SOPs are made available via the SCRIHS website and the electronic IRB submission system. It is the responsibility of the Principal Investigator and Authorized Study Personnel to follow the SOPs.

Revisions to Standard Operating Procedures

1. IRB staff, with advice from the IRB Chair, Vice Chairs, and/or IRB members, determines when to revise an existing SOP. In most cases, designated IRB staff revise the SOP. Any IRB staff member may draft revisions to an SOP where all revisions are in compliance with federal, state, and institutional regulations.

2. In revising SOPs, IRB staff may consult with the IRB Chair, IRB Vice-Chairs, IRB Advisory Panel and/or IRB members on IRB related issues.

3. If the revised SOP involves coordination with another University administrative office, IRB staff route the SOP to the appropriate individual representing that office for review and approval.

4. The revised SOP becomes effective when signed by the IRB Chair and any appropriate coordinating official(s) on the date indicated.

5. Each SOP designates the date on which it originally became effective as well as the most recent revision date, which serves as the effective date for the SOP. The most recent revision date is the version currently in effect.

6. IRB staff save the revised SOPs in the SCRIHS database. The designated IRB staff person also posts the updated SOP to the SCRIHS website and the electronic IRB submission system and advises IRB staff and/or IRB members of the revisions.

7. IRB staff and IRB members are informed of all changes in the SOPs that are relevant to their job functions via email, individual meetings, and/or staff meetings, direct mailings, presentations and/or the SCRIHS website.

8. If an SOP impacts investigators/study personnel, IRB staff or a designee provides this information to them through the SCRIHS website and disseminates changes through a variety of educational initiatives (e.g., mass email, newsletters, presentations).

9. IRB staff or designee informs institutional officials of all changes in the SOPs when appropriate.

Review of Standard Operating Procedures

1. IRB staff or designee conducts a periodic review of all current SOP's, but not less than once every two years for the continued suitability and correctness of the SOPs.

2. IRB staff may review SOPs at any time for accuracy/applicability. The IRB/IRB staff obtain information necessary to update procedures through monitoring of sources including, but not limited to, the U.S. Food & Drug Administration website, Department of Health & Human Services, and the Office for Human Research Protections listserv.

3. If significant or applicable changes to procedures become necessary, IRB staff will then revise the SOP in question following the procedures outlined above. (See *Revisions to Standard Operating Procedure section)*

Suspension or Archiving a SOP

1. When an SOP is suspended or becomes obsolete, the IRB manager or designee informs appropriate staff and/or IRB members, and ensures that IRB staff remove the SOP from the SCRIHS website and electronic IRB submission system, and database and archive it, as appropriate.

Record Keeping

1. IRB staff maintain copies of all current SOPs in electronic files. The designated IRB staff person archives copies of all previous editions of the SOPs in the SCRIHS database.

2. IRB staff place the electronic files into the SOP folder in the SCRIHS database. IRB staff maintain electronic copies of all original and subsequent revisions of all SOPs indefinitely.

REFERENCES

Not applicable

EXTERNAL RESEARCH AND IRB RELIANCE

EFFECTIVE DATE: October 10, 2012

REVISION DATE: September 25, 2015

OBJECTIVE

To describe the procedures for coordination of Southern Illinois University School of Medicine (SIU-SOM) Institutional Review Board (IRB), also known as the Springfield Committee for Research Involving Human Subjects (SCRIHS), research review and oversight for research involving human subjects which is conducted at external site(s).

GENERAL DESCRIPTION

External research activities are subject to special procedures for coordination of research review and may involve more than one IRB responsible for research oversight. In these cases, SIU-SOM IRB has established additional procedures to define the responsibilities of each IRB, coordinate communication among responsible IRB committees, and manage information obtained in external research to ensure protection of human subjects. In coordinating external research reviews, SCRIHS staff, in consultation with SIU-SOM Legal Counsel, takes into consideration the source of funding for the research activity, federal regulations, specific sponsor regulations governing human research protections, and institutional policies.

The SIU-SOM IRB requires additional information and documentation for research that meets the definition of external research. Institutional policies apply to all external research involving human subjects regardless of funding source.

In addition, SIU-SOM IRB may enter into formal agreements with other sites which are not legal entities of SIU-SOM to provide research review (i.e., to act as the relied-upon IRB), to rely on other institutions for research review, or to cooperate in review. SIU-SOM enters into these types of arrangements through an IRB Authorization Agreement.

Definitions

The term *internal research* designates research conducted at performance sites that fall under the authority of SIU-SOM IRB.
The term *external research* designates research conducted at performance sites that are not covered under the authority of SIU-SOM IRB. SIU-SOM requires a letter of acknowledgement/approval from appropriate administrator that the research can be performed at the external site, unless SIU-SOM has a prior written agreement or memorandum of understanding with the site.

PROCEDURES

External Research and Associated Requirements

1. The institution is responsible for ensuring that all performance sites and investigators engaged (See federal guidance on Engagement in Research http://www.hhs.gov/ohrp/policy/engage08.html) in its federally supported research involving human subjects operate under an appropriate Office for

Human Research Protections (OHRP) or other federally approved Assurance. In general, institutions affiliated solely through professional or collaborative arrangements apply to OHRP for their own Assurance. OHRP offers a number of different Assurance mechanisms, including the FWA, Individual Investigator Agreement, and IRB Authorization Agreements. If a federal agency that is not a division of the DHHS supports the research, there may be additional requirements. SCRIHS staff determine these additional requirements on a case-by-case basis with the sponsoring agency.

2. External sites determine the appropriate Assurance mechanism with assistance from the OHRP based on such issues as the funding source, nature of the research, ownership of the performance site, and affiliation of the individuals collecting the data.

3. When a performance site without an IRB is "engaged" in research, SCRIHS advises the PI and assists in obtaining the appropriate Assurance and IRB approvals.

4. External sites submit an application for an Assurance to the OHRP and designate an institutional Signatory Official with authority to represent and commit the entire institution and all of its components to a legally binding agreement. If the Signatory Official is not legally authorized to represent an entity, it may not be covered under the Assurance.

5. In some cases, an institution may operate under another institution's Assurance with the approval of the supporting agency. In such cases, SIU-SOM may enter into a formal IRB Authorization Agreement with the collaborating institution for review, approval, and continuing oversight of the research in question.

6. The institution's Assurance may also cover independent investigators who are not an employee of the institution only in accordance with a formal written agreement of commitment to relevant human subject protection policies and IRB oversight. The institutions may formalize such agreements under the sample OHRP Individual Investigator Agreement or by a commitment agreement developed by the institutions. The institution entering into the commitment agreement maintains the agreement on file and submits copies to OHRP upon request.

<u>Negotiation of an IRB Authorization Agreement with an External Site(s)</u>

1. Under an IRB Authorization Agreement, both institutions agree that one institution is responsible for providing IRB review and the second will rely on the other for IRB review. IRB Authorization Agreements list the federal Assurance number for each institution and designates whether the agreement applies to all human subjects research or is limited to specific project(s).

2. The authorized Signatory Officials for both institutions must approve the agreement in writing. The SIU-SOM Dean and Provost signs all IRB Authorization Agreements as the Signatory Official for SIU-SOM under its Assurance. Both institutions maintain an IRB Authorization Agreement on file and agree to submit the document to OHRP upon request.

3. Cooperative research studies involving multiple institutions may rely on cooperative review. In such cases, participating IRBs enter into a written cooperative review agreement identifying the specific IRB designated to provide review and detailing the respective responsibilities of the IRB and each institution under the review agreement.

4. The IRB which agrees to review studies conducted at another institution (primary IRB) has the responsibility for initial and continuing review of the research. The primary IRB takes into account the required criteria for approval, the applicable regulations (e.g. 21CRF 50 or 56), the facilities and

capabilities of the other institution, the measures to be taken by the participating institution to ensure compliance with the IRB's determinations, and community attitudes or local research context, as appropriate.

5. The primary IRB under an IRB Authorization Agreement is responsible for conveying approvals to the respective PI or directly to the IRB.

6. In cases in which SIU-SOM relies on another designated IRB under an IRB Authorization Agreement, the PI, with assistance from SCRIHS, is responsible for providing information to the external IRB assuring sufficient consideration of local research context for the SIU-SOM component(s) of the study.

7. When the SIU-SOM IRB relies on an external IRB for review of research under an IRB Authorization Agreement, it agrees to abide by the decisions and determinations made by the external IRB.

8. Likewise, individual investigators agree to abide by those same decisions and determinations and may not modify or alter the research protocol without prior written approval of the external IRB.

Sites Operating under a Formal Agreement with the Southern Illinois University School of Medicine IRB

1. SIU-SOM may enter into a formal agreement to serve as the relied-upon IRB for a single external site, which is not a legal entity of SIU-SOM, by signing a Memorandum of Understanding, contract, or other official written agreement. In these cases, the formal agreement outlines the relationship between the institutions and documents the authority granted to the institution to serve as the relied-upon IRB for the external site.

2. Sites operating under a formal agreement must file their own individual Assurance with the OHRP and list SIU-SOM IRB as the designated IRB on the Assurance. The Signatory Official for each institution signs all formal agreements. The Dean and Provost serves as the Signatory Official for SIU-SOM.

3. The terms of the formal agreement specify appropriate human subjects education and training resources for investigators at the cooperating site as well as education and training for SIU-SOM IRB members pertaining to IRB knowledge of the local research context, including distinct subject populations.

IRB Knowledge of Local Research Context

1. In accordance with OHRP guidance, when the SIU-SOM IRB serves as the relied-upon IRB for another institution or when the research involves distinct subject populations (non-English speaking populations, veterans, etc.), the SIU-SOM IRB ensures that it possesses or obtains sufficient knowledge of the local research context even when the IRB is geographically removed from the external research location.
2. The PI supports the IRB in understanding the local research context by providing the IRB necessary information, as appropriate, on:
   - The anticipated scope of the external facility's research activities;
   - The types of subject populations likely to be involved;
   - The size and complexity of the institution;
   - Institutional commitments and regulations;
   - Applicable law;

- Standards of professional conduct and practice;
- Method for equitable selection of subjects;
- Method for protection of privacy of subjects;
- Method for maintenance of confidentiality of data;
- Languages understood by prospective subjects;
- Method for minimizing the possibility of coercion or undue influence in seeking consent;
- Safeguards to protect the rights and welfare of vulnerable subjects.

3. SCRIHS staff assist the PI in addressing the requirements for information on the local research context upon request.

4. SCRIHS staff assist the IRB in identifying appropriate consultants and distributing appropriate review materials pertaining to the local research context to IRB members, as appropriate.

REFERENCES

Office for Human Research Protections (OHRP)
Engagement Memo
Terms of the Federalwide Assurance of Protection for Human Subjects
Sample Unaffiliated Investigator Agreement
Food and Drug Administration (FDA)
Cooperative Research Guidance
Non-Local IRB Review Guidance
21 CFR parts 50 and 56
45 CFR 46.114

TYPES OF IRB REVIEWS

INITIAL FULL BOARD REVIEW

EFFECTIVE DATE: June 8, 2011

REVISION DATE: October 9, 2013; June 11, 2014; July 1, 2015

OBJECTIVE

To describe the policy and procedures for initial full board review by the Institutional Review Board (IRB)

GENERAL DESCRIPTION OF POLICY

The IRB conducts initial review for non-exempt research at convened meetings unless the research is eligible for expedited initial review. The IRB follows the procedures for conducting a convened meeting, the definition of *quorum*, and the requirements for conducting a full board review meeting as described in the Conduct of IRB Meeting SOP. Investigators must submit studies that do not meet the federally mandated criteria for exempt or expedited initial review for full board review. (See Exempt and Expedited Review SOPs.) The IRB only approves research that meets the federal criteria for approval as specified in 45 CFR 46.111 and 21 CFR 56.111. During initial full board review the IRB reviews the informed consent process and documentation as specified in the Informed Consent SOP.

PROCEDURES

Submission and Screening

1. The PI or designee submits an application, following all instructions, for IRB review of a research protocol for initial full board review and submits it to SCRIHS using the electronic IRB system. In addition to the application, the PI or designee should submit the following (when applicable): a protocol, consent form(s), HIPAA authorization, questionnaires, advertisements (or any other subject recruitment materials), and data collection forms. For drug or device related clinical studies an investigator's brochure, technical manual, instructions for use, SCRIHS Study Personnel Conflict of Interest (COI) Disclosure Form, or other materials need to be included as well.

2. SCRIHS staff screen the application to determine whether it is complete (e.g., includes all pertinent forms and appropriate signatures). If it is not complete, SCRIHS staff return the application to the investigator within the electronic IRB system. Once the investigator has provided the missing information the application can be resubmitted to SCRIHS.

3. SCRIHS staff screen the IRB application to ensure compliance with pertinent federal requirements. Examples of screening include, but are not limited to, the items listed below.

    - Using the information on the application, SCRIHS staff screen to determine whether the PI addressed off-site issues following procedures outlined in the External Research and IRB Reliance SOP.

    - If the investigator checks items on the application that indicate the research involves prisoners, SCRIHS staff send the protocol to a prisoner representative for review.

    - If the investigator indicates in the application that the research involves an investigational new drug (IND) or investigational device exemption (IDE), SCRIHS

staff confirm the validity of the IND or IDE number by ensuring that the investigator has included a copy (containing the number) of the detailed protocol from the sponsor and/or verification statement from the sponsor or the Food and Drug Administration (FDA).

- SCRIHS staff screen the application to determine whether research involves vulnerable subjects and/or sensitive types of research/procedures (e.g., HIV screening). If so, SCRIHS staff add a notation on the agenda for the meeting referring IRB members to the pertinent guidance.

- SCRIHS staff screen the SCRIHS Study Personnel Conflict of Interest (COI) Disclosure Form submitted for the Authorized Study Personnel (ASP). If the ASP answered "yes" to any of the questions on the form, SCRIHS staff and the IRB follow procedures outlined in the Conflict of Interest Policy.

Reviewer Assignments and Reviewer Responsibilities

4. SCRIHS staff schedule the IRB submission on the agenda for the next available meeting. The IRB meets once a month.

5. SCRIHS staff assigns a primary and secondary reviewer based on the IRB members' experience, educational background, and expertise. If no IRB member has the appropriate expertise, SCRIHS staff may ask an ad hoc consultant to serve as a tertiary reviewer.

6. For all investigator-initiated protocol applications, SCRIHS staff assign a primary and secondary reviewer and a tertiary reviewer who has adequate knowledge in the area of scientific design.

7. In conducting the initial review of the proposed research, the assigned IRB reviewers utilize the electronic *Reviewer Checklist.*

8. The assigned reviewers are responsible for:
   - Comparing the protocol with the IRB application;
   - Informing the full board IRB of any discrepancies between the detailed protocol and the application materials;
   - Comparing the sections of the approved sample informed consent document with the SCRIHS proposed form to ensure that the sections of the consent are consistent;
   - Conducting an in-depth review.

9. SCRIHS staff screen the protocol to determine whether additional expertise is necessary to conduct the review. If so, SCRIHS staff may ask an ad hoc consultant who has appropriate expertise in the discipline to participate in the review. SCRIHS may contact IRB members, SIU-SOM faculty, or department chairs for advice in identifying consultants.

10. SCRIHS staff ensure that ad hoc consultants do not have a conflict of interest in accordance with the IRB Member and Consultant Conflict of Interest SOP. SCRIHS staff send the ad hoc consultants the same information as voting IRB members and a detailed protocol, if applicable.
11. The IRB encourages PI's or their designees to attend the IRB meeting to present a brief synopsis (3-5 minutes) of their research proposal and to provide clarification or answers to any reviewer questions.

Review Process

1. Approximately five (5) to ten (10) days prior to each convened meeting, SCRIHS staff notify the IRB members of their review assignments. Notices are generated from the electronic IRB system. A copy of the agenda is available to all members, and the Dean, within the electronic IRB system.

2. All IRB members have access to all study materials as they are posted electronically on the IRB agenda. All IRB members have the opportunity to discuss each research protocol during the convened meeting.

3. Ad hoc consultants may provide comments or recommendations in writing to the IRB prior to the meeting or attend the convened meeting to participate in the review. SCRIHS staff maintain documentation of written comments or reports in the protocol file. In cases where the consultant participates in the meeting, the minutes of the meeting document the information provided by the consultant. (See Minutes of IRB Meetings SOP)

4. IRB members are encouraged to contact the PI directly, prior to the meeting, if they have any questions or concerns regarding the protocol review.

IRB Approval Process

    1. A majority of the voting IRB members (or their designated alternates), including at least one member whose primary concerns are in nonscientific areas, must be present in order to conduct a convened meeting. In order for the IRB to approve the proposed research, the protocol must receive the approval of a simple majority of those members present at the meeting. (See The Conduct of IRB Meetings SOP)

    2. When the IRB reviews research that involves categories of human subjects vulnerable to coercion or undue influence, SCRIHS staff ensure that adequate representation or consultation is present for discussions of research involving vulnerable human subjects. (See Protection of Vulnerable Subjects SOP and Membership of IRB SOP)

3. All IRB members attending the meeting have access to the materials listed in the *Submission and Screening* section above, prior to the convened meeting, and have the opportunity to discuss each research protocol during the convened meeting, and participate in the determination of whether the research meets the regulatory criteria for approval.

4. If the PI or designee attends the convened IRB meeting, the IRB reviews each initial full board review submission with the PI or designee present. After the PI or designee leaves the meeting, the IRB reviews the submission and discusses any controverted issues, or any other issues, and their resolution prior to voting.

5. During discussion, the IRB members raise those issues that the committee determines do not meet the federal criteria for approval as specified in 45 CFR 46.111, 21 CFR 56.111, and 38 CFR 16.111. In addition, the IRB determines whether the risk level assigned by the PI is appropriate. The IRB considers whether the PI's preliminary assessment of federally mandated specific findings requirements (e.g., request for waiver of informed consent) is acceptable with respect to meeting federal requirements.

6. For research involving a new drug or new device where the PI or the sponsor has not obtained an IND or IDE, the committee determines what action(s) is needed (whether the PI needs to obtain an

IND/IDE or whether PI needs to contact the FDA for guidance). The PI needs to submit, or the PI needs to request from the study sponsor, documentation of any correspondence with the FDA.

7. A member or consultant with a conflict of interest must leave the room during the vote and only participate in the review by providing information in accordance with the IRB Member and Consultant Conflict of Interest SOP.

Review Outcome(s)

1. An IRB member makes a motion, another member seconds the motion, and then the convened IRB votes for or against or abstains from one of the following actions:

   APPROVED: IRB approval indicates that the IRB has concluded that the research and consent/assent forms meet the federal criteria for approval. IRB approval verifies that the IRB agrees with the assessment of the submission and/or specific findings as described by the PI in the submission. SCRIHS staff send the PI an approval letter accompanied by an informed consent/assent document (if applicable) with the affixed "IRB Approval" validation stamp, which includes valid dates of IRB approval. SCRIHS Staff enter the new study approval into the electronic IRB system. If applicable, SCRIHS notifies each hospital of study approval using the electronic IRB system. The start of the approval period is the date of the IRB meeting.

   APPROVED WITH CONTIGENCIES and/or ADDITIONAL INFORMATION REQUIRED: The IRB has approved the submission pending completion of minor revisions. The IRB can give the IRB Chair or designee the authority to approve the minor revisions which do not involve substantive issues. If there are substantive issues, the assigned IRB reviewers may request to see the revisions before final approval is granted by the IRB Chair or designee. If IRB reviewers request to see the revisions, but cannot complete a review of the revisions in a timely manner then the revisions will be sent to the IRB Chair or designee for review. SCRIHS staff send the PI a letter describing the revisions requested by the IRB.

   The PI responds to the IRB's suggested revisions in the electronic IRB system and submits the response to SCRIHS staff, who submits the response to the IRB Chair or assigned reviewers for further review. The Chair or designee may forward the responses to the entire IRB for additional review, request additional information, or approve.

   Once approved, SCRIHS staff enter the new study approval into the electronic IRB system. If applicable, SCRIHS staff notify each hospital of approval using the electronic IRB system.

   For full board approval with conditions/revisions, the date of the start of the approval period is the date on which the IRB Chair, or designee, has reviewed and approved the requested conditions/revisions.

   TABLED: The IRB withholds approval pending submission of major revisions/additional information. SCRIHS staff send the PI a letter using the electronic IRB system. The letter lists the reasons for tabling the application and includes a description of the revisions or clarifications requested. The IRB can request that the PI attend the future meeting at which the IRB reviews his/her response to discuss or answer IRB concerns or questions. The PI must respond in writing to the requested revisions and/or clarifications. The PI is encouraged to attend the next available meeting to respond to any further questions or points of clarification. SCRIHS staff schedule the PI's response to the requested revisions for review by the full board committee for the next available meeting.

DISAPPROVED: If a research study is disapproved, SCRIHS staff send the PI a letter, using the electronic IRB system, describing the reasons for disapproving the application and give the PI an opportunity to respond in person or in writing. Disapproval of the application usually occurs when the IRB determines that the risk of the procedures outweighs any benefit to be gained or if the proposed research does not meet the federal criteria for IRB approval. Disapproval does not prohibit the PI from revision and resubmission of the protocol.

2. During the convened meeting, the IRB determines the approval period, as appropriate to the degree of risk but not less frequently than once per year. The IRB may set a shorter approval period for high risk protocols or protocols with high risk/low potential benefit ratios.

3. Before issuing approval, SCRIHS staff ensure that all study personnel have completed the required training. If the PI and study personnel have not completed training, SCRIHS staff notify the PI in writing.

4. If the research involves prisoners, SCRIHS staff check to determine whether the PI submitted the protocol for funding to any DHHS agency. If this is the case, and the protocol involves prisoners, SCRIHS staff, with input from the PI, prepare and submit a prisoner certification report to the Office for Human Research Protection (OHRP) in accordance with OHRP requirements and the Mandated Reporting to External Agencies SOP.

5. Once the IRB approves a research study, SCRIHS staff send an approval letter to the PI, which includes the approval period, a reminder to use only the approved consent/assent form, a reminder that the IRB must approve any changes to the protocol, or approved procedures, and a reminder that approval may be necessary from other entities where research is to be conducted prior to initiation of the changes.

6. At IRB approval, it is the PI's responsibility to request an IRB Statement of Compliance if the protocol falls under the International Conference on Harmonisation guidance related to Good Clinic Practice. The SCRIHS office maintains a statement of compliance signed by the IRB Chair and provides that statement upon request.

7. If the PI has concerns regarding the IRB decision/recommendations for changes in the study, he/she may submit them to the IRB via a written document that includes a justification for changing the IRB decision. The IRB reviews the request using the standard procedures.

8. All written correspondence to and from SCRIHS should be conducted using the appropriate mechanisms within the electronic IRB system. This includes outcome letters, responses to stipulations/concerns, documentation of training, and all other written notifications as outlined in the above paragraphs.

REFERENCES

21 CFR 50.25
21 CFR 56.111
45 CFR 46.108
45 CFR 46.111
45 CFR 46.116
45 CFR 46.117
45 CFR 46 Subparts B

45 CFR 46 Subparts C
45 CFR 46 Subparts D & 21 CFR 50 Subpart D

EXPEDITED REVIEW PROCEDURES

EFFECTIVE DATE: August 26, 2009

REVISION DATE: November 13, 2013; March 11, 2015; April 8, 2015

OBJECTIVE

To describe the policies and procedures for conducting initial expedited reviews

GENERAL DESCRIPTION

Southern Illinois University School of Medicine's (SIU-SOM) Institutional Review Board (IRB), SCRIHS, uses an expedited review process to review studies that meet the categories adopted by the Department of Health and Human Services (DHHS) and the Food and Drug Administration (FDA) that involve no greater than "minimal risk." The expedited applicability criteria, including the definition of "minimal risk", and federally mandated categories are attached. Expedited review procedures allow SCRIHS to review and approve studies that meet the criteria in the attached document without convening a meeting of the full IRB. The SCRIHS Chair or one or more experienced reviewers from among the SCRIHS committee conducts expedited reviews.

Expedited reviewers only review and approve research that meets the federal criteria for approval as specified in 45 CFR 46.111 and 21 CFR 56.111. Also, expedited reviewers ensure that the study's informed consent process and documentation meets the requirements as specified in 45 CFR 46.116 and 21 CFR 50.25 unless the IRB waives the requirements in accordance with federal regulations.

Expedited reviewers exercise all of the authority of SCRIHS except that the reviewers may not disapprove the research. The IRB only disapproves a research activity in accordance with non-expedited procedures set forth in the DHHS and FDA regulations.

The IRB agenda for convened meetings advises SCRIHS of research studies approved using expedited review procedures. The IRB minutes also reflect these approvals. Any IRB member can review the entire electronic IRB file for an expedited study.

PROCEDURES

Assigning Reviewers

1. SCRIHS staff assigns initial expedited reviews to the Chair-designated IRB member(s).

2. The expedited reviewer notifies SCRIHS staff if he/she is not available to conduct expedited review or has a conflict of interest.

Review Documents

1. Expedited reviewers will electronically review the following documents and IRB forms:
    - Appropriate SCRIHS Application;
    - Protocol;
    - Informed consent/assent process and forms, including waiver requests,
    - HIPAA language, including waiver requests;

- Any additional materials, including advertisements, data collection forms, letters, etc;
- Vulnerable populations, including determinations for research involving individuals with consent capacity impairment, pregnant women, fetuses and/or neonates, prisoners, or children;

2. Expedited reviewers review all information in the expedited review submission packet in enough depth to be familiar with the protocol, to determine whether the research is eligible for expedited review, and to determine whether the research meets the regulatory criteria for approval.

Submission and Screening

1. The PI/Study personnel makes a preliminary determination that a protocol is eligible for expedited review based on the criteria included in this document. SCRIHS makes the final determination regarding whether a protocol is eligible for expedited review.

2. The PI/Study personnel completes an expedited review application and submits to SCRIHS using the electronic IRB system. All necessary forms and templates needed for expedited study submission are available within the electronic IRB system. The PI/Study Personnel is encouraged to call SCRIHS staff for submission guidance.

3. Upon receipt of the electronic submission packet, SCRIHS staff pre-review for completeness and accuracy and make a preliminary determination that the application meets the criteria for expedited review, including minimal risk and identifies the research categories. If the submission does not meet the criteria for expedited review, SCRIHS staff advise the PI/Study personnel to resubmit the study accordingly.

4. SCRIHS staff review the submission for areas of research requiring federally mandated specific findings (such as research with prisoners, pregnant women, children, etc.). SCRIHS staff use the electronic IRB system to alert the expedited reviewer(s) of the areas requiring determinations.

5. SCRIHS staff also screen for Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule and/or Family Educational Rights and Privacy Act (FERPA) concerns.

6. After completing pre-review screening, SCRIHS staff assign the submission to a reviewer through the electronic IRB system.

Expedited Review Process

1. The assigned reviewer conducts expedited initial review. The reviewer must utilize the electronic IRB system to complete the review. The assigned expedited reviewer conducts expedited reviews outside of a convened meeting. If the assigned reviewer is unable to complete the expedited review, the reviewer must notify SCRIHS staff, via email or phone, within 24 hours of initial assignment. SCRIHS staff will then reassign the expedited review to another reviewer.
2. If the reviewer does not provide assignment feedback within approximately 5 working days, SCRIHS staff either reminds the reviewer of the assignment or forwards the submission to another reviewer.

3. The expedited reviewer contacts the PI/Study personnel for any clarification needed and documents the issues discussed within the electronic IRB system. The expedited reviewer makes determinations for specific findings using the information from the initial submission packet and records his/her determinations in the electronic IRB system's *Reviewer Checklist*.

4. The reviewer also documents any issues pertaining to special findings (e.g., requests for waiver of informed consent or documentation or Subpart B, C, D findings) within the electronic IRB system. The reviewer raises any issues, including controverted issues, that he/she has determined do not meet the federal criteria for approval or Southern Illinois University School of Medicine (SIU-SOM) IRB policies.

5. Upon receipt of the expedited reviewer's recommendations, SCRIHS staff notify the PI of the outcome through the electronic IRB system.

Review Outcomes

1. Expedited reviewers make the final determination as to whether the proposed research activities meet the expedited review criteria outlined in the attached document.

2. Expedited reviewers also determine whether the research meets the federal criteria for approval as outlined in 45 CFR 46.111 and 21 CFR 56.111.

3. Expedited reviewers also ensure that the investigator will conduct the informed consent process and obtain documentation of informed consent, as specified in 45 CFR 46.116 and 117 and 21 CFR 50.25, unless the IRB waives the requirements in accordance with federal regulations.

4. The expedited reviewers raise any issues, including controverted issues, or request changes that they have determined do not meet the federal criteria for approval or SIU-SOM IRB policies.

5. The expedited reviewers document on the *Reviewer Checklist*, in the electronic IRB system, their determinations regarding expedited eligibility, applicable expedited category, and whether the research meets the federal criteria for approval.

6. The expedited reviewers make one of the following three determinations in regard to the protocol and consent forms:

    - APPROVED: SCRIHS approval indicates that the expedited reviewer has concluded that the research and consent forms meet the federal criteria for approval. SCRIHS staff forward the application to the SCRIHS Chair or designee for final approval via the electronic IRB system. The final approval is then routed to the PI/Study personnel through the electronic IRB system.

    - REVISIONS/ADDITIONAL INFORMATION REQUIRED/NO ACTION TAKEN: The expedited reviewer withholds approval pending submission of revisions/additional information. The PI/Study Personnel is notified via the electronic IRB system of the requested revisions/additional information request. The PI/Study Personnel responds to revisions requested by the IRB via the electronic IRB system. SCRIHS staff forward those responses to the expedited reviewer for further review, if requested, or to the SCRIHS Chair or designee for final review and approval via the electronic IRB system.

    - FULL REVIEW REQUIRED: The expedited reviewer may determine that the protocol requires full review by the IRB at a convened meeting.

7. The expedited reviewer can determine that the research is eligible for a less stringent mechanism of review (i.e., the project is exempt from requirements for review or the activities do not fall under the purview of the IRB). In these cases, SCRIHS requires a revision to the application submission

documenting within the electronic IRB system the rationale for determining that the activities do not meet the federal definitions of *research*, *clinical investigation*, or *human subject.*

8. Once the expedited reviewer approves the study, he/she assigns the approval period at intervals appropriate to the degree of risk but not less than once per year. The date the IRB Chair or designee provides final approval on the study is the date the approval period starts.

9. If the PI has concerns regarding the IRB decision/recommendations for changes in the study, he/she may submit his/her concerns to SCRIHS staff via a written document, via the electronic IRB system, that includes justification for changing SCRIHS's decision. SCRIHS staff forward the PI's written concerns to the expedited reviewer and the SCRIHS Chair or designee for final resolution. If the investigator is still dissatisfied with the IRB decision, SCRIHS staff place the submission on the next agenda for the convened SCRIHS meeting for review.

REFERENCES

21 CFR 56.102(i)
21 CFR 56.110
21 CFR 56.111
45 CFR 46.102(i)
45 CFR 46.110
45 CFR 46.111

FEDERALLY MANDATED EXPEDITED REVIEW CRITERIA – EFFECTIVE NOVEMBER 9, 1998 – DEFINITION OF MINIMAL RISK GUIDANCE TO PI AND REVIEWERS

Expedited procedures can only be used to review a study if the only involvement of human subjects fits one or more of the categories specified in the federal regulations and if all of the procedures present no greater than "minimal risk."

The IRB reviewer confirms that **all of the research activities** fit in one or more of the expedited categories. If the research includes activities that do not fit in the categories, the study is not eligible for expedited review even if the research involves "minimal risk."

The Department of Health and Human Services defines *minimal risk* to mean "the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests" [45 CFR 46.102(2)(i)].

Investigators are asked to provide a risk assessment, but it is the IRB reviewer's responsibility to determine whether the research meets the federal definition.

The IRB reviewer must consider two questions:

- Is the probability of the harm or discomfort anticipated in the proposed research greater than that encountered ordinarily in daily life or during the performance of routine physical or psychological examinations or tests? OR

- Is the magnitude of the harm or discomfort greater than that encountered ordinarily in the daily life or during the performance of routine physical or psychological examinations or tests?

If the answer is "yes" to either of these questions, then the research does not meet the definition of minimal risk.

Federal Expedited Review Applicability and Categories

(A) Research activities that (1) present no more than minimal risk to human subjects, and (2) involve only procedures listed in one or more of the following categories, may be reviewed by the IRB through the expedited review procedure authorized by 45 CFR 46.110 and 21 CFR 56.110. 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.

(B) The categories in this list apply regardless of the age of subjects, except as noted.

(C) The expedited review procedure may not be used where identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.

(D) The expedited review procedure may not be used for classified research involving human subjects.

(E) IRBs are reminded that the standard requirements for informed consent (or its waiver, alteration, or exception) apply regardless of the type of review—expedited or convened—utilized by the IRB.

(F) Categories one (1) through seven (7) pertain to both initial and continuing IRB review.

Research Categories

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 expedited 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.

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[1] considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week.

3) Prospective collection of biological specimens for research purposes by noninvasive means. Examples: (a) Hair and nail clippings in a 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.

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 expedited review, including studies of cleared medical devices for new indications.) Examples: (a) Physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject's privacy; (b) weighing or testing sensory acuity; (c) magnetic resonance imaging; (d) electrocardiography,

electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography; (e) moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

5) Research involving materials (data, documents, records, or specimens) that have been collected or will be collected solely for 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.)

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

7) Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies. (Note: Some research in this category may be exempt from the 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.)

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.

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.

EXEMPT REVIEW

EFFECTIVE DATE: February 8, 2012

REVISION DATE: May 29, 2015

OBJECTIVE

To describe the policies and procedures for the exempt review process

GENERAL DESCRIPTION

Research procedures that meet the categories set forth by federal regulations [45 CFR 46.101(b); 21 CFR 56.104(d); 38 CFR 16.102(b)] may qualify for exemption. The Institutional Review Board (IRB), also known as SCRIHS, must review and approve all exemption requests. Research activities are exempt from the human research protection regulations when the only involvement of human subjects falls within one or more categories below.

1. Research conducted in established or commonly accepted educational settings, involving normal education practices, such as:
    - Research on regular or special educational instructional strategies, **or**
    - Research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

    This category does not apply to Food and Drug Administration (FDA) regulated research.

2. Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, unless:
    - Information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; **and**
    - Any disclosure of the human 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.

    This category does not apply to FDA regulated research.

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 the exemption regulations, if:
    - The human subjects are elected or appointed public officials or candidates for public office; **or**
    - Federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.

    This category does not apply to FDA regulated research.
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.

This category does not apply to FDA regulated research.

5. Research and demonstration projects which are conducted by or subject to the approval of federal Department or Agency heads, and which are designed to study, evaluate, or otherwise examine:
    - Public benefit or services programs;
    - Procedures for obtaining benefits or services under those programs;
    - Possible changes in or alternatives to those programs or procedures; or
    - Possible changes in methods or levels of payment for benefits or services under those programs.

    This category does not apply to FDA regulated research.

6. Taste and food quality evaluation and consumer acceptance studies:
    - If wholesome foods without additives are consumed; **or**
    - If a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the FDA or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

The IRB must review research in categories that are exempt from the federal human research requirements to determine whether an exemption is appropriate.

PROCEDURES

Submission and Screening

1. The PI makes a preliminary determination that a protocol is eligible for exempt review based on an assessment of the protocol establishing that it falls into one or more of the categories specified in the federal regulations. The IRB reviewer makes the final determination regarding whether a protocol is eligible for exemption.

2. The PI utilizes the electronic IRB system to submit a study for exempt review. If the investigator has questions he/she may call the SCRIHS office for assistance.

3. Upon receipt of the application, designated SCRIHS staff screens the application including the informed consent process and documentation for completeness and accuracy. The designated SCRIHS staff reviews the PI's exempt category selection for appropriateness. The designated SCRIHS staff forwards the submission packet to an exempt reviewer. If it is clear to the designated SCRIHS staff the application does not meet the criteria for exempt review, the designated SCRIHS staff contacts the PI and recommends that he/she consider resubmitting either an expedited or full review application.

4. In addition, SCRIHS staff screen for Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule and/or Family Educational Rights to Privacy Act (FERPA) concerns. If there is a HIPAA or FERPA concern, SCRIHS staff notifies the exempt reviewer and seek guidance from appropriate sources if necessary.

5. Based on the screening, SCRIHS staff contact the PI for any additional information needed for a thorough review.

Assigning Reviewers

1. SCRIHS staff assigns exemption requests to the IRB Chair or a designated IRB member for review and approval.

2. The assigned reviewer is responsible for notifying the SCRIHS staff if he/she is not able or available to conduct the review during the period assigned. The reviewer is also responsible for notifying SCRIHS staff if he/she has a conflict of interest as outlined in the IRB Member and Consultant Conflict of Interest SOP.

IRB Exempt Review

1. The reviewer for exempt protocols electronically receives the following:
    - Completed exemption application
    - Data collection instruments (if applicable)
    - Any applicable HIPAA forms
    - Any additional information SCRIHS staff may have requested from the PI or SCRIHS recommendations to reviewer

2. The reviewer is responsible for reviewing the application upon receipt to determine that all of the research procedures fit one or more of the exemption categories specified in the federal regulations. The reviewer ensures that the research meets ethical principles and standards for protecting research subjects.

3. During review, the reviewer ensures that the research does not include any of the following:
    - Prisoners;
    - Survey or interview techniques which include children as subjects (this applies to exemption category #2 only);
    - The observation of children where the investigator participates in the activities being observed (this applies to exemption category #2 only);
    - FDA-regulated research (this applies to exemption categories #1-5).

4. The reviewer contacts the PI through the electronic IRB system for any clarification needed.

5. If the reviewer is unable to respond within approximately 5 days, SCRIHS staff sends up to two reminders. If the reviewer is still unable to respond, SCRIHS staff forwards the protocol to the IRB Chair or Vice Chair(s) for review.

Review Outcome(s)

1. The reviewer makes one of the following recommendations by completing the reviewer checklist within the electronic IRB system:
    - Additional information needed to determine exempt status;
    - Required revisions needed to qualify study for exemption;
    - Disapproval of exempt status with rationale for disapproval and recommendations for submission of expedited or full review application;
    - Non-Human Subject Research Determination;
    - Approved.

2. The PI is responsible for submitting any requested revisions to SCRIHS through the electronic IRB system. SCRIHS staff forwards the revisions to the reviewer for review and approval if appropriate. The reviewer determines whether the revisions are sufficient for approval of exempt status, and, if so, the approval is electronically sent to the PI after electronically approved by the Chair or Designee.

3. If the reviewer determines the revisions are inappropriate or insufficient, he/she may request that the PI make further revisions. This review and revision process continues until the research is either approved or disapproved as exempt.

4. If the IRB disapproves the exemption request, the PI may submit the research proposal as an expedited study if the study meets the criteria for an expedited review. If the study does not meet the criteria for an expedited review, the PI submits a full board review application.

5. IRB records for all exempt determinations include the citation of the specific category justifying the exemption.

6. When the IRB has certified a research study as exempt, the IRB does not require continuing reviews. The exemption approval is in effect for a five-year period. Any changes to the approved project must be submitted to the IRB. If the changes are significant, it may require re-submission and a new review. Approximately three months prior to the end of the five-year period, the electronic IRB system automatically notifies the PI that the exemption will expire. The PI must submit a new exemption application if the project is to continue.

7. If the PI has concerns regarding the IRB decision/recommendations for changes in the study, he/she may submit the concerns to the IRB in writing, including a justification for changing the IRB decision. The PI may send the request to the IRB Chair or Vice Chairs for final resolution. If the investigator is still dissatisfied with IRB decision, he/she may send the study to the full board IRB for review.

REFERENCES

45 CFR 46.101(b)
45 CFR 46.102(i)
21 CFR 56.104(d)

CONTINUING REVIEW

EFFECTIVE DATE: June 8, 2011

REVISION DATE: November 13, 2013; October 8, 2014; July 1, 2015

OBJECTIVE

To describe the policies and procedures for conducting continuing review (CR)

GENERAL DESCRIPTION OF POLICY

Southern Illinois University School of Medicine's (SIU-SOM) Institutional Review Board (IRB), SCRIHS, conducts substantive and meaningful CR at intervals appropriate to a protocol's degree of risk but not less than once per year. The research protocol must satisfy the criteria set forth in 45 CFR 46.111 and 21 CFR 56.111 for SCRIHS to approve the protocol for continuation.

PROCEDURES

A. CR Requests, Submissions, and Screening

1. As a courtesy, SCRIHS staff send CR reminders to the PI/study personnel, via the electronic IRB system, before the IRB approval period expires (e.g., approximately 90 days prior to expiration). The PI/study personnel is responsible for responding to the notification in a timely manner. However, the PI is ultimately responsible for submitting CR materials to the IRB in a timely manner.

2. The PI/study personnel completes the electronic IRB system *Continuing Review Submission Form* according to the instructions on the form and submits during the appropriate SCRIHS agenda submission deadline.

3. The PI must submit CR materials for studies as long as the research:
   - Remains open to enroll new subjects;
   - Remains active for long-term follow-up and local participants are included (even when the research is permanently closed to enrollment and all subjects have completed all research-related interventions); and/or
   - Requires analysis of data with identifiers.

4. When the SCRIHS office receives the CR materials, SCRIHS staff conducts a preliminary screening of the materials submitted to ensure the materials are complete and consistent with IRB requirements.

5. Upon receipt of the CR submission, SCRIHS staff screens the CR materials to determine whether the CR is eligible for expedited review.

6. SCRIHS staff screens the CR to determine if the study has been open for three years or more without any local enrollment. If there has not been any local enrollment for three years or more, the PI must justify keeping the protocol open on the CR form within the electronic IRB submission system.

7. SCRIHS staff also screens the CR submission to ensure compliance with selected federal requirements, such as need for prisoner representative review.

8. SCRIHS staff may request additional information or materials from the PI/study personnel, via the electronic IRB system, if the CR submission is not complete. If the PI/study personnel does not respond, SCRIHS staff attempts to contact the PI/study personnel for the additional information/materials, provided there is sufficient time before the end of the approval period.

9. If the SCRIHS office does not receive a response from the PI/study personnel, SCRIHS staff sends the CR to the IRB for review. If the approval period limits the amount of time available to resolve outstanding issues, SCRIHS staff may send the protocol for review "as is" to avoid a lapse of approval. SCRIHS staff forward notes detailing the missing or incomplete materials to the assigned reviewer.

B. Full Board Continuing Review Procedures

1. SIU-SOM IRB conducts full board CR at regularly scheduled convened meetings.

2. A primary reviewer from the IRB committee roster is assigned to review each full board CR submission.

3. Approximately 5-10 days prior to the convened meeting, the primary reviewer receives the complete CR submission for each CR he/she is assigned to review.

4. SCRIHS staff may serve as intermediaries between the PI/study personnel and the IRB primary reviewer. However, the primary reviewer is encouraged to contact the PI/study personnel directly for clarification.

5. All IRB members have access to all study materials as they are posted electronically on the IRB agenda 5-10 days prior to the scheduled convened meeting. All IRB members have the opportunity to discuss each research protocol during the convened meeting.

6. Primary reviewers provide recommendations to the IRB at the convened meeting on issues which they determine do not meet the federal criteria for approval, are controverted or need additional information.

7. If the primary reviewer is unable to attend the meeting, SCRIHS staff provide his/her comments or recommendations in writing for presentation to the IRB at the convened meeting.

8. The convened IRB assesses each CR individually using federal criteria 45 CFR 46.111 and 21 CFR 56.111. At the meeting, the IRB reviews the CR materials and any controverted issues and their resolution prior to voting. During discussion, IRB members only raise those controverted issues that the IRB determines do not meet the federal criteria for approval. IRB approval of the CR materials documents that the IRB agrees with the PI's assessment of any specific findings that might relate to the subject's willingness to continue participation that are included in the CR submission.

9. All IRB decisions/outcomes regarding CR reviews are documented in the IRB meeting minutes.

10. The SIU-SOM Dean and Provost or designee has access to the IRB website and is notified when a new IRB agenda has been posted to the IRB website.

C. Expedited Continuing Review

SCRIHS may use expedited review procedures for CR under the following circumstances:

1. The study was initially eligible and continues to be eligible for expedited review procedures; OR
2. 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
3. Where study personnel have enrolled no subjects locally and no additional risks have been identified either locally or at any site if the research involves a multi-site study; OR
4. The only remaining research activities are limited to data analysis; OR
5. The research involves the study of drugs and/or medical devices AND either does not require an Investigational New Drug (IND) (21 CFR Part 312) and/or an Investigational Device Exemption (IDE) (21 CFR Part 812) and/or the device is approved for marketing and being used in accordance with the approved labeling. SCRIHS must also have determined and documented at a convened meeting that the research is no greater than minimal risk and no additional risks have been identified.

1. The Expedited Review Panel is responsible for the review of expedited CR submissions. If the assigned expedited reviewer has a conflict of interest, is unavailable, or does not have the appropriate expertise to review the CR, SCRIHS staff assign responsibility for the CR to another member of the Expedited Review Panel.

2. SCRIHS staff notify the assigned expedited reviewer, using the electronic IRB system, to complete CR submission for each expedited CR he/she is assigned to review.

3. The assigned expedited reviewer is responsible for reviewing information in the expedited CR reviewer assignment, found within the electronic IRB system, in enough depth to be familiar with the protocol, to determine whether the research is eligible for expedited review, and to determine whether the research meets the regulatory criteria for approval.

4. The expedited reviewer is responsible for making the final recommendation to the IRB Chair that the protocol meets the criteria for expedited review as outlined above. If the expedited reviewer determines full board review is necessary, he/she documents this requirement in the electronic IRB system's *Reviewer Checklist*. Upon receipt of the expedited reviewer's recommendation, SCRIHS staff implement full board CR procedures.

5. The expedited reviewer applies the same criteria for approval as outlined above for full board review (i.e., applies 45 CFR 45.111 and 21 CFR 56.111 and informed consent regulatory criteria). The expedited reviewer raises controverted issues he/she determines do not meet federal criteria and/or may request additional information.

6. When documentation of informed consent/assent is required, the expedited reviewer reviews the informed consent/assent document(s) submitted for re-approval to ensure accuracy and completeness.

7. SCRIHS staff serve as intermediaries between the PI/study personnel and the Expedited Review Panel reviewer. However, the expedited reviewer may contact the PI/study personnel directly for clarification.

8. The expedited reviewer documents any determination pertaining to specific findings, as mandated by federal regulations, that were not previously addressed by the IRB. (Expedited reviewer approval of

the CR materials documents that the reviewer agrees with the PI's assessment of the specific findings).

9. The expedited reviewer ensures that the PI/study personnel provides any significant new findings that might relate to the subject's willingness to continue participation in accordance with regulations.

10. If the approval might lapse before completion of the CR, the expedited reviewer can make a determination to allow subjects currently participating to continue in accord with procedures described in the section below on lapses of approval. (Refer to Section E)

11. Expedited CR approvals are automatically posted on the next available IRB meeting agenda within the electronic IRB system.

D. Review Outcome(s)

1. For full board CR, an IRB member makes a motion, the motion is seconded, and then SCRIHS members vote for, against, or abstain from one of the following actions:

- APPROVED: IRB Approval - IRB concluded that the research and, if applicable, consent forms meet the federal criteria for approval. The IRB's approval vote verifies that the IRB members agree with the information/materials submitted for continuation of the protocol and/or specific findings described in the CR materials by the PI/study personnel. The final approval is then routed to the PI/study personnel and applicable hospitals by SCRIHS staff via the electronic IRB system.

  For full board CR approval without conditions/revisions, the date of the start of the approval period is the date of the IRB meeting. Additionally, *the date of the convened meeting* when the IRB conducts continuing review and approves the study without conditions/revisions determines the latest permissible date of the next continuing review.

- REVISIONS and/or ADDITIONAL INFORMATION REQUIRED: Approval Pending – the IRB has approved the CR pending clarification or minor revisions. The IRB Chair, Vice Chairs, or SCRIHS staff have the authority to approve the minor revisions which do not involve substantive issues. SCRIHS staff will notify the PI/study personnel via the electronic IRB system of the requested revisions.

  The PI/study personnel responds to the IRB's suggested revisions using the electronic IRB system. SCRIHS staff review those responses or forward to the IRB Chair or Vice Chairs (whoever has been designated). Additional information may be requested or the revisions can be approved.

  For full board CR approval with conditions/revisions, the date of the start of the approval period is the date on which the IRB Chair, or designee, has reviewed and approved the requested conditions/revisions. However, *the date of the convened meeting* when the IRB conducts continuing review and approves the study with conditions/revisions determines the latest permissible date of the next continuing review. All submission review outcomes are electronically signed by the SCRIHS Chair or Vice-Chair(s) within the electronic IRB submission system.

- TABLED : The IRB withholds approval pending submission of major revisions/additional information. SCRIHS staff send the PI/study personnel a letter in the electronic IRB system. The letter lists the reasons for tabling and includes a description of the revisions or clarifications requested. SCRIHS staff schedule the PI's response to the requested revisions for review by the full board committee. The IRB does not require the PI/study personnel to attend, but may make such requests as deemed necessary.

  If IRB approval is suspended or terminated, SCRIHS staff must file an incident report with OHRP and FDA if applicable and notify appropriate institutional officials.

  - DISAPPROVED: The IRB disapproves the CR. SCRIHS staff send the PI/study personnel a letter in the electronic IRB system describing the reasons for disapproving the protocol. The PI is given an opportunity to respond in person at the next scheduled IRB meeting or in writing. This outcome usually occurs when the IRB determines that the risk of the procedures outweighs any benefit or if the research does not meet the federal criteria.

  If IRB approval is suspended or terminated, SCRIHS staff must file an incident report with OHRP and FDA if applicable and notify appropriate institutional officials.

2. For expedited CR, the expedited reviewer may make the following determinations: 1) approved; 2) revisions and/or additional information required; 3) review by the full board committee required. The expedited reviewer exercises all the authority of the IRB except he/she may not disapprove the CR. Only the convened IRB may disapprove the CR. For expedited CR, the date of the start of the approval period is the date which the IRB Chair, or designee, electronically signs the CR submission within the electronic IRB submission system. All submission review outcomes are electronically signed by the SCRIHS Chair, Vice-Chair(s) or designee within the electronic IRB submission system.

3. During the convened meeting, the IRB determines the approval period as appropriate to the degree of risk but not less frequently than once per year. The IRB may set a shorter approval period (for CR to occur more often than annually) for high risk protocols or protocols with a high risk/low potential benefit ratio. Some factors to consider are:
   a. Nature of any risk posed by the research project
   b. Degree of uncertainty regarding risks involved
   c. Vulnerability of subject population
   d. Experience of PI conducting the research
   e. IRB's previous experience with PI (compliance history, complaints, etc.)
   f. Projected rate of enrollment
   g. Whether research project involves novel interventions

If the PI has concerns regarding the IRB's decision/recommendations for changes in the study, he/she may submit his/her concerns to the IRB, using the electronic IRB system, with a justification for altering the decision. The IRB reviews the request using the standard IRB review procedures.

E. Lapse of Approval

If the IRB approval expires, the PI must cease all research activities and may not enroll new subjects in the study. Continuation is a violation of federal requirements specified in 45 CFR 46.103(a) and 21 CFR 56.103(a). However, if the IRB Chair, or designee, determines that there is an overriding safety concern and/or ethical issue or that it is in the best interests of the individual subjects to continue participating in

the research activities, the IRB Chair, or designee, may permit the subjects to continue in the study for the time required to complete the CR process.

1. If a PI fails to submit the CR by the end of the approval period, SCRIHS staff notify the PI/study personnel using the electronic IRB system the approval will lapse or has lapsed. SCRIHS staff informs the PI/study personnel that research must cease and no new subject enrollment may occur. SCRIHS staff also informs the PI/study personnel that he/she should, if appropriate, notify subjects that the study approval has lapsed and that, if applicable, it is his/her responsibility to notify the funding agency of the expiration of IRB approval.

2. The PI may ask the IRB for permission to allow subjects currently participating to continue due to an overriding safety concern, ethical issues, or because it is in the best interest of the individual subjects. The IRB Chair, or designee, makes the final determination, if appropriate. SCRIHS staff notifies the PI using the electronic IRB system of that determination.

3. In the case of a study in which the study approval lapses but the PI/study personnel wants to continue the study, the PI/study personnel should submit the CR materials to the IRB, using the electronic IRB system, as soon as possible. The PI should submit an explanation of why the lapse occurred. The IRB may subsequently approve the study for continuation. The PI may resume the study once continuing review and approval by the IRB has occurred. The date of the start of the approval period will be determined as stated in section *D. Review Outcome(s)* above.

4. When CR approval does not occur prior to the end of the approval period, the IRB does not report the expiration as a suspension of approval under Food and Drug Administration or Department of Health and Human Services.

E. Determining the Date for the Second and all Subsequent Continuing Reviews Reviewed by the IRB at Convened Meetings

The date of the convened meeting when the IRB conducts continuing review and approves the study, with or without conditions/revisions, will determine the latest permissible date of the next continuing review.

1. Examples: One Year Approval Period

- The continuing review for a study is approved <u>without</u> conditions/revisions at a convened meeting held on October 8, 2014. The study was given a one year approval period. The latest permissible date for the next continuing review will be October 8, 2015.

- The continuing review for a study is approved <u>with</u> conditions/revisions at a convened meeting on October 8, 2014. The PI makes corrections and resubmits on October 29, 2014. The Chair, or designee, reviews and approves the conditions/revisions on October 30, 2014. The study was given a one year approval period. The latest permissible date for the next continuing review will be October 8, 2015.

2. Examples: Six Month Approval Period

- The continuing review for a study is approved <u>without</u> conditions/revisions at a convened meeting held on October 8, 2014. The study was given a six month approval period. The latest permissible date for the next continuing review will be April 8, 2015.

- The continuing review for a study is approved with conditions/revisions at a convened meeting on October 8, 2014. The PI makes corrections and resubmits on October 10, 2014. The Chair, or designee, reviews and approves the conditions/revisions on October 12, 2014. The study was given a six month approval period. The latest permissible date for the next continuing review will be April 8, 2015.

REFERENCES

21 CFR 56.108(a)(1)&(2)
21 CFR 56.109(f)
21 CFR 56.110
21 CFR 56.111
21 CFR 56.115(a)(3)&(7)
45 CFR 46.103(b)(4)
45 CFR 46.108(b)
45 CFR 46.109(e)
45 CFR 46.110
45 CFR 46.111
45 CFR 46.115(a)(3)&(7)
FDA's February 2012 Guidance for IRBs, Clinical Investigators, and Sponsors: IRB Continuing Review after Clinical Investigation Approval
OHRP's November 10, 2010 Guidance on Continuing Reviews

AMENDMENTS

EFFECTIVE DATE: November 9, 2011

REVISION DATE: September 11, 2013; August 7, 2015

OBJECTIVE

To describe the policies and procedures for reviewing an amendment (revisions/changes) to a previously approved protocol

GENERAL DESCRIPTION

An approved protocol represents the investigator's commitment to conduct an investigation using the methods and documents approved by the Institutional Review Board (IRB). Investigators may not initiate any changes in research procedures or consent/assent form(s) without prior IRB review and approval, except where necessary to eliminate apparent immediate hazards to the subject. All proposed changes must be promptly reported to the IRB. Examples of amendments that require IRB review include, but are not limited to, changes in:

- Study personnel;
- Advertising materials (flyers, radio spots, etc.);
- Research procedures and instruments;
- Subject populations (e.g., age range, number of subjects);
- Location where research will be conducted;
- Consent/assent forms;
- Recruitment procedures; or
- Date for completion of study.

If the investigator makes protocol changes to eliminate apparent hazards to the subject(s) without prior IRB approval, the investigator must immediately report the changes to the IRB for review and a determination as to whether the changes are consistent with the subject's continued welfare.

Investigators must promptly notify the IRB in writing of any change in a protocol's status, such as enrollment status changes, discontinuation or completion of a study via the electronic IRB submission system.

Definitions

Amendments are defined as any change to the IRB approved protocol submission.

PROCEDURES

Submission of Amendments

1. The PI/Study Coordinator is responsible for submitting any requested amendments (revisions/changes) using the appropriate electronic IRB system reporting form, prior to the implementation of any change.

2. To submit the request, the PI/Study Coordinator completes the appropriate form according to the instructions on the form and submits the form to the SCRIHS office via the electronic IRB system.

Screening of Submissions

1. The appropriate SCRIHS staff member screens the submission.

2. If the request is incomplete, SCRIHS staff either returns the submission to the PI/Study Coordinator or requests additional information from the PI/Study Coordinator.

3. If an amendment adds vulnerable populations or requires documentation of specific regulatory findings, SCRIHS staff send the amendment to a designated expedited reviewer for review.

4. Depending on the requested change, SCRIHS staff may also secure additional review (i.e., prisoner representative). The IRB is responsible for applying the applicable regulatory requirements.

5. If an amendment requires consent/assent form changes, SCRIHS staff screens to ensure they conform to the IRB consent/assent template. The IRB Chair or designated reviewer has final authority for requiring consent/assent changes.

6. If an amendment includes additions to study personnel, SCRIHS staff screens to ensure that all new study personnel have completed required human subject protections training through CITI. If not, SCRIHS staff informs the PI/Study Coordinator that the untrained study personnel cannot be added until they have completed required training. SCRIHS staff asks the PI/Coordinator whether he/she wishes to remove the study personnel in question and continue with the amendment request. Alternately, the PI/Study Coordinator may choose to wait until the study personnel in question completes the training. In that case, SCRIHS staff forwards the amendment to the IRB Chair or designee for approval after study personnel training is complete.

7. SCRIHS staff screens for HIPAA concerns. If appropriate, SCRIHS staff forwards the amendment, with noted concerns, to the IRB Chair or designee for review.

Determining Mechanism of Review (i.e., Expedited vs. Full Board Review)

1. If the sponsor or the PI specifically requests full review procedures, SCRIHS staff places the amendment on the next available agenda for full board review.

2. If PI/sponsor does not request a full board review, SCRIHS staff sends the submitted form, with any attachments, to the IRB Chair or designated expedited reviewer for review.

3. The IRB Chair or designated expedited reviewer makes a determination regarding whether the IRB can review the request using expedited or full board review procedures. If the change is minor, the IRB Chair or designated expedited reviewer conducts the review using expedited procedures. A minor change is one which makes no substantial alteration in:
   - The level of risk to subjects;
   - The research design or methodology;
   - The subject population;
   - Qualifications of the research team;
   - The facilities available to support the safe conduct of the research; or
   - Any other factor that would warrant review of the proposed changes by the convened IRB.

Cancer Cooperative Group Amendments

1. If the cooperative group specifically requests full review procedures, SCRIHS staff places the amendment on the next available agenda for full board review. If the amendment includes new or modified risk information, new subjects cannot be enrolled until reviewed and approved by the IRB.

2. If the cooperative group does not request a full board review, SCRIHS staff sends the submitted form, with any attachments, to the IRB Chair or designated expedited reviewer for review.

3. The IRB Chair or designated expedited reviewer makes a determination regarding whether the IRB can review the request using expedited or full board review procedures based on the September 29, 2008 memorandum from the Office for Human Research Protections (OHRP) to the Cancer Therapy Evaluation Program (CTEP).

Expedited/Full Board Review Procedures

1. The IRB Chair or designated expedited reviewer conducts the expedited review using standard expedited review procedures. The expedited reviewer exercises all the authority of the IRB except the reviewer cannot disapprove the research. The listing of the item on the IRB agenda for the convened IRB serves to advise the IRB of the expedited review.

2. The IRB Chair or designated expedited reviewer makes a determination, if applicable, regarding:

    - Eligibility for expedited review;

    - Whether the research meets the criteria for IRB approval;

    - Whether proposed changes to the informed consent/assent process continue to meet requirements as set forth in 45 CFR 46.116 and 117, and 21 CFR 50.25; and

    - Whether the proposed changes affect any research categories of the currently approved protocol.

3. If the IRB Chair or designated expedited reviewer recommends full board review, SCRIHS staff places the amendment on the next available IRB agenda.

4. For an amendment undergoing full board review, SCRIHS staff invites (e.g., phone call or e-mail) the PI to attend if the IRB requires that he/she attend the meeting. The full board IRB reviews the submission applying the federal criteria for approval as applicable to the request.

Review Outcome(s)

1. For expedited review, the outcomes of review are the same as the options outlined in the Initial Expedited Review SOP. SCRIHS staff notifies the PI via the electronic IRB system of the IRB's decision following procedures outlined in the Initial Expedited Review SOP.

2. For full board review, the outcomes of review are the same as the options outlined in the Initial Full Board Review SOP. SCRIHS staff notifies the PI via the electronic IRB system of the IRB's decision following procedures outlined in the Initial Full Review SOP.

3. For full board review, the IRB determines if reconsent of research participants is required. If reconsent is required this is communicated to the PI.

4. If the IRB approves an amendment, the end date of the approval period remains the same as that assigned at initial or continuing review.

5. If the PI has concerns regarding the IRB's decision, the PI may submit his/her concerns to the IRB, using the electronic IRB system with a justification for altering the decision. The IRB reviews the request using the standard IRB review procedures.

REFERENCES

45CFR46.103b(4)(iii)
21CFR56.108(a)(3)&(4)
21 CFR 56.110(b)(2)
45 CFR 46.110(b)(2)
45 CFR 46.111
21 CFR 56.111

ADVERSE EVENT AND UNANTICIPATED PROBLEM REPORTING

EFFECTIVE DATE: April 11, 2012

REVISION DATE: March 9, 2016

OBJECTIVE

To describe the policy and procedures of the Institutional Review Board (IRB), also known as the Springfield Committee for Research Involving Human Subjects (SCRIHS), for defining prompt reporting requirements of unanticipated problems or adverse events, and reporting requirements of problems/adverse events that do not meet prompt reporting requirements to the IRB, appropriate institutional officials, and applicable regulatory agencies.

GENERAL DESCRIPTION

Regulatory guidance provided in the Code of Federal Regulations [45 CFR 46.103(b)(5) and 21 CFR 56.108(b)] requires the IRB to have written procedures in place for ensuring Prompt Reporting of adverse event or series of adverse events meeting the definition of an unanticipated problem involving risk to human subjects or others to the IRB, appropriate institutional officials, and applicable regulatory agencies.

GLOSSARY OF TERMS

Adverse event: 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.

Unexpected Adverse Event: 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:

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

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.

Related: As used throughout this SOP includes:

Possibly Related: There is a reasonable possibility that the adverse event, incident, experience or outcome may have been caused by the procedures involved in the research.

Probably Related: Adverse event and administration of study product are reasonably related in time, and the adverse event is more likely explained by study product than other causes.

Definitely Related: Adverse event and administration of study product are related in time, and a direct association can be demonstrated

External Adverse Event (Non-Local): From the perspective of this Institution (SIUSOM) and affiliated entities engaged in a multicenter clinical trial, *external adverse events* are those adverse events experienced by subjects enrolled by investigators at other institutions engaged in the clinical trial.

Internal Adverse Event (Local): From the perspective of this Institution (SIUSOM) and affiliated entities (e.g. MMC and SJH) engaged in a multicenter clinical trial, *internal adverse events* are those adverse events experienced by subjects enrolled by a Principal Investigator(s)/Study Staff at this Institution and/or affiliated entities. In the context of a single-center clinical trial, all adverse events would be considered *internal adverse events.*

PROCEDURES

Reporting of Adverse Event (AE)/Unanticipated Problem (UP)

<table>
<tr><th colspan="2">Prompt Reporting</th></tr>
<tr><td>Unanticipated Problem must meet ALL of the following:</td><td>Serious Adverse Event (SAE) must meet ANY of the following:</td></tr>
<tr><td>1. Unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied;

2. Related; AND

3. Suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) related to the research than was previously known or recognized.</td><td>1. Results in death;

2. Is life-threatening

3. Results in inpatient hospitalization or prolongation of existing hospitalization;

4. Results in a persistent or significant disability/incapacity;

5. Results in a congenital anomaly/birth defect; OR

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</td></tr>
<tr><td colspan="2">Unanticipated problems that are a SAE should be reported to the IRB within five (5) business days of the investigator becoming aware of the event.

Unanticipated problem(s) that are not a SAE should be reported to the IRB within ten (10) business days of the investigator becoming aware of the problem.

Any death of a study subject that is related to the study procedures should be reported within 48 hours of the investigator’s awareness of the event.</td></tr>
</table>

Other event(s) not meeting prompt reporting requirements may be reported to the IRB if the Principal Investigator feels the event(s) may affect the safety and/or welfare of subjects and/or change the risk level of the study.
Promptly report any problems/adverse events the Sponsor or Cooperative Group require to be reported to the IRB.

Continuing Review Reporting
At the time of Continuing Review a log of all events (both local and non-local) involving subjects since the study was initiated, whether anticipated or unanticipated, serious or not serious, life-threatening or not life-threatening, or related or not related is required. If a sponsored clinical trial utilizes a DSMB/DMC, their reports serve as documentation. Any DSMB/DMC reports not previously submitted to the IRB should be submitted at the time of Continuing Review.

Screening of Submission

1. The Principal Investigator makes the preliminary determination that the event meets the criteria for Prompt Reporting using the above criteria. The Principal Investigator completes the appropriate reporting form in the electronic IRB system within the specified time period outlined in *Submission of AE/UP*.

2. IRB Staff screen the submitted reporting form. If the report is not complete, IRB staff send the Principal Investigator a message via the electronic IRB system describing what is needed to complete the submission.

3. If found complete, the IRB staff assign the submission to the IRB Chair or designee. The IRB Chair or designee receives, at minimum, the completed reporting form. The IRB Chair or designee may also receive related material(s) including documents revised as a result of the unanticipated problem/adverse event or documents that provide additional assessments or summary information.

4. The IRB Chair or designee reviews the report and any other submitted documents such as proposed revisions to the protocol, consent/assent or other study-related materials.

5. When the IRB Chair or designee determines that the unanticipated problem or adverse event involves risks to subjects or others, he/she will document, in the electronic IRB system, the recommended corrective actions to reduce the immediate risk for enrolled subjects and potential subjects.

6. The IRB staff forward the IRB Chair's or designee's recommendations for immediate actions to be taken by the Principal Investigator in order to reduce the risks to subjects and others within the electronic IRB system.

7. IRB staff schedule a review of the unanticipated problem or adverse event by the convened IRB. The IRB staff provide the IRB members attending the next convened meeting with access to the appropriate form and other study related document in the electronic IRB system.

8. If the IRB Chair or designee determines it is not an unanticipated problem or adverse event involving risk to subjects or others, he/she documents his/her review in the electronic IRB system and lists any

concerns/recommendations to identify and manage any potential risks to subjects pending full board review.

9. IRB staff places the item on the next appropriate IRB agenda for review by the convened IRB.

10. If the study is federally funded (e.g., by the US DHHS), or regulated by the Food and Drug Administration (FDA), additional IRB reporting requirements may be in effect. (See Mandated Reporting to External Agencies SOP)

11. The Principal Investigator reports all deaths related to study procedures using the appropriate reporting form in the electronic IRB system and within the period outlined in the Reporting Timeframe section (see page 4).

12. Deaths that are not related to the study procedures (i.e., due to underlying disease progression) are reportable at the time of IRB Continuing Review with the Continuing Review submission.

13. The IRB may request more stringent requirements for reporting events for individual research studies if it determines it to be necessary.

REVIEW OUTCOME(S) AND PRINCIPAL INVESTIGATOR APPEAL PROCESS

1. For all unanticipated problems/adverse events, the IRB determines whether the unanticipated problem/adverse event involves risk to human subjects or others. If it involves risk to subjects or others, the IRB will follow the established reporting policy. (See Mandated Reporting to External Agencies SOP).

   The IRB actions may include:
   • Acceptance without further recommendation;
   • A request for further clarification from the Principal Investigator;
   • Changes in the protocol (e.g., additional test or visits to detect similar events in a timely fashion);
   • Changes in the consent/assent form(s);
   • A requirement to inform subjects already enrolled about additional risks;
   • A change in frequency of review for Continuing Review;
   • Further inquiry into other protocols utilizing the particular drug, device, or procedure in question;
   • Suspension or termination (See Suspension or Termination SOP) of the study; or
   • Request for directed on-site review or other actions deemed appropriate by the IRB.

2. If the IRB accepts the IRB Chair's or designee's review of an unanticipated problem or adverse event without recommendation(s), it is recorded in the IRB minutes by the IRB staff.

3. If the IRB requests clarification or additional information or revisions, the IRB Staff will notify the Principal Investigator via the electronic IRB system of the need for additional information and/or changes. The Principal Investigator responds via the electronic IRB system. The IRB Chair or designee considers this information. The IRB Chair or designee may provide the Full Board with the response(s) for additional review, request additional information, or acknowledge/accept the response without recommendation.

4. When the Principal Investigator has concerns regarding the IRB decision/recommendations for changes in the study, he/she may submit those concerns, including a justification for appealing the IRB decision, to the IRB in writing using the electronic IRB system. The IRB reviews the request and

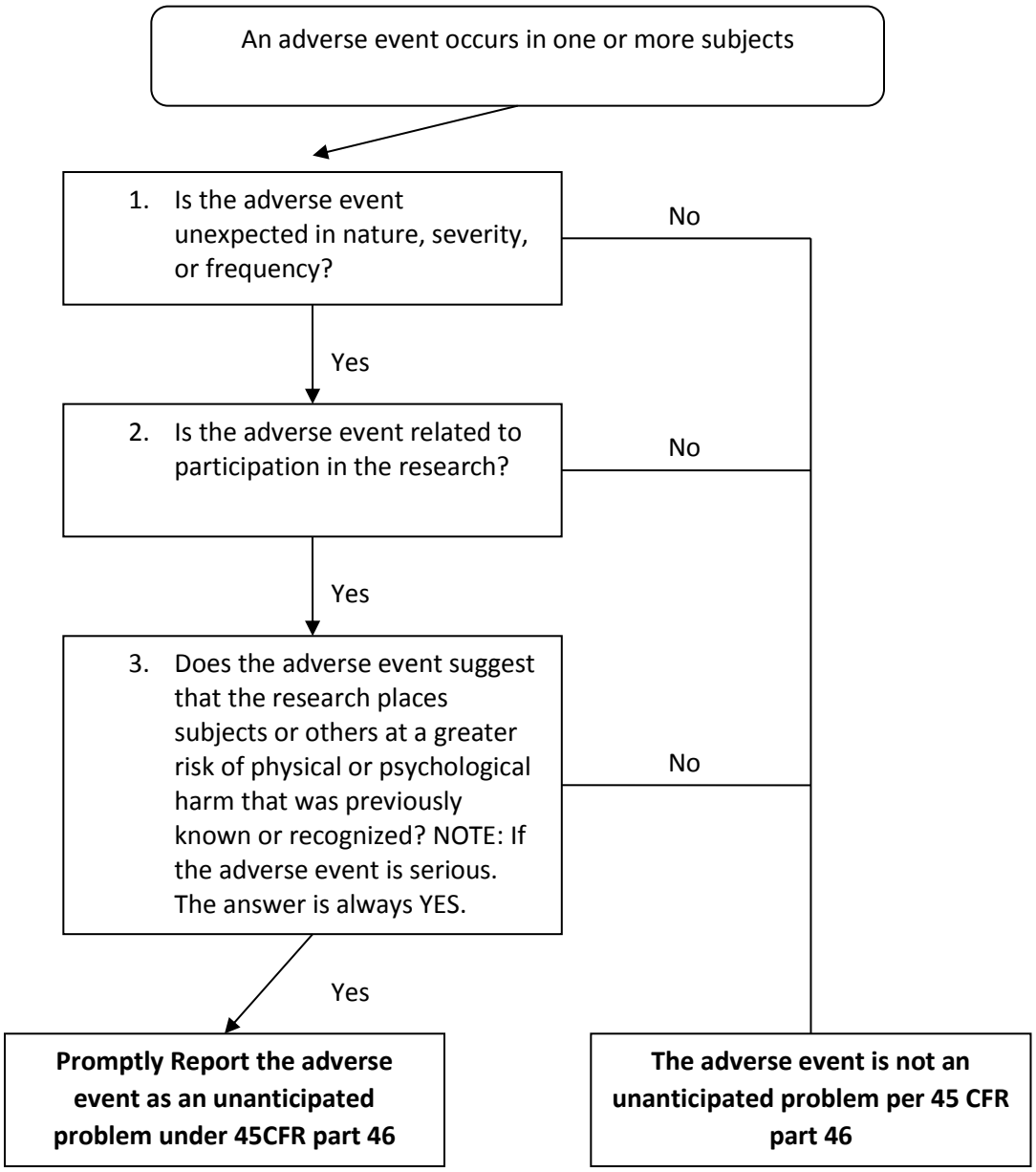
makes a final determination. IRB staff records the IRB's final determinations in the electronic IRB system.

REFERENCES

21 CFR 56.108(b)
45 CFR 46.103(b)(5)
Office of Human Research Protection (OHRP): Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events
Food and Drug Administration (FDA): Guidance for Clinical Investigators, Sponsors, and IRBs: Adverse Event Reporting to IRBs – Improving Human Subject Protection

APPENDIX A

Decision Chart for Determining Whether an Adverse Event is an Unanticipated Problem and Requires Prompt Reporting



APPENDIX B

Examples of adverse events/unanticipated problems that would require Prompt Reporting:

1. Adverse events occurring that are unexpected, related to the research, and involve new or increased risks to participants or others.
2. Adverse events that have been determined by the Sponsor or a Data Safety Monitoring Board to be unanticipated problems involving risks to participants or others.
3. Changes made to the research without prior approval of the IRB in order to eliminate apparent immediate harm.
4. Other unanticipated events, incidents, or problems that are related to the research and that indicate participants or others might be at new or increased risks.
5. Any event that requires prompt reporting according to the research protocol or plan or the sponsor.
6. Any accidental or unintentional change to the research protocol approved by the IRB or plan that involved risks or has the potential to recur.
7. Any change to the research protocol or plan taken without prior IRB review to eliminate apparent immediate hazard to a research participant.
8. Any publication in the literature, safety monitoring report, interim result, or other finding that indicates an unexpected change to the risks or potential benefits of the research.
9. Any complaint of a participant that indicates an unanticipated risk or that cannot be resolved by the research staff.
10. Any other event appropriate to the local context.

PROTOCOL VIOLATIONS, DEVIATIONS AND EXCEPTIONS

EFFECTIVE DATE: January 11, 2012

REVISION DATE: August 7, 2015

OBJECTIVE

To describe the policies and procedures for reviewing a protocol violation, deviation or exception to a previously approved protocol

GENERAL DESCRIPTION

Federal regulations require the IRB to review proposed changes in any research activity and to ensure that the investigator does not initiate such changes in approved research without IRB review and approval except when necessary to eliminate apparent immediate hazards/risks to the subject [45CFR46.103(b)(4)(iii) and 21CFR56.108(a)(4)]. Research activity includes all aspects of the conduct of the research study (e.g., recruitment methods, consent process, procedures used to protect privacy and confidentiality, etc.) and all of the information outlined in the IRB application/protocol reviewed and approved by the IRB.

Definitions

Exceptions or *deviations* are changes that impact individual subjects and do not change the overall protocol. Investigators may not initiate these changes without prior IRB review and approval, except where necessary to eliminate apparent hazards to the subject.

The IRB considers enrollment of a research subject in a protocol that fails to meet current IRB approved protocol inclusion criteria or falls under protocol exclusion criteria to be a protocol *exception*.

The IRB considers a departure from the current IRB approved procedures that impact an individual subject to be a protocol *deviation*.

A *protocol violation* is any exception or deviation involving a single subject that is not approved by the IRB prior to its initiation or implementation. These protocol violations may be major or minor violations.

A *major violation* is one that may impact subject safety; make a substantial alteration to risks of subjects, or any factor determined by IRB Chair or IRB member as warranting review of the violation by the convened IRB. Examples of major violations may include, but are not limited to:

- Failure to obtain informed consent, i.e., there is no documentation of informed consent, or informed consent is obtained after initiation of study procedures;
- Missing subject signature;
- Enrollment of a subject who did not meet all inclusion/exclusion criteria;
- Performing study procedure not approved by the IRB;
- Failure to report serious unanticipated problems/adverse events involving risks to subjects to the IRB and (if applicable), the sponsor;
- Failure to perform a required lab test that, in the opinion of the PI, may affect subject safety or data integrity;
- Drug/study medication dispensing or dosing error;

- Study visit conducted outside of required time frame that, in the opinion of the PI or IRB, may affect subject safety;
- Failure to follow safety monitoring plan.
- Use of unapproved consent form

A *minor violation* is a violation that does not impact subject safety or does not substantially alter risks to subjects. Examples of minor violations may include, but are not limited to:

- Implementation of unapproved recruitment procedures;
- Missing original signed and dated consent form (only a photocopy available);
- Missing pages of executed consent form;
- Inappropriate documentation of informed consent, including:
    - missing investigator signature;
    - copy not given to the person signing the form;
    - someone other than the subject dated the consent form;
    - individual obtaining informed consent was not listed on IRB approved study personnel list.
- Use of invalid consent form (i.e., consent form without IRB approval stamp or outdated/expired consent form);
- Failure to follow the approved study procedure that, in the opinion of the PI, does not affect subject safety or data integrity;
    - Study procedure conducted out of sequence;
    - Omitting an approved portion of the protocol;
    - Failure to perform a required lab test;
    - Missing lab results;
    - Enrollment of ineligible subject (e.g., subject's age was 6 months above age limit);
    - Study visit conducted outside of required timeframe;
- Over-enrollment;
- Enrollment of subjects after IRB-approval of study expired or lapsed;
- Failure to submit continuing review application to the IRB before study expiration.

PROCEDURES

Submission of Protocol Violation, Deviations and Exceptions

1. The PI/Study coordinator must submit any and all protocol violations, deviations, and exceptions that occur during the course of a study to the IRB within ten (10) business days upon initial discovery.

2. The PI/Study coordinator uses the electronic IRB system to submit all protocol violations, deviations, and exceptions.

3. The PI reports all protocol violations, deviations, and exceptions to the sponsor, if applicable, following the sponsor's requirements.

Screening of Submissions

1. SCRIHS staff screens the Protocol Violation, Deviation and Exception Reporting Form for completeness and accuracy. If the submission is incomplete, SCRIHS staff either returns it to the PI/Study coordinator or continue to process the submission but request additional information from the PI/Study coordinator, which they forward to the IRB upon receipt.

2. SCRIHS staff screen to determine whether the incidents involve vulnerable populations or require documentation of specific regulatory findings. If either of the above applies, then SCRIHS staff advises the IRB of any regulatory requirements the IRB should address in conducting the review. The IRB is responsible for applying the regulatory requirements.

3. SCRIHS staff screen submitted protocol incidents for HIPAA concerns and follow the procedures outlined in the HIPAA in Research SOP concerning noncompliance.

Determining Mechanism of Review (i.e., Expedited vs. Full)

1. SCRIHS staff forwards the completed Protocol Violation, Deviation and Exception Reporting Form with any applicable attachments to the IRB Chair or designee.

2. When reviewing a protocol violation, the IRB Chair or designee makes a determination regarding whether the violation is major or minor and whether to review the violation using full or expedited review procedures, respectively, unless the sponsor/PI requests full review. If the violation is minor, the IRB Chair or designee conducts review using expedited procedures. If the violation is major, the IRB Chair or designee determines the review type.

3. If the sponsor or the PI specifically requests full board review procedures, SCRIHS staff places the protocol report on an agenda for full board review.

Expedited/Full Review Procedures for Protocol Violations, Deviations or Exceptions

1. The IRB Chair or designee conducts expedited review using standard expedited review procedures.

2. If the protocol report undergoes full board review, the IRB Chair or designee has the option to invite the investigator to attend the meeting to answer any questions or concerns that the IRB may have concerning the protocol report.

3. SCRIHS staff notifies the PI if he/she must attend the IRB meeting. SCRIHS staff schedules the submission for review and the protocol report is made available on the IRB agenda. The full board committee reviews the protocol reports using the procedures outlined in the Initial Full Review SOP.

4. If the IRB determines that the information provided in the protocol report is reportable to external agencies, SCRIHS staff prepares a report to the applicable federal agency and maintains records as outlined in the Mandated Reporting to External Agencies SOP.

Review Outcome(s)

6. The IRB/SCRIHS staff handle the review and outcomes of review as outlined in the Amendment SOP and/or, if applicable, the Termination or Suspension of Research by the IRB SOP.

7. The IRB may, if appropriate, make a determination that the protocol violation(s) constitute “serious” or “continuing noncompliance”, or an “unanticipated problem involving risks to subjects or others” as defined in the Noncompliance SOP.

8. If the PI has concerns regarding the IRB decision, he/she may submit them to the IRB in a written document that includes justification for changing the IRB decision.

REFERENCES

21CFR 56.108(a)(4)
45CFR 46.103(b)(4)(iii)

HIPAA COMPLIANCE

EFFECTIVE DATE: June 28, 2012

REVISION DATE: September 25, 2015

OBJECTIVE

To describe Institutional Review Board (IRB) policy and procedures for conducting reviews of research involving the use or disclosure of protected health information under the Health Insurance Portability and Accountability Act (HIPAA), also known as the Privacy Rule.

GENERAL DESCRIPTION

The Privacy Rule protects the use and disclosure by *covered entities* of identifiable health information, referred to as "protected health information (PHI)". The Privacy Rule is not intended to interfere with access to and exchange of PHI for traditional, permissible healthcare purposes – treatment, payment for healthcare or healthcare operations. However, the Privacy Rule imposes restrictions on the use or disclosure by *covered entities* of PHI for other purposes, including research.

Definitions

Protected health information is defined as any of the 18 identifiers listed in the HIPAA Privacy Regulations in combination with health information that is created or maintained by the covered entity (CE) that relates to the past, present, or future physical or mental health or conditions of an individual. Health information is "individually identifiable" under the Privacy Rule if it directly identifies an individual or reasonably could be used to identify an individual.

List of 18 Identifiers:
1. Names;
2. All geographical subdivisions smaller than a State, including street address, city, county, precinct, zip code, and their equivalent geocodes, except for the initial three digits of a zip code, if according to the current publicly available data from the Bureau of the Census: (1) The geographic unit formed by combining all zip codes with the same three initial digits contains more than 20,000 people; and (2) The initial three digits of a zip code for all such geographic units containing 20,000 or fewer people is changed to 000.
3. All elements of dates (except year) for dates directly related to an individual, including birth date, admission date, discharge date, date of death; and all ages over 89 and all elements of dates (including year) indicative of such age, except that such ages and elements may be aggregated into a single category of age 90 or older;
4. Phone numbers;
5. Fax numbers;
6. Electronic mail addresses;
7. Social Security numbers;
8. Medical record numbers;
9. Health plan beneficiary numbers;
10. Account numbers;
11. Certificate/license numbers;
12. Vehicle identifiers and serial numbers, including license plate numbers;
13. Device identifiers and serial numbers;

14. Web Universal Resource Locators (URLs);
15. Internet Protocol (IP) address numbers;
16. Biometric identifiers, including finger and voice prints;
17. Full face photographic images and any comparable images; and
18. Any other unique identifying number, characteristic, or code (note this does not mean the unique code assigned by the investigator to code the data)

A *covered entity (CE)* is defined in the HIPAA rules as (1) health plans, (2) health care clearinghouses, and (3) health care providers who electronically transmit any health information in connection with transactions for which the U.S. Department of Health and Human Services has adopted standards. Generally, these transactions concern billing and payment for services or insurance coverage.

A *business associate agreement* is defined as a contract where a person or entity performs certain functions or activities that involve the use and/or disclosure of PHI.

A *data use agreement* is defined as an agreement required by the Privacy Rule between a covered entity and a person or entity that receives a limited data set. The data use agreement must state that the recipient will use or disclose the information in the limited data set only for specific limited purposes.

Options for Obtaining Protected Health Information

An investigator has the following six options for obtaining PHI for research purposes:

- De-identified Information - health information that cannot be linked to an individual;
- Authorization - permission from the research participant to use/disclose PHI collected during the research study for defined purposes;
- Waiver of Authorization - permission to forgo the authorization requirement based on the fact that the disclosure of PHI is a minimal risk to the subject and the research cannot practically be done without access to/use of PHI;
- Limited Data Set - a subset of protected health information that contain the following elements: city, state, zip code, date of birth, death, or date of service;
- Preparatory Work - PHI reviewed for the purpose of designing a research study or identifying potential subjects. PHI cannot be removed from the CE during the review; or
- Decedent Research - research where PHI is collected from a subject(s) that is deceased prior to the initiation of the study.

PROCEDURES

General Procedures

1. IRB members shall not review any research authorizations, waiver of authorization, or de-identification requests in which they have a conflict of interest.

Research Authorization Review Procedures

1. The PI makes a preliminary assessment to determine whether or not the protocol requires research authorization. SCRIHS staff will assist PI and make a determination regarding HIPAA requirements if needed.

2. The PI submits his/her IRB application (i.e., exempt, expedited, or full) in iRIS, the electronic IRB system. The PI uses the IRB's model HIPAA Authorization language that is included in the SCRIHS consent form template, which includes federally and institutionally mandated criteria.

3. SCRIHS staff reviews the submission and determines whether the study is subject to the HIPAA Privacy Rule and if the appropriate HIPAA authorization language needs to be included in the consent form for the study. SCRIHS staff reviews the authorization language to ensure that federally and institutionally mandated criteria are in the document.

4. IRB members use the SCRIHS template HIPAA Authorization language as a guide to assist them with their authorization review. The IRB and/or IRB reviewer make the final determination as to whether the study is subject to the HIPAA Privacy Rule and whether the investigator must revise the authorization language.

5. SCRIHS staff send requests for revisions to the authorization language to the PI, who in turn makes the necessary corrections and resubmits the revised consent form document in iRIS. The IRB Chair or designee reviews revisions to the authorization language and determines whether the federally and institutionally mandated criteria are satisfied.

6. A copy of the IRB approval is usually required to access patient medical records. Contact the appropriate healthcare provider for instructions.

7. The IRB does not review authorizations under the following circumstances:
   - PHI that was created or received either before or after the compliance date (April 14, 2003) may continue to be used and disclosed for research purposes, if any one of the following was obtained prior to the compliance date:
     - An authorization or other express legal permission from the subject to use or disclose PHI for the research; or
     - The informed consent of the subject to participate in the research; or
     - A waiver of informed consent by the IRB in accordance with the federal regulations pertaining to human subject research protection commonly known as the Common Rule or in accordance with an exception under the FDA's human subject protection regulations.

   - If the PI obtains a waiver of informed consent prior to the compliance date, but subsequently seeks informed consent after the compliance date, he/she must obtain the subject's authorization at the time he/she obtains the new informed consent. It is the PI's responsibility to submit a copy of the authorization form for IRB review.

8. The SCRIHS office maintains all versions of the PI's research authorization document for a period of no less than six (6) years after the study closure.

9. SCRIHS staff/IRB revises the IRB's template Authorization language as appropriate.

Research Waiver of Authorization Request Review Procedures

1. The PI makes a preliminary assessment to determine whether his/her proposal needs a HIPAA research waiver of authorization. SCRIHS staff will assist PI and make a determination regarding HIPAA requirements if needed.

2. The PI submits his/her IRB application (i.e., exempt, expedited, or full board) and research waiver of authorization requests in iRIS.

3. SCRIHS staff review protocols and determine whether the study is subject to the HIPAA Privacy Rule and if a research waiver of authorization request is appropriate for the study. SCRIHS staff review the waiver information provided in iRIS to ensure that federally and institutionally mandated criteria are included.

4. The IRB make the final determination as to whether the study is subject to the HIPAA Privacy Rule and whether the investigator must revise the HIPAA language.

5. SCRIHS staff send requests for revisions to the PI/study coordinator, who in turn makes the necessary corrections and resubmits the revised language to SCRIHS. The IRB Chair or designee reviews revisions to the HIPAA Waiver of Authorization Request Form and determines whether the federally and institutionally mandated criteria for waiver of authorization are satisfied.

6. A copy of the IRB approval is usually required to access patient medical records. Contact the appropriate healthcare provider for instructions.

7. The IRB does not require a research waiver of authorization under the following circumstances:

   - A PI may use and disclose for research purposes PHI that was created or received either before or after the compliance date (April 14, 2003) if a waiver of informed consent was reviewed by the IRB in accordance with the federal regulations and obtained prior to the compliance date.
   - If the PI obtains a waiver of informed consent prior to the compliance date, but subsequently seeks informed consent after the Compliance Date, he/she must obtain the subject's authorization at the time he/she obtains the new informed consent.

8. The SCRIHS office maintains all versions of the PI's HIPAA Waiver of Authorization Request for a period of no less than six (6) years after the study closure.

9. SCRIHS staff/IRB revises the IRB's template Authorization language as appropriate.

Research De-identification Review Procedures

1. The PI makes a preliminary assessment to determine whether the protocol meets the criteria for de-identification. SCRIHS staff will assist PI and make a determination regarding HIPAA requirements if needed.

2. The PI submits an IRB application and research de-identification request to SCRIHS, using the electronic IRB system, iRIS.

3. SCRIHS staff review protocols and determine whether de-identification is appropriate for the study.

4. SCRIHS staff forward the necessary review documents, along with any comments, to the appropriate IRB reviewer and/or IRB.

5. The IRB reviewer and/or IRB reviews research de-identification requests as outlined in the corresponding review SOPs. The IRB reviewer and/or IRB makes a final determination as to whether

the study meets the criteria for de-identification. The IRB notifies the PI if the study does not meet the criteria for de-identification.

6. If the IRB denies the de-identification request, SCRIHS staff notify the PI and provide assistance in determining the appropriate HIPAA review type.

7. A copy of the IRB approval is usually required to access patient medical records. Contact the appropriate healthcare provider for instructions.

Research Databases/Repositories Review Procedures

Note: Research utilizing stored data or materials (cells, tissues, fluids, and body parts) from individually identifiable living persons must be reviewed by the IRB. However, if the investigator cannot readily ascertain the identity of the subject from whom the data or materials originated, the research may not meet the definition of "human subject".

1. Individuals who are uncertain whether an activity is human research should submit a request for a Non-Human Subject Research Determination to the IRB.

2. Researchers who wish to establish a new research repository/database or to remove PHI and/or identifiable specimens from a research database or repository must submit an application through iRIS.

3. PIs, IRB members, and SCRIHS staff follow the authorization, waiver of authorization, and de-identification procedures previously outlined in this document.

4. If the research database or repository was established before April 14, 2003, and the following conditions are met, HIPAA requirements may not apply:
   - The information/specimens in the database are de-identified (e.g., all 18 identifiers listed in the HIPAA Privacy are removed); or
   - Subjects signed a consent form; or
   - The IRB waived informed consent.

HIPAA Compliance Procedures for Investigators Working in the Covered Entity

1. Investigators working in a CE must comply with the applicable HIPAA policies and procedures.

2. Any significant noncompliance HIPAA issue, such as a breach or complaint, involving research will be reviewed with the CE's Privacy Officer and Legal Counsel if necessary.

   - If the CE's Privacy Officer receives a HIPAA research complaint or an alleged HIPAA research noncompliance issue, the Privacy Officer will promptly notify the SCRIHS office. The Privacy Officer may confer with SCRIHS staff or the IRB Chair(s) to assess whether the complaint/alleged noncompliance issue falls under the purview of the IRB or both the IRB and the Privacy Officer.

   - If the SCRIHS office receives a HIPAA research complaint or report of an alleged HIPAA research noncompliance issue, SCRIHS staff will promptly notify the CE's Privacy Officer.

SCRIHS staff may confer with the Privacy Officer to assess whether the complaint/alleged noncompliance issue falls under the purview of the IRB or both the IRB and the Privacy Officer.

- If the complaint/alleged noncompliance issue falls under IRB purview, SCRIHS staff will initiate an inquiry following IRB standard operating procedures. The IRB determines whether the incident meets requirements for reporting to the federal regulatory agencies. In making the determination, IRB follows the procedures for reporting.

- After the IRB has completed its review of the complaint/alleged noncompliance issue, SCRIHS staff provides the CE's Privacy Officer with a copy of the final deliberations if the allegation involves both research and a violation of the HIPAA regulations. If SCRIHS staff determine the incident to be reportable to a federal regulatory agency, a copy of the federal report is sent to the Privacy Officer.

- If the complaint/alleged noncompliance falls under the CE's Privacy Officer purview, the Privacy Officer will initiate a review. After the Privacy Officer has completed its review of the complaint/alleged noncompliance, the Privacy Officer provides the SCRIHS office with a copy of the final deliberations if the allegation involves both research and a violation of the HIPAA regulations. If the Privacy Officer determines the incident to be reportable to a federal regulatory agency, the Privacy Officer sends a copy of the federal report to the SCRIHS office.

REFERENCES

45 CFR 164.512
45 CFR 164.532
45 CFR 164.530
45 CFR 164.508
45 CFR 164.514
NIH's Research Repositories, Databases, and the HIPAA Privacy Rule
NIH's Privacy Boards and the HIPAA Privacy Rule
OHRP - Guidance on Research Involving Coded Private Information or Biological Specimens

SUBJECT CONCERNS AND COMPLAINTS

EFFECTIVE DATE: March 14, 2012

REVISION DATE: December 11, 2013; February 19, 2016

OBJECTIVE

To provide guidance in handling concerns, complaints, or questions received regarding a research study involving human subjects

GENERAL DESCRIPTION

The right of research subjects to lodge a concern (e.g., allegation), complaint, or question and to be assured that the concern, complaint, or question is taken seriously and resolved in a timely manner is of prime importance. The SCRIHS office is responsible for investigating concerns, complaints, and questions from subjects and any improprieties involving investigators or their staff. SCRIHS staff handles these issues in a timely manner, assuring protection of human subjects. The IRB holds any violators accountable to the applicable regulation. A research subject (past, current, or prospective), a designated spokesperson, family member, or anyone with a concern about a human research study may raise concerns, complaints, or questions about a research project by telephone, in writing, or in person to the SCRIHS office or IRB Chair. Each IRB approved informed consent document includes the telephone number to reach the SCRIHS office; the telephone number is also listed on the SCRIHS website.

PROCEDURES

Concerns/Complaints/Questions

1. A research subject or anyone with a concern, complaint, or question regarding a research study involving human subjects may raise the concern, complaint, or question with the SCRIHS office or IRB Chair. Upon receipt of a concern (e.g., allegation), complaint, or question, SCRIHS staff gather the following information from the complainant as appropriate:
   - Subject's (or complainant's) name, address, and phone number (This information is NOT MANDATORY, and an individual may report an incident anonymously; however, staff advises the individual that a thorough review may not be possible, and that, without this information, follow-up responses to the individual are not feasible.);

   - Study protocol title (or SCRIHS protocol number) and the name of the PI;
   - Date(s) of the incident, and;
   - An explanation of the concern, complaint, or question.

2. SCRIHS staff assure the individual (or complainant) that he/she will inquire into the circumstances and that the IRB/SCRIHS office will take appropriate measures to address the issue. Furthermore, staff inform the individual that a response to him or her will be forthcoming as rapidly as possible provided that contact information is given (e.g., if possible, within 2 to 3 weeks if the issue is a complaint and if permissible by law). Staff also explain to the individual the limits to confidentiality.

3. SCRIHS staff handle the concern, complaint, or question in a confidential manner to the extent allowed by law. The SCRIHS office limits access to information regarding the concern, complaint or

question to individuals with responsibilities that require knowledge of the concern, complaint, or question.

4. SCRIHS staff convey the information regarding the concern, complaint, or question to the PI of the study at issue, the Director of the Center for Clinical Research (CCR), and the IRB Chair in a timely manner unless confidentiality or discretion requires otherwise to effectively review or investigate the concern, complaint or question.

5. SCRIHS staff promptly investigate the concern, complaint, or question; evaluate the alleged impropriety on a case-by-case basis; and make every effort to correct the issue(s) at the administrative level.

6. If the alleged impropriety involves potential harm to subjects or others, SCRIHS staff notify the IRB Chair for immediate action pending formal inquiry**.** Staff report concerns, complaints, or questions involving serious issues immediately to the IRB Chair, the SCRIHS Advisory Panel and, if appropriate, Legal Counsel.

7. SCRIHS staff manage the inquiry, preparing related correspondence, and maintaining documentation of the review for at least six years from completion of the inquiry or close out of the IRB file, whichever is longer.

8. The IRB Chair or his/her designee, in collaboration with SCRIHS staff, ensures appropriate response to each concern, complaint, or question and reports the action(s) taken to the IRB. If the complaint, concern, or question is of a minor nature such as a payment issue, the IRB Chair, SCRIHS staff, or designee may resolve the issue without bringing it forth for an IRB committee vote. The IRB Chair, SCRIHS staff, or designee refers major issues such as failure to obtain signed informed consent from potential subjects (if required) to the IRB, and the IRB votes on any actions the IRB takes. All actions taken are by the IRB, are appropriate for the circumstances, and the final course of action is dependent on the nature, severity, and seriousness of the findings.

9. Depending on the nature of the event or circumstances, the IRB may take the following actions, including, but not limited to:
   - Further inquiry;
   - Administrative action;
   - Details and recommendations forwarded to the appropriate departments/committees (e.g., IRB, Compliance Office) for consideration;
   - Details and recommendations forwarded to the appropriate department chair for action as appropriate;
   - Details and recommendations forwarded to the Dean and Provost, Associate Dean for Research and Faculty Affairs, and/or Executive Director of Human Resources for action;
   - Details and recommendations forwarded to the appropriate officials at affiliated institutions for notification, action, and/or follow-up, if applicable, and;
   - Other actions as deemed appropriate.

10. SCRIHS staff and the IRB monitor any concerns, complaints, or questions that an individual may lodge for issues of noncompliance. SCRIHS staff bring issues involving noncompliance to the attention of the IRB Chair, the IRB, and the SCRIHS Advisory Panel. (See the Noncompliance SOP.)

REFERENCES

45 CFR 46.116(a)
21 CFR 50.25(a)

NONCOMPLIANCE

EFFECTIVE DATE: July 13, 2011

REVISION DATE: December 11, 2013; February 5, 2016

OBJECTIVE

To describe the policies and procedures the Institutional Review Board (IRB), also known as the Springfield Committee for Research Involving Human Subjects (SCRIHS), follows for handling allegations of noncompliance

GENERAL DESCRIPTION

The ethical conduct of research is a shared responsibility. It requires cooperation, collaboration, and trust among the institution, investigators and their research staff, the subjects who enroll in research, IRB members, and SCRIHS staff. The primary responsibility of the IRB is to ensure protection of the rights and welfare of research subjects. In performing that responsibility, the IRB addresses allegations of noncompliance with IRB requirements and/or federal regulations governing the conduct of human research. SCRIHS staff, IRB members, or IRB consultants do not participate in alleged noncompliance reviews if they have a conflict of interest. (See the IRB Member and Consultant Conflict of Interest SOP.)

Definitions

Noncompliance is defined as conducting research in a manner that disregards or violates federal regulations or institutional policies and procedures applicable to human subjects research. Noncompliance with IRB and/or federal requirements may involve a range of issues from relatively minor or technical violations which result from inadvertent errors, inattention to detail, or inadequate training and supervision of research staff to more serious violations, which pose risk to subjects and/or violations of their rights and welfare.

Continuing noncompliance is a repeated failure to adhere to the laws, regulations, or policies governing human research.

Serious noncompliance is a failure to adhere to the laws, regulations, or policies governing human research that may reasonably be regarded as:

(1) Involving substantive harm, or a genuine risk of substantive harm, to the safety, rights, or welfare of human research subjects, research staff, or others; or
(2) Substantively compromising the effectiveness of a facility's human research protection or human research oversight programs.

PROCEDURES

Submission and Screening of Allegations of Noncompliance

1. Anyone may submit allegations of noncompliance or continuing noncompliance involving human subjects research to the IRB verbally or in writing. The IRB maintains confidentiality regarding the identity of the person submitting the allegation to the extent possible.

2. SCRIHS Staff or designee screens the allegation of noncompliance to determine whether the protocol(s) affected is supported by federal funds.

Determination That an Allegation Is Justified or Unjustified

1. SCRIHS staff, in collaboration with the SCRIHS Advisory Panel (AP), review all allegations to determine whether the facts justify the allegation (i.e., there are supporting documents or statements).

2. If the AP deems the allegations unjustified, the convened IRB reviews the allegation. The convened IRB may dismiss the allegation as unjustified after review of the material(s) and decide to take no action.

3. If the convened IRB finds the allegation is unjustified and takes no action, SCRIHS staff communicate (by phone, email, or letter) the IRB's decision to the complainant (if the identity of the person is known) and to the investigator against whom the allegation was raised (respondent).

4. If the convened IRB finds the allegation is justified, an inquiry into the allegation may be initiated (See *Initiating an Inquiry into an Allegation* section).

5. If the AP or convened IRB determines that an allegation is justified and concerns administrative issues, the IRB Chair or designee manages the concern through communications with the PI.

6. If the complaint/concern is minor or administrative, the IRB Chair or designee may determine not to require a formal inquiry, interview, or summary with opportunity to comment.

7. Upon resolution of the issue, the IRB Chair or designee provides an oral or written summary of the resolution to the IRB at the next convened IRB meeting for review and approval.

Initiating an Inquiry into an Allegation

1. If the allegation involves more serious issues than administrative or minor concerns, the convened IRB, AP or the IRB Chair or designee decides whether to initiate an inquiry. The convened IRB, AP or IRB Chair bases the decision on the seriousness and/or the frequency of violations and/or disregard for the federal regulations or the institutional policies and procedures applicable to human subjects research.

2. If the AP, IRB Chair, or convened IRB determines that an allegation is justified and suggests that subjects are at immediate risk, the IRB Chair or designee informs the convened IRB. In circumstances of immediate risk, the AP or IRB Chair can immediately suspend research activities until the convened IRB meets. The convened IRB considers whether to continue suspension of research activities or to take other actions. However, in most cases, upon receipt of the allegation, the convened IRB takes no formal action until it conducts an inquiry to collect additional information and concludes the review.

3. If the convened IRB or the IRB Chair or designee decides to initiate an inquiry to determine the validity of the allegations, the PI is notified. If the allegation involves a co-investigator or a research assistant, those individuals may be contacted. The IRB Chair or designee makes the initial notification via telephone and/or e-mail. The IRB Chair sends written follow-up correspondence. Note: All research materials must remain intact and unaltered during the course of an investigation.

4. The IRB may appoint one or more voting member(s) or SCRIHS staff (e.g., the IRB Chair or designee) to gather information pertaining to the nature of the allegation, the procedures approved in the IRB protocol, and the procedures followed in conducting the study.

5. The IRB representative interviews the complainant, and in cases where the complainant requests anonymity, the IRB representative maintains the complainant's anonymity to the extent possible. The interviewer prepares a summary of the interview and gives the complainant the opportunity to comment on the written summary. In some cases, the complainant may have already submitted a written complaint, which the IRB representative then verifies. The IRB representative may request additional information from the complainant.

6. The convened IRB, the IRB Chair, or a designated IRB member communicates with the respondent and gives him/her the opportunity to comment on the allegation and provide information. The respondent may submit a written rebuttal to the complaint. The IRB representative may request additional information from the respondent.

7. Depending on the nature of the allegation and the information collected during the communication with the respondent, the convened IRB or its representative may also contact other individuals. In addition, in conducting the review, the convened IRB or its representative may examine research records; correspondence; research data, both published and unpublished; informed consent/assent forms; medical records; inclusion/exclusion criteria; the applicable approved IRB protocol; and any other pertinent information.

8. When appropriate, the IRB member(s) conducting the inquiry prepares, with the assistance of an assigned SCRIHS staff member, a summary report for the convened IRB. The report may consist of a summary of the allegations, interview summaries, and copies of pertinent information or correspondence. The report may or may not include recommendations for IRB action. (In some cases, the IRB representative simply provides the IRB with a summary of the allegations, the interview summaries, and copies of pertinent information without an accompanying written report from the review team.)

Review Procedures

1. SCRIHS staff advise the IRB regarding the applicable institutional, affiliated agencies/entities and federal regulations, assists the IRB in documenting the review, answers questions about the review process, maintains the records as required by state and federal laws, and serves as a liaison with the funding agency or agencies.

2. The IRB reviews the material presented by the review team at a convened meeting at which a quorum is present. The materials provided include the summary report of the noncompliance, the protocol if applicable and the informed consent document if applicable. The convened IRB determines whether to request additional information or whether to interview additional witnesses. The IRB may give the respondent the opportunity to meet with the convened IRB before it takes final action.

Review Outcomes/IRB Actions

1. The convened IRB makes the determination whether the allegation is substantiated, and if so, whether the noncompliance is serious or continuing based on the materials compiled during the inquiry. If the noncompliance is serious or continuing and the research federally funded, the IRB, with the assistance of SCRIHS staff, reports the incident(s) to the applicable agency following procedures outlined in the Mandated Reporting to External Agencies SOP.

2. The convened IRB may take a variety of actions, depending on the outcome of the review, including, but not limited to, the following:

- Approve continuation of research without changes;
- Request formal educational intervention;
- Request minor or major changes in the research procedures and /or consent documents;
- Modify the continuing review schedule;
- Require monitoring of research;
- Require monitoring of the consent process;
- Suspend or terminate IRB approval/disapprove continuation of the study;
- Require audits of other active protocols of the investigator;
- Suspend or disqualify the investigator from conducting research involving human subjects approved by the IRB;
- Determine that the investigator may not use the data collected for publication;
- Require that the investigator contact subjects previously enrolled in the study and provide them with additional information and/or re-consent them;
- Request that the investigator inform publishers and editors if he/she has submitted or published manuscripts emanating from the research;
- Recommend further administrative action to the institution and affiliated agencies/entities; and/or
- Require the PI to notify research sponsors and/or funding agencies

3. The IRB Chair or designee communicates (phone call, email, or letter) to the person raising the allegation (if the identity of the person is known) that the matter has been addressed. The IRB Chair or designee communicates the IRB decision to the respondent.

4. The IRB informs the following individuals of the allegation, the review process, and the findings of the review, if appropriate, depending upon the outcome of the review, the external sponsor, or the requirements of the applicable regulatory agency:
    - Investigator;
    - Complainant;
    - The department chair;
    - Dean and Provost;
    - Legal counsel
    - Affiliated hospitals or other entities as appropriate
    - Office for Human Research Protections and/or the Food and Drug Administration (See Mandated Reporting to External Agencies SOP.);
    - Sponsor, if appropriate;
    - Other administrative personnel as appropriate.

5. The IRB resolves questions or concerns raised by a PI regarding the outcome of a specific IRB noncompliance review through direct communication with the PI.

6. The PI submits concerns in writing to the IRB within thirty days of the date the IRB issues the final decision. The IRB limits concerns to a review of the procedures employed to reach the decision (i.e., claims that the process was faulty in a way that creates a considerable risk that the outcome was incorrect) or grievances against sanctions imposed as a result of a finding of noncompliance. The PI specifies the nature of any claimed procedural error or the perceived unfairness of sanctions issued.

Note: All written letters, emails, and/or correspondence to and from SCRIHS may be generated using the appropriate mechanisms within the electronic IRB system.

REFERENCES

21 CFR 56.123
45 CFR 46.112

TERMINATION OR SUSPENSION OF RESEARCH BY THE IRB

EFFECTIVE DATE: July 13, 2011

REVISION DATE: November 13, 2013; February 12, 2016

OBJECTIVE

To describe policies and procedures for suspending or terminating research approved by the Institutional Review Board (IRB), also known as the Springfield Committee for Research Involving Human Subjects (SCRIHS)

GENERAL DESCRIPTION

The convened IRB has the authority to suspend or terminate approval of research that is not being conducted in accordance with the IRB approval, that has been associated with serious or continuing noncompliance, or that has been associated with harm to the rights and welfare of human subjects (See Noncompliance SOP). Any suspension or termination of approval shall include a statement of the reason for the IRB action.

The IRB Chair or designee has the authority to suspend approval when the continuation of the research may adversely affect the rights and welfare of research subjects or when the IRB needs additional information to ensure that the rights and welfare of subjects are protected and there is insufficient time to have the convened IRB review the situation.

The IRB reports the suspension or termination promptly to the investigator(s), appropriate institutional official(s) and other project sites affected by the suspension or termination (i.e. hospitals). If the research is funded by an extramural agency, federal regulations, if applicable, may dictate whether the funding agency must be informed that IRB approval has been suspended or terminated. Principal investigators (PIs) are responsible for informing the funding agency of any suspension or termination of funded research.

Reporting to federal regulatory agencies may not be required if the PI voluntarily closes down a study to new subject accrual or temporarily halts the research procedures. The IRB, IRB Chair, SCRIHS staff, or administrative officials may recommend voluntary closure to the PI, but the PI makes the decision whether closure is appropriate. However, if the IRB or IRB Chair requires suspension or termination, then the incident is reportable under the Mandated Reporting to External Agencies SOP.

Definitions

A *suspension* of IRB approved research is a temporary interruption in the enrollment of new subjects, activities involving previously enrolled subjects, or other research activities.

A *termination* of IRB approval refers to a permanent halt in the enrollment of new subjects, activities involving previously enrolled subjects, or other research activities.

PROCEDURES

Suspension of IRB Approval

1. If the convened IRB suspends IRB approval, it shall document in the minutes the reasons for suspending the research and any information needed from the PI and/or corrective actions or events that need to take place for the IRB to consider a withdrawal of the suspension.

2. If the IRB Chair or designee suspends IRB approval, the IRB Chair documents the reason for suspension and notifies the PI in writing or requests that SCRIHS staff prepare the correspondence. SCRIHS staff inform the IRB, and the IRB discusses the suspension at a convened meeting.

3. When a suspension involves the withdrawal of current subjects from a research protocol, the IRB considers alternatives that protect subjects currently enrolled to ensure that harm is not incurred from such withdrawal. Such considerations may include possible transfer of subjects to another investigator, arrangement of clinical care outside the research, continuation of some research activities under the supervision of an independent monitor, permitting follow-up of subjects for safety reasons, or requiring reporting of adverse events or outcomes to the IRB and the sponsor.

4. SCRIHS staff notify the PI in writing of the suspension. The correspondence shall include, but is not limited to, the following:
    - An explanation of the extent of the suspension in terms of enrollment, recruitment, interventions, interactions, and data analysis;
    - The reasons for the suspension, an explanation of the reasons for the decision, and an offer to the investigator to respond to the convened IRB in writing;
    - A description of whether follow-up of subjects for safety reasons is permitted or required.
    - If applicable, a request for a description of any procedures needed to protect the rights and welfare of current subjects if the suspension involves currently enrolled subjects. If necessary, the PI and IRB considers the appropriate procedures for withdrawal of enrolled subjects, taking into account their rights and welfare.

5. If instructed by the IRB, the PI notifies enrolled subjects of any suspended research protocols

6. The IRB determines which institutional officials to notify of the suspension and whether to report the suspension to an external agency. (See Mandated IRB Reporting to External Agencies SOP) Also, SCRIHS staff send copies of suspension correspondence to other SIU-SOM administrative units in accordance with the coordination SOPs (e.g., Dean and Provost or designee; Affiliated hospitals; Office of Compliance; Legal).

Termination of IRB Approval

1. If the convened IRB terminates approval, it shall document in the minutes the reasons for terminating the research.

2. When a termination involves the withdrawal of current subjects from a research protocol, the IRB considers alternatives that protect subjects currently enrolled to ensure that harm is not incurred from such withdrawal. Such considerations may include possible transfer of subjects to another investigator, arrangement of clinical care outside the research, continuation of some research activities under the supervision of an independent monitor, permitting follow-up of subjects for safety reasons, or requiring reporting of adverse events or outcomes to the IRB and the sponsor.

3. SCRIHS staff notify the PI of the termination. The notification may include, but is not limited to, the following:
   - An explanation of the extent of the termination in terms of enrollment, recruitment, interventions, interactions, and data analysis;
   - The reasons for the termination, an explanation of the reasons for the decision, and an offer to the investigator to respond to the convened IRB in writing;
   - A request for a description of any procedures that need to be followed to protect the rights and welfare of current subjects if the termination involves currently enrolled subjects;
   - A description of whether follow-up of subjects for safety reasons is permitted or required;
   - An explanation that any request for the IRB to reconsider the termination must be made within 30 days from date of the notification.

4. The PI notifies enrolled subjects of any termination of a research protocol, via an IRB approved action plan, and the PI considers the appropriate procedures for withdrawal of enrolled subjects, taking into account their rights and welfare.

5. The IRB determines which institutional official to notify of the termination and whether a report to an external agency is required. (See Mandated Reporting to External Agencies SOP) Also, SCRIHS staff send copies of the termination notification to other administrative units in accordance with the coordination SOPs (e.g., Dean and Provost or designee; Affiliated hospitals; Office of Compliance; Legal).

Reporting and Recordkeeping of Suspension or Termination

1. See the Mandated Reporting to External Agencies SOP for a description of policies and procedures regarding reporting and recordkeeping of SIU-SOM studies.

Note: Written notification and documentation may be done through the appropriate mechanisms within the electronic IRB system.

REFERENCES

21 CFR 56.113
45 CFR 46.113

THE CONDUCT OF IRB MEETINGS

EFFECTIVE DATE: February 8, 2012

REVISION DATE: May 13, 2015

OBJECTIVE

To describe policies and procedures for the preparation, scheduling, and conduct of convened meetings of the Institutional Review Board (IRB)

GENERAL DESCRIPTION

The IRB, also known as the Springfield Committee for Research Involving Human Subjects (SCRIHS) conducts convened meetings in accordance with applicable federal requirements for full board review (i.e., 21 CFR 56.108, 45 CFR 46.108, and 38 CFR 16.108).

PROCEDURES

Preparation and Distribution of the Agenda

1. SCRIHS staff develop, maintain, and revise the IRB meeting schedule, as appropriate. The dates of scheduled meetings are available on the SCRIHS website, within the electronic IRB system, or by request. SCRIHS staff handle the meeting rooms and catering arrangements for the scheduled meeting dates.

2. SCRIHS staff create an agenda approximately 7-10 calendar days before a meeting and make it available to the IRB within the electronic IRB system. SCRIHS staff review the agenda for accuracy and completeness before distributing it to the IRB. IRB members and other appropriate individuals are notified when the agenda is made available.

3. If special circumstances exist, and items need to be added to the agenda after the agenda has been posted, SCRIHS staff notify the IRB members of the changes prior to the meeting. The decision to post late items on the agenda is at the discretion of SCRIHS staff and/or the IRB Chair/Vice Chairs.

4. For each meeting, SCRIHS staff automatically generate the agenda in the electronic IRB system.

5. The agenda serves as a guideline for the conduct of the meeting. The agenda for the meeting may include additional discussion items at the discretion of the IRB Chair, SCRIHS staff, or IRB members.

Quorum Requirements

1. A quorum is required to conduct any business of the convened IRB.

2. A majority (e.g., Total IRB members = 11; majority = 6) of the IRB members must be present to constitute a quorum.

3. At the convened meeting, at least one member whose primary concerns are in nonscientific areas must be present.

4. When the IRB reviews FDA regulated research, there must be one member present who is a licensed physician.

5. Alternate members may attend in the place of absent regular members in order to meet the quorum requirements.

6. Members must excuse themselves from the meeting during a vote when they have a conflict of interest. In such cases, they do not count as a part of the members necessary to constitute a vote or majority. If the quorum is lost during a meeting (e.g., loss of a majority through excused members with conflicting interests or early departure or absence of a non-scientist member, etc.), the IRB does not take further protocol actions that require a vote unless the quorum is restored.

Review of Protocols

1. The IRB Chair, Vice Chair, or any voting IRB member may chair the convened meeting.

2. For initial full board review, the IRB encourages principal investigators (PIs) to attend the convened meeting. In some circumstances the IRB, IRB Chair/Vice Chairs, or SCRIHS staff may require the PI to attend the convened meeting. The IRB, IRB Chair/Vice Chairs, or SCRIHS staff may grant permission for the co-investigator or knowledgeable party to attend in place of the PI.

3. For other types of review, IRB members, the IRB Chair/Vice Chairs, or SCRIHS staff may also invite or require the PI to attend, when deemed appropriate.

4. Except as required, or as may be permitted, by law, the proceedings of the meetings are confidential. Individuals may request to attend as observers. Upon receipt of these requests, SCRIHS staff or the IRB Chair may grant permission for attendance by these individuals. SCRIHS staff obtain a signed Certification of Confidentiality form from observers who have permission to attend. Observers do not receive agenda items.

5. IRB members do not participate in the review of any component of a project in which the member has a conflict of interest, except to provide information requested by the IRB.

6. See Initial Full Board Review, Continuing Review, Protocol Deviations, Violations and Exceptions, Amendments, and Noncompliance SOPs for discussion of review outcomes and controverted issues.

7. SCRIHS staff are responsible for preparing meeting minutes.

Tele/Videoconference Participation

    1. The IRB may conduct convened meetings by telephone or video conferencing as long as IRB member(s) have received a copy of all of the documents under review at the meeting, a quorum as defined above is present, and discussion occurs in real time.

    2. Members connected through telephone or video conferencing count as part of the quorum and may vote. "Telephone polling" (where SCRIHS staff or others contact IRB members individually by telephone) does not qualify as a convened meeting. To allow for appropriate discussion, all members must be connected simultaneously for a teleconference to take place.

Voting

1. IRB members may not vote by proxy (i.e., members not present at the convened meeting or not participating via tele/videoconference shall not vote on an issue discussed during a convened meeting). Members can provide written comments for IRB consideration, but such members submitting such comments are not counted as present for purposes of voting or quorum.

2. Voting at a convened meeting takes place under the following conditions:

- A majority of the members must be present (or connected via speakerphone/video), to constitute a quorum, for all reviews/actions voted on at a convened meeting;
- A passing vote must consist of a majority of members present (or connected via speakerphone/video) voting in favor of the motion;
- An individual who is not listed on the Office for Human Research Protections (OHRP) membership roster for the IRB may not vote with the IRB;
- Administrative representatives of the IRB may not participate in the vote;
- Ad hoc consultants may not participate in the vote;
  - A non-scientist member must always be present for an IRB vote;
  - A physician must be present for the IRB to vote on FDA regulated research;

3. If the outcome of the IRB vote is a "approved pending revisions and/or additional information", the IRB Chair, or the individual chairing the meeting, may review and approve the PI's response on behalf of the IRB under an expedited review procedure.

REFERENCES

21 CFR 56.108c
21 CFR 56.109
45 CFR 46.108(a & b)
45 CFR 46.103
45 CFR 46.108
45 CFR 46.107(e)

SPECIAL REQUIREMENTS

INFORMED CONSENT

EFFECTIVE DATE: December 14, 2012

REVISION DATE: June 8, 2016

OBJECTIVE

To describe policies and procedures for obtaining and documenting informed consent/assent and for reviewing and requesting waiver of informed consent or waiver of documentation of informed consent for non-exempt human research

GENERAL DESCRIPTION

Informed Consent/Assent Permission: Process and Documentation

A major requirement of research involving human subjects is that investigators must obtain the informed consent of prospective subjects before they include these subjects in research. Informed consent is an ongoing educational process that takes place between the investigator and subject, allowing the investigator and the participant to exchange information and ask questions. In most cases, federal regulations require informed consent and documentation of the process. In certain circumstances, the federal regulations allow a waiver of informed consent documentation or of the process.

The consent document is not a substitute for discussion among investigators and research subjects. To ensure an effective informed consent process, the Institutional Review Board (IRB) and investigators comply with all applicable federal regulations (e.g., 21 CFR 50, 45 CFR 46.116, 117, and 38 CFR 16.116, 117). These regulations mandate the inclusion of eight basic informed consent elements. Additional elements may be required, depending on the nature of the research. (These various elements are further discussed below.) IRB policy also specifies the information to include in the consent process. The SCRIHS informed consent template outlines the required elements of informed consent. The investigator may use a short form if approved by the IRB in accord with applicable federal requirements.

Definitions

Assent is defined as affirmative agreement of a child or an individual who lack decisional capacity to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent.

Permission is defined as the agreement of parent(s) or guardian to the participation of their child or ward in research or clinical investigation. Permission includes the element of consent set forth in federal regulations and outlined in the SCRIHS informed consent template.

In Illinois, the terms *child* or *children* refer to all individuals under 18 years of age unless the individual(s) is legally emancipated. (See section *Emancipated Individuals* for details of Illinois state law.) Individuals under 18 years of age who are not emancipated meet the federal definition for "child" [e.g., Department of Health and Human Services (DHHS), Food and Drug Administration (FDA), and U.S. Department of Education].

Legally Authorized Representative (LAR): Refer to the LAR Consent SOP and Participants Who Lack Decisional Capacity guidance document

Waiver of Informed Consent Process

The IRB has the authority to approve a consent procedure that does not include or which alters some or all of the federally mandated elements of informed consent, provided the approved procedure meets applicable federal regulations. The FDA and DHHS requirements for waiver differ. Consequently, the investigators and IRB must comply with the applicable regulations, which differ depending upon study sponsor or regulatory status of the proposed research. A summary of applicable waiver federal regulations and institutional requirements is as follows:

1. Non-FDA regulated studies: to waive informed consent requirements, the IRB must find and document that the study meets the requirements in 45 CFR 46.116(c)(d).

2. Non-FDA or Non-DHHS funded or regulated studies involving planned emergency research: the IRB does not accept proposals that require a waiver of informed consent for planned emergency research for non-FDA/DHHS regulated research.

3. FDA regulated and/or DHHS funded planned emergency research: the IRB approves exceptions for informed consent requirements if the study meets all of the requirements specified in 21 CFR 50.24 and/or 45 CFR 46.101(i), and SCRIHS policy.

4. Single subject emergency use of a FDA regulated test article: IRB policy is more stringent than the FDA requirements outlined in 21 CFR 50.23. The IRB requires investigators to consult with the IRB Chair or designee before using the test article in a single subject without informed consent. The IRB may allow an exception to consultation, consistent with 21 CFR 50.23.

5. Waiver of parental or guardian permission in non-FDA regulated studies: when consent of parents or guardians is not a reasonable requirement because it poses additional risk to the potential subject or the parents' interest may not adequately reflect the child's interest (e.g., neglected or abused children), the IRB may waive parental or guardian permission in accord with 45 CFR 46 Subpart D and 46.408(c) and Subpart A 46.116.

Waiver of Documentation of Informed Consent

Federal regulations permit an IRB to waive the documentation requirements for obtaining informed consent under special circumstances.

1. FDA regulated studies: IRB may, in its discretion, waive documentation for some or all of the subjects if the study meets the conditions listed in 21 CFR 56.109(c).

2. Non-FDA regulated studies: the IRB may waive the requirement to obtain a signed consent form for some or all of the subjects if the study meets the requirements in 45 CFR 46.117(c).

PROCEDURES

Informed Consent Process and Documentation

1. The PI submits a proposed informed consent procedure and written form with his/her IRB application prior to initiation of research, except in situations such as research proposals that meet exempt criteria (although informed consent(s) may be included). The PI indicates in the IRB application the study personnel who will participate in the informed consent process or individuals the PI will authorize to obtain informed consent on his/her behalf.

2. The IRB has an informed consent template, available in the electronic IRB submission system and on the SCRIHS website. Investigators use this template as a guide unless the IRB grants exceptions or a waiver. The consent template contains the eight required elements, the six additional elements of informed consent, and additional IRB requirements for research involving human subjects. See *Additional Elements Where Appropriate* below.

3. At a minimum, the proposed consent process and form must include the following eight federally required elements:

    - Research statement: a statement that the study involves research, an explanation of the purpose of the research, an explanation of the expected duration of participation, a description of the procedures involved, and identification of any procedures which will be experimental.

    - Reasonably foreseeable risks or discomforts: a statement that describes foreseeable risks or discomforts associated with the research, the likelihood of their occurrence, and the ramifications associated with the risks (e.g., decreased blood count may result in need for a blood transfusion).

    - Reasonably expected benefits to subjects or others: a statement that describes benefits to subjects or others that may reasonably be expected from the research including no benefit, if this is applicable. Payment for participation in a research project is not considered a benefit.

    - Appropriate alternatives: a statement that describes with enough detail any alternative procedures or course of treatment that may benefit the subject. If no alternatives exist, the consent form must state that there are no alternatives except not to participate.

    - Extent of confidentiality: a statement that describes the extent to which the investigator/study personnel will maintain or not maintain confidentiality of records identifying the subject (e.g.,

law requires reporting child abuse, etc.) and describes how the research team will protect subjects' private records during and after the conclusion of proposed research studies. Any research that is subject to audit or inspection must identify who will have access to the subject's record (e.g., FDA, National Institutes of Health (NIH), SCRIHS, Government Accounting Office, sponsors, or contract research organizations).

- Compensation or treatment for injury: for studies with greater than minimal risk, a statement explaining any compensation and an explanation of any medical treatments available if injury occurs or where the subject may obtain further information. The IRB informed consent template contains standard statements in accordance with IRB policy.

- Contact information: a statement that describes contact information details, including telephone numbers, and whom to contact for the following situations: questions about the research (e.g., investigator and other team members), questions about subjects' rights, comments, suggestions, or input (e.g., SCRIHS), and in the event of a research-related injury (depending on the nature of the research, the PI or a physician on the research team).

- Voluntary participation statement: a statement that describes clearly that participation in the research is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

The following additional elements must be included as appropriate. The IRB requires these additional elements unless the item(s) does not apply given the nature of the research or the proposed procedures (e.g., subjects will not receive remuneration for participation).

  - Unforeseeable risks to subjects, embryos, or fetuses: a statement warning subjects that some risks are currently not known or foreseeable, when applicable;

  - Investigator-initiated termination of participation: a statement that describes the instances in which an investigator may terminate a subject's participation (e.g., subject noncompliance, subject not benefiting from research, etc);

  - Additional costs: a statement that describes any additional costs a subject may encounter such as transportation, time away from work, parking, health costs, etc.;

  - Early withdrawal/procedures for termination: a statement that describes a subject's right to withdraw from the study and any procedures that may be necessary after an early withdrawal for subject's safety;

  - Significant new findings: a statement that subjects will be told of any new findings which may affect willingness to continue in the research;

- Approximate number of subjects: a statement that explains the approximate number of subjects to be enrolled in the study, worldwide, nationwide and locally, as applicable;

- Disposition of subject's blood samples: DNA testing, cell lines, development of future products;

- Payment: a statement which includes all information concerning the amount and schedule of payment for participation.

4. If the research involves vulnerable populations or sensitive issues, the investigator must address additional regulatory and/or institutional requirements. The investigator may consult SCRIHS staff for guidance. The vulnerable populations and sensitive issues include, but are not limited to:

   - Research involving the participation of children;
   - Research involving individuals with impaired consent capacity;
   - Research involving HIV screening and/or AIDS research;
   - Research involving DNA banking, genetic research, or gene therapy;
   - Research activities directed toward pregnant women;
   - Research involving prisoners;
   - Research involving students.

5. The investigator also must address the following issues, if applicable to the proposed research:

   - DHHS/NIH-sponsored multicenter clinical trial: the investigator must include a copy of the DHHS/NIH-approved sample informed consent document in the application. The investigator must justify in writing any deletion or substantive modification of information concerning risks or alternative procedures contained in the sample informed consent document, and the IRB must approve these deletions or modifications. For trials sponsored by the National Cancer Institute, investigators must forward copies of such IRB-approved changes, with their justifications to the appropriate Cooperative Group headquarters;
   - Investigational drugs, devices, or biologics: the investigator must inform the subject in the ICF that the study includes evaluation of both safety and effectiveness of the test article and state the test article is investigational, and, if applicable, not approved by the FDA;
   - Applicable FDA regulated clinical trials: the investigator must inform the subject that the clinical trial will be registered on www.ClinicalTrials.gov, a national clinical trial registry;
   - The process of dose escalation;
   - The possibility of risk for an unborn child, a man or woman's ability to procreate, or a woman's ability to conceive or carry a child will include the statement listed in the Instructions for Documentation of Informed Consent, which may be revised to meet the needs of the study;

- Additional requirements as specified in the IRB full and expedited review; applications/informed consent template.

6. If the research involves genetic testing or DNA banking, the PI must address, in the informed consent process and form, the relevant language from the Human Specimen Collection/Tissue Banking consent form template(s).

7. If the research involves establishing a specimen/tissue repository, the PI must address, in the informed consent process and form, the relevant language from the Tissue Banking consent form template.

8. The IRB assesses the PI's description of the informed consent process to ensure that the process meets the general requirements of informed consent (i.e., consent be obtained from the subject or subject's legally authorized representative; be in language understandable to the subject; be obtained under circumstances that provide the subject with the opportunity to consider whether or not to participate and that minimize coercive influences; does not include language through which the subject is made to waive his/her legal rights or inappropriately releases the investigator, sponsor, or institution from liability).

9. Where applicable, the IRB determines whether disclosure of any investigator conflict of interest is warranted in the informed consent process and document.

10. The IRB is responsible for reviewing the proposed informed consent document(s) to ensure that applicable federal and IRB requirements are met.

11. Once the IRB approves the study, SCRIHS staff processes the submission approval in the electronic IRB system. SCRIHS staff route the approval and associated forms with appropriate approval stamps to the investigator. Investigators may only enroll subjects using informed consent/forms which have a valid "IRB approval" stamp unless the IRB grants a waiver from the requirement for informed consent or documentation.

12. The investigator is responsible for ensuring that informed consent is obtained from each research subject or his/her LAR after the subject or the subject's LAR has had an adequate opportunity to read the form and prior to subject participation in any part of the study, using the process and form approved by the IRB.

13. The subject or the subject's LAR and the person providing the information to the subject sign and date the informed consent document at the time of consent. Only study personnel authorized (in the IRB approved protocol submission) to obtain informed consent may provide the informed consent to the subject and sign the informed consent document. The subject, or LAR signing on the subject's behalf, receives a copy of the signed form. A copy of the signed consent form must be placed in the patient's medical record, if applicable, or according to affiliated hospital/SIU HealthCare policies.

Use of the Short Form Written Consent Document

1. The PI may request to use a short form written consent document stating that study personnel have presented the elements of informed consent (as required by 45 CFR 46.116) orally to the subject or the subject's LAR.

2. The IRB reviews the request and may approve the short form option for documentation only if the study meets all of the requirements outlined in 45 CFR 46.117(b), and as applicable, 21 CFR 50.27(b).

3. When the IRB approves use of the short form method:

    - The PI must ensure there will be a witness to the oral presentation. For participants who do not speak English, the PI must ensure the witness is conversant in both English and the language of the participant.
    - The IRB must provide prior approval of a written summary of the oral content presented to the subject or the subject's LAR, which embodies the basic and appropriate elements of disclosure.
    - The subject or the subject's LAR signs and dates the short form.
    - The witness signs both the short form and a copy of the summary.
    - The person actually obtaining consent signs a copy of the summary.
    - The person obtaining consent gives a copy of the summary to the subject or the subject's LAR, in addition to a copy of the short form.

Research Involving Individuals Who Lack Decisional Capacity

1. The PI completes the IRB application, including forms, and after obtaining IRB approval implements the research in accordance with the requirements for assessing decisional capacity specified in the SCRIHS LAP SOP and Participants Who Lack Decisional Capacity guidance document

2. In conducting the review, the IRB uses the recommendations for assessing decisional capacity as a guide to ensure additional safeguards are in place.

Assent

1. The PI must utilize the appropriate Assent Form template document when preparing the IRB application.

2. The PI is responsible for including in the IRB application a description of the process/ procedure for obtaining and documenting assent when research includes:

    - Children and/or;
    - Individuals who lack decisional capacity.

3. The IRB reviews the proposed process and, if applicable, the assent form to ensure compliance with IRB guidance and federal requirements (Refer to Age of Assent Guidance Document and Participants Who Lack Decisional Capacity Guidance Document).

Emancipated Individuals

1. State law defines emancipation of individuals under the age of eighteen in Illinois and who are thus able to consent to participate in some research studies. If necessary, legal counsel will be consulted by SCRIHS staff to advise PIs as to whether the particular subjects are legally emancipated. If pregnant individuals under the age of eighteen are neither married nor living on their own (i.e., living at home under the care of their parents or some other adult), they are not legally emancipated, and both parental permission and subject assent are needed.

2. When conducting the study, given the variety of living situations that an individual may find him or herself living in, investigators may need to make decisions on a subject-by-subject basis. If there are questions relating to whether an individual meets the state statutory requirements to be emancipated, the investigator may consult SIU legal counsel.

3. If a child or a class of subjects is deemed to be emancipated, then 45 CFR 46 Subpart D and 21 CFR 50 Subpart D do not apply, and the subject may provide informed consent as an adult.

Obtaining Informed Consent outside the State of Illinois

1. If the PI conducts the research outside the state of Illinois and the research involves children, an LAR, or a guardian, the investigator must follow the requirements of the state/country in which he/she will conduct the research. The PI must also determine which individuals meet the federal definitions for child/children, LAR, or guardian in the location outside the state of Illinois.

2. The PI identifies the state law(s) applicable to the determination of legally authorized representative and contacts SIU legal counsel for review and determination prior to approval by the IRB.

Non-English Speaking Subjects

1. Investigators must deliver all information regarding informed consent/assent to potential subjects or their LAR in the subject's native language(s) or one that the subject understands. The investigator must provide the IRB and prospective subjects a translated version of the consent/assent form.

2. SCRIHS staff identifies a cultural consultant to review the study and informed consent/assent document for accuracy and cultural appropriateness. If SCRIHS staff are unable to identify an individual to serve as a cultural consultant, the investigator provides a cultural consultant for review of accuracy of the informed consent form and cultural appropriateness.

3. SCRIHS staff ensures that the consultant does not have a conflict of interest.

4. The IRB may use expedited review procedures in approving such documents if the IRB has already approved the English language consent/assent document, and the cultural consultant attests to the accuracy of the translation.

Research that Requires Monitoring of Informed Consent/Assent Process and Procedures

1. The IRB determines which research requires monitoring of the informed consent/assent process and the procedure and frequency with which such monitoring will occur based on the degree of risk to subjects, the need for protection of vulnerable subjects, or concerns related to an incident of noncompliance.

2. A designated IRB member(s), SCRIHS staff, or other designee (as determined by the IRB) may monitor the informed consent/assent process. The monitoring may involve direct observation, interviews of subjects, surveys of subjects, or other means as deemed appropriate by the IRB for the circumstances.

Recordkeeping

1. For studies conducted at the affiliated hospitals or SIU HealthCare clinics, the PI should defer to those applicable policies for maintaining research documents in medical records. The PI must also keep the original signed consent/assent document in the research records in accord with the IRB-approved protocol.

2. For studies conducted in other settings, the PI keeps the original signed informed consent form and, if applicable, assent form in accord with the SCRIHS/IRB Recordkeeping SOP and the study procedures as approved by the IRB.

3. The IRB documents its review as delineated in the applicable procedures for a particular review mechanism (e.g., initial full review, expedited review, modification review, etc.) and the SCRIHS/IRB Recordkeeping SOP.

Waiver of Informed Consent for Non-FDA Regulated Studies

1. The PI makes a preliminary decision to seek waiver of informed consent and submits a justification, addressing the reason for each criteria for alteration, for the waiver request in the IRB application.

    - The IRB may waive the requirements or alter elements, in its discretion, if it finds and documents:
        - The research involves no more than minimal risk to the subjects;
        - The research will not adversely affect the rights and welfare of subjects ;
        - The investigator could not practicably conduct the research without the waiver or alteration.
        - Whenever appropriate, study personnel provide subjects additional pertinent information after they begin participation in the study.

2. The IRB may also waive the requirement to obtain informed consent or alter some of the elements, in its discretion, if the IRB finds and documents that:

    - The research or demonstration project is to be conducted by or is subject to approval of state or local government officials and is designed to study, evaluate or examine public benefit of service programs, procedures, methods or levels of payment; AND
    - The investigator could not practicably conduct the research without the waiver or alteration.

3. If the IRB reviews the protocol at a convened meeting, and if approved, SCRIHS staff document the waiver of informed consent approval in the IRB meeting minutes.

4. If the protocol is eligible for expedited review, the expedited reviewer documents whether the study meets each of the criteria.

Waiver of Informed Consent for FDA Regulated and/or DHHS Funded Planned Emergency Research

1. The PI completes the IRB application following the procedures outlined in the Initial Full Board Review SOP. SCRIHS staff screen the application using procedures outlined in the Initial Full Board Review SOP. SCRIHS staff asks the PI to address any additional issues not included in the standard IRB application, such as plans for public disclosure in communities prior to initiation.

2. At the convened meeting, SCRIHS staff provide the IRB Chair or designee with a copy of 21 CFR 50.24 and/or 45 CFR 46.101(i). The individual chairing the meeting goes through each regulatory requirement. The IRB discusses whether the research meets each requirement and raises any applicable controverted issues. The outcomes of the review are the same as those listed in the Initial Full Board Review SOP. SCRIHS staff record the discussion in the minutes.

Exception from Informed Consent Requirement for Use of FDA-Regulated Test Articles in a Single Subject

1. The PI must obtain informed consent, even in an emergency use situation, unless the study meets certain conditions. (See Emergency Use SOP)

Waiver of Parental or Guardian Permission for Research Involving Children in Non-FDA Regulated Research

1. The PI makes a preliminary decision to seek waiver of parental or guardian permission for participation of children in accord with 45 CFR Subpart D 46.408 (c) or 45 CFR 46.116(c)(d). The PI includes justification for the waiver and a description of a substituted appropriate mechanism for protecting the children who will participate in the research.

2. The IRB may approve, in its discretion, the request provided the study meets the conditions outlined in 45 CFR Subpart D 46.408(c) or 45 CFR 46.116 (c)(d).

3. If the IRB reviews the research at a convened meeting, SCRIHS staff record the discussion in the minutes.

4. If the IRB reviews the study using expedited procedures, the expedited reviewer documents whether the research meets the criteria.

Waiver of Documentation of Informed Consent for FDA-Regulated Research

1. The PI makes an initial request to waive the documentation requirements for obtaining informed consent, as specified in the IRB application.

2. The IRB may waive the documentation requirement to obtain a signed consent, in its discretion, if the research presents no more than minimal risk and involves no procedures for which the IRB normally requires written consent.

3. When the IRB waives the requirement to obtain written documentation of informed consent, the IRB reviews a written description of the information that the PI will give to the subjects.

4. In cases in which the IRB waives the documentation requirement, the IRB has the authority to require the investigator to provide subjects with a written statement regarding the research.

5. If the IRB reviews the request at a convened meeting, SCRIHS staff include the discussion in the IRB minutes.

6. If the IRB reviews the study using expedited procedures, the expedited reviewer documents whether the research meets each of the criteria.

Waiver of Documentation of Informed Consent for Non-FDA Regulated Studies

1. The PI makes an initial request to waive the documentation requirements for obtaining informed consent, as specified in the IRB application.

2. The IRB may waive the documentation requirements to obtain a signed consent, in its discretion, if:

    - The only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Study personnel must ask each subject whether the he/she wants documentation regarding the research; or
    - The research presents no more than minimal risk to subjects and involves no procedures for which written consent is normally required (i.e., a cover letter or a phone script).

3. In cases in which the IRB waives the documentation requirement, the IRB has the authority to require the investigator to provide subjects with a written statement regarding the research.

4. When the IRB waives the requirement to obtain written documentation of informed consent, the IRB reviews a written description of the information that subjects will receive.

5. If the IRB reviews the request at a convened meeting, SCRIHS staff includes the discussion in the meeting minutes.

6. If the IRB reviews the protocol using expedited procedures, the expedited reviewer documents whether the research meets each of the criteria.

REFERENCES

21 CFR 50.20
21 CFR 50.23-25
21 CFR 50.27
21 CFR 56.109 (b),(c)
45 CFR 46.101(i)
45 CFR 46.109 (b),(c)
45 CFR 46.111
45 CFR 46.116
45 CFR 46.117
34 CFR 97 [Department of Education Subpart D]

PROTECTION OF VULNERABLE SUBJECTS

EFFECTIVE DATE: March 14, 2012

REVISION DATE: December 4, 2015; December 11, 2015

OBJECTIVE

To describe policies and procedures for reviewing research involving vulnerable subjects

GENERAL DESCRIPTION

The Institutional Review Board (IRB) gives special consideration to protecting the welfare of vulnerable subjects such as children, prisoners, fetuses/neonates, pregnant women, and individuals with consent capacity impairment. The IRB also recognizes that additional populations such as students may qualify as vulnerable populations and need safeguards in place for their protection during study participation.

PROCEDURES

Screening and Educational Guidance

1. The PI identifies the categories of vulnerable subjects (e.g., individuals with consent capacity impairment, children, prisoners, pregnant women, and students) involved in the research in the electronic IRB application.

2. Upon receipt of an IRB application, SCRIHS staff conduct a preliminary screening. When applicable, SCRIHS staff provide any necessary materials/guidance to the IRB on the regulations pertaining to vulnerable subjects.

3. SCRIHS staff, IRB Chair, or designee requests a consultant review if additional expertise is needed.

4. IRB membership includes representation with expertise in selected vulnerable populations routinely reviewed by the IRB, such as children or prisoners. SCRIHS staff screen the application to ensure that designated representatives review research involving children or prisoners. Depending upon the type of review, designated representatives either attend the convened meeting or provide comments in writing.

Protocol Review Process

1. The IRB reviews the IRB application to determine whether the study protocol includes enrollment of vulnerable subjects and whether appropriate safeguards are in place.

2. As applicable, the IRB considers the following elements when reviewing research involving vulnerable subjects:
   - Inclusion/exclusion criteria;

   - Over-selection or exclusion of certain groups based on perceived limitations (i.e., targeting prisoners as research subjects because they are a readily available "captive" population);

- Knowledge of applicable or local laws that bear on the decision-making process (i.e., emancipated individuals, legally authorized representatives, age of majority for research consent).

3. The IRB follows applicable federal and state regulations and IRB policy to assist in reviewing and approving proposed research that involves vulnerable subjects such as:

   - Pregnant Women, Human Fetuses and Neonates (45 CFR 46, Subpart B)
   - Research Involving Prisoners (45 CFR 46, Subpart C)
   - Research Involving Children (45 CFR 46, Subpart D, 21 CFR 50, Subpart D and U.S. Department of Education, Subpart D)
   - Research Involving Individuals with Impaired Consent Capacity
   - Research involving students

4. The IRB considers each of the specific findings discussed in the IRB application for research involving vulnerable subjects, as documented by IRB approval. IRB approval also documents that the IRB members acknowledge and agree with the preliminary description of safeguards and risk assessment of the protocol as described in the application by the PI. SCRIHS staff document in the minutes discussions of controverted issues at convened meetings.

5. SCRIHS staff document specific findings in the meeting minutes or other appropriate sections of the electronic system. The IRB does not amend the categories during subsequent reviews unless changes to the protocol dictate otherwise.

6. The IRB may require review more frequently than once a year for protocols involving vulnerable populations based on the nature of the research and the level of risk.

REFERENCES

45 CFR 46 Subpart B
45 CFR 46 Subpart C
45 CFR 46 Subpart D
21 CFR 50 Subpart D
34 CFR 97 Subpart D

MEDICAL DEVICES

EFFECTIVE DATE: August 8, 2012

REVISION DATE:

OBJECTIVE

To describe the procedures for Institutional Review Board (IRB) determinations of Significant Risk (SR) and Non-Significant Risk (NSR) investigational devices and evaluation of investigator plans to control investigational devices as required by the Food and Drug Administration (FDA) Investigational Device Exemption (IDE) Regulations.

GENERAL DESCRIPTION

The sponsor and the IRB categorize the device investigation as either Significant Risk (SR) or Non-significant Risk (NSR). The sponsor makes the initial determination of risk. The principal investigator (PI) submits the proposed study to a convened IRB for formal determination of the appropriate SR/NSR category.

Unless the study is exempt from Investigational Device Exemption (IDE) requirements, a SR device study must be conducted under an FDA approved IDE. A NSR device study may be conducted under an abbreviated IDE with the IRB acting as surrogate for the FDA. An exemption from the IDE requirement is not an exemption from the requirement for prospective IRB review or informed consent.

Each PI receiving investigational device(s) for human research purposes is responsible for control of the device(s) in accordance with regulatory requirements and any corresponding institutional requirements. The PI is required to submit a plan for control, storage, and accountability of the device(s) for IRB review and approval. During review of the research proposal, the IRB will evaluate the plan. The PI assumes sole responsibility for implementing the plan as approved by the IRB. Post IRB-approval monitoring to evaluate adherence to the IRB approved plan may be conducted by SCRIHS staff or appointed an IRB member(s).

If uncertainty exists regarding the need for an IDE, the IRB can request that the PI consult with the FDA and provide documentation of the FDA response.

If a protocol involving a medical device is subject to review under more than one department or agency's regulations, the protocol must meet the requirements of each set of regulations.

Definitions

A *medical devic*e is defined as any health care product that does not achieve its primary intended purposes by chemical action or by being metabolized.

An *investigational device* is a medical device which is the subject of a clinical study designed to evaluate the effectiveness and/or safety of the device.

A *significant risk device study* is a study of a device that presents a potential for serious risk to the health, safety, or welfare of a participant and (1) is intended as an implant; or (2) is used in supporting or sustaining human life; or (3) is of substantial importance in diagnosing, curing, mitigating, or treating

disease, or otherwise prevents impairment of human health; or (4) otherwise presents a potential for serious risk to the health, safety, or welfare of a participant.

A *nonsignificant risk device study* is one that does not meet the definition for an SR study. A study is considered NSR if it (1) is noninvasive; (2) does not require an invasive sampling procedure that presents significant risk; (3) does not by design or intention introduce energy into a subject; and (4) is not used as a diagnostic procedure without confirmation of the diagnosis by another medically established diagnostic product or procedure.

An *Investigational Device Exemption* (IDE) permits a device, which otherwise would be required to comply with a performance standard or to have premarket approval, to be shipped lawfully for the purpose of conducting investigations of that device. An approved IDE exempts a device from specific Food and Drug Administration (FDA) requirements as laid out under 21 CFR 812. An approved IDE means that the IRB (and FDA for SR devices) has approved the sponsor's study application and that the study meets all the requirements under 21 CFR 812.

PROCEDURES

Significant vs. Nonsignificant Risk Determination

1. An investigator conducting research that involves collection of safety or efficacy data on a medical device completes the applicable device section of the electronic IRB application.

2. If the study is being conducted under a valid IDE, the PI includes in the electronic IRB application the IDE number, name of IDE holder/sponsor, and sponsor protocol imprinted with number or written communication from FDA or the sponsor documenting the IDE number.

3. If the study is not being conducted under a valid IDE at time of IRB submission, the PI includes in the IRB application the sponsor's initial assessment of the risk (SR or NSR), and the rationale used in making the risk determination. The PI includes FDA correspondence or documentation if available.

4. The IRB makes its own determination of the risk category (SR or NSR). The IRB reviews reports of prior investigations conducted with the device, the proposed investigational plan, a description of subject selection criteria, monitoring procedures, and any other information the IRB deems necessary to make its decision.

5. The IRB may request that the PI consult with the FDA as appropriate. If FDA provides a determination, it is considered final and the IRB does not duplicate the effort.

6. If the IRB determines that a protocol submitted for approval involves a SR device, which has been deemed NSR by the sponsor, the IRB notifies the investigator who notifies the sponsor. The sponsor notifies the FDA that the IRB has made an SR determination.

7. If the IRB determines that a study involves the use of a SR device, the PI must obtain an IDE and IRB approval before the study begins and must conduct the study in accordance with full IDE requirements.

8. If the PI considers a SR device to be exempt from IDE requirements, he/she references the exemption category being claimed and provides documentation from FDA or sufficient justification to support the exemption category.

9. The PI is responsible for consulting FDA to determine if the device meets specific criteria to be exempt from IDE requirements.

10. If the IRB determines that the study is NSR, there is no requirement for submission of an IDE application to the FDA. The PI conducts the study in accordance with abbreviated IDE requirements.

11. After making the risk determination, the IRB conducts the review of the study using the same criteria it would use in considering approval of any full review application. The IRB considers the risks and benefits of the medical device compared to the risks and benefits of alternate devices or procedures as listed in the electronic IRB application.

12. The IRB may approve or disapprove the proposed research based on local context and its responsibilities to protect human subjects in research.

13. SCRIHS staff document the decision of the IRB (both risk assessment and approval) in correspondence sent to the PI and in the meeting minutes or electronic protocol file depending on the type of review.

14. In a study of an investigational device in which an unanticipated problem/adverse event to subjects or others occurs, the investigator submits to the sponsor and to the IRB a report of the problem or adverse event occurring during the investigation. (See Unanticipated Problems and Adverse Event Reporting SOP.)

IRB Evaluation of PI's Plan to Control Device

1. During review of the research proposal, the IRB evaluates the information provided by the PI that describes plans for control of the investigational device(s) including policies and procedures for storage, control, dispensing, and accountability.

2. If the IRB determines the PI's plans are inadequate, the IRB may request changes and/or additional information.

3. SCRIHS staff may periodically review protocols involving use of an investigational device.

4. SCRIHS staff provide the IRB with any follow-up evaluation regarding whether the PI is meeting investigator responsibilities for control, storage, and accountability of the device.

REFERENCES

21 CFR 812.2
21 CFR 56
21 CFR 50
21 CFR 812.66
21 CFR 56.108(a)(1)
21 CFR 812.2(b)

HUMANITARIAN USE DEVICES

EFFECTIVE DATE: November 9, 2011

REVISION DATE: March 1. 2012; March 11, 2016; July 22, 2016; August 08, 2018

OBJECTIVE

To describe the process for review of a humanitarian use device (HUD) for clinical, emergency, compassionate, and investigational use

GENERAL DESCRIPTION

The Southern Illinois University School of Medicine IRB, also known as SCRIHS, may approve the following situations involving the use of a HUD:

- Clinical use of a HUD per legally marketed Humanitarian Device Exemption (HDE) indication; OR
- Clinical Investigation or Investigational Use of a HUD ; OR
- Emergency or Compassionate Use of a HUD based on a healthcare provider/principal investigator (PI) request that meet IRB criteria.

Definitions

Humanitarian Use Device (HUD): A medical device intended to treat or diagnose a disease or condition that affects or is manifested in fewer than 8,000 individuals in the United States per year.

A Humanitarian Device Exemption (HDE): A type of application granted by the U.S. Food and Drug Administration (FDA) that authorizes the marketing of the HUD. Approval of an HDE is based on safety and probable benefit and allows the "***use"*** of an HUD for a specific indication in fewer than 8,000 individuals in the United States per year. Although the device is authorized by Federal Law, the effectiveness of the device for the specific indication has not been demonstrated.

"Use" of an HUD according to an approved HDE does not require the collection of safety and effectiveness data per 21 CFR 814.

"Clinical Investigation" of an HUD refers to research involving a HUD, conducted in accordance with approved indication(s), where safety and effectiveness data are collected.

"Investigational Use" of an HUD refers to an investigation of the HUD other than the approved indication(s). Investigators are required to comply with the IDE regulations (21 CFR Part 812) in addition to complying with the requirements for IRB approval (21 CFR Part 56) and protection of human subjects (21 CFR Part 50).

"Investigational Device Exemption **(IDE)"** refers to the regulations under 21 CFR 812. An approved IDE means that the IRB (and FDA for significant risk devices) has approved the sponsor's study application, and the proposed use meets all the requirements of 21 CFR 812.

PROCEDURES

Clinical Use for Treatment or Diagnosis Consistent with HDE Approved Labeling

1. The healthcare provider proposing the use of the HDE must submit an application to the IRB following the Initial Full Board Review SOP. SCRIHS approval is required before the HDE can be used.

2. The IRB will review the clinical use of a HUD at a convened meeting per full board review criteria and procedures. The IRB approves the use of the HUD device consistent with the scope of the FDA-approved HDE indications for groups of patients meeting clinical criteria.

3. The IRB may choose to require informed consent or allow use of a modified clinical consent, or patient information brochure consistent with the approved labeling.

4. The healthcare provider is required to submit a report to FDA and to the IRB whenever a HUD may have caused or contributed to a death or serious injury or has malfunctioned and would be likely to cause or contribute to a death or serious injury if the malfunction were to recur (21 CFR 814.126(a)).

5. The healthcare provider labels and stores the HUD in a secure manner to assure accountability and traceability and to clearly display use limitations or restrictions designated by the IRB or HDE holder.

6. IRB approval may not be sufficient to use a HUD in clinical practice. Hospitals and clinical groups have separate requirements for approval and use of HUDs.

Clinical Investigations of an HUD Consistent with Labeling

1. The IRB may approve an application for the clinical investigation of a HUD to collect safety and effectiveness data consistent with the scope of the FDA-approved indications. The clinical investigation is exempt from the requirement for an IDE as long as the HUD is used in accordance with its approved indication(s). However, IRB approval (21 CFR Part 56) and protection of human subjects (21 CFR Part 50) are still needed, as required for all FDA-regulated clinical studies. Informed consent, and additional safeguards for children (if applicable) required for the clinical investigations of an HUD are separate and distinct from the IRB approval associated with the use of the HUD.

2. The PI submits an IRB application following the Initial Full Board Review SOP. The IRB will review the submission at a convened IRB meeting.

Investigational Use of an HUD Off-label

1. The IRB may, at its discretion, approve an application for the investigational study of an HUD device beyond its approved indication(s). Investigational use of an HUD beyond its approved indications(s) must be conducted in compliance with the IDE regulations at 21 CFR Part 812, in addition to requiring IRB approval (21 CFR Part 56) and protection of human subjects (21 CFR Part 50). When the proposed use is in compliance with IDE regulations 21CFR 812 requiring an IDE if there is significant risk.

2. The PI submits an IRB application following the Initial Full Board Review SOP. The IRB will review the submission at a convened IRB meeting.

3. In the event that IRB approval for research of a HUD for an indication other than its approved indication(s) is requested without first obtaining an FDA-approved IDE, the IRB can make a SR/NSR determination as described in 21 CFR 812.66. If the HUD carries significant risk, the PI may conduct the study following FDA approval of an IDE application.

Continuing Review Requirements for HUDs

1. The IRB shall conduct continuing review of all HUD approvals at intervals appropriate to the degree of risk, but not less than once per year (45 CFR 46.109 / 21 CFR 56.109).

HUD Emergency Use

1. Per 21 CFR 814.124: if a physician in an emergency situation determines that IRB approval for the use of the HUD at the facility cannot be obtained in time to prevent serious harm or death to a patient, a HUD may be used without prior IRB approval. **The physician should follow the SCRIHS Emergency Use SOP.** Additionally, the physician must provide a report to the IRB.This report will include:

    - The identification of the patient involved;
    - The date on which the device was used;
    - The reason for the use;
    - The patient has a life-threatening condition, OR;
    - The patient has a serious medical condition that can reasonably be expected to benefit from the use of the HUD, AND;
    - This is the best acceptable treatment alternative for the patient; AND;
    - Alternative treatments pose greater risks for the patient or are deemed to provide less benefit than the HUD.

HUD Compassionate Use

1. The healthcare provider submits the request to the IRB via the electronic submission system. The title should include "HUD Compassionate Use". The following are required for review at a convened meeting prior to proceeding with the procedure:
    - A letter from the Primary Investigator describing the patient's condition and the circumstances necessitating treatment. This should include a discussion of why alternative therapies are unsatisfactory and why the probable risk of using the device is no greater than the probable risk from the disease or condition;
    - A written assessment from another physician, not involved in the patient's care, stating that no generally acceptable alternative treatment for the condition exists;
    - A letter from the sponsor authorizing the compassionate use;
    - A copy of the informed consent form document and the compassionate use protocol that will be followed;
    - Clearance from the institution where the treatment will be conducted;
    - A schedule for monitoring the patient after treatment..

2. The healthcare provider provides the HDE holder and the IRB with information addressing the criteria listed in item 1.

3. In addition, the healthcare provider requests that the HDE holder submit an HDE amendment for FDA approval prior to the compassionate use of the device. If the FDA grants approval, the healthcare provider reports the use of the HUD to the IRB and the HDE holder for subsequent submission to the FDA database.

4. The full IRB reviews compassionate use in a convened meeting using all standard full review criteria and procedures. The approval applies to the single case requested and does not apply to a class of patients.

5. The healthcare provider obtains informed consent from the patient or the patient's legally authorized representative using an IRB-approved consent form or approved modified clinical consent or operative permit that is consistent with or combined with the approved labeling and/or patient information packet..

6. The healthcare provider monitors the patient and submits a follow-up report including any safety-related information to the FDA or the HDE holder.

7. The healthcare provider submits a report to FDA and to the IRB whenever a HUD may have caused or contributed to a death or serious injury or has malfunctioned and would be likely to cause or contribute to a death or serious injury if the malfunction were to recur (21 CFR 814.126(a).

8. The healthcare provider submits a final report to include the final patient outcome via the Notification of Study Closure form in the electronic submission system.

REFERENCES

Food and Drug Administration
Guidance for HDE Holders, Institutional Review Boards (IRBs), Clinical Investigators, and FDA Staff - Humanitarian Device Exemption (HDE) Regulation: Questions and Answers (July 8, 2010)
Information Sheet Guidance: Frequently Asked Questions about Medical Devices (January 2006)
21 CFR 812.35(a)
21 CFR 814.24
21 CFR 50.23
21 CFR 56.109
45 CFR 46.109

EMERGENCY USE

TITLE: Emergency Use

EFFECTIVE DATE: August 8, 2012

REVISION DATE: March 8, 2013; October 9, 2013; July 22, 2016, August 8, 2018

OBJECTIVE

To describe the procedure for the emergency use of a Food and Drug Administration (FDA) regulated investigational drug, biologic, or device in a single subject

GENERAL DESCRIPTION

The need for an investigational drug, biologic, or device may arise in an emergency situation that does not allow time for submission of an investigational new drug (IND) application or investigational device exemption (IDE) in accordance with federal regulations.

Although the FDA may exempt the requirement for prior review and approval by the IRB in emergency use cases [21 CFR 56.104(c)], SCRIHS Institutional Review Board (IRB) policy requires prior review and confirmation that use of the article meets FDA criteria by the IRB Chair, Vice Chair(s), or physician IRB member in these situations. In accord with FDA regulations, investigators who administer an investigational treatment, in an emergency situation, without IRB approval, must submit a report of the use to the IRB within five working days.

In addition, any subsequent use of the test article in another subject must first receive full IRB review. The FDA acknowledges, however, that it would be inappropriate to deny emergency treatment to a second individual if the only obstacle is that the IRB has not had sufficient time to convene a meeting to review the issue.

In activities regulated by 45 CFR 46, an investigator may not use data related to emergency care (i.e., single patient administration) as a prospectively planned systematic investigation designed to contribute to generalizable knowledge. Investigators may not aggregate such data with research data, even if the emergency protocol is identical to that of a research protocol subsequently approved by the IRB, nor may the investigator include the outcome of such care in any report of a research activity.

If the activity involves emergency use of an FDA regulated test article in a life-threatening situation, the activity is research under FDA regulations, and the patient is a subject under FDA regulations. The FDA may require data from an emergency use of a test article in a life-threatening situation to be reported in a marketing application.
If use is for a life-threatening or serious disease but time is sufficient to obtain IRB approval, follow procedures in the Expanded Access Program (EAP) for Drugs SOP, Humanitarian Use Devices SOP, or other SOPs as applicable.

Definitions

Emergency Use is defined as the use of a test article (e.g., investigational drug, biologic, or device) on a human subject in a life-threatening situation in which no standard acceptable treatment is available and in which there is not sufficient time to obtain IRB approval.

Life-threatening, for the purposes of section [21 CFR 56.102(d)], includes the scope of both life-threatening and severely debilitating, as defined below.

- *Life-threatening* means diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted and diseases or conditions with potentially fatal outcomes, where the end point of clinical trial analysis is survival. The criteria for life-threatening do not require the condition to be immediately life-threatening or to immediately result in death. Rather, the subjects must be in a life-threatening situation requiring intervention before review at a convened meeting of the IRB is feasible.

- *Severely debilitating* means diseases or conditions that cause major irreversible morbidity. Examples of severely debilitating conditions include blindness, loss of arm, leg, hand or foot, loss of hearing, paralysis or stroke.

PROCEDURES

1. If possible, before administering, the PI submits the following information directly to the IRB Chair, or designee, for review and confirmation for emergency use of a test article in a single subject:

    - A letter from the PI describing the patient's condition and the circumstances necessitating treatment;
    - An assessment from another physician, not involved in the patient's care, stating that no generally acceptable alternative treatment for the condition exists;
    - A copy of the informed consent form document and the treatment plan that will be followed;
    - Documented clearance from the institution where the treatment will be conducted;
    - A detailed schedule for monitoring the patient after treatment has been performed.

2. However, if the immediate use of the test article is, in the healthcare provider's opinion, required to preserve the life of the patient and time is not sufficient to obtain assessment by the IRB chair or designee, then the PI submits a report in writing within five working days as described below.

3. If the PI proposes to administer the test article in emergency use situations without informed consent, the request to the IRB Chair should include a statement certifying in writing that all of the conditions per [21 CFR 50.23] are met. These conditions are as follows:
    - The subject is confronted by a life-threatening situation necessitating the use of the test article;
    - Informed consent cannot be obtained because of an inability to communicate with or obtain legally effective consent from the subject;
    - Time is insufficient to obtain consent from the subject's legal representative; and
    - There is no alternative method of approved or generally recognized therapy available that will provide an equal or greater likelihood of saving the subject's life.

    If possible, this statement should include evaluation by a physician who is not participating in the clinical investigation. However, if the immediate use of the test article without informed consent is, in the investigator's opinion, required to preserve the life of the subject and time is not sufficient to obtain the independent determination by nonparticipating physician then the independent evaluation must be included in writing in the five working days report described below.

    NOTE: It is the PI's responsibility to obtain any needed institutional approval from the institution where treatment will be conducted prior to emergency use.

4. If the IRB Chair is not available, the PI should submit the information listed in item 1 or if applicable, item 2, to the SCRIHS office.

5. In the event that a PI submits an emergency use request to the SCRIHS office, SCRIHS staff forward the materials to the IRB Chair, Vice Chair(s), or physician IRB member, as available.

6. The IRB Chair, Vice Chair(s), or physician IRB member assesses the request to determine whether it meets the regulatory requirements for emergency use and responds to the PI in writing. The IRB Chair, Vice Chair(s), or physician IRB member may determine the PI can proceed or may withhold confirmation.

7. The IRB Chair, Vice Chair(s), or physician IRB member forwards the request and his/her response to SCRIHS staff and SCRIHS staff process the request.

8. Within five working days of the emergency use, the PI must submit a report to the IRB regarding the emergency use of the test article. That report is to include:

    - A brief description of the life-threatening situation;
    - Justification for use of the test article;
    - Signed consent form or justification for administration without informed consent;
    - Statement of review and evaluation of the situation by a physician who is not participating in the clinical investigation (if administered without informed consent); and,
    - A description of outcome of administration.

9. At a convened IRB meeting, SCRIHS staff inform the IRB that the IRB Chair, Vice Chair(s), or physician IRB member has assessed a request for emergency use using the regulatory definition, and the committee verifies the following criteria for emergency use:

    - The subject was confronted by a life-threatening situation necessitating the use of the investigational drug, biologic, or device;
    - No alternative method of approved or generally recognized therapy was available that provides an equal or greater likelihood of saving the subject's life; and
    - Time was not sufficient to obtain IRB approval.

10. If an investigator fails to submit a request involving emergency use of an investigational test article to the IRB for review and confirmation prior to initiation, the IRB retrospectively reviews the situation to determine if the test article administration met the regulatory definition and whether failure to comply with this SOP meets the IRB definition of noncompliance. (See the Noncompliance SOP.)

REFERENCES

21 CFR 56.102(d)
21 CFR 56.104(c)
21 CFR 50.23
21 CFR 312.36
21 CFR 312.310

EXPANDED ACCESS PROGRAM (EAP) FOR DRUGS

EFFECTIVE DATE: September 12, 2012

REVISION DATE: January 29, 2016

OBJECTIVE

To describe the procedures for utilizing the Food and Drug Administration (FDA) Expanded Access Program (EAP) including individual patient and intermediate or large population treatment investigational new drug (IND) applications

GENERAL DESCRIPTION

Definitions

Expanded Access, (sometimes called Compassionate Use), is a mechanism to facilitate availability of investigational drugs (as early in the drug development process as possible) for patients with serious or immediately life-threatening disease or conditions for which there are no satisfactory alternative treatments.

The FDA defines an *immediately life-threatening disease* as a stage of a disease in which there is a reasonable likelihood that death will occur within a matter of months or in which premature death is likely without early treatment.

A *Serious disease* means a disease or condition associated with morbidity that has substantial impact on day-to-day functioning. Short-lived and self-limiting morbidity will usually not be sufficient, but the morbidity need not be irreversible, provided it is persistent or recurrent.

A *treatment IND* is a large scale expanded access program typically following resolution of phase III or during phase II where sufficient safety data is available.

General Requirements

The FDA will permit an investigational drug to be used under the expanded access program (EAP) after sufficient data have been collected to show that the drug "may be effective" or does not have unreasonable risks relative to the risk of the condition of treatment.

FDA describes three distinct categories of EAP based on the number of people who need access and the level of risk. An expanded access IND submission is required for each type of expanded access.

1. Individual patient IND, including emergency use IND (21 CFR 312.310) commonly held by the treating physician or investigator for treatment of an individual patient.

2. Intermediate population treatment IND (21 CFR 312.315) commonly held by the sponsor (manufacturer) for use in a population smaller than a typical treatment IND or treatment protocol. The investigational drug for intermediate population treatment INDs may be in active development or may be an FDA approved drug that is unavailable or in limited supply.

3. Large population treatment IND or treatment protocol (21 CFR 312.320) commonly held by the sponsor for widespread treatment use. For a large population treatment INDs, the sponsor must be pursuing marketing approval.

Before submitting an Individual Patient IND to FDA, a physician or PI must confirm the manufacturer will provide the drug. If a large or intermediate scale EAP is available through the manufacturer, the PI may coordinate access to the drug through the manufacturer's approved Treatment IND rather than filing a separate Individual Patient IND.

FDA regulations require prospective review by the full board, convened IRB.

FDA policy specifies that "the provision for emergency use would rarely apply to a treatment protocol or treatment IND because these are planned uses of the test article and sufficient time is available to obtain IRB review and approval." In rare cases in which emergency use does apply for individual patients, administration takes place according to emergency use federal regulations (21 CFR 56.104) following procedures in the Emergency Use SOP.

The FDA identifies special considerations when a patient is to be treated under an EAP:

- Drug Development: In considering EAP use, individual needs must be balanced against societal needs. The FDA stipulates that expanded access use should not compromise enrollment or interfere with active clinical investigations that could support approval of the drug.

- Informed Consent: Informed consent is especially important in expanded access use situations because the subjects are desperately ill and particularly vulnerable. They will receive medications which have not been proven either safe or effective in a clinical setting. Both the setting and their desperation may work against their ability to make an informed assessment of the risk involved. Therefore, the PI must ensure that potential subjects are fully aware of the risks involved in the participation.

- Charging for Treatment INDs: The FDA permits charging for the drug, agent, or biologic when used in an EAP when regulatory criteria are met. Therefore, the IRB must pay particular attention to EAPs in which the subjects will be charged for the cost of the drugs. If subjects will be charged for use of the test article, economically disadvantaged persons may inadvertently be excluded from participation. Charging for participation may preclude economically disadvantaged persons as a class from receiving access to test articles. The IRB must balance this interest against the possibility that unless the sponsor can charge for the drug, it will not be available for treatment use until it receives full FDA approval.

- Regulatory Responsibilities: Per FDA a licensed physician under whose immediate direction an investigational drug is administered for an expanded access use is considered an investigator assuming applicable regulatory responsibilities. An individual who submits an IND for expanded access use is considered a *sponsor-investigator*, assuming applicable responsibilities for sponsors and investigators (21 CFR 312.305 (c). Additional training requirements may be required.

PROCEDURES

Individual Patient IND

1. The physician or PI submits the following for full board review by the convened IRB:

- Inclusion of the phrase "INDIVIDUAL PATIENT IND" in the title of electronic submission application; and
- brief description of patient situation and treatment plan; and
- individual patient IND approval letter from FDA; and
- investigator's brochure if applicable; and
- copy of the informed consent form.

2. SCRIHS staff screen the IRB submission and verify the IND number according to procedures described in the Initial Full Board Review SOP.

3. The IRB reviews the submission as outlined in the Initial Full Board Review SOP and according to federal regulations.

4. At the conclusion of treatment, the physician or PI reports a written summary of the results of the expanded access use, including any safety related information, to the IND sponsor or FDA and the IRB.

Individual Patient IND with Central IRB Approval

1. In cases where the expanded access protocol has received central IRB approval, SCRIHS may defer responsibility for IRB review of the individual patient use to the central IRB where appropriate agreements and required approvals are obtained consistent with the External Research and IRB Reliance SOP.

Individual Patient IND in an Emergency Situation

1. In the rare cases in which an emergency requires that the patient be treated before a written IND submission can be made, the PI obtains authorization for individual use from FDA by telephone or electronic communication with subsequent submission of IND paperwork (21 CFR 312.310).

2. The PI follows procedures described in the Emergency Use SOP, submitting emergency use information directly to the IRB Chair, with the following addition:
    - documentation of FDA telephone or electronic authorization for emergency IND.

3. The IRB Chair, SCRIHS staff, and/or the IRB follow review procedures as described in the Emergency Use SOP.

Intermediate or Large Population Treatment IND

1. The PI follows procedures described in the Initial Full Board Review SOP with the following additions and provisions:
    - inclusion of the phrase "TREATMENT IND" in the title on the electronic submission application; and
    - treatment IND approval letter from FDA; and
    - related materials including the treatment protocol, investigator's brochure, informed consent form, and potential investigational drug costs.

2. SCRIHS staff screen the IRB submission following procedures described in the Initial Full Board Review SOP.

3. The full board IRB reviews the protocol as outlined in the Initial Full Board Review SOP and according to federal regulations.

4. At the conclusion of treatment, the physician or PI reports a written summary of the results of the expanded access use, including any safety related information, to the IND sponsor or FDA and the IRB.

REFERENCES

21 CFR 312.300
21 CFR 312.8

DATA AND SAFETY MONITORING PLANS

EFFECTIVE DATE: October 10, 2012

REVISION DATE:

OBJECTIVE

To describe Institutional Review Board (IRB) review of data and safety monitoring plan(s) (DSMP) to ensure adequate protection is in place for subjects

GENERAL DESCRIPTION

Investigators develop data and safety monitoring plans as a mechanism for assuring the safety of human subjects and human research data, the validity of data, and the appropriate termination of studies.

All clinical trials require some form of monitoring. Risk and complexity are identified as the most important determinants of the degree and method of monitoring. The IRB requires review and approval of data and safety monitoring plans (DSMP) for greater than minimal risk research, or clinical investigations funded by the National Institutes of Health (NIH) or regulated by the Food and Drug Administration (FDA).

- Minimal risk studies (exempt, expedited) do not usually require a monitoring plan.

- Early studies (non-therapeutic, Phase 1, some Phase 2) are allowed great flexibility in monitoring; it is specifically allowed that the Principal Investigator (PI) conduct the monitoring. However, the policy requires written policies and procedures, and also requires that regardless of the method used, monitoring must be performed on a regular basis.

- Some Phase 2 and all Phase-3 studies require a formal DSM plan, which may include the establishment of a Data Safety Monitoring Board (DSMB), also referred to as Data Monitoring Committees (DMC), Independent Safety Review Committees (ISRC) by the sponsoring company, institute, study site or at the lead institution of a multi-center trial.

PROCEDURES

1. At initial review, investigators conducting greater than minimal risk research, or NIH funded/FDA regulated clinical investigations include a description of the proposed data and safety monitoring plan (DSMP) in the IRB application.

2. During initial review, the IRB reviews the general description of the DSMP to determine that adequate protections for human subjects are in place.

3. The IRB recognizes that the elements of a monitoring plan may vary depending on the potential risks, complexity, and nature of the trial. The IRB reviews several elements of the DSMP, which may include but are not limited to:

    - Plans for monitoring the progress of the trial and the safety of subjects;
    - Plans for assuring compliance with requirements regarding the reporting of adverse events;
    - Plans for review or analysis of cumulative safety data to determine whether harm is occurring;

- Any stopping or suspension rules to protect subjects;
- Any rules for dose escalation or reduction;
- Plans for assuring that any action resulting in a temporary or permanent suspension of a clinical trial is reported to the appropriate agencies;
- Plans for assuring data accuracy and protocol compliance;
- Plans for assuring communication among multi-center sites adequately protect the subjects.

4. The IRB may request additional information regarding the DSMP at initial review.

5. After reviewing the plan, the IRB may determine that a study requires a Data and Safety Monitoring Board (DSMB). A DSMB is recommended when:

   - The study endpoint is such that a highly favorable or unfavorable result, or even a finding of futility, at an interim analysis might ethically require termination of the study before its planned completion;
   - There are *a priori* reasons for a particular safety concern, as, for example, if the procedure for administering the treatment is particularly invasive;
   - There is prior information suggesting the possibility of serious toxicity with the study treatment;
   - The study is being performed in a potentially fragile population such as children, pregnant women or the very elderly, or other vulnerable populations, such as those who are terminally ill or of diminished mental capacity;
   - The study is being performed in a population at elevated risk of death or other serious outcomes, even when the study objective addresses a lesser endpoint;
   - The study includes small numbers of subjects and toxicity may become more apparent through close monitoring of individual subjects, while in larger studies risk may be better addressed through statistical comparisons of treatment groups;
   - The study is large, of long duration, and multi-center.
   - For any controlled trial of any size that will compare mortality or major morbidity.

6. If the IRB (or an external entity) determines the DSMP of an investigator-initiated protocol must include a Data and Safety Monitoring Board (DSMB), the IRB evaluates the DSMB for membership, charter, and DSMB responsibilities. (See DSMB Charter Template for guidance)

7. The PI submits documentation of data and safety monitoring activities (i.e., summary report, meeting minutes) to the IRB prior to continuing review if provided to the PI by the sponsor or prepared by the PI, as described in the DSMP. The IRB reviews these materials prior to continuing review as an Amendment.

8. The PI is responsible for acquiring evidence that data and safety monitoring activities have occurred if the sponsor has not been providing the documentation. At the time of continuing review of the study, the PI submits documentation representing data and safety monitoring activities (i.e., summary report, meeting minutes) not previously submitted to the IRB.

9. At continuing review, the IRB reassesses the risk and determines whether the PI should provide additional information in the informed consent document based on the information provided in the data and safety monitoring reports/minutes.

REFERENCES

NIH Policy for Data and Safety Monitoring,
http://grants.nih.gov/grants/guide/notice-files/not98-084.html

Establishment and Operation of Clinical Trial Data Monitoring Committees,
http://www.fda.gov/RegulatoryInformation/Guidances/ucm127069.htm

LEGALLY AUTHORIZED REPRESENTATIVE CONSENT

EFFECTIVE DATE: September 8, 2010

REVISION DATE: June 8, 2016; October 12, 2016

OBJECTIVE

This policy provides guidance and direction for obtaining a valid informed consent from a Legally Authorized Representative ("LAR") decision maker in order for an adult subject who lacks decisional capacity to participate in a research study in Illinois. Investigators are to follow this policy when obtaining permission for adults unable to consent to take part in research. It is the policy of SCRIHS to review, approve, and provide guidance as to ethical considerations to afford additional protections when decisionally-impaired subjects are involved in human subject research, to uphold their rights and welfare, and to prevent coercion or undue influence. An investigator must also follow the SCRIHS guidance document "Participants Who Lack Decisional Capacity". Protocols intending to use LAR consent must outline the procedures applicable to the study protocol in the application for SCRIHS approval.

GENERAL DESCRIPTION OF POLICY

Unless the IRB has waived the requirement to obtain consent (45 CFR 46.116(c)), when research in Illinois involves ADULTS unable to consent, permission must be obtained from the following legally authorized representatives (LARs) in order of priority:

Priority	Type of Legally Authorized Representative
1	Guardian of Person – Court order gives the power to make Healthcare Decisions
2	Power of Attorney for Healthcare - unrevoked
3	Guardian of the Person – Court order does not specify that the Guardian of the Person has the power to make healthcare decisions
4	Spouse of subject
5	Adult Son or Daughter of subject
6	Parent of adult subject
7	Adult Brother or sister of subject
8	Adult grandchild of subject
None	Guardian of Estate; Power of Attorney for Property

RESEARCH OUTSIDE OF ILLINOIS

For research outside of Illinois, a determination of who is an LAR is to be made with consultation from legal counsel.

Definitions

DECISIONAL CAPACITY: The ability to understand and appreciate the nature and consequences of a decision regarding medical treatment or forgoing life-sustaining treatment and the ability to reach and communicate an informed decision in the matter as determined by the investigator(s).

LEGALLY AUTHORIZED REPRESENTATIVE (LAR): DHHS and the FDA define a legally authorized representative as "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." (21 CFR 50.3; 45 CFR 46.102(c))

PROCEDURES

If no LAR can be identified, then the subject shall not be enrolled in a research study.

If multiple LARs exist at the same priority level and all of the LARs in that priority level do not unanimously agree regarding the subject's enrollment in a research study, then the subject shall not be enrolled in the research study.

- Once identified, and if the LAR(s) agree(s), the LAR shall complete and sign and date the appropriate signature section of the informed consent document for the research study. At least one LAR must act as the designee to complete the LAR signature section to identify the other LAR(s) and certify the other LAR(s) concurrence with the subject's enrollment.

- Investigators shall describe to the highest ranking LAR(s) the nature of the ongoing decisions during the study regarding the subject's participation, decision to participate in certain procedures, changes to the study, etc., in order to ensure that the LAR will be willing to undertake these on-going responsibilities.

- LARs are prohibited from receiving any financial compensation for providing consent.

- Potential LAR(s) must be advised that if a higher-ranking LAR is identified at any time, the investigator will defer to the higher-ranking LAR's decision regarding the subject's participation in the research.

Re-consenting Subjects

Consenting is an ongoing process. All applicable criteria that would trigger re-consenting a subject in any study shall apply to subjects whose consent has been provided by a LAR. In addition:

- A subject who regains decisional capacity to consent, as determined by the principal investigator or another physician, must be re-consented using standard consenting procedures.

- In the event that the LAR dies, or otherwise becomes unavailable, and another LAR is available, the new LAR must give consent and the subject must be re-consented subsequently upon any event that would otherwise trigger re-consenting the subject.

- In the event that the LAR dies, or otherwise becomes unavailable, and another LAR is not available, the subject must be safely withdrawn from the study.

Risk and Benefit Considerations:

The following issues are considered by SCRIHS during its review of research involving adult subjects who are decisionally-impaired as a result of a life-threatening injury or illness.

a. SCRIHS must find that appropriate provisions are made in accordance with the level of risk and the prospect of benefit for determining the subject's ability to provide consent or their ability to withdraw, such as the following:

    1. The ability to make a choice;
    2. The ability to understand relevant information;
    3. The ability to appreciate the situation and its likely consequences; and
    4. The ability to think through information rationally.

b. SCRIHS must consider the degree of ability of the potential subject, the level of risk, and the prospect of benefit to the individual subject.

c. The research should not impose a risk of harm, unless the research is intended to benefit the subject and the probability of benefit is greater than the probability of harm.

For research involving adult subjects who lack decisional capacity as a result of a life-threatening injury or illness, the investigator(s) must be an attending physician. The investigator(s) is then responsible for obtaining LAR consent from the appropriate person.

REFERENCES

45 CFR §46.102, 45 CFR §46.402, 45 CFR 46.116
21 CFR §50.3
Illinois Health Care Surrogate Act (755 ILCS 40/1 et seq.)
Illinois Power of Attorney Act (755 ILCS 45)
Medical Patient Rights Act (410 ILCS 50/3.1)
45 CFR 46, Subpart A and 21 CFR 50 Subpart B

LEGALLY AUTHORIZED REPRESENTATIVE CONSENT FOR RESEARCH FORM

SELF-CERTIFICATION

Section 1:

I am willing to serve as a Legally Authorized Representative ("LAR") decision maker for

_____

(Potential Subject's Name)

to participate in *[Title of Study]* conducted by *[Principal Investigator's Name]*.

Section 2:
Category of Potential LAR (ORDERED BY PRIORITY)
Please check the LAR description that applies to you:

☐ 1. Subject's guardian of the person with authority to make healthcare decisions *(I understand and agree I must provide the principal investigator a copy of the applicable, valid guardianship documents if I am a legally appointed guardian and that a copy of the document(s) will be kept with the consent form and the medical record.*);

☐ 2. Authorized agent under a power of attorney for health care under the Illinois Power of Attorney Act when the patient's condition falls within the coverage of the power of attorney for health c*are (I understand and agree I must provide to the principal investigator a copy of the valid power of attorney document and that the document must be reviewed to ensure that there are no limitations in it that would preclude consent to a research protocol and that a copy of the document(s) will be kept with the consent form and the medical record.*);

☐ 3. Guardian of the person when court order does not grant the power to make health care decisions. *(I understand and agree I must provide the principal investigator a copy of the applicable, valid guardianship documents if I am a legally appointed guardian and that a copy of the document(s) will be kept with the consent form and the medical record.*)

☐ 4. Spouse of subject;

☐ 5. Adult son or daughter of subject;

☐ 6. Parent of the subject;

☐ 7. Adult brother or sister of the subject;

☐ 8. Adult grandchild of the subject.

Section 3:
LAR's Contact Information:

Name: _____ Home Phone: ( ) _____

Address: _____ Work Phone: ( ) _____

_____ Cell Phone: ( ) _____

E-mail: _____

Note: Other individuals at the same priority level must all agree in order to use an LAR to consent to research. For example, all adult siblings must agree in order for a parent to be enrolled in a research study.

Section 4:
Signatures

_____

Signature of Legally Authorized Representative Date

_____

Signature of Investigator Date

RECORDKEEPING AND REPORTING

MINUTES OF IRB MEETINGS

EFFECTIVE DATE: January 11, 2012

REVISION DATE: August 14, 2015

OBJECTIVE

To describe the policies and procedures for completing the minutes of the convened meetings of the Springfield Committee for Research Involving Human Subjects (SCRIHS), an Institutional Review Board (IRB)

GENERAL DESCRIPTION

The federal policies for the protection of human subjects [45 CFR 46.115 (a)(2)] require that "Minutes of IRB meetings shall be in sufficient detail to show attendance at the meeting; actions taken by the IRB; the vote on these actions including the number of members voting for, against, and abstaining; the basis for requiring changes in or disapproving research; and a written summary of the discussion of controverted issues and their resolution." (Office for Human Research Protections)

Complete minutes enable a reader who was not present at the meeting to determine exactly how and with what justification the IRB arrived at its decisions. They also provide the IRB itself with sufficient detail to help it reconstruct its discussions at a later date, if necessary. Comprehensive minutes also demonstrate respect for the human subjects of research. Meeting minutes do not have to contain information provided in protocols the IRB has previously approved. This process assumes that if IRB members do not discuss a particular issue, the IRB deems the issue acceptable.

PROCEDURES

Minutes Preparation

1. The SCRIHS staff member(s) attending the convened IRB meeting draft detailed notes to document IRB discussions and determinations in the electronic IRB system. Examples of the type of information included in the minutes are as follows:
    - The location of the meeting and the time the IRB convened the meeting and adjourned; Documentation of attendance to include:
    - Initial and continued presence of a majority of members (i.e., quorum), including at least one nonscientist;
    - Whether an alternate is voting and for whom he/she is voting;
    - When a member leaves the room or leaves the meeting;
    - When a member returns to the room;
    - When a member cannot attend the meeting but provided written reviews for protocol assignments;
    - Minutes on the review of each protocol include the following:
    - The names of IRB member recused from the meeting due to a conflict of interest during the discussion and vote of the study;
    - Separate deliberations for each action taken by the IRB;
    - A summary of the discussion of any controverted issues and their resolutions;
    - The vote on these actions, including the number of voting “for,” “opposed,” or “abstaining”;

- In order to document the continued existence of a quorum, SCRIHS staff record votes in the minutes using the following format: VOTE: Total = 15; For = 14, Against = 0, Abstained = 1;
- The IRB's determination on frequency of continuing review (based on the degree of risk or the risk/benefit ratio);
- Name of investigators and any other guests attending the meeting;
- The basis for requiring changes in the research;
- The level of risk determined by the IRB (at initial review; on all other reviews, the minutes only list level of risk if it has changed).

2. When the IRB disapproves a protocol, SCRIHS staff document the basis for the disapproval in the minutes and document discussion of the controverted issues.

3. SCRIHS staff write IRB meeting minutes impersonally and do not attribute opinions expressed by IRB members. Typically, the minutes only identify members by name when they recuse themselves from a particular review due to conflict of interest or leave the meeting for any reason.

4. The IRB considers written comments and/or information provided by ad hoc reviewers or consultants in the review process. Ad hoc reviewers or consultants may provide comments or recommendations electronically to the IRB prior to the meeting or attend the convened meeting to participate in the review. In cases where the consultant participates in the meeting, the minutes of the meeting document the information provided by the consultant.

Alternates

1. IRB meeting minutes document when an alternate IRB member replaces a voting IRB member and for whom the alternate is substituting.

2. When alternates substitute for a primary member, the alternate member receives and reviews the same material that the primary reviewer received or would have received.

Specific Findings

1. When the IRB makes specific findings at convened meetings, SCRIHS staff document these findings in the minutes of the meeting and include protocol-specific information justifying each finding. Examples of specific findings include, but are not limited to:
   - Alteration or Waiver of the Informed Consent Process in Non FDA Requested Research: When the convened IRB reviews a procedure that alters or waives the requirements of informed consent, the minutes document the IRB's determinations required by the federal regulations (45 CFR 46.116).
   - Waiver of Documentation of Informed Consent: When the convened IRB reviews a procedure that waives the requirements for obtaining a signed informed consent document, the minutes document that the IRB made the findings in accordance with federal regulations (45 CFR 46.117, 21 CFR 56.109).
   - Research Involving Deception: When the convened IRB reviews research involving deception, the minutes document that the IRB made the findings in accordance with 45 CFR 46.116.
   - Research Involving Prisoners: When the IRB reviews research involving prisoners, the minutes indicate that the research meets the findings required by 45 CFR 46.305(a) and represents one of the categories of research permissible under Health and Human Services (HHS) regulations required by HHS 45 CFR 46.306(a)(2).

  - At least one member of the IRB is a prisoner or a prisoner representative with appropriate background and experience to serve in that capacity.
  - In cases where more than one IRB reviews a particular research project, only one IRB need satisfy this requirement.
- Research Involving Children: When the IRB reviews research involving children, the minutes document that the IRB made the findings in accordance with IRB policy and federal regulations (HHS 45 CFR 46 Subpart D 46.404-46.407 and FDA 21 CFR Subpart D 50.50-50.55).
- Wards of the State or Other Agency: When the IRB reviews research involving children who are wards of the state or any other agency, institution, or entity, the minutes document that the IRB made the findings in accordance with federal regulations (45 CFR 46.409 and 21 CFR 50.56).
- Research Involving Pregnant Women, Human Fetuses and Neonates: When the IRB reviews research involving pregnant women, human fetuses, and neonates, the minutes must document that the IRB made the findings in accordance with federal regulations (45 CFR 46 Subpart B).
- Research Involving Individuals with Impaired Consent Capacity: When the IRB reviews research involving individuals who are determined to be cognitively impaired and/or lack consent capacity, the minutes document that the IRB made the findings in accordance with federal regulations [45 CFR 46.111(b), 21 CFR 56.111(b)], and local policy.
- Investigational New Devices: The minutes document the IRB's determination of significant or nonsignificant risk for Investigational New Devices and the rationale for that decision, in accordance with federal regulations [(21 CFR 812.3(m)].

Department of Health and Human Services (DHHS) Approved Sample Consent Documents (e.g., NIH-Supported Multi-center Clinical Trials)

1. When the IRB reviews DHHS-approved informed consent documents (e.g., NIH-supported multi-center clinical trials), the minutes include justification for any instance in which the IRB requested or approved the investigator's deletions or substantive modifications of information concerning risks or alternative procedures contained in the DHHS-approved sample informed consent document.

Tele/Videoconference Participation

1. At a meeting in which IRB members participate via telephone/teleconference, meeting minutes document that the IRB member:
   - Has received all pertinent material prior to the meeting; and
   - Can actively and equally participate in the discussion of and vote on all protocols.

Distribution of Minutes

1. SCRIHS staff drafts the IRB meeting minutes in the electronic IRB system.

2. The minutes are included with the IRB agenda for the meeting at which the minutes are scheduled to be approved.

3. Prior to the convened meeting, each IRB member reviews the minutes. IRB members then forward any necessary revisions to the appropriate SCRIHS staff member or discuss the revisions at the convened meeting. The IRB then approves the minutes at the convened meeting. The IRB delegates to SCRIHS staff the authority to correct administrative errors in meeting minutes as appropriate.

4. IRB minutes are confidential and not available to the public for review. Approved minutes are available on the electronic IRB system to appropriate institutional officials, SCRIHS staff and IRB members and any others deemed appropriate by SCRIHS or the IRB, unless otherwise required by law.

Record Keeping

1. SCRIHS staff maintains electronic copies of the IRB minutes.

REFERENCES

45CFR 46.107
45 CFR 46.108
45 CFR 46.111
45 CFR 46.115 (a)(2)
45 CFR 46.116
45 CFR 46.117
45 CFR 46.409
21 CFR 812.3(m)
21 CFR 50.23
21 CFR 50.24
21 CFR 50.56

INSPECTIONS BY REGULATORY AGENCIES

EFFECTIVE DATE: April 11, 2012

REVISION DATE: January 22, 2016

OBJECTIVE

To describe the policies and procedures for SCRIHS/Institutional Review Board (IRB) with respect to inspections by external regulatory agencies

GENERAL DESCRIPTION

IRB/SCRIHS records are subject to regulation and inspection by governmental agencies [e.g., Food and Drug Administration (FDA) or the Office for Human Research Protections (OHRP)].

PROCEDURES

Upon Notice of Inspection

1. SCRIHS staff/IRB Chair(s) ask all inspectors to identify themselves by name and title and show appropriate identification. Inspectors must inform SCRIHS staff/IRB Chair(s) what agency they represent and state the reason for the inspection. If an inspector is unable to provide identification, IRB Chair(s)/SCRIHS staff will request that he/she return with the appropriate identification. Inspectors with the FDA must present a Form 482 upon arrival.

2. In the event the IRB is notified of the inspection in advance by email, letter or phone, the IRB Manager is responsible for notifying the IRB Chair(s), Director of the Center for Clinical Research (CCR), Southern Illinois University School of Medicine (SIU-SOM) Dean and Provost, and SIU-SOM Legal Counsel of the pending inspection.

3. After the inspector has identified her/himself, the IRB Manager must be notified of the inspection. The IRB Manager then notifies the IRB Chair, CCR Director, SIU-SOM Dean and Provost, and SIU-SOM Legal Counsel of the inspection.

4. In instances when the IRB Manager is not available, SCRIHS staff offer to assist but inform the inspector that the supervisor is not present in the office. SCRIHS staff then suggest that while they will do their best to help him/her, rescheduling the inspection for a time when the IRB Manager is available is preferred, as the IRB Manager might be better equipped to answer questions. If the IRB Manager is not present and the federal inspector decides to stay and conduct the inspection, SCRIHS staff must contact the IRB Chair(s) and the CCR Director immediately.

5. When the purpose of the inspection relates to a specific clinical trial, the Principal Investigator will be notified and SIU-SOM Legal Counsel will review existing clinical trials contracts for obligations to notify the sponsor.

During Inspection

1. The IRB Manager or designee and a designated SCRIHS staff member are available to the inspector throughout the inspection.

2. The IRB Manager or designee, the designated SCRIHS staff member, the IRB Chair, if available, and the CCR Director, if available, may meet with the inspector at the beginning of the inspection.

3. SCRIHS staff and the IRB Chair answer all inspector questions or concerns accurately, honestly, and succinctly and answer only the questions asked.

4. The federal inspector has the right to visually observe and inspect all facilities and records of the IRB.

5. If the inspector requests duplicate copies of IRB records, SCRIHS staff comply with the requests and keep a list of the records the inspector has received for duplication. The inspector may ask to duplicate these records at a Southern Illinois University School of Medicine (SIU-SOM) facility or ask office personnel to duplicate the records. SCRIHS staff members are available to duplicate these records. If the inspector decides to use duplicating equipment outside the SCRIHS offices, a SCRIHS employee must travel with the inspector to the duplication office to verify the documents copied.

6. At the conclusion of the inspection, the IRB Manager or designee, designated SCRIHS staff member, the IRB Chair, if available, and the CCR Director, if available, may attend the exit interview. If an inspector identifies deficiencies, he/she may leave a copy of the findings with SCRIHS staff, documenting the results of the inspection. If the inspector does not identify any problems during the inspection, the IRB Manager/IRB Chair receives a letter following the inspection from agency headquarters confirming the outcome.

Following the Inspection

1. The IRB Manager or designee maintains a record of everything reviewed by the inspector following the inspection, along with copies of any correspondence provided at the conclusion of the inspection or received after the inspection.

2. The IRB Manager or designee forwards copies of correspondence received from the inspector to the IRB Chair and the CCR Director. The IRB Chair, CCR Director, and SCRIHS staff discuss any corrective action and prepare and implement a response plan as appropriate.

3. The IRB/SCRIHS submits a written response regarding the inspection to the appropriate authority, if required. The IRB Manager forwards the written response to the IRB Chair, CCR Director, SIU-SOM Dean and Provost and Legal Counsel for approval. The final response is kept on file in the SCRIHS office. The final response is presented to the IRB at a convened meeting.

REFERENCES

Not applicable

MANDATED REPORTING TO EXTERNAL AGENCIES

EFFECTIVE DATE: July 13, 2011

REVISION DATE: January 29, 2016

OBJECTIVE

To describe policies and procedures for ensuring prompt Institutional Review Board (IRB), also known as the Springfield Committee for Research Involving Human Subjects (SCRIHS), reporting of events to institutional official(s), sponsor, coordinating center, and the appropriate federal agencies.

GENERAL DESCRIPTION

IRB, institutional and affiliated agencies/entities policies require compliance with all applicable local, state, and federal reporting requirements in the conduct of research involving human subjects. The IRB notifies appropriate officials when research falls under the purview of a federal regulatory agency and one or more of the following occurs:

- Unanticipated problems involving risks to subjects or others; and/or
- Serious or continuing noncompliance with the regulations or requirements of the IRB; and/or
- Suspension or termination of IRB approval for research due to noncompliance; and/or
- Department of Health and Human (DHHS) submitted or funded studies that are not otherwise approvable under 45 CFR 46 Subpart B, which include pregnant women, fetuses, and neonates; and/or
- DHHS submitted or funded studies which include prisoners; and/or
- Food and Drug Administration (FDA) regulated or DHHS or U.S. Department of Education submitted or funded studies which include children and are not otherwise approvable under applicable subparts; and/or
- Changes in IRB membership; and/or
- Exceptions to informed consent in emergency medical research; and/or
- Regulatory agency requests for a report;
- Inquiries or sanctions from government oversight agencies.

Reporting to regulatory federal agencies is not required if the principal investigator (PI) voluntarily closes down a study to new subject accrual or temporarily halts the research procedures. The IRB, IRB Chair, SCRIHS staff, or administrative officials may recommend voluntary closure to the PI, but the PI makes the decision whether closure is appropriate. However, if the IRB or IRB Chair requires suspension or termination, then the incident may be reportable under this policy.

Lapses of approval as outlined in the Continuing Review SOP are not reportable under provisions of the SOP.

Definitions

Unanticipated Problem Involving Risks: See Unanticipated Problem Reporting Policy

Serious Noncompliance: See Noncompliance SOP.

Continuing Noncompliance: See Noncompliance SOP.

PROCEDURES

Unanticipated Problems Involving Risks to Subjects

1. When the IRB discovers or is made aware of unanticipated problems involving risk to the subject or others, the IRB Chair or designee prepares a report within fifteen business days from the date the IRB conducts final review of the unanticipated problem. The report includes:
    - the title of the research protocol and/or grant proposal;
    - name of the PI on the protocol;
    - IRB number assigned to the research protocol;
    - the number (project identifier) of any applicable federal award(s) (grant, contract, or cooperative agreement);
    - the nature of the event; the findings of the institution, affiliated agencies/entities or the IRB;
    - and actions taken by the PI, institution, affiliated agencies/entities and/or the IRB to address the issue.

2. SCRIHS staff, in consultation with the IRB Chair, approves the report, which is then sent through the IRB Chair and the Dean and Provost to the federal agency with a copy to the IRB, PI, and other University administrators as determined by the IRB. (See also Unanticipated/ Anticipated Problem/Adverse Event Reporting SOP.)

3. If the research is FDA regulated, the IRB requires the PI to report to the sponsor, who report to the FDA. The sponsor's report to the FDA must be submitted to the IRB. If the PI is the sponsor, the PI is required to report to the FDA. The IRB may choose to prepare and send the report directly to the FDA.

4. If the DHHS conducts or funds the research, SCRIHS staff send the report to the OHRP.

5. If an agency that is subject to the "Common Rule," other than the DHHS, conducts or funds the research, SCRIHS staff send the report to the agency as required by the agency and OHRP.

6. A copy of the federal report(s) and any final IRB actions are placed in the IRB file by SCRIHS staff.

Serious or Continuing Noncompliance

1. When the IRB discovers or is made aware of serious or continuing noncompliance, the IRB Chair or designee prepares a report within fifteen business days from the date the IRB conducts final review of the serious and/or continuing noncompliance. The report includes:
    - the title of the research protocol and/or grant proposal;
    - name of the PI on the protocol; IRB number assigned to the research protocol;
    - the number (project identifier) of any applicable federal award(s) (grant, contract, or cooperative agreement);
    - the nature of the event;
    - the findings of the institution, affiliated agencies/entities or the IRB;
    - and actions taken by the PI, institution, affiliated agencies/entities, and/or the IRB to address the issue.

2. SCRIHS staff, in consultation with the IRB Chair, approves the report. The report is sent through the IRB Chair and the Dean and Provost to the federal agency with a copy to the IRB, PI, and other University administrators as determined by the IRB. (See also Noncompliance SOP.)

3. If the research is FDA regulated, the IRB requires the PI to report to the sponsor, who reports to the FDA. The sponsor's report to the FDA must be submitted to the IRB. If the PI is the sponsor, the PI is required to report to the FDA. The IRB may choose to prepare and send the report directly to the FDA.

4. If the DHHS conducts or funds the research, SCRIHS staff send the report to OHRP.

5. If an agency that is subject to the "Common Rule," other than the DHHS, conducts or funds the research, SCRIHS staff send the report to the agency as required by the agency and OHRP.

6. SCRIHS staff maintain all correspondence relating to the serious or continuing noncompliance in the SCRIHS office. A copy of the federal report(s) and any final IRB actions are placed in the IRB file by SCRIHS staff.

Suspension or Termination of Research

1. When the IRB suspends or terminates approval of a research protocol, the IRB Chair or designee prepares a report to the applicable federal agency within fifteen days from the date the IRB conducts final review of the suspension or termination. The report include

- the title of the research protocol and/or grant proposal;
- name of the PI on the protocol;
- IRB number assigned to the research protocol;
- the number (project identifier) of any applicable federal award(s) (grant, contract, or cooperative agreement);
- the nature of the event;
- the findings of SIU-SOM or the IRB; and actions taken by the PI, SIU-SOM, and/or the IRB to address the issue.

2. SCRIHS staff, who may consult with the IRB Chair, approves the report, which is sent through the IRB Chair and the Dean and Provost to the federal agency with a copy to the IRB, PI, and other University administrators as determined by the IRB.

3. If the DHHS conducts or funds the research, SCRIHS staff send the report to the OHRP.

4. If an agency that is subject to the "Common Rule," other than the DHHS, conducts or funds the research, SCRIHS staff send the report to the agency as required by the agency and OHRP.

5. When research is FDA regulated, the IRB requires the PI to report to the sponsor, who must report to the FDA with a copy to the IRB. If the PI is also the sponsor, then the IRB requires the PI to report to the FDA. The IRB may choose to prepare and send the report directly to the FDA.

6. SCRIHS staff maintain all correspondence relating to the suspension or termination in the SCRIHS office. A copy of the federal report(s) and any final IRB actions are placed in the IRB file by SCRIHS staff.

Pregnant Women, Fetuses, and Neonates

1. Upon receipt of an IRB application, SCRIHS staff screen protocols for inclusion of pregnant women, fetuses, or neonates in research submitted to or funded by the DHHS.

2. If the IRB finds that the research is not otherwise approvable for pregnant women, nonviable neonates, or neonates of uncertain viability under 45 CFR 46 Subpart B and the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses, or neonates, SCRIHS staff, with input from the IRB and the PI, prepare a report to the DHHS based on the current guidance from OHRP. The IRB, in consultation with SCRIHS staff, approves the report, which SCRIHS staff send through the IRB Chair and Dean and Provost with a copy to the PI and to OHRP per OHRP guidance within fifteen business days of IRB approval of the report.

3. SCRIHS staff place a copy of all correspondence in the IRB protocol file and database.

4. If the OHRP disagrees with the IRB findings on the research involving pregnant women, fetuses, nonviable neonates, or neonates of uncertain viability, SCRIHS staff share the information from OHRP with the IRB and the PI and may take steps to attempt to reconcile the differences.

5. IRB approval is contingent on OHRP approval. The research cannot proceed without OHRP approval.

Prisoners

1. Upon receipt of an IRB application or request, SCRIHS staff screen protocols for any inclusion of prisoners in research submitted to or funded by DHHS.

2. SCRIHS staff notify the PI of the DHHS reporting requirement if it finds that the PI has submitted the protocol to DHHS or that the research is DHHS funded and includes prisoners.

3. With guidance from the IRB and/or the PI, SCRIHS staff prepare a report to the DHHS based on the current guidance from OHRP on research which includes prisoners. SCRIHS staff approve the report and send it to OHRP within fifteen days of IRB approval of the report. SCRIHS staff place a copy of all correspondence in the IRB file.

4. If the OHRP disagrees with the IRB classification of the research involving prisoner(s), SCRIHS staff share the information from OHRP with the IRB and the PI and may take steps to attempt to reconcile the differences.

5. IRB approval is contingent on OHRP approval. The research cannot proceed without OHRP approval.

Children

1. Upon receipt of an IRB application or request, SCRIHS staff screen protocols for any inclusion of children in research submitted to or funded by DHHS or the U.S. Department of Education or regulated by FDA.

2. If the IRB finds that the research is not otherwise approvable but presents an opportunity to understand, prevent, or alleviate serious problems affecting the health or welfare of children under the applicable FDA, DHHS, or U.S. Department of Education subpart, SCRIHS staff, with input from the IRB and the PI, prepare a report to the DHHS based on the current guidance from the applicable agency. The IRB, in consultation with SCRIHS staff, approves the report and sends it through the IRB Chair and Dean and Provost with a copy to the PI within fifteen days of IRB approval of the report. SCRIHS staff submit a copy to the institutional official of the applicable federal agency (e.g., Secretary of DHHS through OHRP, Secretary of U.S. Department of Education, or Commissioner of FDA) based on current guidance from the agency. SCRIHS staff place a copy of all correspondence in the IRB protocol file and database.

3. If the applicable federal agency disagrees with the IRB findings on the research involving children, SCRIHS staff share the information from the agency with the IRB and the PI and may take steps to attempt to reconcile the differences.

4. IRB approval is contingent on OHRP approval. The research cannot proceed without OHRP approval

Changes in IRB Membership/Registration

1. When a change in IRB membership occurs, SCRIHS staff notify OHRP/FDA via the online registration system. SCRIHS staff or designee enters the required information regarding the changes in membership and submits to OHRP/FDA within 90 days.

2. SCRIHS staff are responsible for revising registration information such as changes in IRB member contact or Chair contact information within 90 days of the change, changes in the IRB's decision to review or discontinue review of types of FDA products or FDA clinical investigations within 30 days, or the University's decision to disband an IRB within 30 days of permanent cessation of the IRB's review of research.

Exception to Informed Consent in Emergency Medical Research

1. When the IRB approves an exception from the general informed consent requirements for emergency research under FDA and DHHS regulations, the PI provides the sponsor with a copy of the information publicly disclosed prior to the initiation and at the completion of the study. The PI is responsible for maintaining a copy of the report.
2. When the IRB does not approve an exception from the general informed consent requirements for emergency research under FDA and DHHS requirements, SCRIHS staff, with input from the IRB, prepare a report of the reasons why the IRB did not approve the exception. The IRB Chair, in consultation with SCRIHS staff, approves the report. SCRIHS staff submit the report to the sponsor and the PI within fifteen days of approval.

3. SCRIHS staff place a copy of the report in the IRB files. (See Informed Consent SOP.)

Agency-Requested Reports

1. A federal agency may periodically ask the IRB, institution, or affiliated agencies/entities for a specific report on a variety of issues (e.g., alleged noncompliance submitted to a federal agency). SCRIHS staff are responsible for informing the IRB Chair of any inquiries from a government oversight office, such as OHRP or FDA or any other agencies. SCRIHS staff or designee reviews the request and assist the IRB/affiliated entities with preparation of the report.

2. The designated SCRIHS staff member prepares the report in accordance with the agency's request relative to content and timing.

3. The IRB Chair, in consultation with the SCRIHS staff, approves the report. SCRIHS staff and/or IRB Chair determines who receives a copy of the report depending on the nature of the request.

Reports: IRB Determination of Entities to Receive Copy of Reports

1. The IRB/SCRIHS staff determine appropriate institutional officials and/or affiliated entities to receive a copy of a report on a case-by-case basis when the IRB/SCRIHS staff send any of the federally mandated reports discussed in this SOP to a federal agency. These determinations are in accordance with applicable federal requirements.

   Examples of institutional officials and affiliated entities who may receive copies of a report include, but are not limited to, the following:
   - Dean and Provost;
   - Associate Dean of Research and Faculty Affairs;
   - Department Chair;
   - Legal Counsel;
   - Affiliated Hospitals
   - Privacy Officer;
   - Other appropriate administrators as determined by the IRB /SCRIHS staff

REFERENCES

45 CFR 46 Subpart B
45 CFR 46 Subpart C
45 CFR 46 Subpart D
21 CFR 50 Subpart D
May 2003 OHRP Guidance on the Involvement of Prisoners in Research
May 2005 OHRP Guidance on the HHS 45 CFR 46.407 Review Process for Children Involved as Subjects in Research

STUDY CLOSURE

EFFECTIVE DATE: December 14, 2011

REVISION DATE: November 13, 2013; October 30, 2015

OBJECTIVE

To describe the policies and procedures followed to close a study

GENERAL DESCRIPTION

The principal investigator (PI) and/or the Institutional Review Board (IRB) may close approved protocols under certain circumstances. The PI is responsible for promptly closing out an IRB approved study if any of the following conditions exist:

1. All research/clinical investigation activities including data analysis and reporting are complete;
2. The PI never initiated the study;
3. Subject accrual is finished, all data collection is complete and the only remaining activity is analysis of the data, the data are de-identified, and there are no identifying links or codes to the de-identified data;
4. The PI plans to leave the University or institution of employment and intends to continue the research activities at another institution;
5. The PI plans to leave the University or institution of employment and does not have a qualified investigator to assume the role of PI.
6. The study has been open for a period of three or more years and there has been no local enrollment.
7. The study sponsor initiates closure of the study

The PI/Study personnel completes and submits the electronic form "Notification of Study Closure" to the SCRIHS office. When closing out a study, the PI submits a final study report unless: 1) he/she never initiated the study or; 2) the study received initial/continuing review within the last six months and the PI has enrolled no subjects in the last six months.

The PI cannot close out an active IRB approval if:

1. He/she is still following subjects or;
2. He/she is analyzing identifiable data (including data with codes or links to identifiers).

The IRB may notify a PI that IRB approval or active IRB status has expired or that the IRB has inactivated IRB approval due to non-response from the PI to IRB requests. The IRB may suspend or terminate IRB approval. (See the Termination or Suspension of Research SOP.)

If a study has been open for a period of three or more years and the PI has not enrolled subjects in the study, the IRB requires study closure unless there are extenuating circumstances for keeping the project open (e.g., the study is about a rarely seen condition).

Procedures for closing a study fall into five categories:

- Project complete;
- Non-response from PI to IRB requests for revisions at initial review;

- Closure due to non-enrollment;
- Lapse of approval due to non-response to requests for continuing review (See Continuing Review SOP);
- PI or Sponsor initiated withdrawal.

Regardless of the category for study closure, the expiration date for IRB approval falls on the first day after the approval period end date.

PROCEDURES

Project Complete

1. When a study is completed, the PI completes and electronically submits the "Notification of Study Closure" form to SCRIHS using the electronic IRB system. A final study report should be included with the form. The final study report should include the following information:
    - Final findings;
    - Final adverse event report;
    - Final enrollment number (including withdrawals); and
    - Any patient complaints

2. Regardless of initial review type (full or expedited), protocols undergo expedited review procedures for final review, unless the IRB reviewer determines the circumstances surrounding the request for closure require full review. SCRIHS staff screens the study closure form and final study report and the IRB Chair or designee conducts the review.

3. The IRB Chair or designee can request full board review of study closure if there are concerns or issues. Otherwise, the IRB Chair or designee electronically signs off on the "Notification of Study Closure" form. The study is considered officially closed by SCRIHS on the date the IRB Chair/designee completes the form.

4. Once the IRB issues approval for closure, SCRIHS staff code the protocol records as closed in the electronic IRB system. If the protocol was approved before the implementation of the electronic IRB system SCRIHS staff will print the closure letter generated by the electronic IRB system and place it in the original paper file. SCRIHS staff store the protocol files for at least six years from closure date.

5. The PI may be required to retain study records for a longer period of time. This may be dependent on the agreement in the original study contract. If you are unsure please contact the Clinical Trials Contract Coordinator in the Center for Clinical Research for guidance.

Closure Due to Non-Response

1. If, at initial review, the PI fails to respond to the IRB's request for additional information/ revisions within a specified period of time (e.g., approximately three months), the IRB may require a re-submission of the protocol if the PI wants consideration for IRB approval again. SCRIHS staff may administratively withdraw the original submission within the electronic IRB system if the PI fails to respond to the IRB's requests.

2. A study may be closed if the PI fails to submit or return a Continuing Review Submission form, Notification of Study Closure form, or respond to requested information. If closed, SCRIHS staff will send the PI a notification letter ending IRB approval.

Closure Due to Non-Enrollment

1. If, at continuing review, the PI reports to the IRB that he/she has never enrolled local subjects into the study and the study has been open for a period of three or more years, the IRB requests that the PI justifies continuing the study within the continuing review submission.

2. If the IRB agrees that there are extenuating circumstances to keep the study open, the continuing review will be approved and processed as usual. (See Continuing Review SOP)

3. If the IRB determines that the extenuating circumstances do not justify leaving the study open, SCRIHS staff process the materials submitted for closure. SCRIHS staff notify the PI the study has been closed due to lack of enrollment.

PI or Sponsor Initiated Withdrawal

1. During an approval period, the PI or study sponsor may request study closure. Upon receipt of a study closure request, SCRIHS staff determines, based on the date of the study's last review and research activity to date, whether a final study report should be submitted.
2. If it has been 6 months since the initial approval or last continuing review and the PI has enrolled subjects since the last review, SCRIHS staff notifies the PI that a final study report must be submitted in order to appropriately close the study.

3. The IRB Chair or designee reviews and signs the Notification of Study Closure form. SCRIHS staff sends the signed form to the PI after processing the request.

4. When a PI leaves the University or institution of employment, he/she should close out his/her protocol(s) or notify SCRIHS in writing to transfer the protocol(s) to another PI who will take responsibility for the research. This transfer may require an amendment request and/or further IRB review and approval.

5. If applicable, when a PI transfers a protocol, the new PI submits appropriate changes to consent forms, advertisements, etc. to the IRB for review and approval.

Reactivating IRB Approval

1. A PI may re-initiate research previously inactivated by the IRB by following the procedures for initial full review or expedited initial review as determined by the IRB Chair, Vice Chairs, or SCRIHS staff. Be advised, the electronic IRB system will generate a new protocol number upon submission. The PI/Study personnel will need to reference the previously assigned SCRIHS protocol number in the new application.

Note: All notifications and correspondence to and from SCRIHS should be completed using the appropriate mechanisms within the electronic IRB system.

REFERENCES

Not applicable

IRB/SCRIHS RECORDKEEPING

EFFECTIVE DATE: September 12, 2012

REVISION DATE: August 14, 2015

OBJECTIVE

To describe policies and procedures for the Institutional Review Board (IRB)/SCRIHS office recordkeeping

GENERAL DESCRIPTION

The SCRIHS office maintains IRB records in accord with applicable regulatory and institutional requirements.

PROCEDURES

Storage of and Access to Records

1. SCRIHS staff secure all active IRB records in the SCRIHS office area and within the electronic IRB system (iRIS). Access is limited to the IRB Chair, IRB members, Director, Center for Clinical Research, SCRIHS staff and officials of federal and state regulatory agencies, the Office for Human Research Protections (OHRP), the Food and Drug Administration (FDA), and accrediting bodies. SCRIHS staff may grant SIU-SOM employees with administrative appointments and affiliated hospitals administration access to the records on an as-needed basis for official SIU-SOM business. Investigators and/or their authorized study personnel have reasonable access to files related to their research activities. SCRIHS staff limit all other access to IRB records to those who have legitimate need for them, as determined by the SCRIHS staff and/or SIU-SOM Legal Counsel when submitted through state open records statutes.

2. Administrative requests for access (e.g., Associate Dean, Department Chair, Compliance Officer, Hospital Administration) must be in writing and contain the following information:
    - The name of the person requesting the information;
    - The information requested;
    - The reason for the request;
    - Assurance of confidentiality.

3. When the SCRIHS office receives a request for IRB records, SCRIHS staff check to see whether the request is from a PI or his/her authorized personnel. If the person requesting the record is listed as study personnel on the record requested, the SCRIHS staff may copy pertinent parts of the record for that person to pick up or may fax, mail, or e-mail the record.

4. If the individual requests a substantial amount of material, SCRIHS staff allow access to the record and a copy machine in the SCRIHS office area for use by the person requesting the material. Please note charges may apply.

5. If the person requesting the record is not listed as study personnel on the record requested, SCRIHS staff make a determination before releasing any records as to whether the request is from appropriate accreditation bodies, University officials, administrators, or regulatory agencies that should have

access. Unless the individual states an acceptable reason for not informing the PI of the request for a record, and depending on the circumstance, SCRIHS staff may inform the PI that SCRIHS has received a request for access to the applicable protocol.

6. The SCRIHS office maintains protocol records for a minimum of six years after a study is closed. This storage requirement applies even if the study has not enrolled a single subject. SCRIHS staff may destroy protocol records for studies that have been closed for six years unless it conflicts with other record retention agreements/policies (contracts, records management, etc.).

7. In addition to protocol files, the SCRIHS office maintains the following information and records. SCRIHS staff organize and store records in files or binders or in electronic documents as appropriate which include, but are not limited to, the following categories:
   - Standard operating procedures;
   - IRB membership rosters;
   - Meeting minutes, which include documentation of convened IRB meetings;
   - Federalwide Assurance;
   - IRB correspondence;
   - Agendas for IRB meetings, which include all items to be reviewed and documentation of expedited and exempt reviews;
   - Alleged noncompliance case records;
   - Mandated reports;
   - Resumes of currently active IRB members;
   - Electronic records documenting completion of mandatory IRB training for study personnel, IRB members, and SCRIHS staff.
   - Internal/External Audit results

8. The SCRIHS office also maintains communications to and from the IRB in the SCRIHS office and keeps any relevant communication related to a specific research protocol in the protocol record.

Protocol Records

1. SCRIHS staff maintain a separate record for every research application. The IRB protocol record may include, but is not limited to:

   Full Board Review Protocol
   - Initial IRB application;
   - Scientific evaluations of the proposed research if any;
   - For drugs, the investigator's brochure;
   - For devices, a report of prior investigations and instructions for use manual;
   - Data Safety and Monitoring Board reports, if any;
   - Results of human subjects research compliance reviews, if any;
   - IRB approved informed consent document and assent document, if applicable, with the approval date stamp;
   - Documentation of all IRB review and approval actions, modifications and all relevant correspondence to and from the investigator, including initial and, if applicable, IRB continuation review and modification, deviation, exception review;
   - Documentation of type of review;
   - Documentation of study close-out;
   - Specific findings (federal and institutional requirements);

- Continuing/final review materials;
- Significant new findings provided to human subjects, if any;
- Reports of unanticipated problems/adverse events involving risks to subjects or others;
- Reports of protocol violations;
- All relevant correspondence to and from the investigator and any other correspondence related to the protocol either hard copy or e-mail;
- Applications for funding/sponsorship, if applicable;
- Advertising or recruiting materials, if applicable;
- Protocol amendments or modifications;
- Instrument to be used for data collection, if applicable;
- Department of Health and Human Services/National Institutes of Health (NIH) approved sample informed consent form and protocol, if applicable;
- Copy of the package insert, drug monograph, or FDA approved label for drug or device studies using the FDA approved medication/device for approved medical indication;
- Sponsor's grant, contract, or device proposal if the protocol does not involve the administration of drugs, if applicable;
- Human subject protection training dates for principal investigators and study personnel;
- Other committee approvals/correspondence, if applicable;
- Mandated reports, if applicable;
- Criteria for IRB Approval: Reviewer Checklist;
- Protocol Specific Conflict of Interest forms

Expedited Review Protocol

- All of the items listed above under full board review protocol, as applicable to individual studies;
- Documentation and determinations required by the regulations and protocol-specific findings justifying those determinations, including that the study is eligible for expedited review and the applicable expedited review category;
- Description of action taken by the expedited reviewer.

Exempt Review Protocol

- Initial application for exempt review;
- All items listed under full board review protocol, if applicable to individual studies;
- Documentation and determinations required by the regulations and protocol specific findings justifying the determinations, including documentation of exempt eligibility and specifying appropriate exemption category;
- Description of action taken by exempt reviewer.

SCRIHS Electronic IRB system (iRIS)

1. The SCRIHS office maintains an electronic, web-based IRB system (iRIS). As of February 1, 2012, all new SCRIHS submissions are entered into iRIS. Examples of data included in iRIS include the following:
   - IRB number, IRB providing review, and SCRIHS staff managing review;
   - Current status (active/inactive);
   - Title of the research project (protocol);
   - Protocol process type (full, expedited, exempt);
   - Risk category;
   - Dates of research period (initial approval date and anticipated ending date);
   - Approval period;

- Names of the PI, co-investigators, study coordinators, and other study personnel as appropriate;
- Number and age level of subjects;
- Subject demographics;
- Enrollment status (open or closed to accrual);
- Drug information;
- Other committee approvals, if applicable;
- Funding source type;
- Research sites (if other than SIU-SOM);
- Date of initial approval;
- Date of most recent continuing review approval;
- If applicable, prior notice of end of current approval period;
- Submission and review dates for each protocol event (initial review, continuing review, final review, amendment review, unanticipated problem review);
- Human Subjects Research Protection training dates
- Protocol Specific Conflict of Interest forms

REFERENCES

45 CFR 46.115
21 CFR 56.115

MONITORING AND ASSESSMENTS

HUMAN SUBJECTS RESEARCH COMPLIANCE ASSESSMENT

EFFECTIVE DATE: July 12, 2012

REVISION DATE: December 11, 2013; July 10, 2015

OBJECTIVE

To describe policies and procedures for the human subjects research compliance assessment component of the SCRIHS office

GENERAL DESCRIPTION

The SCRIHS office serves to assure and improve human research protections. One of the primary quality improvement activities is the compliance assessment.

SCRIHS staff conducts research compliance assessments at the request of the IRB, the Dean and Provost of Southern Illinois University School of Medicine (SIU-SOM), the Director of the Center for Clinical Research, affiliated hospitals or other entities, due to unusual circumstances, significant risks to subjects, routine failure on the part of an investigator to comply with federal and/or institutional requirements, or allegations or concerns about the conduct of the study. The IRB may also conduct periodic assessments to evaluate whether investigators meet their responsibilities within specific areas of research (e.g., investigators conducting research using an investigational device). If appropriate, compliance assessments also encompass elements of informed consent evaluations. The IRB may request measures to monitor the consent process to determine whether procedures for administration of informed consent are proper. If necessary, SCRIHS staff may review IRB records to determine accuracy and consistency with the investigator's research records and to verify that the investigator made no material changes to the protocol.

A Principal Investigator may request SCRIHS to conduct a compliance assessment of their research to ensure regulatory compliance at any time. SCRIHS will process these requests as schedules allow.

SCRIHS staff shares findings pertaining to the assessment with the principal investigator (PI)/research staff and reports these findings to the IRB. To maintain confidentiality, SCRIHS staff does not disseminate subjects' protected health information in the compliance assessment findings disseminated to the IRB.

If in reviewing the results of a compliance assessment, the IRB determines that the exposed deficiencies warrant action to be taken, the IRB develops a plan for follow-up, which may require further review.

SCRIHS may develop or assign educational programs for investigators, their research staff, SCRIHS staff, and IRB members based on the results of the compliance assessments. When the IRB receives reports of findings from compliance assessments, if necessary, the IRB determines whether to report the findings to the Food and Drug Administration (FDA), the Office for Human Research Protections (OHRP), the study sponsor, the Dean and Provost, or other necessary administration.

PROCEDURES

1. If the IRB, the Dean and Provost, or the Director of the Center for Clinical Research requests a compliance assessment and does not identify a specific protocol, SCRIHS staff may use the following criteria to identify protocol(s) for inspection: for example - federal, state, or industry-funded projects;

currently approved and active for two years; level of risk to subjects; or subjects currently enrolled in study.

2. For compliance assessments that provide post-IRB approval evaluations to determine whether the PI is meeting responsibilities in a specific area of research (e.g., research using an investigational device), SCRIHS staff runs a report to capture all protocols falling under the targeted area of research.

3. Once SCRIHS staff determines which protocol(s) will undergo inspection, staff notifies the PI by phone and/or in writing of the upcoming compliance assessment. Generally, within five working days after initial notification of the PI, SCRIHS staff communicates with the PI and/or the study personnel to schedule the date(s) for the assessment at the earliest time possible.

4. If the nature of the compliance assessment requires it, SCRIHS staff conducts entrance and exit interviews with the PI. The IRB Chair(s) or a designated IRB member may participate in these interviews. At the PI's or SCRIHS's discretion, select study personnel may also attend.

5. Prior to the entrance interview, SCRIHS staff may review the initial review meeting minutes, IRB records, and related SCRIHS databases to become familiar with the protocol(s) and to identify issues to address during the compliance assessment process.

6. The entrance interview precedes SCRIHS staff's on-site assessment of the PI's research records. SCRIHS staff and/or IRB Chair/IRB member may use this time to explain the goals of the compliance assessment. It also allows the PI/ study personnel an opportunity to explain what the protocol entails, respond to the issues which instigated the compliance assessment, and answer any questions arising from SCRIHS staff's review of the IRB protocol records.

7. The records reviewed by SCRIHS staff and/or IRB Chair/IRB member at the PI's site may consist of, but are not limited to, the following:

- Protocol Binder/Regulatory Documentation – SCRIHS staff reviews materials and notes whether the records retained meet federal, International Conference on Harmonisation/Good Clinical Practice, Sponsor requirements and IRB guidelines;
- IRB Documentation – SCRIHS staff compares the PI's records with the IRB's records. Review of IRB documentation affords the opportunity to determine whether the PI made material changes prior to IRB approval;
- Consent Forms – SCRIHS staff examines consent forms used to enroll subjects to ensure that the subjects signed the appropriate consent form for their respective study and that study personnel and subjects properly signed and dated the forms;
- Case Report Forms (CRF) – When applicable, SCRIHS staff may randomly select or request at least three subjects' records for the assessment. SCRIHS staff determines whether the subjects met the inclusion/exclusion criteria for their respective study and whether the PI/study personnel recorded and documented items properly;
- Medical Records – If applicable, SCRIHS staff may review medical records or other source documents to verify the information in the CRFs;
- Grant Application – If applicable, SCRIHS staff may compare the grant application to the IRB approved protocol.

For assistance/clarification during the assessment, SCRIHS staff may contact the PI directly or, if applicable, inquire with the PI's study personnel.

9. SCRIHS staff and/or IRB Chair/IRB member may also request a tour of the facilities to verify control, storage, and accountability of investigational new test articles and research records and/or to confirm availability of related research equipment.

10. The IRB may request monitoring of the consent process as part of the compliance review, using procedures which include, but are not limited to:

    - Surveying research subjects enrolled in the study about the informed consent process and their experience as a research participant;
    - Observing study personnel administration of informed consent to subject candidates by the SCRIHS staff and/or IRB member. The IRB determines the frequency of consent process monitoring on a case-by-case basis; examples of determining factors include level of risk, enrollment activity, funding agency, and targeted subject population.

11. SCRIHS staff and/or IRB Chair/IRB member conducts the exit interview after SCRIHS staff completes a review of the PI's records and may request clarification regarding the protocol or research procedures at that time. SCRIHS staff and/or IRB Chair/IRB member provides the investigator with a verbal summary of the findings and explains the remaining procedures for conclusion of the compliance assessment.

12. After the exit interview, SCRIHS staff writes a report outlining the findings of the compliance assessment pertinent to the PI's records. If the IRB Chair/IRB member participates in the compliance assessment, SCRIHS staff may give the IRB Chair/IRB member the opportunity to review and edit the report prior to sending it to the PI.

13. Once the compliance assessment report is complete, SCRIHS staff sends it to the PI with a requested response date determined on a case-by-case basis. Typically, the PI has two to three weeks to submit a response.

14. Upon receipt of the PI's response, SCRIHS staff forward the response to the IRB Chair or Designee for review.

15. For any compliance assessment findings requiring review by the full committee, as determined by the IRB Chair/IRB Advisory Panel/SCRIHS staff, the IRB members vote for one of the following actions:

    - Approved – No further action is required. SCRIHS staff sends the PI a letter describing the outcome of IRB review.
    - Revisions/additional information requested – The IRB withholds approval pending submission of revisions/additional information. The IRB may give the individual chairing the meeting the authority to approve non-substantial revisions/additional information or require review of substantial revisions/additional information at a convened meeting. If the IRB request necessitates further compliance assessment, SCRIHS staff acts accordingly and processes any additional findings/information for review based on the IRB's determination at the convened meeting (either gives them to the individual who chaired the IRB meeting or assigns them to a convened IRB meeting for review). If the IRB request necessitates a response from the PI, SCRIHS staff sends the PI a letter describing the IRB's request. When the PI responds to the IRB's request in writing, SCRIHS staff processes the response based on the IRB's determination at the convened meeting (either gives it to the individual who chaired the IRB meeting or assigns it to a convened IRB meeting for review). If the individual who chaired the meeting is the IRB's designated reviewer,

he/she may decide to forward the response to the entire IRB for additional review, request additional information, or approve.

- Suspension or termination of the research - SCRIHS staff sends the PI a letter describing the outcome of the IRB review.

  Note: Letters may be sent electronically through email or through the electronic IRB system

16. SCRIHS staff maintain documentation for protocol-specific assessments for a minimum of six years after the study closure.

REFERENCES

45CFR46.103(b)(4)(ii)
21CFR56.108(a)(2)

ADMINISTRATIVE ASSESSMENT REVIEW

EFFECTIVE DATE: December 12, 2012

REVISION DATE: September 11, 2013; January 29, 2016

OBJECTIVE

To describe policies and procedures for the administrative assessment of SCRIHS/IRB procedures and/or operations

GENERAL DESCRIPTION

SCRIHS/Institutional Review Board (IRB) serves to improve human research protections. One of the primary quality improvement activities is the administrative assessment review.

SCRIHS staff conducts administrative assessment reviews as necessary or at the direction of the Director of the Center for Clinical Research (CCR). These reviews measure the effectiveness and/or efficiency of SCRIHS/IRB procedures for protection of human subjects in research. Examples of areas that may be periodically assessed include, but are not limited to:

- IRB member performance;
- Proper use of expedited and exemption categories;
- Timeliness of SCRIHS staff responses to investigators/study personnel and/or of IRB review;
- Appropriate consideration and documentation for protecting vulnerable or potentially vulnerable populations;
- Timeliness of continuing review of approved research;
- Appropriate documentation for and approval of waivers of informed consent and/or alteration of elements of informed consent;
- Inclusion of all the elements of informed consent as required by the IRB;
- IRB consideration for data and safety monitoring;
- Completeness of IRB minutes;
- Quality of SCRIHS office operations and IRB system.

Any performance evaluation topic described under this SOP may be incorporated into a human subjects research compliance assessment at the discretion of SCRIHS staff, the Director of CCR, and/or the IRB Chair(s). SCRIHS staff shares the results of an administrative assessment with the Director of CCR and the SCRIHS Chair(s). The results may impact current practices and may require additional educational activities for SCRIHS staff and IRB members.

PROCEDURES

Administrative Assessment

1. An administrative assessment may require selection of specific protocols for examination of a variety of topics including, but not limited to: review type, funding source, external research, event types, special research categories, and/or assigned SCRIHS staff. Generally, the IRB Manager chooses protocols meeting the criteria for the particular administrative assessment randomly; however, the IRB Manager or the Director of CCR have the discretion to identify specific studies for assessment. If

identifying specific protocols is not necessary for the type of administrative assessment conducted (e.g., review of meeting minutes, review of a committee's workload, evaluation of the performance of IRB members), the designated SCRIHS staff obtains and reviews other related materials.

2. After identifying the protocols and/or related materials for examination, SCRIHS staff or designee conducts an in-depth review of either the IRB records for each protocol or related materials. This may entail review of the electronic IRB system, electronic or physical IRB records maintained by SCRIHS, and the IRB meeting minutes.

3. SCRIHS staff shares the results of the review with the Director of CCR and IRB Chair. Based on performance results, the Director, Chair or designee takes measures to strengthen certain areas of the SCRIHS office.

4. SCRIHS staff or designee educates other SCRIHS staff and/or the IRB on areas in need of strengthening as identified by analysis of the results (e.g., QI presentation at an IRB meeting, staff meeting, in-service presentations, etc.). SCRIHS staff informs the SCRIHS Advisory Panel and/or the IRB of specific findings only if the findings reveal significant or numerous deficiencies in protection of human subjects in research.

5. If exposed significant deficiencies necessitate reporting to the SCRIHS Advisory Panel and the IRB, the IRB determines whether to report the findings to the FDA, OHRP, or the study sponsor, and/or other applicable internal departmental faculty/staff. (See Mandated Reporting SOP.)

6. To support continuous improvement when policy or procedure changes as a result of assessment review findings, SCRIHS staff may perform a follow-up assessment review to determine whether the existing processes remain effective.

Assessment of Expedited Review

If SCRIHS staff conducts an assessment for protocols reviewed using expedited procedures, he/she verifies conformance with policies and procedures which may include, but are not limited to:

- Assignment to appropriate expedited reviewer;
- Notification of IRB members of expedited reviews;
- Review of protocols using expedited procedures according to the eligibility requirements for expedited review (proper use of expedited category);
- Documentation for the basis of allowing expedited review (expedited category selected);
- Performance of expedited reviewer
- Timely processing of applications by SCRIHS staff and/or the IRB reviewer.

Assessment of Exempt Review

If SCRIHS staff conduct an assessment for protocols reviewed for exemption certification, he/she verifies conformance with policies and procedures which may include, but are not limited to:

- Allowable category of exempted research;
- Assignment to appropriate reviewer;
- Documentation for the basis (allowable category) of making the exempt determination;
- Timely processing of applications by SCRIHS staff and/or IRB.

Assessment of Risks and Benefits

If SCRIHS staff conduct an assessment of the IRB's determination of risk versus potential benefit for a protocol, including designation of minimal risk when appropriate, he/she verifies documentation in the research records which includes, but is not limited to:

- Documentation in the meeting minutes or IRB records of the IRB's evaluation of risks of the research;
- Provisions for safety monitoring;
- Determination that risks to participants are minimized by using procedures that are consistent with sound research design and which do not unnecessarily expose subjects to risk, and whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes;
- Determination of the level of risk;
- Determination of the risk level of investigational device, if applicable;
- Appropriate disclosure of risks and benefits in the informed consent process.

Evaluation of IRB Member Performance

1. The SCRIHS Advisory Panel will consider IRB membership representation of appropriate knowledge, skills, and abilities respective to IRB membership annually. Areas of assessment include, but are not limited to:
    - Participation (e.g., attendance);
    - Knowledge of the federal regulations and ethical principles that serve as guidelines for responsible research and whether additional training is necessary to facilitate appropriate reviews;
    - Effective communication (e.g. disruptive, negative, overall attitude);
    - Committee competence in relation to appropriate review (e.g., expertise, representation).
    - Completeness of reviews.
    - IRB Chair leadership

2. Any concerns or issues with individual members will be handled by the IRB Chair(s) based upon recommendations from the Director of CCR, SCRIHS staff or the SCRIHS Advisory Panel.

SCRIHS Office Evaluation

1. The SCRIHS office is assessed at least once every five years. The IRB manager, with input from the Director of CCR, conducts the assessment.

2. SCRIHS staff, the IRB, investigators, and/or other administrative units may participate in the assessment process.

3. Throughout the course of the assessment, SCRIHS staff or the Director of CCR may determine the need for revisions to current SCRIHS policies, procedures, and/or practices in order to ensure compliance with federal regulations and institutional policies. Appropriate education plans will be developed as needed based on results of the assessment.

Elements of Informed Consent Evaluation

1. When SCRIHS staff conducts a review to evaluate appropriate inclusion of the elements of informed consent, he/she verifies conformance with the required elements of informed consent according to

IRB policy using the Consent/Assent templates as a guide. Protocols selected for compliance review are also subject to this informed consent evaluation.

2. The nature of the research dictates whether some additional elements of informed consent are necessary, but for required additional elements which have been excluded (e.g., significant new findings statement), SCRIHS staff confirm the IRB records contain appropriate documentation of the IRB's determination.

3. Upon completion of the informed consent evaluation, SCRIHS staff share the results with the Director of CCR and, if appropriate, the IRB Chair(s).

4. If the informed consent evaluation identifies deficiencies, SCRIHS staff and/or IRB Chair(s) provide follow-up training to IRB members.

Assessment for Appropriate Representation and Expertise for Vulnerable Population Protocol Reviews

1. If SCRIHS staff conduct an assessment for appropriate representation and expertise for full review research involving vulnerable populations (e.g., children, prisoners), he/she verifies that the appropriate IRB representative(s) was either present at the convened meeting or available via teleconference at the convened meeting (OHRP conditions met if so). If research involving vulnerable populations is eligible for expedited review, SCRIHS staff verifies the Expedited Reviewer had appropriate expertise or a consultant review was obtained.

2. SCRIHS staff or the Director of CCR may decide to focus this assessment on a specific vulnerable population during a particular time period.

REFERENCES

Not applicable

COORDINATION

CONFLICT OF INTEREST ("COI POLICY")

All investigators and authorized study personnel must be familiar with this policy. Any individual engaged in the design, conduct, or reporting of human subjects research (anything needing the Institutional Review Board (IRB) approval) must report in each protocol application, any personal financial interests related to the research. For example, an individual should disclose any financial interests with the sponsor of the study, the supporting organization, or the company that owns or licenses the technology/drug being studied. It is the investigator's responsibility to ensure that the protocol application reflects the appropriate disclosures for all study team members.

A SCRIHS Study Personnel Conflict of Interest Disclosure form ("COI Form") must be completed and signed upon submission of a human subjects research protocol to the Springfield Committee for Research Involving Human Subjects ("SCRIHS"). If an actual or potential conflict develops after submission of the protocol to SCRIHS, the investigator or authorized study person must complete and submit a revised COI Form (via an amendment) to SCRIHS at that time.

Introduction:

All members of the SIU SOM research community should be sensitive to the potential impacts of financial interests and/or non-financial relationships with commercial sponsors or other external entities on the conduct of research and the participation and protection of human research subjects. In compliance with federal regulations, guidance, and SIU SOM policy, SCRIHS considers such relationships and determines whether they might influence or appear to influence the outcome of a research project involving human subjects, the objectivity of the investigator during the performance of such a project, or the investigator's interactions with research subjects who participate in the project. Accordingly, SCRIHS, through the Compliance Office, reviews relevant information regarding the financial interests of all investigators and authorized study personnel participating in an externally funded and/or industry sponsored protocol involving human research subjects prior to approving or approving a continuing review of that protocol.

Definitions:

"Authorized study personnel" means those persons involved in the design, conduct, and/or the data analysis of the research involving human subjects.

"Relationships" that may be considered to be conflicts include, but are not limited to, the following: ownership of stocks, bonds, options, patent or royalty interests, receipt of consulting, honoraria or speaking fees, salary, grants, equipment, loans, memberships on non-federal or other scientific advisory boards.

The Role of SCRIHS:

SCRIHS is the primary authority at SIU SOM responsible for ensuring that human research subjects are protected in accordance with federal regulations, SIU SOM policies, and ethical principles. One of the primary responsibilities of SCRIHS is to ensure that human research subjects receive all information needed to provide informed consent. SCRIHS will ensure (1) that the informed consent process provides the subjects with the facts necessary to make a knowledgeable and sound decision as to whether they wish to participate in the study; and (2) that no conflict exists that would otherwise compromise the protection of human subjects.

Role of Investigators and Authorized Study Personnel:

For all new externally funded and/or industry sponsored protocols submitted to SCRIHS, each participating investigator and authorized study personnel must read this COI policy. Each participating investigator and authorized study personnel must complete and sign the COI Form.

If there is an indication of a potential conflict of interest on the COI Form, the Committee will evaluate such conflicts and will determine (1) whether the conflict is permissible in the context of the protocol, and, if so, (2) whether the conflict warrants disclosure to potential subjects as part of the informed consent process. Where required, identified COIs will be forwarded to the SIU COI Committee for review.

Note**In the COI process, the confidentiality of investigators and authorized study persons will be respected. Financial disclosure forms will be kept confidential and information will be shared only on a need-to-know basis.

Instructions for Investigators and Authorized Study Personnel

For new protocols: Investigators and authorized study personnel must submit a completed COI Form to SCRIHS with the original protocol submission in iRIS. During the course of the study, if any answers on the originally submitted COI Form should change, the investigator or authorized study personnel must submit a revised COI Form for review relevant to the affected protocol(s) in iRIS.

For amendments: The participating investigator and authorized study personnel will be required to indicate on amendments that there is no new conflict of interest or if a conflict of interest has arisen, a revised COI Form must be submitted for review. If new study personnel are added to a protocol during the course of a study (via an amendment), the COI Form must be revised to include the new study personnel's certification.

For continuing review: At the time of annual continuing review, a new form will be required. In iRIS a revision of the SCRIHS COI Form in iRIS will need to be created and attached to the continuing review submission. This revised form should include all authorized study personnel.

SIU SOM Conflict of Interest Instructions – There are 2 components

Please note this Intuitional requirement is in addition to the SCRIHS COI requirement and applies only to SIU faculty and staff.

1. COI TRAINING - on CITI before submitting an application for PHS funding.
Follow this link and **register** (if you have not done so previously) https://www.citiprogram.org/default.asp?language=english

2. COI DISCLOSURE & ATTESTATION - To complete your SIU SOM disclosures and do your attestation use this link: https://coi.siumed.edu/ Enter your Employee ID (numeric values only from the back of your ID badge) and click "Log In".
"Start a new submission"

When COI disclosure forms are completed, please click the "Research and CME Reporting tab" click box #1 and hit "submit".

Instructions for Cancer Cooperative Group Protocols:

Cancer cooperative group protocols fall under the purview of the National Cancer Institute (NCI) and the Cancer Therapy Evaluation Program (CTEP). Per CTEP guidelines, all investigators are required to complete the "Confidential Financial Disclosure Form" annually to satisfy conflict of interest reporting requirements.

A copy of all participating investigators' "Confidential Financial Disclosure Form" statements must be submitted to SCRIHS to be kept on file. Updated statements must be submitted annually, when they are updated for CTEP.