



Institutional Review Board

University of Missouri-Columbia

Standard Operating Procedure

Initial Review

Initial Review

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1.0 Purpose

To aid in assuring knowledge and compliance of all persons involved in any aspect of human subject research by documenting the procedure for initial review of non-exempt research.

2.0 Scope

The SOP applies to all human subject research falling under the purview of the University of Missouri Institutional Review Board.

3.0 Policy/Procedure

General Information

In conducting the initial review of proposed research, IRBs must obtain information in sufficient detail to make the determinations required in 45 CFR 46.111, 21 CFR 56.111 and 38 CFR 16.111.

Submission Requirements:

Materials required to assist the IRB in its review of proposed research, include but are not limited to the following, as applicable to the research project:

- Application form and applicable sub-forms (submitted electronically through the eCompliance system)
- Advisor Approval Form (required when a student investigator is the Principal Investigator)

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- PI Assurance Form
- Protocol (Biomedical, Social/Behavioral/Educational, or Sponsor-Provided)
- DHHS-approved protocol (when one exists)
- Proposed informed consent and assent documents
- Authorization Agreements (if there is reliance on our IRB)
- Clinical Investigator's Drug Brochure
- *Data safety monitoring plan
- Any recruitment materials, including advertisements intended to be seen or heard by potential subjects
- Questionnaires, handouts, or any other applicable instruments
- HIPAA alterations or waivers

*For research involving greater than minimal risk, the investigator is required to submit a safety monitoring plan within the application or refer to a plan attached to the application. The overall elements of a plan may vary depending on the potential risks, complexity, and nature of the research activity. The method and degree of monitoring may vary as well depending on the scope and size of the research effort.

NIH Awardees – Certificates of Confidentiality

NIH awardees no longer have to apply for a Certificate of Confidentiality. All ongoing or new research funded by the NIH as of December 13, 2016 that is collecting or using identifiable, sensitive information is automatically issued a Certificate of Confidentiality through a term and condition of award.

For the purposes of this Policy, consistent with subsection 301(d) of the Public Health Service Act (42 U.S.C 241), the term “identifiable, sensitive information” means information about an individual that is gathered or used during biomedical, behavioral, clinical, or other research, where the following may occur:

- An individual is identified; or
- For which there is at least a very small risk, that some combination of the information, a request for the information, and other available data sources could be used to deduce the identity of an individual.

The NIH will continue to consider requests for Certificates of Confidentiality for specific projects that are not funded by NIH, or other HHS agencies that issue Certificates. Such requests need to be submitted through the NIH online system in accordance with current NIH procedures for issuing Certificates.

All recipients of a Certificate shall not:

- Disclose or provide, in any Federal, State, or local civil, criminal, administrative, legislative, or other proceeding, the name of such individual or any such information, document, or biospecimen that contains identifiable, sensitive information about the individual and that was created or compiled for purposes of the research, unless such disclosure or use is made with the consent of the individual to whom the information, document, or biospecimen pertains; or

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- Disclose or provide to any other person not connected with the research the name of such an individual or any information, document, or biospecimen that contains identifiable, sensitive information about such an individual and that was created or compiled for purposes of the research.

Disclosure is permitted only when:

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

Researchers must inform participants (for example, in the consent document) of the protections and limitations of certificates of confidentiality.

When identifiable, sensitive information is provided to other researchers or organizations, the other researcher or organization must comply with applicable certificate of confidentiality requirements.

See <https://humansubjects.nih.gov/coc/index> for examples of research automatically covered and for other information.

Full Board Submission Deadline:

The full board deadline is the 25th of the month for review at the following month's board meeting.

Administrative Processing and Review

1. Applications submitted to the IRB office will be reviewed in the order they are received. All applications are sorted internally within eCompliance by the type of application (Biomedical or Social/Behavioral/Educational) initially selected by the investigator. The IRB staff trained in these specific areas will conduct a preliminary review of the submission materials to determine:
 - a. the completeness of the packet;
 - b. to determine if, in their opinion, the project may qualify for expedited or full-board review; and
 - c. to request clarifications and/or additional materials to provide the reviewer with a complete application that meets regulation and institutional requirements.

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2. Any incomplete submissions will be left in returned status until all required materials are received. The principal investigator or designated contact person will be notified via e-mail that the packet is incomplete and a list of the materials necessary to complete the packet. A project that is incomplete will not be forwarded for review by the IRB until all the necessary elements and clarifications have been received.
3. Prior to final approval being granted on any project, the IRB office will determine if all study personnel have completed the required CITI educational modules, including the ethical conduct of research expectations. IRB approval will be held until the required CITI training has been completed for all key personnel. Clinical trials will require current CITI GCP training. All training is active for three years, and the refresher courses must be taken to maintain active status.
4. The IRB staff will ensure the investigator documented they have the resources necessary to protect participants, including:
 - a. Adequate time for the researchers to conduct and complete the research;
 - b. Adequate number of qualified staff;
 - c. Adequate facilities;
 - d. Access to a population that will allow recruitment of the necessary number of participants;
 - e. Availability of medical or psychological resources that participants may need as a consequence of the research.
5. If the study qualifies for expedited review, it is assigned to a primary reviewer; otherwise, it is placed on the appropriate full board agenda.
6. The IRB staff will ensure the primary reviewer has the necessary scholarly or scientific expertise. For any review, if the primary reviewer feels he/she does not have the necessary expertise to review the project, he/she may contact the IRB staff and the project will be reassigned to another primary reviewer with the necessary expertise. In addition, if an assigned reviewer has a conflict of interest they should contact the IRB staff and the study will be re-assigned.
7. If the IRB staff determines that there is not at least one person on the IRB with the necessary scholarly or scientific expertise, they will invite individuals (consultants) with competence in that area to assist in the review of issues. (see Board Structure and Responsibilities SOP)

Additional Reviews

The nature and type of study may necessitate additional institutional reviews and/or consultations prior to subject enrollment. Investigators will be informed within their IRB approval letter if enrollment cannot begin because all institutional reviews have not yet

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been secured, if applicable. Documentation of each additional review will be entered into the eCompliance database.

1. *Devices* - If the project includes the use of an experimental device, a copy of the application, the protocol and the device information will be sent to the designated device consultant, if needed, prior to review (per 45 CFR 46.107(f)). The device review and recommendation will be sent to the assigned reviewer as part of the review packet.
2. *Radiation* – If the project involves radiation therapy and the investigator marked all therapy is standard of care, the project will be sent to a consultant to confirm standard of care and the consultant checklist will be completed in eCompliance. If the project involves therapy that falls outside of standard of care, it will be forwarded to the Radiation Safety office for review and approval. Subject enrollment cannot begin until the Radiation Safety approval is received. A consultant may review projects that involve research-only radiation procedures (i.e. x-rays, CT Scans) if safety is a concern. The IRB can invite a consultant when necessary (see Board Structure and Responsibilities SOP regarding consultants).
3. *Biosafety* - If the project includes biohazardous materials requiring biosafety review, a copy of the application, consent, and the protocol will be sent to the Biosafety office for review and approval. Subject enrollment cannot begin until biosafety approval is received for both the material being utilized and the location where it will be utilized/stored. Specific items requiring review by the Biosafety office include human material with recombinant or synthetic nucleic acid molecule technology or blood borne pathogens; infectious or zoonotic agents (viruses, bacteria, etc.); biological toxins; or other biohazardous material.
4. *Investigational Drug Services (IDS)* – Pharmacy (IDS) controls the storage, dispensing, labeling, and distribution of investigational drugs or biologics. If the project includes the use of drugs or biologics, the IRB office will notify the Investigational Drug Pharmacist. Trials involving the dispensing of investigational medications must be reviewed and approved by the IDS before subject enrollment may begin. All trials must receive IRB approval prior to Pharmacy's dispensing any medications pursuant to that protocol.
5. *Conflict of Interest* – If a conflict of interest is identified with the investigator and/or study staff and the proposed research, review by the Conflict of Interest (COI) committee is required. The investigator and the Office of Research will be notified about the possible conflict. The investigator may be required to submit additional paperwork for review by the COI committee. Depending on the level of conflict and the degree to which it impacts the proposed study, IRB approval may be delayed until a resolution or management of the conflict has been developed.
6. *Veterans* – If the proposed research is going to be conducted by investigators serving on VA compensated, VA without compensation, or Intergovernmental Personnel Act appointments, review by the VA Research and Development Committee is required. VA

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R&D approval is required prior to conducting any portion of the proposed research at the VA Hospital. See the Truman VA Hospital Human Subjects Research - Special Considerations SOP for more information.

7. *Tissues/Specimens* – If a proposed study includes establishment of a research biorepository, an IRB application must be completed in the eCompliance system. If a proposed study includes solid tissue, blood, urine, saliva, or specimen data for tissue/specimens collected as part of a MU Health Care (Hospital and Clinics) health encounter, a consultant may be utilized. Any researcher utilizing tissues/specimens obtained from an internal or external tissue or blood bank, biorepository, or external laboratory not part of MU Health Care will need to provide proof to the IRB that appropriate consent and collection processes were utilized to obtain samples and provide support regarding the identifiable or de-identifiable nature of the tissue/specimen.

8. *Coverage Analysis* – If a proposed study is a clinical trial or will result in charges in a hospital or clinical setting, investigators must provide an initial coverage analysis/billing grid detailing charges according to standard of care or research only criteria. A final, Medicare coverage analysis will be performed by the Human Subjects Research Protections Program (HRPP) to ensure compliance with CMS guidelines and adherence to MU Health policies and guidelines regarding research billing and pricing.

9. *Study Type/Department Specific* – In certain circumstances, the nature of the study will require additional approval by a committee or department chair or supervisor. The IRB application system will provide a mechanism for these approvals to be acknowledged.

When needed, General Counsel for the University will be consulted on legal issues, to include interpretation of State law and to resolve conflicts between federal, national, and other applicable laws.

Expedited Review Process

Only appropriately trained IRB members may conduct reviews using the Expedited procedure. See Board Structure and Responsibilities SOP regarding primary reviewer eligibility and experience. The IRB staff will select and assign a primary reviewer based on their qualifications, education, and expertise with the type of research under review. The research is not classified.

1. The primary reviewer documents compliance with the applicable regulations permitting expedited review (45 CFR 46.110, 21 CFR 56.110 and 38 CFR 16.110).
2. The review is generally completed within two weeks of receipt of the materials, and the review recommendation is sent to the IRB administrative office for final processing. The primary reviewer always has the option to contact the IRB staff and request that the project be reviewed at the next full board meeting if the reviewer determines the project does not meet the requirements for expedited

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review or if the reviewer is more comfortable having the project reviewed by the full board.

3. The reviewer determines and documents the following:
 - a. All applicable criteria are met and all research activities fall into one or more categories of research allowing review by the expedited procedure.
 - b. Any other determinations required by the regulations, including protocol specific findings that justify those determinations.
 - c. The rationale for an expedited reviewer's determination under 46.110(b)(1)(i) that research appearing on the expedited review list described in 46.110(a) is more than minimal risk. These studies will follow the full board review process discussed below.
 - d. The justification for expediting a study not falling under any of the existing expedited categories, but the reviewer determined the study involves no more than minimal risk and can be reviewed expedited. The study cannot be FDA regulated.
4. The primary reviewer will determine the study is approved, approved with minor modifications or requires substantive clarifications.
 - a. If the primary reviewer requests any ***minor modifications or clarifications** (see examples below under Full Board Review Process) requiring simple concurrence by the investigator, the IRB office will notify the investigator. This request and the written response will be documented in the file. The IRB staff will review, for completeness, the clarifications or documented changes when they are received and approve the study.
 - b. For clarifications that they are directly relevant to the expedited determinations under 45 CFR 46.110, 21 CFR 56.110 and 38 CFR 16.110, the IRB staff will contact the investigator and request the modifications or clarifications in writing. The request and response will be documented in the file. The primary reviewer will re-review the study once the modifications have been made and determine the approval status.
5. If the investigator is unwilling to make requested modifications, the project will be placed on the agenda for the next full board meeting along with the justification from the investigator. The board will deliberate and decide to approve or disapprove. See Full Board Review Process below.
6. During an expedited review, if the primary reviewer determines the application cannot be approved by expedited procedures, the application will be placed on the next available full board docket. A research project will not be disapproved without convened IRB review at which a majority of the members of the IRB are present. (45 CFR 46.108(b))

Full Board Review Process

1. The applications for full board review are conducted using a primary reviewer and secondary reviewer process. The primary reviewer documents compliance with regulatory requirements as applicable including, but not limited to 45 CFR 46.116, 21 CFR 56.116 and 38 CFR 16.116. All board members are expected to have a working knowledge of all submitted materials and be able to engage in a meaningful discussion. The secondary reviewer primarily focuses on the consent process/documents. (See Board Meeting Procedures and Minutes SOP and Board Structure and Responsibilities SOP for further information). The IRB will defer to another meeting or obtain a consultant if there is not at least one person on the IRB with appropriate scientific or scholarly expertise or other expertise or knowledge to conduct an in-depth review of the protocol.
2. Once all discussion has ceased on a project, a vote on the motion on the table will be taken. All motions, discussions and actions taking place during the convened Board meeting will be documented in the written minutes of the meeting. (See Board Meeting Procedure and Minutes SOP for further information)
3. The convened board will determine if the study is approved, approved with minor modifications or requires substantive clarifications, or disapproved.
 - a. If the board requests any ***minor modifications or clarifications** requiring simple concurrence by the investigator, the IRB office will notify the investigator. This request and the written response will be documented in the file. The clarifications are subsequently reviewed and approved by the primary reviewer or another designee in a timely fashion. The Minutes will document whether the minor modifications or clarifications can be reviewed administratively or using expedited procedures.

***Minor Modifications or Clarifications:**

- Those modifications or clarifications that do not involve potential for increased risk or decreased benefit to the human subjects.
 - Protocol revisions that entail no more than minimal risk to participants.
 - Changes to informed consent documents that do not affect the rights and welfare of study participants, do not involve increased risk, or significant changes in the study procedures.
 - New or revised recruitment advertisements or scripts.
- b. When the convened IRB requests **Substantive Clarifications or Modifications** regarding the protocol or informed consent documents that are directly relevant to the determinations required by the IRB for research under 45 CFR 46.111, 21 CFR 56.111 and 38CFR 16.111, the convened IRB must review the revisions.

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- i. The project will be re-reviewed with the documented modifications at the next convened board meeting to determine approval status.
 - ii. The investigator may request to attend the meeting to discuss the study under review and answer questions or provide explanation. In addition, the board may request that the investigator attend the meeting to address concerns of the study.
4. If the study is disapproved by the convened board, the Principal Investigator will be notified in writing and the decision will be documented in the Minutes. The letter will include the reason(s) for disapproval and recommendations, if any, on how to proceed in an attempt to have the study approved. The investigator will be given the opportunity to respond. (See Appeals SOP)

Setting Approval Dates

1. When the IRB Reviews and Approves Research *Without Conditions*:
 - a. For expedited review, the approval date is the date the primary reviewer approved the study.
 - b. For full board review, the approval date is the date of the board meeting in which the convened board approved the study.
2. When the IRB Reviews and Approves Research *With Minor Modifications or Clarifications*:
 - a. The approval date is set to the date of the board meeting in which the convened board approved the modifications or the date on which the primary reviewer or IRB designee reviewed and accepted all clarifications.
3. When the IRB Reviews and Defers Approval requiring *further review by the IRB at a subsequent convened meeting*:
 - a. If the study is approved at the subsequent convened meeting without conditions, the approval date is the date of the boards meeting in which the convened board approved the study.
 - b. If the study is approved with minor modifications, the approval date is set to the date of the board meeting in which the convened board approved the modifications or the date on which the primary reviewer or IRB designee reviewed and accepted all clarifications.
 - c. If the study is deferred once more, step 3 will repeat until the study is either approved or disapproved.

Expiration Dates

1. For expedited studies, the initial expiration date is set to one year after the date the primary reviewer approved the study, but cannot extend past that one year interval. Shorter continuing review intervals may be requested, as necessary.

2. For full board studies, the expiration date is set to one year after the date of the IRB meeting at which the research project was initially approved. Shorter continuing review intervals may be requested, as necessary.

The expiration date is defined as the first day that the protocol is no longer approved without continuing review and approval by the IRB.

Approval Notification

The IRB will notify investigators in writing of its decision to approve the proposed research activity, the risk level assigned, the consent requirements, approved documents, and the continuing review interval within the final approval letter. A copy of the approval letter and approved documents are located in eCompliance under attached files.

Activities Determined not to be Human Subject Research

1. Quality Improvement (QI): The IRB provides the investigator the ability to submit a QI Determination Form so the IRB can determine and document the activity proposed is not human subject research, but fits under quality improvement not requiring IRB review. Documentation is often needed for publishers or departments within the University. These are reviewed administratively by the IRB office. Confirmation by a board member may be required on a case-by-case basis.
2. Case Report Form: The retrospective review of three or less cases is not considered human subject research. The IRB requires physicians to complete this form to ensure HIPAA compliance. These are reviewed administratively by the IRB office.
3. Human Subject Research Determination Form: The IRB provides the investigator the ability to submit a form to help determine whether what they are doing is considered research. These are reviewed administratively by the HRPP office. Confirmation by a board member may be required on a case-by-case basis. If it is determined not to be research, the investigator will receive a determination letter stating this. If it is human subject research, the investigator will be notified to submit the IRB application for review and approval.
4. Research Involving Cadavers: The IRB does not require review of research involving cadavers. DHHS defines a human subject as living, and FDA defines a human subject as a healthy individual or a patient. These definitions would exclude non-living humans. *Note: HIPAA regulations would apply if protected health information were disclosed on decedent's relatives, employers, or household members. An IRB application would be required to comply with HIPAA regulations in this case.*
5. Publicly or commercially available information or biospecimens with no restrictions on the use of the information or biospecimens.

DHHS Determined the Following Activities are NOT Human Subject Research

Regardless of funding, the MU IRB will also apply the same non-humans subject research determinations to non-federally funded research.

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1. Scholarly and journalistic activities (e.g. oral history, journalism, biography, literary criticism, legal research, and historical scholarship), including the collection and use of information, that focus directly on the specific individuals about whom the information is collected.
2. Public health surveillance activities, including the collection and testing of information or biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health authority. Such activities are limited to those necessary to allow public health authority to identify, monitor, assess, or investigate potential public health signals, onsets of disease outbreaks, or conditions of public health importance (including trends, signals, risk factors, patterns in diseases, or increases in injuries from using consumer products). Such activities include those associated with providing timely situational awareness and priority setting during the course of an event or crisis that threatens public health (including natural or man-made disasters).
3. Collection and analysis of information, biospecimens, or records by or for criminal justice agency for activities authorized by law or court solely for criminal justice or criminal investigative purposes.
4. Authorized operational activities (as determined by each federal agency) in support of intelligence, homeland security, defense, or other national security missions.

References:

Policy Revision Dates Prior to January 21, 2019:

September 1, 2004; December 9, 2005; December 1, 2006; June 10, 2010; August 12, 2010; July 1, 2011; March 1, 2015; July 1, 2015; January 29, 2016; June 8, 2017; May 3, 2018