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”How to” for PIs

OAK RIDGE SITE-WIDE INSTITUTIONAL REVIEW BOARD (ORSIRB)

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Purpose and Background

This document includes excerpts of the Oak Ridge Site-wide Institutional Review Board's (ORSIRB's) policy and procedures relevant to obtaining and/or maintaining ORSIRB approval of research activities and is intended as a quick reference guide only. For complete documentation please refer to the complete ORSIRB Standard Operating Policy and Procedures.

Responsibilities of Principal Investigators

Principal Investigators (PI) have primary responsibility for protecting the rights and welfare of human research subjects and for complying with all applicable provisions of federal law and any requirements of the Board.

Determination of "Human Subject"

45 CFR 46.102(f): *Human subject* means a living individual about whom an investigator (whether professional or student) conducting research obtains: (1) data through intervention or interaction with the individual, or (2) identifiable private information. Intervention includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes. Interaction includes communication or interpersonal contact between investigator and subject. Private information includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record). Private information must be individually identifiable (i.e., the identity of the subject is or may be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects.

If the answer to any of the following questions is "yes" it is determined that human subjects are involved in research.

A. Does the study involve intervention or interaction with a "human subject"?
B. Does the study involve access to identifiable private information?
C. Are data/specimens <u>received</u> by the Investigator with identifiable private information?
D. Are the data/specimen(s) coded such that a link exists that could allow the data/specimen(s) to be re-identified?

Determination of "Research"

45 CFR 46.102(d): *Research* means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. Activities, which meet this definition, constitute research for purposes of this policy, whether or not they are conducted or supported under a program which is considered research for other purposes.

If the answer to any of the following questions, it is determined that research is being conducted.

A. Is the data/specimen(s) obtained in a systematic manner?
B. Is the intent of the data/specimen collection for the purpose of contributing to generalizable knowledge?

Review and Approval Process

Initial Review of New Studies by ORSIRB

Before initiating the research, the ORSIRB shall be notified by the PIs' institutions of all new proposals to conduct research. Research projects that will involve human participants should be clearly identified as human subjects research as early as possible in proposal preparation and the review process. As the person who designs and implements the research proposal and often interacts personally with research participants, the researcher plays a vital role in the protection of human subjects. The types of research that fall into this category are not necessarily obvious. Human subjects research includes a broader range of research than may investigators and program managers realize. For example, certain types of surveys and interviews are considered research.

PIs may request the level of review they consider appropriate, but only the ORSIRB Administrator or chair will determine whether or not the proposed activity requires review and approval, as well as the level of review required.

In the absence of a timely scheduled meeting of the ORSIRB, the ORSIRB Chair or his/or designee(s) will review protocols requiring Full Board review for interim approval and notify the PI of the outcome within five working days of the receipt of the protocol from the PI. Interim approval allows planning and other preliminary work on the study to proceed, but data collection and subject contact, interviews, etc., must await Full Board review and approval.

When the ORSIRB's approval of a protocol is final, the PI provides clean copies of all revised documents as approved to the ORSIRB Administrator. The ORSIRB Administrator returns them to the PI, stamped as applicable to show the date and duration of the ORSIRB's approval, keeping a copy of each for the files.

Continuation Review

Federal regulations at 45 CFR 46.109 (e) require that approved protocols be periodically reviewed to ensure the continuing protection of human subjects over the course of the research. The scheduling of these reviews should be appropriate to the level of risk involved in the study but must be no less than every 12 months. The ORSIRB Administrator will notify the PI sixty (60) days in advance of the scheduled date of continuation review of each protocol. As with the initial review of new protocols, the continuation review may be conducted either by the Full Board or by an expedited process, depending on the **level of risk** involved in the research.

Protocols Requiring Initial or Continuing Reviews by Multiple IRBs

It must be recognized that some research may be subject to review by both the site and institutional IRB of the principal investigator and/or collaborating institutions. Arrangements will be made on a case-by-case basis to maximize the efficiency of initial and continuing reviews of individual research studies/projects by multiple IRBs.

Levels of Review

Federal regulations at 45 CFR 46 allow for three levels of review: (1) exempt, (2) expedited, and (3) Full Board. The level of potential risk to the subjects determines the level of review required. **The higher the risk, the greater the rigor of review**. **Note**: The ORSIRB makes the **final determination** of the type of review the protocol warrants.

Exempt Review

Certain low-risk research activities are exempt from rigorous IRB review; however, the ORSIRB Chair must conduct a preliminary review to determine whether the research meets the criteria for exemption. Regardless of the determination of the local/site institutional IRBs, the final determination shall be made by the ORSIRB.

Expedited Review

To be considered for expedited review, proposed research must meet two conditions:

(1) It must present no more than ***minimal risk*** to subjects, and
(2) It must fit into one of the identified research categories.

An expedited review, rather than requiring the consideration of the full ORSIRB at a convened meeting, may be conducted by the ORSIRB Chair, a designated voting member, or a group of voting members designated by the Chair. Following an expedited review, the ORSIRB Chair may approve a proposal, ask for modifications to achieve approval, or refer it to the Full Board. Proposed research cannot be disapproved under expedited review.

Expedited review may also be used for minor changes to approved research and for continuation reviews of previously approved protocols. The requirements for approval of a protocol under the expedited review mechanism are the same as those which apply to a Full Board review (e.g. sound scientific protocol, proper informed consent procedures, minimization of research risks, etc.). The only difference is that an expedited review may be performed by a single board member whereas higher risk studies require deliberation by the Full Board.

Full Board Review

All other human subjects research subject to ORSIRB review requires review at a convened meeting by a valid quorum of ORSIRB members. This is the highest level of review, and to be approved, proposed research must receive the approval of a majority of those voting members present.

Materials to be Submitted to the ORSIRB for New Protocol Review

Principal Investigators shall prepare protocols giving a complete description of the scientific and ethical aspects of proposed research including provisions for the adequate protection of the rights and welfare of prospective research subjects and ensuring that pertinent laws and regulations are observed. This is required even in situations in which the research is exempt under 45 CFR 46.101. The proposal review package must include the following for the initial review:

- Project protocol (including background and rationale for the study, details of the scientific design and methodologies, human subjects protection methodologies, sampling plan/statistical design, data management and data security/ confidentiality plan, dissemination and notification plan, recruiting materials).
- Any copies of supporting technical/peer reviews, internal or external, of the protocol.
- Current protocol or project handbook, if appropriate (to include all current local site and ORSIRB-approved consent forms, fact sheets, data collection instruments)
- Documentation of compliance with Privacy Provisions of HIPAA, where appropriate (copies of approved authorizations from participating covered entities)
- Informed Consent Document and Procedure

Informed Consent

Investigators shall include with the protocol, a draft of all applicable informed consent documents that address all the elements of informed consent as prescribed in 45 CFR 46, section 116, and other elements recommended by the ORSIRB to be routinely included in a consent form. Principal Investigators are responsible for ensuring that legally effective informed consent shall:

- Be obtained using a consent form that has been reviewed and approved by the local site and ORSIRB within the previous 12 months or less as previously prescribed by the IRB.
- Be obtained from the subject or the subject's legally authorized representative.
- Be in non-technical language understandable to the subject or his/her representative.
- Clearly state that participation is voluntary.
- Be obtained under circumstances that offer the subject or the representative sufficient opportunity to consider whether the subject should or should not participate.
- Not include exculpatory language through which the subject or the representative is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the Principal Investigator, the sponsor, the institution or its agents from liability for negligence.

Unless otherwise authorized by the Board, Principal Investigators at a minimum shall provide the following to each subject in the informed consent document:

- The names, affiliation, addresses of the principal and any co-investigator(s), the sponsor (funding source), and location at which the research will be conducted.
- A statement that the study involves research, an explanation of the purposes of the research, and the expected duration of the subject's participation; a description of the procedures to be followed as they involve human subjects, and identification of any procedures that are experimental.
- A description of any benefits to the subject or to others that may reasonably be expected from the research.
- A disclosure of appropriate alternative procedures or courses of treatment, if any, which might be available.
- A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained and identifying the individuals (by title), institutions, and/or agencies that may routinely use or access the records.
- For research involving more than minimal risk, explanations as to whether any compensation or medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained.
- A statement describing how, where, for how long, and in what form the data will be used, stored and maintained, and how and to whom the results of the research will be reported to assure the privacy of the subject and the confidentiality of the subject's personally sensitive information.
- Immediate and direct access at the time of consent to an individual capable of answering any questions related to the study.
- An explanation of whom to contact for answers to pertinent questions about (a) any research-related injury to the subject, and (b) the research and research subjects rights and responsibilities; this shall include identification of "the Chair, ORSIRB" as an alternate source of information about subjects' rights.
- A statement that participation is voluntary, and refusal to participate or discontinue participation at any time will not result in any penalty or loss of benefits to which the subject is otherwise entitled.
- A statement of the action, if any, to be taken by the subject if he/she decides to withdraw from the research before its completion, and of the disposition of the subject's data compiled up to the time of withdrawal.
- A copy of the consent form.

When required by the Board, the Principal Investigator also shall provide one or more of the following additional elements of information to each subject:

- A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant), which are currently unforeseeable.
- A statement that the Principal Investigator may decide to withdraw the subject from the research, and the sponsor might terminate funding, without notification.

- Anticipated circumstances under which the subject's participation may be terminated by the research investigator without regard to the subject's consent.
- Any additional costs to the subject that may result from participation in the research.
- The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject.
- A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject.
- The approximate number of subjects involved in the study.

The ORSIRB may permit the Principal Investigator to use a consent form that is either:

- A written consent document that embodies the elements of informed consent required by 45 CFR 46.116. This form may be read to the subject or the subject's legally authorized representative, but in any event, the research investigator or other person obtaining the consent shall document by signing that either the subject or the representative has been given adequate opportunity to read or to listen to a recording of the form before signing it.
- A "short form" written consent document stating that the elements of informed consent required by 45 CFR 46.116 have been presented orally to the subject or the subject's legally authorized representative. When the "short form" is used, PI shall ensure that:
    - The written summary of what is to be said to the subject or the representative receives the prior approval of the Board.
    - A witness is present at the oral presentation.
    - The subject or the representative signs the short form; the witness signs both the short form and a copy of the written summary of the oral presentation.
    - The person obtaining consent signs a copy of the summary.
    - The names of all signatories also shall be printed or typed, with the date and time.
    - A copy of both the short form and summary is given to the subject or the representative.

Waiver or Alteration of Informed Consent

At the request of the PI, the ORSIRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth in 45 CFR 46.116 (a) and (b), or waive the requirement to obtain informed consent provided the Board finds and documents that:

- The research is to be conducted for the purpose of demonstrating or evaluating federal, state or local benefit or service programs that are not themselves research programs; or, procedures for obtaining benefits or services under these programs, or possible changes in or alternatives to these programs or procedures.

- The research involves no more than minimal risk to the subjects.
- The waiver or alteration will not adversely affect the rights and welfare of the subjects
- The research could not practicably be carried out without the waiver or alteration.
- Whenever appropriate the subjects will be provided with additional pertinent information after participation.

Disposition of a Protocol Following ORSIRB Review

When the ORSIRB reviews a proposed protocol, it has four options:

- **Approve** as is (protocol is approved as submitted).
- **Approve with conditions** (review package requires modifications or PI must furnish additional information-within 21 working days). If verification cannot be made, the proposal cannot be approved.
- **Table** (protocol/review package needs major work before the ORSIRB can complete review or the Board has unresolved questions and the PI is not available to address them). The PI is also informed that no work or recruitment of subjects may begin until this documentation is received and reviewed for approval by the Full Board at its next scheduled meeting.
- **Disapprove** (protocol does not meet the minimum criteria required for approval). Investigators have the right to request the ORSIRB to reconsider research proposals that it did not approve.

Documentation

After ORSIRB approval and before beginning a research protocol, the PI must be able to show that the proposed research and consent documents have been reviewed and approved by the ORSIRB and all subjects are fully informed, and that their consent has been documented in signed consent forms (unless the signature requirement was specifically waived by the ORSIRB). The Chair will determine the level of review required prior to implementation of any amendments.

Frequency of Review

The Board shall determine, in its initial review of research protocols, the schedule for continuation review. Such a determination will be made by the Board based primarily on the nature and magnitude of the risk(s) of the research to the subjects. The minimum requirement is no less than once annually. For all approved protocols, the PI will be notified of the schedule for follow-up continuation review.

POST-APPROVAL REVIEW OF NEW PROTOCOLS

Serious Adverse Events

The PI must immediately report to his/her institution's IRB and the ORSIRB all serious adverse events within 48 hours, even if there is no obvious causal relationship between the study activities and the event. The institution's IRB, in turn, is responsible for

reporting all adverse events to the institution's management, to DOE/HQ, and to any other federal agency funding the research protocol, and notifying the ORSIRB of the report. The responsibility for reporting the serious adverse event to the Office of Human Research Protections (OHRP), devising a remediation plan, and for all related follow-up activities will be conducted in accordance with the multi-site review agreements negotiated by the ORSIRB and institutional and site IRBs for each research project.

Amendments/Modifications to an Approved Protocol

A completed Modification Form for all proposed modifications or amendments to an approved protocol shall be submitted to the ORSIRB administrator to initiate ORSIRB review and approval prior to their implementation. As with the review of new protocols and continuation reviews, the review of modifications to an existing protocol may be conducted by either the Full Board or the expedited mechanism depending on the level of risk involved and the scope of the proposed changes. The level of review required will be determined by the Chair of the ORSIRB. No changes to an approved protocol shall be implemented without their approval by the ORSIRB.

Completion/Termination

When a study is completed or the PI wishes to terminate it, the PI must notify the ORSIRB, at which time the protocol will be placed on inactive status for a period of 5 years. During this time, a PI may request re-activation of the protocol without submitting a new protocol (unless there are significant changes in the protocol). After a protocol has been on inactive status for 5 years, it is then discontinued.

MONITORING

Research Conduct

During the course of the research, the PI must comply with all ORSIRB decisions and conditions and the responsibilities described in these Guidelines.

Note: The ORSIRB may contact subjects directly or monitor the research to evaluate the PI's conduct and compliance with requirements.

Deviation from Approved Protocol

The PI may not deviate from an approved protocol without written ORSIRB approval, except when such deviation is necessary to eliminate an immediate hazard to a study subject.

Suspension/Termination Procedure

The ORSIRB has both the authority and the responsibility to suspend or terminate any research involving human subjects that is not being conducted in accordance with ORSIRB requirements or that has been associated with any unexpected serious harm to subjects. Any such suspension or termination of approval must be reported promptly to the PI and shall include a statement of the reasons for the suspension. The ORSIRB Chair must also notify the institution's director, DOE/HQ, and DHHS/OHRP.

MEETINGS

Scheduled Meetings

At least two convened meetings of the Board shall occur within a 12-month period. Meetings may be held more frequently as necessary to assure that the Board meets its responsibilities in accordance with 45 CFR 46. A PI may request, or be requested, to attend a meeting in person or by teleconference call to discuss his/her protocol; however, no PI may be present during a vote on his/her proposal.

RECORD KEEPING

PI Records

The PI must retain all research-related records that originate with the PI or the research team for the length of time as required by law, terms of DOE contract or grant, or as stated in the Federal Register.

Link to Forms