

**The University of Tennessee, Knoxville**  
**Institutional Review Board**  
**Member Guide**



THE UNIVERSITY OF  
**TENNESSEE**  
KNOXVILLE

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OFFICE OF  
RESEARCH INTEGRITY

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## **1. IRB Member Conflict of Interest**

IRB members who have a conflict of interest with any research activity (new submission, amendment, continuing review, etc.) being reviewed cannot deliberate or vote on that research activity and must identify the conflict prior to review, deliberation or voting on the activity occurs (45 CFR 46.107(d)).

An IRB member is said to have a conflict of interest whenever that person, his or her spouse, or dependent child falls under any of the following conditions:

1. Is an investigator or sub-investigator on the protocol.
2. Has entered into a financial arrangement with the sponsor or agent of the sponsor, whereby the outcome of the study could influence the value of the economic interest.
3. Acts as an officer or a director of the sponsor or an agent of the sponsor.
4. Has an equity interest in the sponsor.
5. The member, spouse and dependent children has received payments or other incentives from any sponsor that when aggregated exceed the institutional conflict of interest threshold.
6. Has identified him or herself for any other reason as having conflict of interest.

## **2. Review**

### **2.1 Criteria for IRB Approval of Research (45 CFR 46.111 and 21 CFR 56.111)**

In order to approve human subject research, the IRB shall determine that **all** of the following requirements are satisfied:

1. Risks to subjects are minimized: (i) By using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and (ii) whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.
2. Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result. In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research). The IRB should not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.
3. Selection of subjects is equitable. In making this assessment the IRB should consider the purposes of the research and the setting in which the research will be conducted and should be particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons.
4. Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by 45 CFR 46.116 (or 21 CFR 50.25 if FDA-regulated).
5. Informed consent will be appropriately documented, in accordance with, and to the

extent required by 45 CFR 46.117 (or 21 CFR 50.27 if FDA-regulated).

6. When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.
7. When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.
8. When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects.

### 3. Informed Consent

#### 3.1 Informed Consent Required Elements (45 CFR 46.116)

1. A statement that the study involves research.
2. An explanation of the purposes of the research.
3. The expected duration of the subject's participation.
4. A description of the procedures to be followed.
5. Identification of which procedures are experimental.
6. A description of reasonably foreseeable risks or discomforts that the subjects may encounter, and if appropriate, a statement that some risks are currently unforeseeable.
7. A description of possible benefits, if any, to the subject and others which may be reasonably expected. It should be stated that since it is an experimental treatment or procedure, no benefits can be guaranteed.
8. A disclosure of appropriate alternative procedures or treatments, if any, which are available and might be advantageous to the subject. One alternative might be to choose not to participate in the research.
9. A statement describing the manner and extent, if any, to which confidentiality of records identifying the subject will be maintained and, if applicable, a statement that the IRB, FDA and other entities may inspect the records.
10. One of the following statements about any research that involves the collection of identifiable private information or identifiable biospecimens:
  - a. A statement that **identifiers might be removed** from the identifiable private information or identifiable biospecimens **and that**, after such removal, the information or biospecimens **could be used** for future research studies or distributed to another investigator for future research studies **without additional informed consent** from the subject or the legally authorized representative, if this might be a possibility; or

- b. A statement that the subject's information or biospecimens collected as part of the research, even if identifiers are removed, **will not be used or distributed** for future research studies.
- 11. For research involving more than minimal risk, an explanation as to whether any compensation or any medical treatments are available if injury occurs and, if so, what they consist of or where further information may be obtained.
- 12. When applicable, a description of whether or not reimbursement for time, inconvenience, etc. will be given, including the schedule of payments.
- 13. An explanation of who to contact for answers about the research and in the event there is a research- related injury (This is generally the PI or another staff member closely associated with the study). A separate contact must be named for questions concerning the subject's rights.
- 14. A statement that the subjects' participation is voluntary, that refusal to participate will not involve penalty or loss of benefits to which the subject is entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is entitled.

### **3.2 Additional Elements of Informed Consent, If Applicable (45 CFR 46.116)**

- 1. A statement that the particular treatment and/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.
- 2. Anticipated circumstances under which the subject's participation may be terminated by the investigator with or without the subject's consent.
- 3. A description of any additional costs for which the subject will be responsible, that may result from participation in the research study.
- 4. A description of the consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject.
- 5. A statement that significant new findings developed during the course of the research that may relate to the subject's willingness to continue participation will be provided to the subject.
- 6. The approximate number of subjects that will be involved in the study.
- 7. A statement that the subject's biospecimens (even if identifiers are removed) may be used for commercial profit and whether the subject will or will not share in this commercial profit.
- 8. A statement regarding whether clinically relevant research results, including individual research results, will be disclosed to subjects, and if so, under what conditions.
- 9. For research involving biospecimens, whether the research will (or might) include whole genome sequencing (i.e., sequencing of a human germline or somatic specimen with the

intent to generate the genome or exome sequence of that specimen).

### **3.3 Waiver or Alteration of Informed Consent (45 CFR 46.116(d))**

An IRB may waive or alter the requirement to obtain informed consent provided:

1. The research presents no more than minimal risk to subjects.
2. The waiver will not adversely affect the rights and welfare of subjects
3. If the research involves using identifiable private information or identifiable biospecimens, the research could not be carried out without using such information or biospecimens in an identifiable format.
4. The research could not practicably be carried out without the requested waiver.
5. Whenever appropriate, the subjects will be provided with additional pertinent information after they have participated in the study.
6. The study is not FDA regulated.

OR

1. The research or demonstration project is to be conducted by or subject to the approval of state or local government officials and is designed to study, evaluate, or otherwise examine:
  - a. Public benefit or service programs;
  - b. Procedures for obtaining benefits or services under those programs;
  - c. Possible changes in or alternatives to those programs or procedures; or
  - d. Possible changes in methods or levels of payment for benefits or services under those programs; and
2. The research could not practicably be carried out without the waiver or alteration.

#### **For screening, recruiting or determining eligibility**

The IRB may approve a research proposal in which an investigator will obtain information or biospecimens for the purpose of screening, recruiting, or determining the eligibility of prospective subjects without the informed consent of the prospective subject or the subject's legally authorized representative, if either of the following conditions are met:

1. The investigator will obtain information through oral or written communication with the prospective subject or legally authorized representative, or
2. The investigator will obtain identifiable private information or identifiable biospecimens by accessing records or stored identifiable biospecimens.

### 3.4 Waiver or Alteration of the Requirement for Documentation of Informed Consent (45 CFR 46.117(c))

The IRB may waive or alter the requirement for the investigator to obtain a signed consent form for some or all subjects if it finds any of the following:

1. The only record linking the subject and the research would be the informed consent form and the principal risk would be potential harm from a breach of confidentiality (e.g., domestic violence research where the primary risk is discovery by the abuser). Each subject (or LAR) will be asked whether they want documentation linking them with the research, and their wishes must govern.

This option **does not** apply to FDA-regulated research.

OR

2. The research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context. Procedures such as non-sensitive surveys, questionnaires and interviews generally do not require written consent when conducted by non-investigators (e.g., marketing surveys, telemarketing).

This option **does** apply to FDA-regulated research (most commonly in the context of [minimal risk screening activities](#) that are necessary to determine eligibility for enrollment in a clinical trial).

OR

3. If the subjects or LARs are members of a distinct cultural group or community in which signing forms is not the norm, that the research presents no more than minimal risk of harm to subjects and provided there is an appropriate alternative mechanism for documenting that informed consent was obtained.

This option **does not** apply to research subject to the **pre-2018 Common Rule** or to **FDA or DOJ** regulations.

## 4. Review of Non-Compliance Issues

When it has been determined that non-compliance has occurred and that the non-compliance may meet the definition of serious or continuing non-compliance, the report of non-compliance is referred for review by the IRB.

At this stage, the IRB may:

1. Find that there is no issue of non-compliance.
2. Find that there is non-compliance that is neither serious nor continuing and that an adequate corrective and/or preventive action plan is in place.
3. Find that there is serious or continuing non-compliance and modify or require a corrective and/or preventive action plan.

4. Find that additional information is required to make a final determination. In this instance, the committee will request additional information, and indicate whether such information will be reviewed by the full committee or a subcommittee thereof; if the latter, a report will be written by the subcommittee for review by the full committee for final determination.

If all information required to make a determination is present, the IRB must make a final determination as to whether the non-compliance is **serious and/or continuing**. Upon a finding of serious or continuing non-compliance, the IRB's possible actions could include, but are not limited to:

1. Request a corrective and/or preventive action plan from the investigator.
2. Verification that participant selection is appropriate.
3. Observation of informed consent.
4. Require an increase in data and safety monitoring of the research activity.
5. Request a directed audit of areas of concern.
6. Request a status report after each participant receives intervention.
7. Modify the continuing review cycle.
8. Require additional investigator and staff education.
9. Notify current participants (e.g., if the information about the non-compliance might affect their willingness to continue participation).
10. Require modification of the protocol/research plan.
11. Require modification of the information disclosed during the consent process.
12. Require current participants to re-consent to participation.
13. Suspend the study; or
14. Terminate the study.

## **5. Unanticipated Problem Report**

If the following three conditions apply, then the incident must be reported to the IRB and to OHRP and/or FDA, depending on the regulatory agency with oversight.

1. The event was **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. The event was **related or possibly related** to participation in the research (in this guidance document, possibly related means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research).
3. The event suggests that the research places subjects or others at a **greater risk** of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

If all three criteria are met, the IRB must consider what actions, if any, must be taken to assure subject safety. Consideration should include, but not be limited to:

1. Whether the risk/benefit ratio for the study is still acceptable.
2. Whether a modification is needed in the protocol to better define and/or minimize the risk.
3. Whether the current consent/permission form appropriately describes the event.
4. Whether the protocol requires any revisions.
5. Whether the consent/permission form requires any revisions.
6. Whether all research subjects should be informed of the event.
7. Whether the study still meets the criteria of 45 CFR 46.111.
8. Whether the event represents an incident of non-compliance.
9. Whether the study should continue.