

# Human Research Protection Program Policies & Procedures



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## Modifications to Approved Research

### Background

IRB review is an ongoing process. Federal regulations require that IRBs have written procedures for ensuring prompt reporting to the IRB of any changes in approved research and for ensuring that such changes are not implemented without prior IRB approval, except when necessary to eliminate apparent immediate hazards to subjects.

### I. Scope

This policy describes how and when modifications must be made to previously approved IRB protocols.

### II. Responsible Parties

- A. Investigators
- B. OHSU IRB
- C. IRB Staff

### III. Policy

- A. All changes to currently approved research must be approved by the IRB prior to implementation, except when necessary to eliminate apparent immediate hazards to the human subjects.
- B. Minor changes to currently approved research may be reviewed by expedited review procedures. Additionally, changes to protocols that have previously been reviewed under the expedited review procedures may be reviewed under the expedited review procedures.
- C. The criteria for approval of changes to previously approved research are the same as those for initial review. The IRB must determine that, in light of the proposed changes, the research continues to satisfy 45 CFR 46.111 and/or 21 CFR 56.111, as applicable.
- D. Changes made for a single subject (often called "protocol exceptions" or "protocol waivers") should be submitted for prospective IRB review and approval whenever possible. If prospective review is not achieved, the event must be reported if required by the Protocol Deviations policy.

#### IV. Procedure

##### A. Submitting a Modification to the IRB for Review

- A. All proposed modifications to study submissions must be submitted via the eIRB prior to instituting the change. If the change has already happened without prior IRB approval, a protocol deviation report must be submitted when required by the Protocol Deviations policy.
- B. Examples of modifications that must be submitted via the eIRB include, but are not limited to, changes in:
  - a. Study Personnel
  - b. Enrollment numbers
  - c. Duration of study
  - d. Recruitment methods
  - e. Consent form
  - f. Investigator Brochure or device information
  - g. Study design, methods, procedures, or randomization
  - h. Adding or dropping an arm of the study
  - i. Questionnaires, surveys, interview scripts, advertising
  - j. Funding
  - k. Title of the protocol
  - l. Data and Safety Monitoring plan
- C. Investigators must provide the IRB with complete descriptions of the modifications, including the rationale(s) for the modifications and the anticipated impact upon current and future subjects, as well as revised versions of those study materials affected by the modifications.

##### B. IRB Review

- A. Upon receipt of a modification request, IRB staff and/or a Chair will pre-review the submission to determine the appropriate level of IRB review required.
  - a. Modifications containing minor changes in previously approved research may be forwarded to the Chair or his/her designee for consideration under the expedited review procedures. The Chair has discretion to forward such changes to the full board for review if appropriate.
  - b. Modifications that represent more than a minor change will be forwarded to the full board for review if the research originally required full board review.
  - c. Modifications to research initially eligible for expedited review may be reviewed using expedited procedures. However, modifications that render a research study ineligible for expedited review under the applicable regulatory categories will be reviewed by the full board.
  - d. Some modifications, such as study staff changes (other than the PI) or fixing typos or formatting errors in study documents, are not considered changes in the research. They still must be submitted through the eIRB for administrative purposes, but may be approved administratively by IRB staff.
  - e. See **Appendix A** for examples of minor and major changes to research.
  - f. See **Appendix B** for examples of administrative modifications that do not constitute changes in the research.
- B. All modifications will undergo initial evaluation by ORIO staff to make sure the submission is complete and correct and the changes are consistent with the applicable administrative and regulatory requirements.
- C. The convened IRB, or the IRB Chair/designee using expedited review procedures, will determine whether the research, in light of the proposed changes, continues

to satisfy the applicable criteria for approval. This includes determining whether the proposed changes reflect new information that may relate to a subject's willingness to continue participation, thus warranting re-consent or notification of subjects (see [Re-Consent and Notification Policy](#)).

- D. Approval of a modification to a study does not result in a change to the approval period for the study.
- E. The IRB or IRB staff will provide investigators with written notice of approval (including administrative approval where appropriate), required modifications to secure approval, or disapproval of the modification request.
  - a. Note that the IRB staff does not issue formal approval memos for modifications that only involve staff changes. Approval of these modifications is documented in the eIRB system.
  - b. A modification may only be disapproved by the convened IRB.

## V. Authority

**45 CFR 46.103(b)(4)(iii) and 21 CFR 56.108(a)(4)** require written procedures for ensuring prompt reporting to the IRB of proposed changes in a research activity, and for ensuring that such changes in approved research, during the period for which IRB approval has already been given, may not be initiated without IRB review and approval except when necessary to eliminate apparent immediate hazards to the subject.

**45 CFR 46.110(b)(2) and 21 CFR 56.110(b)(2)** state that expedited review procedures may be used for minor changes in previously approved research during the period (of one year or less) for which approval is authorized.

[OHRP Guidance on IRB Approval of Research with Conditions \(November 10, 2010\), Section E](#), states that protocol corrections that are only administrative in nature (e.g., correction of typographical and spelling errors in the protocol) do not need additional IRB review because OHRP does not consider such corrections to be changes to the research.

## VI. Definitions

**Minor Change** - is a change in research that does not materially alter the required elements of informed consent or any of the criteria for IRB approval under 45 CFR 46.111 and/or 21 CFR 56.111 and does not substantially change the specific aims or design of the study.

## VII. Additional Resources

Expedited Review  
Full Board Review  
Initial Evaluation of Submitted Projects: Administrative and Regulatory Review  
Communicating Research Determinations  
Re-Consent and Notification  
Protocol Deviations

**Appendix A: Examples of Minor and Major Changes** (not an all-inclusive list)

Area of study affected by modification	Examples of minor change	Example of major changes
Elements of consent	<ul style="list-style-type: none"> <li>-- Changes to improve the clarity of statements or to correct grammatical errors, provided that such a change does not alter the substantive content or intent of the language</li> <li>-- Addition of safety information limited to non-serious risks</li> </ul>	<ul style="list-style-type: none"> <li>-- Alter or waive informed consent</li> <li>-- Use of surrogate consent for incapacitated or incompetent adult subjects</li> <li>-- Addition of new safety information that may affect the subjects willingness to participate (e.g., new unanticipated problems involving risks)</li> </ul>
IRB Approval 46.111 – Risks minimized	<ul style="list-style-type: none"> <li>-- Clarification of risks without changing the expected nature, severity or frequency of risks</li> <li>-- Addition of research activities that would be considered exempt or expedited if considered independent from the main research protocol</li> <li>-- Modification of the study design that will not change or will reduce the likelihood or magnitude of harm while still addressing the purpose (e.g., increase hospital stay to improve safety monitoring)</li> <li>-- Modification of the study population that will not change or will reduce the likelihood or magnitude of harm while still addressing the purpose (e.g., broaden exclusion criteria or narrow inclusion criteria)</li> <li>-- Modification of a study procedure that will not change or will reduce the likelihood or magnitude of harm while still addressing the purpose (e.g., reduce the number procedures or reduce amount collected or administered)</li> </ul>	<ul style="list-style-type: none"> <li>-- Add a new procedure with an expected serious harm;</li> <li>-- Add a new risk to existing procedures that is considered serious</li> <li>-- Change in severity of an expected risk from not serious to serious</li> <li>-- An increase in the incidence of an expected serious risk (either from rare to likely or less likely or less likely to likely)</li> <li>-- Modification of the study design that will increase the likelihood or magnitude of harm</li> <li>-- Modification of the study population that will increase the likelihood or magnitude of harm</li> <li>-- Modification of a study procedure that will increase the likelihood or magnitude of harm</li> </ul>
IRB Approval 46.111 – Risks reasonable relative to benefits	<ul style="list-style-type: none"> <li>-- Modifications with no affect on the risks or benefits</li> <li>-- Modifications that improved the acceptability of the risks in relation to the harms</li> <li>-- Addition of a direct benefit to the subjects enrolled</li> </ul>	<ul style="list-style-type: none"> <li>-- Modifications that worsen the acceptability of the risks in relation to the harms</li> <li>-- Removal of a direct benefit to the subjects enrolled</li> </ul>
IRB Approval 46.111 – equitable selection of subjects	<ul style="list-style-type: none"> <li>-- Addition/modification of recruitment procedures or materials</li> <li>-- Addition/modification of payments to subjects that will not unduly influence the subject</li> <li>-- Addition of children under 46.404</li> </ul>	<ul style="list-style-type: none"> <li>-- Addition of children under 46.405 – 408</li> <li>-- Addition of a pregnancy women/fetus population</li> <li>-- Addition of a prisoner population</li> </ul>

IRB Approval 46.111 – adequate safety monitoring	-- Addition/modification of safety monitoring plan that will likely improve the safety of subjects	-- Modifications to the safety monitoring plan that will reduce the current protections
IRB Approval 46.111 – adequate protection of privacy and maintenance of confidentiality	-- Addition/modification of privacy or confidentiality safeguards that will likely improve the protections	-- Modifications to the privacy or confidentiality safeguards that will reduce the current protections
Qualification of the research team	-- Change in principal investigator -- Additional training or changes to scope of practice	-- Suspension/lapse of investigator privileges that directly affect research procedures
Facilities available to support safe conduct of the study	-- Changes in study sites	-- Withdraw of institution/staff support for research that directly affects safe conduct of research
<b>Note: Changes, which in the opinion of the expedited reviewer do not meet the criteria or intent of a minor modification, will be forwarded to the convened IRB for review.</b>		

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#### **Appendix B: Examples of Administrative Modifications**

The following examples (not an all-inclusive list) usually do not constitute changes in the research and may be approved administratively by IRB staff:

- Study staff changes, not including a change in PI
- Addition of an alternate-language short form that is either:
  - Posted on the OHSU IRB Forms website, or
  - Translated from the English version on the website and submitted with an appropriate certificate of translation
- Closure to enrollment in a manner consistent with the approved protocol and unrelated to safety concerns
- Correction of typographical errors and formatting
- Changes in study staff contact information