

# Submitting Modification Requests to the IRB

SOP 115.4  
Revised: February 11, 2019

## Purpose and Scope

This Standard Operating Procedure (SOP) documents the requirements for Investigators to obtain University of Hawai'i (UH) Institutional Review Board (IRB) approval for proposed changes in IRB-approved research.

This SOP applies to all non-exempt research being performed under the approval of a UH IRB whether the modification is initiated by the sponsor or the investigator. It only covers procedures additional to or different from those during initial review.

## Definitions

**Major Modification:** A proposed change in research-related activities that materially affects an assessment of the risks and potential benefits of the study or substantially changes the specific aims or design of the study.

**Minor Modification:** A proposed change in research-related activities that does not materially affect an assessment of the risks and potential benefits of the study and does not substantially change the specific aims or design of the study.

Note: A modification may also be referred to as an “amendment,” a “revision,” or a “change.”

## Procedures

### *What Kind of Changes Are Modifications and, Thus Require the Submission of a Modification Request?*

The DHHS and FDA regulations require review and approval by an IRB before an investigator initiates any modification to a study.<sup>1</sup>

A change made to correct a typographical or grammatical error in an IRB-approved document is not considered to be a modification and, thus, a modification request is not required. The HSP may administratively approve a request to correct typographical errors and other non-modification changes.

A modification includes a change in the following:

1. study design, study methods, or procedures, including removal of a procedure;
2. the study title or sponsor;
3. recruitment strategies or procedures;

<sup>1</sup> 45 C.F.R. § 46.103(b)(4)(iii) (2012); 21 C.F.R. §§ 56.108(a)(3)–(4) (2013).

4. the IRB-approved informed consent process or consent form, questionnaires, recruitment materials, e.g., advertisements, contact letters or postcards, scripts, or other study-related documents;
5. investigators, including the addition or withdrawal of sub-investigators and co-investigators; or
6. study sites or sub-sites, including the addition or removal of sites.

## **Level of Review**

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### **Expedited Review**

#### **If the Study Meets the Criteria for Expedited Review:**

The modification request will be reviewed under expedited review.

#### **If the Study Does Not Meet the Criteria for Expedited Review, Expedited Review May still Be Used to Review Minor Modifications<sup>2</sup>:**

Federal regulations allow IRBs to review requests for minor modifications using an expedited review procedure. To qualify as a minor modification, the proposed change must not materially:

1. alter the assessment of risks and potential benefits of the study;
2. increase the level of risk to the physical, emotional, or psychological well-being of participants, including loss of confidentiality; or
3. change the specific aims or design of the study.

**Examples of minor modifications** for the purpose of expedited review include:

1. Substituting assessment procedures and tools with alternate assessment procedures and tools when the changes do not increase the level of risk to participants;
2. Adding new study tools, e.g., questionnaires or recruitment notices, that do not increase the level of risk to participants;
3. Revising a consent form to make:
  - (a) administrative changes, e.g., changes in an address or telephone number;
  - (b) Minor changes in compensation, e.g., from \$30 to \$50, or estimated time for participation, e.g., from 3 hours to 4 hours; or
  - (c) Improvements in the accuracy or clarity of information provided to participants, provided that the change does not alter the content or intent of the statements;
4. Making administrative or editorial changes to other study documents or modifying the documents to improve formatting or clarity, provided that the change does not alter the content or intent of the information or statements;
5. Increasing or decreasing enrollment supported by a reasonable justification;
6. Narrowing the range of inclusion criteria;
7. Broadening the range of exclusion criteria;
8. Decreasing the number or volume of biological sample to be collected, provided that the change does not affect the nature of the information to be collected;
9. Adding or deleting qualified investigators;
10. Adding or deleting study sites; and
11. Other minor modifications determined by the HSP to meet federal requirements.

#### **Notification to IRB Members:**

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<sup>2</sup> 45 C.F.R. § 46.110(b)(2); Guidance on Expedited Review Procedures, DHHS (Aug. 11, 2003), <http://www.hhs.gov/ohrp/policy/exprev.html>.

Like studies under expedited initial or continuing review, all IRB members will be notified in writing of modifications approved under this procedure.<sup>3</sup>

### Convened IRB

#### **Major Modifications:**

Modifications that do not qualify as “minor” are considered to be “major” and require review by the convened IRB at a scheduled meeting.

Major modifications are reviewed by a convened IRB unless the study meets the criteria of expedited review.

### *Types of Actions*

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The types of allowable actions are the same as those during initial review, which depend on the level of review. See the Section entitled Types of Actions for expedited review or convened-IRB review.

### *Expiration Date*

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The approval of a modification request does not affect expiration date of the study and the UH policies related to the expiration date unless the request is reviewed at the same time as the continuing review of the study. In that case, the expiration date follows the policy on continuing review.

### *Review Process*

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#### **I. Primary Reviewer System**

A primary reviewer will be assigned to review a modification request.

#### **II. Prescreening by the HSP**

The HSP staff prescreens the request to check whether all required materials have been submitted and determine the level of review on the request.

#### **III. No Modification Implemented Before Approval with the Exception of Removing an Apparent Immediate Hazard.**

The investigator may not initiate a modification in any IRB-approved study or study-related document without obtaining prior IRB approval on the change except as necessary to remove an apparent immediate hazard to research participants.<sup>4</sup>

- a. If the investigator initiates a modification in the emergency situation without prior IRB approval, the investigator must notify the IRB within five business days of the modification. The IRB will review the changes and determine whether each change was consistent in ensuring the participants' welfare.
  - i. The change notice must include a description of the modification, the reason for implementing the change without prior IRB approval, and the date and results of the implementation.
  - ii. If the IRB determines the protocol modification without prior IRB approval was not necessary to remove an apparent immediate hazard, the modification is considered to be a protocol violation and subject to **SOP 108, Determining and Reporting Non-Compliance and Protocol Violations**.

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<sup>3</sup> 45 C.F.R. § 46.110(c)(2) (2012); Guidance on IRB Approval of Research with Conditions, OHRP (Nov. 10, 2010), <http://www.hhs.gov/ohrp/policy/conditionalapproval2010.html>.

<sup>4</sup> 45 C.F.R. § 46.103(b)(4)(iii); 21 C.F.R. § 56.108(a)(4).

- iii. If an unapproved modification is deemed to have a potentially-adverse impact on participants, the IRB may determine it to be an unanticipated problem.

**IV. Forms for Modification Requests.** The investigator will submit a **Modification Request Form** through eProtocol when applying for IRB approval of a modification.

- a. This form is required for applications that will be reviewed at a convened IRB meeting and for applications that will be reviewed under an expedited procedure. It should be used for all UH IRBs: Biomedical, Social & Behavioral Sciences, and Cooperative.
- b. Application is to be submitted electronically via eProtocol or by email to [uhirb@hawaii.edu](mailto:uhirb@hawaii.edu).
  - i. Current submission requirements are posted on the HSP website at <https://www.hawaii.edu/researchcompliance/modify-protocol>.

**V. Sponsor-Initiated Changes.** For sponsor-initiated changes to the study or other IRB-approved study documents, the investigator must summarize the changes on the modification request form and describe the potential impact of the changes on participants.

- a. The HSP will not accept the form if an investigator writes “see attached” referencing the sponsor’s document to describe the proposed change.

**VI. What Information Should Be Included in a Modification Request?** The modification request should include the following information:

- a. Description of the modification;
- b. Purpose of the modification;
- c. Party initiating the modification, investigator or sponsor;
- d. Enrollment status of the study, e.g., open, closed, or the number of locally enrolled participants; and
- e. An explanation of the likely effects from the modification on participants in sufficient detail for the IRB to determine the risks and potential benefits of the proposed change;
- f. Because investigators must relay information relating to modifications to participants when the changes may affect the participants’ willingness to continue with the study, the investigators should, as applicable, address in the modification request whether they will notify the changes to currently enrolled participants;
  - i. The investigator should recommend to the IRB the method of communication to participants, e.g., whether they should be re-consented, provided with a notice explaining the change, or have the change explained at the next study visit.

**VII. Materials Additional to a Modification Request.** If proposed changes affect the study such as its objectives, design, methods, procedures, targeted population, or inclusion or exclusion criteria, the investigator must append a revised protocol or protocol amendment to the modification request.

**VIII. How to Submit Consent Forms?** The investigator will append a “track” and a “clean” copy of the consent form with requested changes, as applicable, to the modification request.

- a. If the investigators are revising the consent form, they will append a red-lined version, using track changes, of the currently-approved consent form instead of a clean copy (see section VII below).
- b. The “clean” copy of the consent where the track changes applied to the current IRB-approved consent form have been accepted.

**IX. How to Submit Changes to IRB-Approved Documents?** The investigator will append “track” and “clean” copies of all IRB-approved documents being modified to the modification request, with:

- a. “track” versions indicating changes to documents using “track changes” or another editing function that clearly shows the specific changes being made, and
- b. “clean” versions in which the track changes have been accepted.

**X. When to Submit a Modification Request?**

- a. **When to Submit the Request if the Application Requires Convened-IRB Review?** The investigator will submit the modification request and associated documents by the IRB’s posted submission deadline, posted at <https://www.hawaii.edu/researchcompliance/institutional-review-board-irb-0>. Applications not received by the deadline will be placed on the agenda of the following month’s meeting.
- b. **When to Submit a Request Qualified for Expedited Review?** Applications that qualify for expedited review can be submitted at any time.

**XI. Prescreening by the HSP.** The HSP staff will screen each modification request and determine whether it qualifies for expedited review.

**XII. Distribution of Materials to the Members.** The HSP will distribute all materials for a modification request to the members about two weekends before the meeting.

**XIII. The Review.** The review follows the procedures of corresponding level of review, expedited or convened-IRB review.

**XIV. Notification of IRB's Decisions.** Following review of the modification request, the IRB will notify the investigator in writing of its decision.

- a. It will also request any clarification or additional information or documents from the investigator in writing.

**XV. Investigator's Responsibility if the Study Is Approved with Stipulations.** The investigator will promptly address any concerns, questions, and stipulations generated by the convened IRB, IRB Chair, or other expedited reviewer.

- a. **Failure to Respond Within Three Months.** If the investigator fails to respond to the stipulations within three months, the modification request will be considered withdrawn.

**XVI. When May an Investigator Initiate the Modification?** Investigators may initiate the modification after they have received final written approval of the requested modification, not approval with stipulations.

**XVII. Investigator's Responsibilities After Approval.** The investigator will notify the co- or sub-investigators, external collaborators, and sponsor, as applicable, of IRB decisions regarding modifications.

- a. It is the investigator's responsibility to distribute revised consent forms and other revised study documents to collaborators and members of the study team along with relevant instructions from the IRB.

## Materials

- APP 05 Modification Request Form
- WKSH 311 Reviewer Worksheet for Continuing Review, Modification or Study Closure
- TMP 418 Modification – Letter of Approval - Expedited

- TMP 419 Modification – Letter of Approval = Full-Board
- TMP 420 Modification – Letter of Approval with Stipulations – Full-Board
- TMP 421 Modification – Letter of Deferral – Full-Board
- TMP 422 Modification – Letter of Disapproval – Full-Board
- TMP 439 TMP 439 Modification – Letter Accepting Responses to Stipulations

## References

- The IRB has and follows written policies and procedures to conduct reviews by the convened IRB (**AAHRPP Element II.2.D.**).
  - Element II.2.D.3. – Review of proposed modifications to previously approved research
- The IRB has and follows written policies and procedures to conduct reviews by the expedited procedure (**AAHRPP II.2.E.**).
  - Element II.2.E.3. – Review of proposed modifications to previously approved research