

Policy Number: 17

Title: Modifications to Previously Approved or Registered Research

Date of Last Revision: 08/10/05; 08/23/10; 05/01/13, 06/05/13, 04/23/15, 07/21/15, 08/05/15, 03/05/16, 05/01/16, 10/1/18, 11/13/19, 04/29/20, 08/27/20

Policy:

It is the policy of the UC Irvine (UCI) Institutional Review Board (IRB) to review all requests for modifications to previously approved research projects to determine if a change in the risk/benefit ratio of the study has occurred.

Research activities in which the only involvement of human subjects will be in one or more of the categories specified under 45 CFR 46.104 (d) are exempt from the requirements of the basic Health and Human Services Policy for the Protection of Human Research Subjects (Subpart A). As such, and in an effort to promote efficiencies, for research confirmed as exempt by the UCI IRB, minor changes may be made without prospective IRB review and approval.

In addition, for specific types of research self-confirmed via the Exempt Self Determination Tool changes may also be made without prospective IRB review and approval.

- I. **Modifications: For previously IRB approved or IRB confirmed research all planned changes in the conduct of a study and/or changes to the informed consent document must be approved by the IRB prior to initiation. Exceptions for exempt research are noted below in Section E.**
- II. **In addition, effective May 1, 2020, listing new, as well as, the addition and removal of research personnel is no longer required unless the role of the research personnel mandates accordingly. See Section G below.**
 - A. The Investigator may make a modification to research activities to avoid an immediate hazard to the participant but must report this to the IRB via the Unanticipated Problems reporting process, as applicable (See IRB Policy 19).
 - B. Investigators must submit the electronic modification request along with revisions to the research protocol and any proposed changes to the consent document or other documents to the IRB.
 - C. Modifications to the previously approved research must meet the regulatory criteria for approval when one or more regulatory criteria are affected.
 - D. Full Committee Review: Modifications that do not meet the criteria for expedited review must be **reviewed by the Full Committee** at a convened meeting. Table 1 below provides examples of types of modifications that may qualify for full committee review. *The decision to send a modification request to the full committee is based on the impact to the risk / benefit ratio and also is made with IRB Chair's discretion, based on their expertise.*
 - E. Expedited Review: Modifications that meet the criteria for expedited

review will be reviewed by a Chair or designee according the expedited review procedures. Table 1 below provides examples of types of modifications that may qualify for an expedited review process.

F. Exempt Protocols: Research activities in which the only involvement of human subjects will be in one or more of the categories specified under 45 CFR 46.104 (d) are exempt from the requirements of the basic Health and Human Services Policy for the Protection of Human Research Subjects (Subpart A). As such, and in an effort to promote efficiencies, for research confirmed as exempt by the UCI IRB, minor changes may be made without prospective IRB review and approval.

1. **Examples of minor changes to exempt research: Do NOT submit a modification to the UCI IRB when:**

- a) Making editorial or administrative revisions to consent documents or other study documents
- b) Adding non-sensitive questions to a survey or interview or revising current questions
- c) Adding a new recruitment material that follows IRB guidelines
- d) Increasing or decreasing the number of participants - unless adding a new population as noted below**
- e) Making study team/personnel changes - except a change in Lead Researcher (LR)

2. **Examples of significant changes to exempt research: DO submit a modification to the UCI IRB when:**

- a) Adding a new population as follows:
 1. A targeted recruitment of children
 2. A targeted recruitment of adults (age 18 or older) who may not be legally/mentally/cognitively competent to consent
 3. A targeted recruitment of prisoners
 4. A targeted recruitment of American Indian/Alaska Native tribes
 5. A targeted recruitment of undocumented people
 - b) Adding non-UCI personnel engaged in research: a) intervening or interacting with the participants and/or b) having access to participant identifiable private information for research purposes.
 - c) Adding an international research site
 - d) Adding questions about sensitive aspects of the participants' behavior such as illegal conduct, drug use, sexual behavior or use of alcohol – to a survey or interview
 - e) For a change in study LR
 - f) To disclosure a new financial interest
 - g) When adding Department of Justice (DOJ) funding
 - h) For any change that makes the study no longer eligible for Certification of Exemption (study will require expedited or full committee review)
3. In addition, for research self-confirmed via the Exempt Self Determination Tool (that qualifies for the self-confirmation) changes may also be made without prospective IRB review and approval.

- G. **Research Personnel:** Only list those research personnel in the IRB Application and Protocol Narrative who may be involved in the following tasks. The Lead Researcher is required to maintain the Study Team log or something similar to track Research Personnel independently. Prior to engaging in human subject research, all Research Personnel must complete the applicable CITI human subject training course, including HIPAA if research involves PHI.

Research Personnel Heat Map

Role of Research Personnel	Minimal Risk Protocol	Greater Than Minimal Risk Protocol	
Access to subject identifiable data including Protected Health Information (PHI) for screening/ determining eligibility	<p>List only the LR and Co-Researcher(s) in the UCI IRB Application & Protocol Narrative. The LR is required to <u>maintain a Study Team log</u> or something similar to track Research Personnel independently.</p>		
Recruiting subjects directly via phone, email or in person			
Access to subject identifiable data which may include PHI for data collection purposes			
Involvement in the informed consent process (i.e., explaining the study to prospective subject)			
Interacting with subjects as part of study procedures; for greater than minimal risk research this may include more invasive procedures			<p>List the LR, Co-Researcher(s) and Research Personnel in the UCI IRB Application & Protocol Narrative.</p>
Involvement in the interpretation of study data			
Finalization of the informed consent process (i.e., able to sign off as the individual obtaining consent)			
Has a <u>disclosable financial conflict of interest</u>			

III. Types of Modifications

- A. Minor Modifications:
 Minor modifications may be reviewed and confirmed by the following;
- a) **IRB MEMBER**
 - b) **HRP STAFF REVIEWER: Tier 1** and **Tier 2**
- B. Delegation is provided in the HRP Staff Reviewer Delegation of Authority document maintained on the HRP WIKI page – and signed by the IRB Chairs for A, B and C, as well as the Director, Human Research Protections. Definition of HRP Staff Reviewers is noted in Section III below.
- C. Authority examples and exceptions are summarized below and further delineated in Table 1b.
- D. An HRP Staff Reviewer (both tiers) may review modifications **except under the following conditions:**
- a) Changes that are exceptions as noted in Policies #12 and #13
 - b) Any change that makes the study no longer eligible for exempt (when the modification is applicable) or expedited review

1. For protocols approved as involving greater than minimal risk:
 - c) Changes involving vulnerable populations
 - d) Changes involving FDA-regulated research activities
 - e) Adding new procedures
 - f) Adding a new study site
 - g) Adding questions about *sensitive aspects of the subjects' behavior and health status* (e.g., Hepatitis/HIV status, illegal behavior, abuse, alcohol/drug use, sexual behavior, or use of alcohol – to a survey or interview
 - h) Disclosure of a new financial interest
 - i) Change in LR or FS or a member of the study team who holds a critical role in the study
 - j) Addition of newly-identified risk
 - k) Changes to consent process
 - l) Changes to compensation plan

Examples of Acceptable Modifications to be reviewed by designated reviewers:

- Adding or removing research personnel (*as applicable – See Policy 17, Section II. G. above*)
 - Fixing typographical errors or minor word changes to study documents
 - Revisions to or adding data collection instruments
 - Adding new recruitment materials
 - Increasing or decreasing the number of subjects
2. For protocols approved as involving greater than minimal risk, proposed changes:
 - a) Do not increase risk to subjects;
 - b) Constitute a minor change to previously approved research; and
 - c) Involve procedures that fall within Exempt categories 1 – 6 or Expedited categories 1 - 7.
 - d) Authority examples and exceptions are summarized in Table 1b below.

E. Major Modifications:

When a proposed change in a research study does not constitute a minor modification, the IRB must review and approve changes at a convened meeting (See Procedure 14.A).

IV. IRB Reviewers and Delegation of Authority

1. IRB Reviewers:

- a) **IRB MEMBER:**
 - (1) Chair, Vice Chair or another designated IRB member or alternate member. These are not HRPP Staff members.
- b) **HRP STAFF REVIEWER**

- (1) **Tier 1:** Administrator or above, CIP or CCRP certified and appointed as IRB members or alternate members may review transactions related to exempt and expedited level protocols. Exceptions are noted as applicable. Those without current CIP or CCRP have been designated by an IRB Chair or the Director, Human Research Protections to have the appropriate experience to review transactions related to exempt and expedited protocols.
- (2) **Tier 2:** Analysts or above, CIP or CCRP certified may review transactions related to exempt and expedited level protocols. Those without current CIP or CCRP have been designated by an IRB Chair or the Director, Human Research Protections to have the appropriate experience to review transactions related to exempt and expedited protocols.
- (3) The IRB will determine that any significant new findings that arise from the review process that might be related to participants' willingness to continue participation are provided to participants.

V. Table 1a – Review of modifications submitted for expedited studies (and exempt when applicable)

Modification Type	To be reviewed by ____ (or above)	Example	Exceptions
Minor Change	HRP STAFF REVIEWER: Tier 2	Adding or removing research team personnel <i>(as applicable – See Policy 17, Section II. G. above)</i>	Change in LR or FS or a member of the study team who holds a critical role in the study (e.g., removal of a co- researcher who is performing a critical study assessment, etc.) must be reviewed by HRP STAFF REVIEWER: Tier 1 or an IRB MEMBER (expedited).
Minor Change	HRP STAFF REVIEWER: Tier 2	Minor non-administrative wording changes in the approved consent form, recruitment materials, or other documents. For example, minor changes to <i>time commitment, and location.</i>	Addition of new study sites for expedited research must be reviewed by HRP STAFF REVIEWER: Tier 1 or an IRB MEMBER
Minor Change	HRP STAFF REVIEWER: Tier 2	Changing study documents such as surveys, questionnaires or brochures including removing questions or components of a survey/questionnaire, addition of questions or components to a survey/questionnaire that are similar in nature to existing components.	When vulnerable populations are targeted enrollees the modification must be reviewed by the IRB MEMBER.
Minor Change	HRP STAFF REVIEWER: Tier 1	Adding new recruitment materials.	
Minor Change	HRP STAFF REVIEWER: Tier 1	Increasing or decreasing maximum or target sample size.	
Minor Change	HRP STAFF REVIEWER: Tier 1	Adding study sites (which may require a Federal Wide Assurance (FWA) and appropriate IRB approval) or the removal of study sites	
Minor Change	HRP STAFF REVIEWER: Tier 1	Decreasing the number or volume of biological sample collections, provided that such a change does not affect the collection of information related to safety evaluations	
Minor Change	HRP STAFF REVIEWER: Tier 1	New study documents to be distributed to or seen by subjects that include information or questions that are substantively different from materials already approved by the IRB	
Minor Change	IRB MEMBER	New or revised financial conflict of interest management plans.	
Minor Change	IRB MEMBER	An increase in risk to subjects not previously disclosed as part of the IRB approved study materials	
Major Change	IRB MEMBER	Changing study documents such as surveys, questionnaires or brochures including removing questions or components of a survey/questionnaire where the new questions would reasonably place subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, insurability, reputation, or be stigmatizing if the answers became known outside of the study context	

VI. Table 1b – Review of modifications submitted for greater than minimal risk studies

Modification Type	To be reviewed by _____ (or above)	Example	Exceptions
Minor Change	HRP STAFF REVIEWER: Tier 1 and Tier 2	Minor non-administrative wording changes in the approved consent form, recruitment materials, or other documents. For example, minor changes to <i>time commitment</i> .	Addition of new study sites _____ must be reviewed by the IRB MEMBER .
Minor Change	HRP STAFF REVIEWER: Tier 1 and Tier 2	Changing study documents such as surveys, questionnaires or brochures including removing questions or components of a survey/questionnaire, addition of questions or components to a survey/questionnaire that are similar in nature to existing components.	When vulnerable populations are targeted enrollees the modification must be reviewed by the IRB MEMBER .
Minor Change	HRP STAFF REVIEWER: Tier 1	Adding or removing research team personnel (as applicable – See Policy 17, Section II. G. above)	Change in LR or FS or a member of the study team who holds a critical role in the study (e.g., removal of a co-researcher who is performing a critical study assessment, etc.) must be reviewed by an IRB MEMBER (expedited).
Minor Change	IRB MEMBER	Adding new recruitment materials.	
Minor Change	IRB MEMBER	Increasing or decreasing maximum or target sample size.	
Minor Change	IRB MEMBER	Adding study sites (which may require a Federal Wide Assurance (FWA) and appropriate IRB approval) or the removal of study sites	
Minor Change	IRB MEMBER	Minor changes specifically requested by the Conflict of Interest Oversight Committee (COIOC); Institutional Biosafety Committee (IBC); or other University Committees with jurisdiction over the research	
Minor Change	IRB MEMBER	Changes in inclusion/exclusion criteria.	
Minor Change	IRB MEMBER	Altering the dosage form (e.g., tablet to capsule or oral liquid) of an administered drug, provided the dose and route of administration remain constant	
Minor Change	IRB MEMBER	Decreasing the number or volume of biological sample collections, provided that such a change does not affect the collection of information related to safety evaluations	
Minor Change	IRB MEMBER	Decreasing the length of hospitalization or number of study visits, provided that such a decrease does not affect the collection of information related to safety evaluations	
Major Change	IRB MEMBER / Full Committee	New study documents to be distributed to or seen by subjects that include information or questions that are substantively different from materials already approved by the IRB	

Major Change	IRB MEMBER / Full Committee	New or revised financial conflict of interest management plans.	
Major Change	IRB MEMBER / Full Committee	An increase in risk to subjects not previously disclosed as part of the IRB approved study materials	
Major Change	IRB MEMBER / Full Committee	Changing study documents such as surveys, questionnaires or brochures including removing questions or components of a survey/questionnaire where the new questions would reasonably place subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, insurability, reputation, or be stigmatizing if the answers became known outside of the study context	
Major Change	IRB MEMBER / Full Committee	Add Relying Sites	

VII. Special Composition Requirements for Vulnerable Populations

When a study requires review by the full IRB Committee, it must meet special composition requirements (See IRB Procedures 36.A, 37.A, 38.A, 39.A, and 40.A) when conducting reviews of significant modifications/amendments.

VIII. Re-consent/Notification of Participants

The IRB will render a determination of whether the changes to the research activities constitute significant new findings that might relate to participants' willingness to continue participation. The IRB will also assess how currently enrolled participants will be informed of the new findings (e.g., change in the ICDs) and, if and how participants who have completed research interventions should be notified.

References:

21 CFR 56.110(b)(2)

45 CFR 46.110(b)(2)

Procedure Number 17.A

Title: Procedure for Modifications to Previously Approved or Registered Research

Procedure:

This procedure provides guidance for submission, review and approval of modifications to previously approved or registered research projects.

- I. **Lead Researcher (LR) Responsibilities**
 - A. The LR will complete the electronic "Modification Request" (MOD) and explain the requested change along with a justification for the change. All revisions must be incorporated into the corresponding documents such as the protocol narrative, informed consent documents (ICDs) or other documents should be revised and submitted along with the MOD. Changes to the documents should be underlined or highlighted.
 - B. If, in the LR's opinion, the risk/benefit ratio has changed, such that it constitutes a significant change that might affect a subject's willingness to participate, the LR should provide a revised ICD to re-consent currently enrolled participants. The IRB Committee may also request re-consenting of the participants.
 - C. Except as outlines in the current Policy 17, Section 1E, any proposed or anticipated changes in UCI confirmed exempt research must also be submitted to the IRB for approval prior to initiation of the change. The research will then be evaluated for appropriate IRB review.
 - D. When the LR makes changes to avoid an immediate hazard to the participant, the LR completes an electronic "Unanticipated Problems" Report (UP). The Investigator is required to submit the form to the IRB in accordance with IRB Policy 19.
- II. **IRB Committee Responsibilities**
 - A. The IRB Chairperson or his/her designee may review and approve research that meets the definition of a minor modification/amendment (see Procedure 13.A). A IRB Reviewer Modification checklist must be completed unless the minor modification request is limited to the following changes:
 1. Personnel change (*as applicable – See Policy 17, Section II. G. above*)
 2. Recruitment material
 3. Revising typographical errors
 - B. When a proposed change in a research study represents a significant modification, the full IRB Committee must review and approve the changes. Only one Reviewer is required for review of significant modifications. The Reviewer and Committee members will receive via electronic agenda:
 1. The MOD form and applicable appendices.
 2. All revised documentation highlighted or underlined including the revised protocol narrative, revised informed consent document, if applicable.
 3. The Sponsor Protocol, if applicable.
 4. The last approved Investigator's Brochure, if applicable.
 5. Any additional pertinent material (e.g., questionnaires, advertisements, DSMB reports, DHHS-grant application, etc.).
 6. The IRB Reviewer Checklist.

- C. The IRB Committee must determine whether the regulatory criteria for approval are met when the modification affects one or more regulatory criteria.
- D. The IRB will determine that any significant new findings that arise from the review process and that might be related to participants' willingness to continue participation are provided to participants. When considering notification regarding significant new findings that arise from the review process, the IRB must take into account the prospective participants, participants enrolled in the study and, if applicable, participants who have completed the research.

III. IRB Analyst or Higher Responsibilities

- A. The Analyst will review the MOD request and determine if it reflects a significant or minor change.
- B. Changes meeting the criteria for minor modifications will be reviewed and approved by the IRB Chairperson or his/her designee.
- C. Requested changes meeting the criteria for significant modifications will be prepared for full IRB Committee review, placing the study on the next available Committee agenda, and preparation of materials for the Reviewer and Committee members.
- D. For significant modifications, the Analyst prepares the "Reviewer's Checklist." For minor modifications, use of the "Reviewer's Checklist" is recommended when there are multiple types changes (e.g. procedure change, updating inclusion/exclusion criteria, etc.) and/or when re-consenting may be necessary.
- E. The "IRB Reviewer's Checklist" is signed by the Reviewer.
- F. Letters denoting the IRB Committee determinations will be drafted using the appropriate template.
- G. The Analyst will assist in obtaining any additional information requested by the Committee Chairperson or Reviewer.
- H. At any time, the Analyst may consult with the IRB Committee Chairperson for assistance in determining the type of review that is required to process the modification.
- I. The Analyst will process the approved documents and make the appropriate HPS database entries.