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

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

I. Modifications:
For previously IRB approved or registered 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.

A. 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.

B. Modifications to the previously approved research must meet the regulatory criteria for approval when one or more regulatory criteria are affected.

C. 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.

D. 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.

1. Reviewers:
   a) IRB MEMBER:
      (1) Chair, Vice Chair or another designated IRB member or alternate member.
   b) HRP STAFF REVIEWER

2. An HRP Staff Reviewer is defined as follows:
   a) 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.
      (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 Executive Director of Research Protections to have the appropriate experience to review transactions related to exempt and expedited protocols. Exceptions are noted as applicable.

E. 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.

F. 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).

II. 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 Executive Director of Research Protections.

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 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
- 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
1. 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).
**III. Table 1a – Review of modifications submitted for exempt and expedited studies**

<table>
<thead>
<tr>
<th>Modification Type</th>
<th>To be reviewed by (or above)</th>
<th>Example</th>
<th>Exceptions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minor Change</td>
<td>HRP STAFF REVIEWER: Tier 2</td>
<td>Adding or removing research team personnel</td>
<td>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). Case by case assessment for exempt.</td>
</tr>
<tr>
<td>Minor Change</td>
<td>HRP STAFF REVIEWER: Tier 2</td>
<td>Minor non-administrative wording changes in the approved consent form, recruitment materials, or other documents. For example, minor changes to time commitment, and location.</td>
<td>Addition of new study sites for expedited research must be reviewed by HRP STAFF REVIEWER: Tier 1 or an IRB MEMBER</td>
</tr>
<tr>
<td>Minor Change</td>
<td>HRP STAFF REVIEWER: Tier 2</td>
<td>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.</td>
<td>When vulnerable populations are targeted enrollees the modification must be reviewed by the IRB MEMBER.</td>
</tr>
<tr>
<td>Minor Change</td>
<td>HRP STAFF REVIEWER: Tier 1</td>
<td>Adding new recruitment materials.</td>
<td></td>
</tr>
<tr>
<td>Minor Change</td>
<td>HRP STAFF REVIEWER: Tier 1</td>
<td>Increasing or decreasing maximum or target sample size.</td>
<td></td>
</tr>
<tr>
<td>Minor Change</td>
<td>HRP STAFF REVIEWER: Tier 1</td>
<td>Adding study sites (which may require a Federal Wide Assurance (FWA) and appropriate IRB approval) or the removal of study sites</td>
<td></td>
</tr>
<tr>
<td>Minor Change</td>
<td>HRP STAFF REVIEWER: Tier 1</td>
<td>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</td>
<td></td>
</tr>
<tr>
<td>Minor Change</td>
<td>HRP STAFF REVIEWER: Tier 1</td>
<td>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</td>
<td></td>
</tr>
<tr>
<td>Minor Change</td>
<td>IRB MEMBER</td>
<td>New or revised financial conflict of interest management plans.</td>
<td></td>
</tr>
<tr>
<td>Minor Change</td>
<td>IRB MEMBER</td>
<td>An increase in risk to subjects not previously disclosed as part of the IRB approved study materials</td>
<td></td>
</tr>
<tr>
<td>Major Change</td>
<td>IRB MEMBER</td>
<td>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</td>
<td></td>
</tr>
</tbody>
</table>
### IV. Table 1b – Review of modifications submitted for greater than minimal risk studies

<table>
<thead>
<tr>
<th>Modification Type</th>
<th>To be reviewed by (or above)</th>
<th>Example</th>
<th>Exceptions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minor Change</td>
<td>HRP STAFF REVIEWER: Tier 1 and Tier 2</td>
<td>Minor non-administrative wording changes in the approved consent form, recruitment materials, or other documents. For example, minor changes to time commitment.</td>
<td>Addition of new study sites must be reviewed by the IRB MEMBER.</td>
</tr>
<tr>
<td>Minor Change</td>
<td>HRP STAFF REVIEWER: Tier 1 and Tier 2</td>
<td>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.</td>
<td>When vulnerable populations are targeted enrollees the modification must be reviewed by the IRB MEMBER.</td>
</tr>
<tr>
<td>Minor Change</td>
<td>HRP STAFF REVIEWER: Tier 1</td>
<td>Adding or removing research team personnel</td>
<td>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).</td>
</tr>
<tr>
<td>Minor Change</td>
<td>IRB MEMBER</td>
<td>Adding new recruitment materials.</td>
<td></td>
</tr>
<tr>
<td>Minor Change</td>
<td>IRB MEMBER</td>
<td>Increasing or decreasing maximum or target sample size.</td>
<td></td>
</tr>
<tr>
<td>Minor Change</td>
<td>IRB MEMBER</td>
<td>Adding study sites (which may require a Federal Wide Assurance (FWA) and appropriate IRB approval) or the removal of study sites</td>
<td></td>
</tr>
<tr>
<td>Minor Change</td>
<td>IRB MEMBER</td>
<td>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</td>
<td></td>
</tr>
<tr>
<td>Minor Change</td>
<td>IRB MEMBER</td>
<td>Changes in inclusion/exclusion criteria.</td>
<td></td>
</tr>
<tr>
<td>Minor Change</td>
<td>IRB MEMBER</td>
<td>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</td>
<td></td>
</tr>
<tr>
<td>Minor Change</td>
<td>IRB MEMBER</td>
<td>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</td>
<td></td>
</tr>
<tr>
<td>Minor Change</td>
<td>IRB MEMBER</td>
<td>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</td>
<td></td>
</tr>
<tr>
<td>Major Change</td>
<td>IRB MEMBER / Full Committee</td>
<td>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</td>
<td></td>
</tr>
<tr>
<td>Major Change</td>
<td>IRB MEMBER / Full Committee</td>
<td>New or revised financial conflict of interest management plans.</td>
<td></td>
</tr>
<tr>
<td>Major Change</td>
<td>IRB MEMBER / Full Committee</td>
<td>An increase in risk to subjects not previously disclosed as part of the IRB approved study materials</td>
<td></td>
</tr>
<tr>
<td>Major Change</td>
<td>IRB MEMBER / Full Committee</td>
<td>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</td>
<td></td>
</tr>
<tr>
<td>Major Change</td>
<td>IRB MEMBER / Full Committee</td>
<td>Add Relying Sites</td>
<td></td>
</tr>
</tbody>
</table>
V. Special Composition Requirements for Vulnerable Populations

VI. 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.

VII. Exempt Research
Any proposed or anticipated changes in an exempt study must also be submitted to the IRB for review and approval by experienced HRP personnel prior to initiation of the change. If the proposed changes affect the level of review, the Reviewer will seek the consultation of the IRB Chair to determine the appropriate level of review (i.e., Expedited or full Committee).

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. Any proposed or anticipated changes in 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
   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” and any applicable “Reviewer’s Supplemental Checklists.” 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” and any “Supplemental Reviewer’s Checklists” are 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.