

<b>Title:</b>	Modification to Ongoing Activities
<b>Responsible Office:</b>	Institutional Review Office (IRO)
<b>Responsible Official:</b>	Karen Hansen, IRO Director
	<i>Signature/date</i>
<b>Effective Date:</b>	January 14, 2008
<b>Policy:</b>	2.5

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## **POLICY STATEMENT**

It is the policy of Fred Hutchinson Cancer Research Center (FHRC) that all proposed changes made to an IRB approved research study must first receive IRB review and approval prior to implementation of the modification.

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## **DEFINITIONS**

**Modification:** Any change to a research study that is made after initial IRB review and approval. Modifications include, but are not limited to, research participant population, recruitment, procedures; study design, study sites, changes to research personnel, or reports to the IRB regarding premature completion of a study.

**Minor Modification:** A modification that does not cause increased risk to the research participants. Minor modifications may include and are not limited to the following: reduction in the risk/discomfort to the research participant, changing a funding source document, adding study staff, or making editorial changes to a consent form. Examples are listed in the *Modification to on Going Activities Procedure*.

**Major Modification:** Any modification that is not a minor modification. Examples are listed in the *Modification to on Going Activities Procedure*.

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## **REFERENCES**

21 CFR 56.108 (a)(3) & (4)

21 CFR 56.109

45 CFR 46.110 (b)(2)

45 CFR 46.109 (a) & (b)

45 CFR 46.103 (b)(4)(iii)

45 CFR 46.116(b)(5)

Food and Drug Administration. Information Sheets: Guidance for Institutional Review Boards and Clinical Investigators Updated September 1998

Food and Drug Administration. Information Sheets: Continuing Review After Study Approval

Food and Drug Administration. Information Sheets: Frequently Asked Questions: IRB Procedures

OHRP Guidance on Written Institutional Review Board (IRB) Procedures

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## INDIVIDUALS AFFECTED BY THIS POLICY

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The contents of this policy apply to Institutional Review Office (IRO) staff, IRB members, employees of FHCRC and investigators from other institutions who submit research studies to the FHCRC IRB for review and approval.

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## ALLOWABLE EXCEPTIONS

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This policy is meant to be followed without deviation. However, the only exception is a modification that is necessary to eliminate apparent immediate hazards to the research participant [21 CFR 56.108(a) (4); 45A, Part 46, Section 103(b) (4) (iii)]. In such a case, after notification of the change, (See IRB Policy 2.6 for reporting Unanticipated Problems Involving Risks to Subjects or Others), the IRB reviews the change to determine that it is consistent with ensuring the research participants' continued welfare.

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## PROCEDURES

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Modification review and approval procedures will depend on whether the modifications are minor or major. Federal guidelines allow expedited review procedures for minor modifications, while major modifications require full IRB committee review. The *Protocol Modification Form* must be attached to all modification requests.

### 1. Review of Minor Modifications (Expedited Review)

The FHCRC follows the following steps for expedited review:

- a. The FHCRC IRB outlines submission procedures for investigators in the *Modification to On - Going Activities Procedure*.
- b. The IRB Staff follows the *Modification to On-Going Activities Procedure* and the *Screener: Protocol Modification* when screening all modifications that are submitted to the IRB.
- c. When screening the modifications, the IRB Staff will note if the modification falls under the "Major" or "Minor" criteria. This information will be provided to the IRB Chair or appropriate IRB member (A designee would include any IRB member who is delegated expedited review responsibilities by the IRB Chair.).
- d. The IRB Staff will send the modification to the Chair or designee with a copy of *the IRB Member Checklist* and the *IRB Chair or Designee Review Type Determination form*.
- e. The modification will be reviewed by the IRB Chair or designee. The IRB Chair or designee will make the final determination if the modification is a "Major" or "Minor" modification. The IRB Chair or designee may not singularly disapprove a modification. Alternatively, they can send the modification to full review if they are not satisfied that the modification meets the expedited review criteria.
- f. The IRB Staff will follow the *Screener: Protocol Modification* for final processing.
- g. At the convened IRB meeting, when members are voting on the expedited review and approved items on the agenda, the IRB members may request that an expedited review item receive full committee review or request additional information about the expedited review item.

### 2. Review of Major Modifications (Full Review)

The FHCRC IRB follows the following steps for full review:

- a. The FHCRC IRB outlines submission procedures for investigators *Modification to On-Going Activities Procedure*.

- b. The IRB Staff follows the *Modification to On-Going Activities Procedure* and the *Protocol Screener: Protocol Modification* when screening all modifications that are submitted to the IRB. The IRB Staff must address every question on the modification screening form.
- c. The IRB Staff places major modifications on the next IRB agenda for full IRB Committee review at a convened meeting. The IRB members will use the *IRB Member Checklist* to assist in the review process.
- d. The IRB Staff will follow the *Screener: Protocol Modification* for final processing.
- e. If not approved, the IRB will advise the Principal Investigator (PI)/research study staff that the modification was not approved and the reasons for the disapproval within 24 hours of the IRB meeting. The IRB may also make recommendations to the PI that include possible changes to the modification that could be resubmitted to the IRB for review and reconsideration.

### 3. Examples of Major and Minor Modifications:

<p><b><u>Major modifications - Full Review Criteria:</u></b></p> <ul style="list-style-type: none"> <li>• Increasing the physical or psychological risk/discomfort to the participant or others</li> <li>• The modification requested is in response to an event which involved increased risk to the participant or others</li> <li>• Major change in the design or goal of the study</li> <li>• Adding procedures that are not allowable in the Expedited review Categories (Section A) such as: <b><u>Skin Biopsies or Bone Marrow collections</u></b></li> <li>• Making multiple changes in the protocol, instruments, or consent</li> <li>• Adding a new consent form</li> <li>• Expanding the eligibility criteria</li> <li>• Increasing the number of participants at risk</li> <li>• Adding questions asking for sensitive information e.g. depression or sexuality</li> <li>• Adding an element that may breach the confidentiality of the participant (example: adding focus groups)</li> <li>• Numerous modifications throughout the year where there may be confusion or a question as to the full scope of the study</li> <li>• Whenever a study is closed for safety reasons e.g. FDA, DSMB, or PI initiated the closure will be referred to the full Board for review</li> <li>• Gene Therapy Trial - unless minor administrative changes or the IRB Chair determines that the risk/discomfort is reduced to the participant.</li> </ul>	<p><b><u>Minor modifications - Expedited Review Criteria:</u></b></p> <ul style="list-style-type: none"> <li>• Reduction of risk/discomfort to the participant</li> <li>• Adding or removing an institution</li> <li>• Changes to recruitment and advertising</li> <li>• Adding a questionnaire or instrument similar to the one already approved e.g. uses many of the same questions</li> <li>• Removing question from a questionnaire or instrument</li> <li>• Minor editorial modifications to the protocol, questionnaire, or consent that do not alter the meaning or procedure (spelling change, grammar, etc)</li> <li>• Consent form modifications that:</li> <li>• Add or remove information from the consent form so that it is consistent with an already approved IRB requirement</li> <li>• Defining a phrase more clearly in lay language</li> <li>• Updating a consent form to use IRB approved boiler plate language</li> </ul>
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**NOTE:** The above examples are presented as general guidelines only. Specific amendment classifications are made on a case-by-case basis.

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### SUPPORTING DOCUMENTS

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Modification To On-Going Activities Procedure  
 Screener: Protocol Modification  
 IRB Member Checklist

Protocol Modification Form  
Approval Date Guidelines  
IRB Chair or Designee Review Type Determination