Marshfield Clinic

Changes/Amendments to Approved Research

1. SCOPE

1.1. System-Wide

2. DEFINITIONS & EXPLANATIONS OF TERMS

2.1 None

3. PROCEDURE BODY

Federal regulations 45 CFR 46.103(b)(4) and 21 CFR 56.108(a)(4) require this institution to have written procedures for ensuring prompt reporting of proposed changes in a research activity to the Marshfield Clinic Research Foundation Institutional Review Board (MCRF IRB). The regulations also require procedures for ensuring that such changes, 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 subjects.

3.1. Determining Whether IRB Review is Required Before Change / Amendment is Implemented

a. In almost all circumstances, changes or amendments to approved research require MCRF IRB review prior to being implemented. Approval letters inform Principal Investigators (PIs) that changes and amendments require IRB review, and investigators and researchers are also informed via the required Human Subjects Protection Training.

b. Changes / Amendments Not Requiring Prior IRB Review and Approval

- Changes or amendments to eliminate an apparent immediate hazard to subjects may be made without prior IRB approval, but they must be reported to the IRB within five working days of taking place. The IRB will then review the change or amendment to determine whether it was consistent with ensuring the continued welfare of research participants.
- Planned, not-for-cause study suspensions and closures to accrual by sponsors, as anticipated and described in the protocol, do not represent a change and therefore do not require IRB review.

c. Changes / Amendments Requiring Prior IRB Review and Approval

- Prior IRB approval is required before any modification can be made to the information that was provided in any of the following IRB-approved items:
  - Submitted IRB application;
  - Protocol;
  - Informed consent document or process;
  - Oral consent scripts or information sheets used when documentation of informed consent has been waived;
  - Investigational Drug Brochures; or

- Recruitment materials.

Examples of such changes or amendments include, but are not limited to:

- New or additional research tests or procedures;
- Additional study aims or questions;
- Additional population(s) to be studied;
- Consent form revisions;

  If the sponsor does not specify a requirement for re-consent, all subjects who are potentially affected by the change or amendment should be re-consented if the new information reflects an increase in risk.
- Proposed increase in total study enrollment;
- Changes to, or additional ICH GCP required materials;
- Changes to, or additional recruitment methods or documents;
- Changes to the following protocol tools: surveys, interview questions, questionnaires, letters to participants, phone scripts, participant information materials, newsletters; case report forms that capture information that was not specifically described in the protocol.
- New disclosures of research data and/or materials;
- Change of Principal Investigator (PI);
- Addition or removal of co-investigators and performance sites; New or different subject incentives; or
- Premature completion of a study (see also "Ending IRB Oversight" procedure").

3.2. Submitting Proposed Changes in, or Amendments to, Approved Research

a. A proposed change to a research activity must be submitted to ORIP before it can be implemented using the Change or Update to Original Submission Form.

b. Amendments to protocols approved after January 1, 2010 must include a redlined protocol or revised protocol pages, with the specific changes clearly documented.

c. Sponsor-initiated, non-emergent changes or amendments in a research activity must be reported promptly to ORIP, by no later than 30 calendar days from the date that the change or amendment is received by research staff.

3.3. Review of Proposed Changes or Amendments

a. Depending upon the nature of the proposed change or amendment, MCRF IRB conducts review via expedited review or by convened IRB. The IRB will consider whether the criteria for IRB approval of the research activity are still met if the change or update is approved (see "Criteria for IRB Approval" procedure).

Expedited Review

- 45 CFR 46.110 and 21 CFR 56.110 allow for the use of an expedited review process for minor changes in previously approved research

during the period for which approval is authorized. Expedited review is allowed when a change is to a project previously approved through expedited review, and the proposed change does not pose more than minimal risk to subjects, and does not remove the project from within categories 1-7 of 63 FR 60363-60367, or when it falls under the list of minor changes in the procedure document, "Expedited Review."

- Expedited review will be carried out by the MCRF IRB Chairperson, Vice Chair or a physician or PhD IRB member designated by the Chair with one year or more of experience as an IRB member or ORIP IRB Administrator (who is also an IRB member). Before conducting review, the expedited reviewer will consider whether he or she has a conflict of interest precluding review of the item consistent with the document, "IRB Consideration of Conflict of Interest: Member and Investigator."
- The expedited reviewer will receive for review a copy of the submitted documents, and a reviewer guide. ORIP staff may also develop a summary of the change or amendment before it is routed to the expedited reviewer including a citation of the regulation(s) under which the research may be expedited.
- The reviewer will first verify that the item qualifies for the expedited review mechanism and that the regulation(s) cited are correct. The reviewer will then apply the criteria noted.
- The expedited reviewer may then:

  Approve - Criteria for IRB approval are the same as for review by the convened IRB; see the document, "Criteria for IRB Approval."

  Table - The item will receive further review once the expedited reviewer receives the requested responsive material from the investigator

  Defer to the convened IRB for review.
- Disapproval is not allowed via expedited review therefore reviewer may request that convened board make a determination.
- The expedited reviewer will indicate and document approval.
- A summary of all items approved through expedited review will be provided to each IRB member monthly in the form of written minutes. IRB members may request that any item approved via expedited review be brought for re-review by the convened MCRF IRB.

b. Convened MCRF IRB Review

For convened IRB review of proposed changes or amendments, all members receive copies of all modified documents for review prior to the convened meeting.

Primary Reviewers

- ORIP staff will assign two members of MCRF IRB to serve as primary reviewers for each change or amendment request. Primary reviewers

receive a copy of the amendment information submitted, including any accompanying documents, within one to two weeks prior to a scheduled meeting.

- If, upon initial review of the materials, a primary reviewer decides that in congress with the members of the convened MCRF IRB, he or she does not have the expertise needed to evaluate the change or amendment, ORIP staff will either assign a different primary reviewer or arrange for a consultant to conduct review of the request.
- Primary reviewers complete a primary reviewer document in IRIS, which are collected and stored electronically after the meeting, as available. Primary reviewers are expected to forward any questions or concerns with the study to the ORIP review committee coordinator responsible for the meeting. He or she will coordinate questions and facilitate communication with the PI so that, whenever possible, the primary reviewers' questions and PI's response can be shared and considered at the meeting.

4. ADDITIONAL RESOURCES

4.1. References:
- Reviewers Guide for Review of Changes

4.2. IRB Form for Submission:
- *Change or Update to Original Submission (IRB)*

5. DOCUMENT HISTORY

Version No.	Revision Description
1.0	New Document in Document Control System transferred from Policy & Handbook Library - #712.9. Changed IRB submission form title from ARU form to Change or Update to Original Submission form. Removed ORIP personnel no longer with institution and updated professional title(s) of ORIP staff.
2.0	Added hyperlink to IRB form: Change or Update to Original Submission Added hyperlink for referenced policies/procedures.

6. DOCUMENT PROPERTIES

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