McLeod Health
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Institutional Review Board Policy Manual

Protocol Deviations

PURPOSE: To provide a procedure for the accurate and timely reporting of protocol deviations to the McLeod Health Institutional Review Board (IRB).

POLICY: It is the policy of the IRB that any protocol deviation (unanticipated problem) that involves non-compliance in the conduct of an IRB approved protocol be reviewed by the Board and Chair/Vice Chair of the IRB.

DEFINITION

The term **"protocol deviation"** is not defined by either of the federal regulations 45 CFR 46or 21 CFR 50. For McLeod Health purposes, a protocol deviation is a minor or a major departure from the protocol procedures as approved by the IRB without prior IRB approval.

PROCEDURE

1. Deviations that are **minor** are eligible for expedited review under the provisions of 45 CFR 46.110(b)(2) and 21 CFR 56.110(b)(2), as applicable. A minor protocol deviation is any change, divergence, or departure from the protocol specified procedures or ICH Guideline for Good Clinical Practice (GCP) that has not been approved by the IRB which **does not** have a major impact on the subject's rights, safety or well-being, or the completeness, accuracy and reliability of the study data.

2. Deviations that are major do not qualify for expedited review and therefore must be reviewed by the full IRB. A **major** protocol deviation is a deviation from the IRB approved specified procedures or ICH Guideline for Good Clinical Practice (GCP) **that may** affect the subject's rights, safety, or wellbeing and/or the completeness, accuracy and reliability of the study data. The ethical principles were violated.

3. The principal investigator submits all protocol deviations that occur during the course of a study to the IRB immediately upon discovering them and within 14 calendar days following the discovery. The PI also reports all protocol deviations to the sponsor, if applicable, following the sponsor's requirements.

4. IRB coordinator screens the protocol deviation form for completeness and accuracy. If the submission is incomplete, IRB coordinator requests additional information from the principal investigator, which is returned to the IRB upon completion.

5. The IRB coordinator sends the completed protocol deviation form with any applicable attachments to the IRB Chair or designee for review. If it is decided that the deviation is considered a **major** unanticipated problem it will be reported at the next convened Board

meeting for a full board review. If the deviation is **minor**, the IRB Chair or his/her designee conducts expedited review.

6. If the protocol deviation report undergoes full board review, the IRB Chair will require the principal investigator to attend the meeting to explain what has occurred. In addition, the PI will have to answer any questions or concerns that the IRB may have relating to the protocol deviation.

7. If the IRB determines that the deviation is reportable to external agencies, the IRB Chair will promptly notify the Institutional Official. The Institutional Official will review the event and discuss the report with the IRB Chair or designee. The IRB Chair or designee will notify OHRP, the FDA (if appropriate), the sponsor, and other agency officials as appropriate.

SUSPENSION AND CORRECTIVE ACTION

1. If the protocol deviation is seen as a **"major"** event by the sponsor, they have the option of suspending the study. The IRB will receive documentation of any suspension by the sponsor from the principal investigator. The IRB coordinator will forward the suspension documentation to the IRB Chair and IRB Vice-Chair.

2. An initial response from the IRB will be forwarded to the principal investigator by the IRB Chair acknowledging the suspension. At this time, the Institutional Official will receive a copy of the letter. The suspension will be reported at the next convened full board meeting. The PI will be invited to attend the meeting and present why the suspension occurred.

3. A review will take place before the meeting to verify if the sponsor had reported this suspension to a federal regulating agency (i.e. FDA). The IRB's Federalwide Assurance (FWA) will determine how the IRB is to report this situation. Depending on the sponsor (i.e. federally funded or private industry study) and the IRB's FWA will determine to whom the IRB will report this matter.

4. During the meeting, the IRB will request from the PI the action(s) that will be taken on his/her part to prevent any future deviations. The PI should be prepared to present this at the Board meeting.

5. A corrective action plan will be developed by the IRB and Chair for the PI. All areas of concern will be taken into consideration and addressed in the action plan. The importance of compliance and adhering to federal regulations, the McLeod Health IRB policies and procedures, and the study protocol will be stressed. This plan is to be put in place effective immediately.

6. The corrective action plan from the IRB could consist of continued suspension of the study, reduce the length of continuing review, and/or no review of future protocol submissions until further notice. Other options will be available depending on the severity of the suspension.

EXAMPLES of various degrees of deviations may include, but not limited to:

* Failure to obtain informed consent (i.e., there is no documentation of informed consent, or informed consent is obtained after initiation of study procedures);

* Enrollment of a subject who did not meet all inclusion/exclusion criteria;

* Performing study procedure not approved by the IRB;

* Failure to report serious unanticipated problems/adverse events involving risks to subjects to the IRB and (if applicable) the sponsor;

* Study visit conducted outside of window as listed in the IRB-approved protocol;

* Inappropriate documentation of informed consent, including:

- someone other than the subject signed the consent form;
- consent form used was not current IRB-approved (without IRB approval stamp) or outdated/expired consent form;
- consent form does not include updates or information required by IRB
- missing investigator signature;
- original consent form signed after patient started on treatment
- copy not given to the person signing the form;

Applicable Regulations and Guidelines

Code of Federal Regulations – 21 CFR 56.108(b)
Code of Federal Regulations – 45 CFR 46.103(b)(5)
ICH Guideline for Good Clinical Practice (4 – 4.5)
Protocol Deviation Form

Approved: 5/14/15
Revised:
18039.IRB.P-30