Decatur Memorial Hospital

INSTITUTIONAL REVIEW BOARD
SOP 409: Unanticipated Problems Involving Risks to Subjects and Others

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POLICY

Decatur Memorial Hospital requires researchers to comply with all applicable local, state, and federal laws and regulations in the conduct of research studies. As part of this requirement, researchers are required to submit to the IRB of record any problem or event that meets the regulatory definition of "unanticipated problems involving risks to subjects and others" (UPIRSOs). Problems or events labeled as "unexpected adverse events" in research involving investigational drugs or devices may or may not meet the regulatory definition of a UPIRSO. The UPIRSO Checklist will be utilized by the research team to assist in making this determination.

Federal regulations 45 CFR 46.103(a) and 21 CFR 56.108(b)(1-3) require "prompt reporting" to the IRB of record, appropriate institutional officials, and agency heads (OHRP, and when involving a regulated product, the FDA) of:

- Any unanticipated problems involving risks to human subjects or others.
- Any serious or continuing noncompliance with the regulations or the requirements or determinations of the IRB.
- Suspension or termination of IRB approval.

Prompt reporting of UPIRSOs should occur as soon as possible after the research team learns of the problem or event. After learning of the problem or event, the research team will need to submit the UPIRSO within 10 business days.

PROCEDURES

1. Regulatory Definition of an Unanticipated Problem Involving Risks to Subjects and Others

1.1 The incident, experience, or outcome is unexpected (in terms of nature, severity, or frequency) given the research procedures that are described in the protocol or the investigator's brochure and the characteristics of the subject population being studied while the protocol was followed as written;

1.2 There is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research; and

1.3 Participants or others are at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized due to the incident, experience, or outcome.

2. DMH IRB Definition of Serious or Continuing Noncompliance

2.1 Serious noncompliance is defined as noncompliance that adversely affects the rights and welfare of study subjects or results in any untoward medical occurrence that meets the criteria of "serious" or significantly impacts the integrity of study data.

2.1.1 Examples: Conducting research without IRB approval, or treating a research subject with investigational drug despite having a lesion indicating progressive disease.

2.2 Continuing noncompliance is defined as a pattern that, if unaddressed, could jeopardize the rights and welfare of research subjects or the integrity of the study data due to noncompliance with the protocol, federal regulations, and/or the requirements of the IRB.

2.2.1 Example: Protocol requires a blood draw at a specific time, but the physician tells multiple research subjects they can have the blood draw at a later time that is more convenient.

3. Local Adverse Events and Protocol Deviations

3.1 The research team is expected to complete the UPIRSO Checklist to determine if the event or problem is a UPIRSO. If the event or problem is not deemed a UPIRSO, the signed checklist shall be placed in the patient's chart and regulatory binder (for pharmaceutical trials). If the event or problem is deemed a UPIRSO, a submission form will need to be completed in IMEDRIS and the signed checklist must be attached to the submission form along with any other supporting documentation.

3.2 Regardless of the determination reached, all local adverse events and protocol deviations must be reported to a monitoring entity (e.g. the research sponsor, a coordinating or statistical center, or an independent medical monitor) if required under the monitoring provisions described in the IRB-approved protocol.

4. Multi-Institutional Off-Site Adverse Events

4.1 NCORP Trials

4.1.1 All NCORP-funded external adverse events received will be centralized and assessed using the UPIRSO Checklist. Any external adverse event that is deemed a UPIRSO requires reporting to the IRB of record.

4.1.2 If the NCORP-funded external adverse event does not meet the definition of a UPIRSO, a table of events along with the reports will be submitted to the Principal Investigator or his designee for review and signature. These documents are not to be submitted to the IRB of record. Instead, the signed table and UPIRSO Checklist are scanned for record retention.

4.1.3 All NCORP-funded external adverse events will be entered into the CREDIT systems.

4.2 Industry Sponsored Trials / Non-Federal Sponsor

4.2.1 The entity that oversees the global conduct of the clinical trial, or their designee, is accountable for the process of reviewing and analyzing the significance of individual external adverse events received by the sponsor from study sites in multi-center clinical trials. The onus is NOT on each principal investigator, nor the local IRB. To that end, principal investigators will not be required to acknowledge receipt or review of these documents, and the DMH IRB will not accept them, either.

4.2.2 Industry sponsor refers specifically to pharmaceutical companies, biotechnology companies and medical device manufacturers.

4.2.3 Non-federal sponsor refers specifically to nonprofits, and institutions of higher learning.

5. IRB Review of UPIRSOs

5.1 Unanticipated problems as defined by the regulations require prompt reporting to the IRB of record as these problems potentially place research subjects or others at greater risk of physical or psychological harm than was previously recognized and warrant consideration of substantive changes in the protocol, consent form, or consent process or other action in order to protect the safety, welfare, and rights of research subjects.

5.2 The IRB of record shall review and determine whether or not the incident, experience, or outcome is an unanticipated problem and/or an issue of serious or continuing noncompliance. The IRB of record will consider whether risks to subjects are still minimized and reasonable in relation to the anticipated benefits, if any, to the subjects and the importance of the knowledge that may reasonably be expected to result.

5.3 The Principal Investigator shall be notified of the determination reached by the IRB of record and whether any additional action is required.

6. Reporting to OHRP and FDA

6.1 The DMH IRB will report (affirmative) determinations of unanticipated problems and/or serious or continuing noncompliance to OHRP and FDA, if applicable. Individuals included on the original correspondence will also be included in the report to OHRP and FDA.

6.2 The DMH IRB will also report any suspensions or terminations of DMH IRB approval to OHRP and FDA. The notification letter will be drafted by an IRB Co-Chair, and will outline the circumstances for the suspension and/or termination.

SCOPE

This SOP applies to all IRB members, the IRB administrator, and members of the research community.