Issuing Department: Human Subjects Protection Program (HSPP)
Policy Number: 2009-001.0
Policy Title: Reporting Unanticipated Problems to the Institutional Review Board

Purpose

The purpose of this policy is to identify events that may constitute an unanticipated problem involving risk to subjects or others (unanticipated problem) that must be reported to the Institutional Review Board (IRB), the time frame within which the reporting must occur, the elements of the report, and the mechanism for filing the report.

This policy does not excuse principal investigators from their obligation to assess all adverse events and to report internal events to the sponsor of study in accordance with the sponsor's requirements.

Definitions

See policy 2011-007 for definition of:

Unanticipated Problem Involving Risk to Subjects or Others (including examples)

Policy

It is the policy of the HSPP that a Principal Investigator (PI) must report occurrences that may constitute an unanticipated problem to the IRB Office within five business days of becoming aware of the occurrence.

While an IRB Chair may determine that an event does not constitute an unanticipated problem, only the convened IRB will make the final determination as to whether an occurrence does constitute an unanticipated problem, inclusive of problems presenting no more than minimal risk. If the convened IRB determines that the occurrence does constitute an unanticipated problem, the PI must also report the occurrence at the time of continuing review or study closure, whichever is first.

The IRB will not review external adverse events (e.g. individual adverse event reports, IND safety reports, MedWatch reports, line listings of suspected unexpected serious adverse reactions (SUSARS) etc.) unless 1) the sponsor has deemed the event(s) to be an unanticipated problem that a) has been reported to the FDA and b) that requires that corrective measures be taken or 2) unless the UConn Health PI disagrees with the sponsor and believes the event is an unanticipated problem and recommends corrective actions.

The IRB will not review internal expected adverse events that are already disclosed in the informed consent form unless the PI states that the severity or frequency of the event(s) has been greater than anticipated.

Procedure

Occurrences that may constitute an unanticipated problem are reported to the IRB in one of two ways. Either the investigator self reports or an audit finding is referred to the IRB for determination.

Self Reporting:

PIs are to report to the IRB any occurrence that may be an unanticipated problem within 5 business days of becoming aware of the event. An occurrence that may constitute an unanticipated problem is to be reported even if detected after a subject withdraws from a study, after a subject has completed the study intervention, or for up to 30 days after study completion.

The PI is to complete the Problem Report Form (PRF) found within the electronic IRB submission system for reporting to the IRB. The PRF addresses all information that is required for submission. If the PI proposes a corrective action that will require a change to the protocol or study related documents, the PI must submit a request for modification form.

Upon receipt of a PRF, the Regulatory Specialist (RS) will assign an IRB Chair* of the corresponding panel to review the submission and make a determination. The Chair will be provided with the PRF Reviewer Form to use in the review process. The IRB Chair has access to the complete IRB file of the study to which the occurrence relates.

The IRB Chair may determine that the occurrence does not constitute an unanticipated problem, or may refer the occurrence to the convened board for review and determination. The Chair may also seek guidance from other individuals (e.g. someone with a specific medical expertise) in making the initial determination, providing the individual does not have a conflict with the study. In reviewing the PRF the Chair may also require the PI to take corrective actions. Any required actions will be communicated to the PI through correspondence from the RS as directed by the Chair. The Chair may determine that an occurrence is not an unanticipated problem by evaluating the reported occurrence in relation to the definition of an unanticipated problem. The determination of the Chair is documented on the PRF reviewer form.

Self-Reported Occurrences That Are Deemed Not to be Unanticipated Problems: If the Chair determines that the occurrence does not constitute an unanticipated problem, the RS will return the submission to the PI with an outcome of "Not Reportable". For informational purposes, the determination will be presented to the convened board at the next convened meeting for which the submission deadline has not passed on the expedited and exempt agenda activity listing. Any member of the board may request that the convened board review the report and corresponding information. In such case, the determination of the convened board would stand.

Self-Reported Occurrences Referred to Convened Board: If the Chair refers the PRF to the convened board for review the RS will place the submission on the next available agenda as a discussion item. For any PRF referred to the convened board, IRB members will have access to the PRF and all documents that have been associated to the electronic study file. A primary reviewer system will be utilized and the assigned reviewers will have access to the PRF reviewer form. The Chair will also determine whether any additional supporting documentation is required and direct the RS to obtain information accordingly.

Referral of Audit Findings:

The Research Compliance Monitor (RCM) is responsible for ensuring that audit letters are reviewed by a Chair to determine whether any findings are to be referred to the Board. If so, the RCM will provide

the relevant material, the audit letter and PI responses at a minimum, to the RS for inclusion on the next available meeting agenda. Because there is not a specific submission associated with an audit report, when an audit is referred to the convened IRB, the RS will attach the audit material and the discussion item reviewer form (i.e. a pdf version of the PRF reviewer form) to the agenda such that the information is available to all members. The referring Chair will act as the primary reviewer leading the discussion at the meeting.

If the PRF or audit response is accompanied by a request for modification form, the IRB staff will list the modification and discussion item separately on the agenda. Procedures described elsewhere for the submission and review of modifications will be used for review and approval of the modification.

Actions of the IRB:

Upon initial review of a PRF or audit report, the Chair may elect to suspend the approval for the study, in whole or in part, until such time as the convened board can review the information. (Refer to procedure for imposing a study suspension).

The IRB may require corrective action including, but not limited to, a modification of the protocol or information disclosed in the informed consent document and process, that information be provided to past participants, that current participants be informed if the information may relate to their willingness to participate, re-consenting of currently enrolled subjects, more frequent continuing review, monitoring of the consent process or research project by a third party, or requiring additional education. The IRB may also consider a suspension of approval of the research; or termination of approval of the research. The IRB may seek counsel from other institutional areas (e.g. legal counsel, risk management, research compliance) in determining corrective action plans. The IRB may make recommendations regarding employment status but has no authority over an individual's employment status.

When reviewing a PRF or audit finding, any member of the IRB may request additional information from the investigator, to review the complete IRB file, or to review previous minutes relating to the study. Requests for additional information from the investigator will be done through correspondence from the IRB member or from the RS at the direction of the IRB member.

The RS will note the outcome of the discussion and determination of the IRB in the minutes. The determinations of the board, including any required corrective actions, will be communicated to the PI in a letter prepared by the RS and sent to the PI through the electronic IRB submission system. For determinations of UPs, the letter will first be routed to the Chair for sign-off.

If the IRB instructed the PI to make specific changes, the resulting request for modification may be reviewed through the expedited review process (i.e. the PI responds according to the directives provided by the IRB) or may require full board review (e.g. the responses provided by the PI do not match the directives of the IRB).

Additional Reporting From Investigators:

If the convened IRB determines that an occurrence is an unanticipated problem, the PI must also report the unanticipated problem(s) at the time of continuing review on the continuation addendum form, or at the time of study closure on the request for study closure form, whichever comes first.

*Throughout the policy/procedure, while a Chair is the default reviewer, the task may be designated to another qualified member if necessary (e.g. if a referring Chair will not be present at the next scheduled meeting).

Related Policies

2009-002 Reporting Non-Compliance to the IRB
2009-003 Imposing a Suspension or Termination of IRB Approval
2009-004 Reporting to External Agencies and Institutional Officials
2009-05.0 Monitoring of IRB Approved Studies

Basis

45 CFR 46 – Protection of Human Subjects
21 CFR 56 – Institutional Review Boards
Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events" Office for Human Research Protections (OHRP) 2007
Guidance for Clinical Investigators, Sponsors, and IRBs: Adverse Event Reporting-Improving Human Subject Protection" Food and Drug Administration (FDA), 2009

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Reviewed and Approved By:

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