Institutional Review Board (IRB)
Human Subjects Protection Office
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STANDARD OPERATING PROCEDURE ADDENDUM

IRB Review of Protocol Exceptions

A. Definitions

1. Protocol Exception: A one time, intentional action or process that departs from the IRB-approved study protocol, intended for one occurrence or applied to a single individual. This action is approved by the sponsor or funding agency, IRB, and the FDA, if applicable, prior to its implementation. An example of an exception may include: the potential enrollment, following approval of the sponsor, of a participant who fails to meet all of the protocol eligibility criteria.

This policy does not apply to emergency protocol deviations where changes to a study are made without prior IRB approval to eliminate apparent immediate hazards to participants. Such situations are covered separately under IRB Standard Operating Procedure, Section X.C - Modifications and IRB Standard Operating Procedure Addendum: Reporting of Unanticipated Problems Involving Risks to Participants and Others.

B. Policy

It is the policy of the Penn State University (PSU) Institutional Review Board (IRB) to review all protocol exceptions to an IRB-approved protocol prior to their initiation or implementation except in situations where changes to a study are made to eliminate apparent immediate hazards to a participant.

A. The protocol exception is evaluated by the IRB in order to determine that it does not increase the risk to the participant, or jeopardize the integrity of the research data.

B. Protocol exceptions can be reviewed either by the expedited review process or by the convened board depending upon the type of research and nature of the exception request. An IRB Chair or designated, experienced IRB member will determine the level of review required as outlined in IRB Standard Operating Procedure, Section X.C - Modifications.

C. If the research involves an investigational agent (drug, biologic, or device) prior approval of the protocol exception by the sponsor and/or funding agency is also required.

D. When the research involves an investigational significant risk device and the protocol exception may affect the scientific soundness of the plan or the rights, safety, or welfare of the participants, FDA pre-approval is also required [21 CFR 812.150(4)].

References:

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

45 CFR 46.103(b)(4)

21 CFR 312.66

21 CFR 812.150(a)(4)

C. Procedure

This procedure provides guidance for submission, review and approval of protocol exceptions.

I. Investigator Responsibilities

A. Except where necessary to eliminate apparent immediate hazards to a participant, protocol exceptions must be submitted to the IRB prior to implementation using the Protocol Exception Request Form along with any supporting documentation.

1. Investigators must provide justification for how the protocol exception serves the best interest of the participant.
2. Documentation of pre-approval of the protocol exception by the sponsor and/or FDA, if applicable, must be included as supporting documentation.

B. Documentation of pre-approval by the sponsor and/or FDA, if applicable, and IRB approval of the exception should be maintained in the investigator's research study file.

C. If the review of a protocol exception is required urgently after regular HSPO business hours, the investigator should contact an IRB Chair or Vice-Chair with the protocol exception request. A list of the IRB Chairs and Vice-Chairs is available on the IRB web site.

D. If an investigator is unable to contact an IRB Chair or Vice-Chair about a protocol exception request needed after regular HSPO business hours, the investigator should use his/her best clinical judgment to determine how to proceed. Any emergency protocol deviation must be reported to the IRB according to the "IRB Standard Operating Procedure Addendum: Reporting of Unanticipated Problems Involving Risks to Participants or Others".

II. IRB Responsibilities

A. The IRB Chair or his/her designee will determine the level of review required for the protocol exception according to IRB Standard Operating Procedure, Section X.C - Modifications.

B. The IRB Chair or his/her designee may review and approve a protocol exception that meets the definition of a minor change or one for research that involves minimal risk.

C. All other protocol exceptions must be reviewed by the convened IRB. All board members will receive:

1. The Protocol Exception Form;
2. Supporting materials submitted with the Protocol Exception Form;
3. Protocol Summary Abstract; and
4. Current IRB-approved consent form.

The primary reviewer will receive the above materials plus:

1. The current approved protocol; and
2. Any additional pertinent material.

D. The possible determinations the IRB can make regarding exceptions includes:

1. Exception approved as submitted;
2. Modifications required;
3. Referred for convened review (expedited review only);
4. Disapproval (convened review only); or
5. Tabled – further justification or information required (convened review only).

E. The primary reviewer, or for expedited review the chair or designee, documents his/her initial determinations regarding the protocol exception on the IRB Reviewer Checklist and Summary: Protocol Exception Review.

F. The IRB meeting minutes document the discussion and final determination of the IRB regarding the protocol exception. For protocol exceptions receiving expedited review, the approval memo documents the final determination of the IRB.

III. HSPO Responsibilities

A. A Staff Assistant logs in the submission in PRAMS as a modification and gives the materials directly to an IRB Coordinator.

B. An experienced IRB Coordinator reviews the submission for completeness and determines the level of review or assigns it to an IRB Chair for review level determination.

C. If the protocol exception qualifies for expedited review procedures:

1. An IRB Coordinator assigns the review of the protocol exception request to an IRB Chair or his/her designee.
2. An IRB Coordinator issues an approval memo from the IRB when the review is completed.
3. An IRB Coordinator makes the appropriate PRAMS database entries.
4. The issue is included in a report to the IRB of actions undergoing expedited review.

D. If the protocol exception requires convened board review:

1. An IRB Coordinator places the protocol exception request on the next available IRB agenda. If the protocol exception request requires IRB review before the next regular IRB meeting, the HSPO Associate Director, with the approval of the HSPO Director, convenes a meeting of the Urgent Issue IRB (Board D) to review this request.
2. An IRB Coordinator assigns a primary reviewer.
3. An IRB Coordinator prepares the primary reviewer and IRB member packets.
4. An IRB Coordinator assists in obtaining any additional information requested by the IRB Chair or primary reviewer.
5. Following the IRB meeting the Staff Assistant drafts meeting minutes for the review of the protocol exception.
6. An IRB Coordinator reviews the meeting minutes for completeness.
7. A Staff Assistant makes the appropriate database entries and makes copies of the IRB minutes for the study file.

8. A Staff Assistant sends the original minutes, which includes the IRB decision regarding the protocol exception, to the principal investigator.

Institutional Review Board The Pennsylvania State University Penn State College of Medicine Penn State Milton S. Hershey Medical Center	PENNSTATE 1855
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