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I. PURPOSE

The purpose of this standard operating procedure is to outline the documentation requirements when seeking IRB approval, through the initial, continuing, or amendment review processes, to obtain an exemption determination, and to meet reporting requirements for unanticipated problems involving risks to subjects or others. These requirements apply when CHOP serves as the Reviewing IRB.

To enable the IRB members to meet their regulatory obligations, they rely on this documentation to systemically evaluate each research study to assure the protection of human subjects and adhere to the appropriate regulatory requirements.

II. POLICY STATEMENT

The IRB must have adequate information to review and approve, or determine to be exempt, all human subjects research activity.

III. SCOPE

These policies and procedures apply to all investigators, study staff, Chairs, IRB members and alternates, and IRB Office staff.

IV. DEFINITIONS

eIRB: The electronic IRB management system.


Investigator: An individual at the institution who participates in the design, conduct, analysis, or reporting of research activities.

Principal Investigator: The individual at each institution responsible for the overall conduct of a specified research study or clinical investigation.

Scientific Review Committee (SRC): A committee composed of representatives from a division/department/special interest group whose charge is to complete scientific review.

Unanticipated Problems Involving Risks to Subjects or Others: Any incident, experience, or outcome that meets all of the following criteria:

- Unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied;
- Related or possibly related to a subject's participation in the research; and
- Suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) related to the research than was previously known or recognized.


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V. PROCEDURES

A. Submission Requirements for Initial Review

1. The IRB must review complete information in order to understand the proposed research activities and how the research will be conducted at CHOP. The documents required for initial IRB review include, but are not limited to, the following:

- (a) The complete protocol (for non-exempt human subjects research)
 - (1) For multi-center research, the protocol prepared by the study sponsor (pharmaceutical company, steering committee, overall Principal Investigator (PI) or data coordinating center) and distributed to all sites, will be considered the official study protocol and must adhere to sound, scientific-design standards. Supplementary materials that augment the protocol may be required by the IRB in order to demonstrate that the research adheres to sound scientific-design standards. These could include items such as a detailed statistical analysis plan, manual of operations or CHOP-specific recruitment materials.
 - (2) When a multi-center protocol does not exist (e.g., single center research), the protocol prepared by the CHOP investigator must adhere to sound, scientific design standards (e.g., following one of the IRB-provided research protocol templates).
 - (3) Submissions for an exemption determination do not require a protocol.
- (b) Application completed in eIRB.
- (c) Informed consent document(s) (if applicable).
- (d) The Sponsor-approved sample informed consent document (when one exists).
- (e) Investigators' Brochure (IB) or product label (if applicable).
- (f) Device manual or other supporting information (if applicable).
- (g) Scientific review and acceptance in accordance with the CHOP Research Institute Policy. When the SRC requires minor modifications, the investigator's responses to the SRC review may be submitted directly to the IRB; when the SRC requires major modifications (i.e., if the SRC requires major modifications [the protocol is not acceptable as currently written], then the SRC will review the responses prior to IRB submission).
- (h) Additional supporting materials (if applicable)
 - (1) Key literature articles from the Reference list in the protocol.

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(2) Recruitment materials.

(3) Study instruments that are not included on the IRB's list of validated instruments.

(4) For multi-center studies where the CHOP Principal Investigator is the overall Principal Investigator for the study, information about study oversight and operations (data coordinating center activities).

B. Submission Requirements for Continuing Review

1. When conducting continuing review, the IRB applies the same regulatory criteria for IRB approval of research used for initial approval of the research. In order for the IRB to conduct a substantive and meaningful review of the research at the time of continuing review, investigators submit documentation to inform the IRB about study progress to date. Required documentation in the Continuing Review Application includes, but is not limited to:

(a) Summary of the research activity since the previous initial or continuing review, including:

(1) study enrollment and recruitment activities, information about any subject withdrawal or discontinuation, and plans for improving lagging enrollment (when applicable).

(2) When the study is conducted at multiple institutions, the study enrollment at all sites.


i. 3. When the IRB review is limited to the conduct of the study by a CHOP PI, research activities conducted at CHOP.

ii. 4. When the IRB review includes the conduct of the study at CHOP and Relying Institutions, research activities conducted at all sites for which CHOP provides IRB oversight.

(b) New information documenting changes in the potential for risk or prospect for benefit, including information that appears in the literature and reports of all previously unreported unanticipated problems involving risk to research subjects or others (see **SOP 408**) and protocol deviations (may be included in summary form).

(c) Reports of all previously unreported unanticipated problems involving risk to research subjects or others (see SOP 408 and section D below).

(d) A brief summary of previously unreported minor protocol

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deviation/violations.

(e) A summary of any other important adverse event experiences that occurred in the past year, that did not meet the definition of an unanticipated problem involving risks to subjects or others (i.e., did not require prompt reporting to the IRB). The determination of what is important is left to the investigator's judgment.

(f) Data Safety Monitoring Reports (if applicable).

(g) Audit/Monitoring Reports/FDA correspondence (if applicable).

(h) Other materials as specified by the IRB.

2. Proposed changes to the IRB approved materials, including protocol, consent documents or recruitment materials may not be included in the Continuing Review; investigators must submit these changes via an Amendment.

C. Submission Requirements for Amendments

1. Any proposed change in a protocol, or the conduct of the protocol, must be reviewed and approved by the IRB prior to implementation, except where an immediate change is necessary to eliminate a hazard to the subjects.

2. Investigators submit the following documents for IRB review (as applicable):

(a) Electronic application.

(b) Explanation/justification (scientific or other) for the proposed changes.

(c) A list of the proposed changes to the research.

(d) New or revised documents, including protocol, consent form(s), recruitment materials, Investigators' Brochures (as applicable). If the amendment includes revised documents, the submission should include both a tracked-changes version and a clean version.


D. Submission Requirements for Unanticipated Events and Protocol Deviations

1. Investigators are responsible for notifying the IRB of unanticipated problems involving risks to subjects or others.

(a) These reportable events will be submitted as described in **SOP 408**.

(b) When applicable, the report should include the investigator's action plans implemented to prevent recurrence.

2. Investigators are responsible for promptly notifying the IRB of major protocol

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deviations (non-compliance with the approved research plan). Major deviations include those that produce actual harm or had the potential to produce harm to a participant or others (an AE) and those that negatively impacted the scientific validity of the research. Examples of the latter are enrollment of an ineligible subject; events that cause a subject to be withdrawn from the study; and events that prevent a subject from being evaluable for the study's primary endpoint.

- (a) Reports summarizing major protocol deviations will be submitted through the electronic IRB management system.
- (b) When applicable, the report should include the investigator's action plan to prevent recurrence of similar events.

VI. APPLICABLE REGULATIONS AND GUIDELINES


45 CFR 46.109	21 CFR 56.108(a)(4),
45 CFR 46.110	21 CFR 312
45 CFR 46.111	21 CFR 812
45 CFR 46.115	

VII. REFERENCES TO OTHER APPLICABLE SOPS

SOP 408: Unanticipated Problem Involving Risks to Subjects or Others	
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VIII. RESPONSIBILITIES

Title	Responsibility
Director, Human Subjects Research	Responsible for maintaining current research submission requirements for interested investigators and for preliminary triage of non-routine submissions. The required requirements and forms will be maintained on the CHOP IRB website.
IRB Analyst	Responsible for preparing member review materials and reviewing submission elements.
Resource Coordinator	Responsible for submission receipt, tracking and acknowledgements

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IX. ATTACHMENTS

Example cover letters for amendments and continuing reviews are available on the IRB website at: <https://irb.research.chop.edu/cover-letters>

IRB website page on Reportable Events including unanticipated events and protocol deviations is located at: <https://irb.research.chop.edu/reportable-events>

The Research Institute intranet page on the Scientific Review of Protocols is located at: <https://intranet.research.chop.edu/display/deptoctr/Scientific+Review+of+Protocols>

IRB website page listing accepted, Validated Instruments is located at: <https://irb.research.chop.edu/validated-instruments>

X. REVISIONS:

- 11-10-08 Revised to incorporate AAHRPP recommendations and changes to IRB office staff responsibilities
- 6-9-2010 Revised to provide clarification and removed references to paper application forms that have been replaced with the electronic IRB system.
- 01-11-2013 Revised to include the submission requirements related to The CHOP Research Institute's requirement for peer or internal scientific review. Other revisions include the requirements for supporting device information and procedures for reporting major protocol deviations.
- 09-25-2018 Revised to include references to Relying Institutions, edited SOP title (including 'human subjects', and editorial updates, including web links.

XI. APPROVAL:

Director, Human Subjects Research

Date

Chair, Committees for the Protection of Human Subjects

Date