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. These requirements apply when CHOP serves as the IRB of record.

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 regulatory requirements.

II. POLICY STATEMENT

The IRB must have adequate information to review and approve all human subject research activity

III. SCOPE

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

IV. DEFINITIONS

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

Principal Investigator: The individual at the institution responsible for the overall conduct of the research activity. Only individuals meeting the requirements of the Office of Research Compliance and Regulatory Affairs policy "Principal Investigator Eligibility Policy for Protocol Submissions may serve as a principal investigator.

http://intranet.research.chop.edu/x/LIEa

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

(1) For multi-center research, the protocol prepared by the study sponsor (pharmaceutical company, steering committee, overall 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., one of the IRB-provided research protocol templates).

(b) Application completed in the electronic IRB management system.

(c) Complete research grant for federally-funded research.

(d) Informed consent document(s) and assent document(s) (if applicable).

(e) The Sponsor-approved sample informed consent document (when one exists).

(f) Investigators' Brochure or product label (if applicable).

(g) Device manual or other supporting information (if applicable).

(h) Scientific review and approval in accordance with the CHOP Research Institute Policy. http://intranet.research.chop.edu/x/iIROAQ

(1) Internal scientific review is not required for studies that have undergone peer-review by a federal-funding agency or national foundation, that are supported by an industry sponsor or will be conducted without direct human subject involvement.

(2) Investigator-initiated studies that have not undergone peer review must be reviewed and approved by one of the CHOP Scientific Review Committees (SRC).

(3) The details of the SRC's policies are available on the Clinical and Translational Research intranet site. In brief, when the SRC requires minor modifications, the revised protocol and the investigator's responses to the SRC review may be submitted directly to the IRB; when the SRC requires major modifications (the protocol is not approvable), then the SRC will review the responses and must approve the study prior to IRB submission.

(i) Additional supporting materials (if applicable)

(1) Key literature articles from the Reference list in the protocol.

(2) Recruitment materials.

(3) For Multi-center studies where the CHOP Principal Investigator is the Lead 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 a summary of study enrollment and recruitment activities, number and reasons for subject withdrawal or discontinuation, and plans for improving lagging enrollment (when applicable). When the study is conducted at multiple institutions, the summary should include study enrollment as a whole including information regarding equitable subject selection. If the CHOP PI is not the overall PI, the most recent study report should be provided.

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

(c) A brief summary of significant minor protocol deviation/violations. (Major deviations, including unanticipated problem involving risks to subjects or others, should have been reported promptly; see Section D, below)

(d) 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.

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

(f) Audit Reports/FDA correspondence (if applicable).

(g) 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:

(a) Electronic amendment application

(b) Explanation and justification (scientific or other) for the proposed changes;

(c) A list of the proposed changes to the protocol including:

(1) Current wording in the protocol, recruitment plan or application

(2) Proposed new wording;

(d) New or revised documents, including protocol and consent form(s) (if applicable). If the amendment includes revised documents, the submission should include both tracked-changes copy and a clean copy.

(e) Revised grant application (if applicable).

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 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 enrollment of an ineligible subject, events that cause a subject to be withdrawn from the study; events that prevent a subject from being evaluable for the study's primary endpoint; and enrollment of more than the IRB-approved number of subjects.

(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 302: Exempt Research	SOP 401: Review Using Expedited Procedures
SOP 402: Criteria for Initial IRB Approval	SOP 408: Unanticipated Problem Involving Risks to Subjects or Others

VIII. RESPONSIBILITIES

Title	Responsibility
Director, Human Subject 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

IX. ATTACHMENTS

Example cover letters for amendments and continuing reviews are available on the IRB website at:
https://intranet.research.chop.edu/display/cmtirb/Application+Submission+Forms

IRB website page on Reportable Events including unanticipated events and protocol deviations is located at:
https://intranet.research.chop.edu/display/cmtirb/Reportable+Events

The Clinical and Translational Research webpage on the Scientific Review of Protocols is located at:

https://intranet.research.chop.edu/display/deptoctr/Scientific+Review+of+Protocols

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.

XI. APPROVAL:

Director, Human Subject Research _____ Date _____

Chair, Committees for the Protection of Human Subjects _____ Date _____