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1. Purpose

The purpose of this SOP is to describe how protocol amendments are managed and reviewed by the IRB.

2. Scope

This SOP applies to previously approved study protocols but later being amended and submitted for approval by the IRB. Amendments made to protocols may not be implemented until reviewed and approved by the IRB.

3. Responsibility

It is the responsibility of the IRB Secretariat to manage protocol amendments. Investigators may amend the contents of protocols from time to time. Protocol amendments may be submitted for either "expedited" review by the Chairperson / Secretariat/members / reviewers or full board review.

4. Flow chart

No.	Activity	Responsibility
1	Manage the Amendment Package	IRB Secretariat
	↓	
2	Notify the Chairperson of the IRB	IRB Secretariat
	↓	
3	Determine whether Expedited or Full Board Review	Chairperson
	↓	
4	Expedited Review	IRB Secretariat/chairperson/ members/consultants
	↓	
5	Full Board Review	IRB Secretariat / members / Chairperson
	↓	
6	Amendment Review Process	IRB Secretariat / members / Chairperson
	↓	
7	Notify the Principal Investigator	IRB Secretariat
	↓	
8	Documentation	IRB Secretariat

5. Detailed instructions

5.1. Manage the Amendment Package.

- The amendment package is prepared by the PI.
- Upon receipt of the amendment package, the Secretariat of the IRB should follow protocol submission procedure (EPHI-IRB SOP/007/02.0), using document receipt form (EPHI-IRB AF 02-007/02.0) and maintaining confidentiality (SOP# EPHI-IRB 027/02.0)
- Procedure for Maintaining Confidentiality of IRB Documents.
    - **Request for Amendment Memorandum** of the Protocol by the Principal Investigator on an existing and previously approved protocol. The memorandum should:
        - State/describe the amendment
        - Provide the reason for the amendment
        - State any untoward effects with original protocol
        - State expected untoward effects because of the amendment
    - **Original Amendment Submission Form**
        - Check for completeness and for the presence of the required signatures (Principal Investigator or senior relevant expertise or Medical Advisor of the Institute, if applicable). See Annex 1: EPHI-IRB AF 01-014/02.0
    - **Protocol and Related Documents**
        - The amended version of the protocol and related documents should be provided
        - A separate letter indicating the changes or modifications made (addition or deletion) to the document with citation of the page, paragraph and statement lines on the document to describe where the changes or modifications are made

5.2. Notify the Chairperson of the IRB

- Upon receipt of the amendment package, the Secretariat should inform the Chairperson of the IRB in writing (electronically or paper based)
- Keep “Sent” and “Received” mail related to the notification of the Chairperson in the protocol file under the Correspondence section
- Send the request for amendment memorandum and the protocol and related documents to the Chairperson within one working day of receipt by the Secretariat
- Follow EPHI-IRB SOP/027/02.0 to maintain confidentially

- After review of the materials, the Chairperson will determine whether the protocol requires expedited or full board review

5.3. Determine whether expedited or full board review

- Refer EPHI-IRB SOP/010/02.0 for Expedited Review
- Refer EPHI-IRB SOP/011/02.0 for initial review of application protocol)
- Protocol amendment which increase risk to study participants, as judged by the Chairperson, such as a change in study design, which may include but is not limited to:
  - additional treatments or the deletion of treatments
  - any changes in inclusion/exclusion criteria
  - change in method of dosage formulation, such as, oral changed to intravenous
  - significant change in the number of subjects (Increase: if there are <20 subjects enrolled, change of 5 is significant; if there are >20 subjects enrolled, a change of 20% is significant – Decrease: if the decrease in the number of subjects alters the fundamental characteristics of the study, it is significant)
  - significant decrease or increase in dosage amount
- If the Chairperson decides the protocol requires full IRB approval, the Chairperson will indicate this decision on the Checklist, sign and date the form
- The Secretariat places the protocol amendment request on the agenda for the next convened meeting
- The following documents are distributed to each IRB member:
  - the amendment's revision documents to clearly identify each change
  - requested changes to the consent form, if applicable
- If an amendment is received just prior to the IRB meeting, the Chairperson may decide to review the amendment in full IRB, even though the amendment may be expedited

5.4. Expedited Review

- Refer EPHI-IRB SOP/010/02.0 for expedited review procedure

5.5. Full board review by the IRB

- Refer EPHI-IRB SOP/011/02.0 (for initial review of application protocol)
- See section 5.6

5.6. Protocol Amendment Review Process

5.6.1 Review amended protocols

- Use the process outlined in the Application Assessment Form (EPHI-IRB/008/02.0 to review amended protocols and protocol-related documents
- Note recommendations for changes to the protocol and/or informed consent requested by IRB Members in the minutes as with modifications made by EPHI and will be communicated to the principal investigator or clinical trial office
- The Chairperson or designee calls for a vote on the proposed amendment to:
  - Approve the protocol amendment as is with no modification of the informed consent
  - Require a modification to the proposed amendment or informed consent documents, stating the reason and action required to sustain the study with follow-up by the Chairperson
  - Require a modification to the proposed amendment or informed consent documents, stating the reason and action required to sustain the study with follow-up by the Chairperson
  - Require a modification to the proposed amendment or informed consent documents, stating the reason and action required to sustain the study with a follow-up full IRB review
  - Suspend the study, until further information is obtained
  - Not suspend the study as currently approved, but request further information regarding the amendment and the effects of the amendments on the approved study
  - Not approve the amendment request, stating the reason – but allow the study to continue as previously approved

- If the IRB approves the protocol amendment, the Secretariat staff communicates this decision to the principal investigator
- If the IRB does not approve the protocol amendment, the Chairperson immediately notifies the principal investigator in writing of the decision and the reason for not approving the amendment
- If the IRB votes to require modifications to any of the documents, or the protocol amendment, the Secretariat sends a written request about the specific changes to the principal investigator asking him or her to make the necessary changes and resubmit the documents to EPHI-IRB.
- The Chairperson completes a decision form (EPHI-IRB AF 02-008/02.0) after the IRB has reached its decision

- Keep the forms, minutes of the meeting relevant to the discussion and the decision reached by the IRB as the official records of the amendment review process

5.6.2 Completion of the Amendment Submission Form

- The Chairperson must sign and date the original version of this form and return this to the Secretariat no later than 5 working days after the review
- Addition of Amendment to the Protocol Number

  The Secretariat assigns a letter to the protocol number that corresponds to the number of the amendment. For example:
  The third amendment to EPHI-IRB-015-2019 would be formatted as: EPHI-IRB-015-2019C
- Record the amended protocol number on the form
- The Secretariat signs and dates the original version of the form

5.7. Notify the Principal Investigator.

- Send a signed and dated Amendment Submission Form to the Principal Investigator for their records no later than 7 working days
- The Clinical Trials Office or the P.I. should then provide a "clean" copy (*underlining and highlighting removed*) of the protocol and related documents as well as the "clean" PDF electronic version to the Secretariat of the IRB.

5.8. Documentation

- Place the original completed documents, the "clean" version of the protocol and related documents in the protocol file with the other documents pertaining to the amendment

6. Glossary

Amendment protocol package	A package of the amended parts and related documents of the protocol, previously approved by the IRB. In the course of the study, the PI may decide to make changes in the protocol.
Clinical trial office	An institute or an office where the study takes place and where the principal investigator and/or his/her staff may be reached.
Expedited approval	An IRB approval granted only by the Chairperson of the EPHI-IRB or a designated IRB member (not the full IRB) for minor changes to current IRB approved research

activities and for research which involves no more than minimal risk, as stated in the SOP# EPHI-IRB SOP/010/02.0

8. References

1. World Health Organization, Standards and Operational Guidance for Ethics Review of Health-Related Research with Human Participant, 2011.
2. International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use Guidance for Good Clinical Practice (ICH GCP) E6(R2), 2016.
3. Code of Federal Regulations (45 CFR 46): Protection of Human Subjects, Department of Health and Human Services, USA, 2009.
4. Relevant SOPs: EPHI-IRB SOP 007/02.0, EPHI-IRB SOP/008/02.0, EPHI-IRB SOP/010/02.0, EPHI-IRB SOP/011/02.0, EPHI-IRB 027/02.0.

7. Annex

Annex 1: Protocol Amendment Submission Form
(EPHI-IRB AF 01-014/02.0)

PROTOCOL NUMBER: EPHI-IRB-☐☐☐-☐☐☐☐	SUBMITTED DATE:
PROTOCOL TITLE:	
PRINCIPAL INVESTIGATOR:	
INSTITUTE:	Telephone:
APPROVED DATE:	NO. OF AMENDMENT:
DESCRIPTION AND REASON FOR THE AMENDMENT:	
TYPE OF AMENDMENT REQUESTED: ☐ EXPEDITED (Minor changes) ☐ FULL BOARD REVIEW BY IRB (More than minor changes or that amendment "materially affects risks to subjects") SIGNATURES: _____ Date:…….. Principal Investigator	
COMMENTS: ☐ EXPEDITED (Minor changes) ☐ FULL BOARD REVIEWED APPROVALS _____ Date: …….. Chairperson, EPHI-IRB COMPLETION _____ Date: …….. Secretary, EPHI-IRB	