CHAPTER 4.2

REVIEW OF PROTOCOL AMENDMENTS

SOP NUMBER: SOP/014/01

INSTITUTIONAL REVIEW BOARD
(IRB)

Khesar Gyalpo University of Medical Sciences of Bhutan

www.kgumsb.edu.bt

Effective Date: October 1, 2021
Supersedes: SOP/013/yy

Author: SOP Team — Date: September 29, 2021
Approved by: Chairperson, IRB — Date: September 30, 2021
Name: ***Dr. Karma Tenzin***

Table of Contents

1. PURPOSE

The purpose of this procedure is to describe how protocol amendments shall be managed and reviewed by the IRB.

2. SCOPE

This SOP shall apply 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

The IRB Secretariat shall be responsible 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 IRB review.

4. FLOW CHART

No.	Activity	Responsibility
1	Receive Amendment Package ↓	IRB Member Secretary
2	Notify the Chairperson of the IRB ↓	IRB Member Secretary
3	Determine the review channel - Expedited or Full Review ↓	IRB Member Secretary / Chairperson
4	Amendment Review Process ↓	IRB Secretariat / members / Chairperson
5	Communicate the decision to the investigator ↓	IRB Secretariat
6	Storage of the documents	IRB Secretariat

5. DETAILED INSTRUCTIONS

5.1. Complete the submission process of Amendment Package.

5.1.1. The amendment package is prepared by the principal investigator.

5.1.2. Upon receipt of the amendment package, the IRB Secretariat shall follow the receiving procedure in SOP/008/01 (Management of Protocol Submission) and SOP/027/01 - Procedure for Maintaining Confidentiality of IRB Documents.

5.1.2.1. **Request for Amendment Memorandum** of the Protocol by the Principal Investigator on an existing and previously approved protocol. The memorandum shall:

5.1.2.1.1. State/describe the amendment

5.1.2.1.2. Provide the reason for the amendment

5.1.2.1.3. State any untoward effects with original protocol

5.1.2.1.4. State expected untoward effects because of the amendment

5.1.2.2. Application Form for Protocol Amendment Review

5.1.2.2.1. Check for completeness and for the presence of the required signatures (Principal Investigator or Medical Advisor of the Institute, if applicable). See ANNEX- AF/01-014/01

5.1.2.3. Protocol and Related Documents

5.1.2.3.1. The amended version of the protocol and related documents shall be provided.

5.1.2.3.2. The changes or modifications shall be underlined or highlighted.

5.2. Notify the Chairperson of the IRB

5.2.1. Upon receipt of the amendment package, the Secretariat shall inform the Chairperson of the IRB verbally or in writing.

5.2.2. Keep "Sent" and "Received" mail related to the notification of the Chairperson in the protocol file under the Correspondence section.

5.2.3. Send the request for amendment memorandum and the protocol and related documents to the Chairperson within 3 working days of receipt by the Secretariat.

5.2.4. Follow IRB SOP/027/01 in preparing and distributing the documents.

5.2.5. After review of the materials, the Chairperson shall determine whether the protocol requires expedited or full review.

5.3. Determine whether expedited or full review.

5.3.1. Refer to SOP/009/01 for Expedited Review.

5.3.2. Refer to SOP/010/01 for Full Review.

5.3.3. Protocol amendment which increases risk to study participants, as judged by the Chairperson, shall be reviewed by the full board. Such as a change in study design, which may include but is not limited to:

5.3.3.1. additional treatments or the deletion of treatments

5.3.3.2. any changes in inclusion/exclusion criteria

5.3.3.3. change in method of dosage formulation, such as, oral changed to intravenous

5.3.3.4. 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)

5.3.3.5. significant decrease or increase in dosage amount

5.3.4. 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.

5.3.5. The Chairperson shall indicate his/her decision on the Application Form (AF/01-014/01), sign and date the form, and return this to the Secretariat no later than 5 working days after the review.

5.4. Protocol Amendment Review Process

5.4.1. Expedited Review

5.4.1.1. Refer to SOP/009/01 for expedited review procedure.

5.4.2. Full Board Review by the IRB

5.4.2.1. The Secretariat shall place the protocol amendment request on the agenda for the next IRB meeting.

5.4.3. The following documents are distributed to each IRB member:

5.4.3.1. - the amendment's revision documents to clearly identify each change

5.4.3.2. - requested changes to the consent form, if applicable

5.4.4. Refer to SOP/010/01 for full board review.

5.4.5. Review amended protocols

5.4.5.1. Use the process outlined in the Application Form for Initial Review, ANNEX – AF/01-014/01 to review amended protocols and protocol-related documents.

5.4.5.2. Note recommendations for changes to the protocol and/or informed consent requested by IRB Members in the minutes as "with modifications made by IRB" and shall be communicated to the clinical trial office or investigator.

5.4.5.3. The Chairperson or designee shall call for a vote on the proposed amendment to:

5.4.5.3.1. Approve the protocol amendment as is with no modification of the informed consent

5.4.5.3.2. 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

5.4.5.3.3. 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 board review

5.4.5.3.4. Suspend the study, until further information is obtained

5.4.5.3.5. Not suspend the study as currently approved, but request further information regarding the amendment and the effects of the amendments on the approved study

5.4.5.3.6. Not approve the amendment request, stating the reason – but allow the study to continue as previously approved

5.5. Communicate the Decision to the investigator

5.5.1. The Secretariat shall prepare an action letter (see SOP/012/01) to clearly state the IRB's review decision and recommendation. The letter shall list the documents reviewed by the board.

5.5.2. For the decision disapproval, the letter to the investigator or the project manager shall state the followings:

- "If you wish to appeal to this decision, please contact the IRB and submit your appeal in writing, addressed to the IRB Chairperson with justification as to why the appeal shall be granted"

5.5.3. The Chairperson shall review, approve and sign the letters.

5.5.4. The Secretariat shall forward the Board decision to the applicant or principal investigator within 5 working days after the review has taken place, in the form of action letter.

5.6. Storage of the documents

5.6.1. Keep a copy of the Action Letter in the protocol file.

5.6.2. If the amendment is approved, the Secretariat shall assign a letter to the protocol number that corresponds to the number of the amendment. For example: The third amendment to the protocol number PN/2021/003 would be formatted as: PN/2021/003C. Record the amended protocol number on the application form.

5.6.3. 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 or a designated IRB (not the full board) for minor changes to current IRB approved research activities and for research which involves no more than minimal risk, as stated in the SOP/009/01.

7. REFERENCES

7.1. World Health Organization, Standards and operational guidance for ethics review of health-related research with human participants, 2011.
7.2. World Health Organization, Operational Guidelines for Ethics Committees that Review Biomedical Research, 2000.
7.3. International Conference on Harmonization, Guidance on Good Clinical Practice (ICH GCP) 2016.
7.4. Code of Federal Regulation (CFR), 21 §56.110, The United States of America, 1998

7.5. Relevant SOPs: SOP/008/01, SOP/009/01, SOP/0010/01, SOP/011/01 and SOP/027/01

8. ANNEX

ANNEX 1 AF/01-014/01 Protocol Amendment Application Form

ANNEX 1
AF/01-014/01

APPLICATION FORM for Protocol Amendment Review

PROTOCOL NUMBER:	SUBMITTED DATE:
Protocol version number: Dated	
PROTOCOL TITLE:	
PRINCIPAL INVESTIGATOR: INSTITUTE: Telephone/Mobile No.: Responsible Unit or Proponent of the study:	
Co-PI:	
Amendments: (List all the amendments)	
REASON FOR THE AMENDMENT: Signature of _____ Date:…….. Principal Investigator	
(**FOR IRB USE ONLY**) ☐ EXPEDITED REVIEW (Minor changes) ☐ FULL BOARD REVIEW COMMENTS, if any: COMPLETION IRB Member Secretary _____ Date APPROVALS Chairperson _____ Date	