CHAPTER 3.4

INITIAL REVIEW OF RESEARCH PROTOCOL

SOP NUMBER: SOP/010/01

INSTITUTIONAL REVIEW BOARD
(IRB)

Khesar Gyalpo University of Medical Sciences of Bhutan

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1. PURPOSE

This standard operating procedure describes how the IRB manages to review an initially submitted protocol.

2. SCOPE

This SOP shall apply to the review process of the study protocol package submitted for the first time.

3. RESPONSIBILITY

The assigned primary reviewers shall be responsible to thoroughly review the study protocols delivered to them, give their decision, observation and comments to the IRB in the Assessment Form and return to the Secretariat Office on the due date. The IRB shall make the review decision during the full board IRB meeting. The IRB Secretariat shall be responsible to communicate the decision to the investigators and store the documents.

4. FLOW CHART

No.	Activity	Responsibility
1	Designate primary reviewers to review the study protocols ↓	Chairperson
2	Distribute the protocol packages to the primary reviewers ↓	IRB Secretariat
3	Receive and verify the distributed protocol package ↓	IRB Members/Reviewer
4	Review the protocol and complete the Assessment Form ↓	IRB Members/Reviewers
5	Discuss in an IRB meeting ↓	IRB Members / Reviewers Secretariat / Chairperson
6	Communicate the decision to the investigator ↓	IRB Secretariat / Chairperson
7	Storage of the Documents	IRB Secretariat

5. DETAILED INSTRUCTIONS

5.1. Designate the primary reviewers to review the study protocol

5.1.1. The Chairperson shall designate 2-3 members of IRB with relevant expertise to review the study protocols and present to the full board meeting.

5.2. Send the protocol packages to the primary reviewers

5.2.1. Prepare the protocol package, including the protocol & relevant documents, Assessment Form (AF/01-012/01), Assessment Report Form (AF/03-012/01), the information of the due date for the review and the meeting date.

5.2.2. Send the protocol package to the primary reviewers at least 3 weeks before the due date of the review.

5.3. Receive and verify the sent protocol package

5.3.1. Sign and date an acknowledgement form upon receiving the packages.

5.3.2. Return the receipt form back to the delivery person / IRB secretariat.

5.3.3. Check the sent packages and notify the IRB Secretariat if there are documents missing, or the specified meeting date cannot be met.

5.4. Review the Protocol and complete the review forms

5.4.1. Assessment Form, ANNEX - AF/01-012/01)

5.4.1.1. Use the Assessment Form, AF/01-012/01 to guide the review and deliberation process.

Note: The completed Assessment Form is the official record of the decision reached by the IRB for the specific protocol.

5.4.1.2. Consider the following criteria when performing the review:

- 5.4.1.2.1. minimize risks to participants;
- 5.4.1.2.2. risks must be reasonable in relation to anticipated benefits;
- 5.4.1.2.3. participants are selected equitably;
- 5.4.1.2.4. informed consent is adequate, easy to understand and properly documented;
- 5.4.1.2.5. the research plan makes adequate provision for monitoring the data collected to ensure the safety of participants, where appropriate;
- 5.4.1.2.6. there are adequate provisions to protect the privacy of participants and to maintain the confidentiality of data, where appropriate; and
- 5.4.1.2.7. Appropriate safeguards are included to protect vulnerable participants.

5.4.1.3. Make comments where appropriate.

5.4.1.4. Sign and date the reviewer's name.

5.4.2. Assessment Report form, Annex- AF/02-012/01

5.4.2.1. The reviewer records the review decision and comments by completing the assessment report form (AF/03/012/01) and sends it to the IRB secretariat. (Refer to SOP 011-Use of Study Assessment Form.

5.5. IRB Meeting

5.5.1. The primary reviewer presents a brief oral or written summary of the study design and his/her comments.

5.5.2. The chairperson may ask the principal investigator / applicant to present the protocol to the IRB meeting, if required based on the recommendations of the reviewers.

5.5.3. The Chairperson or designee entertains discussion on each document under consideration (e.g., protocol, informed consent, investigators and site qualifications, advertisements).

5.5.4. Recommendations for modifications to the protocol, consent form, and/or advertisements as requested by the Board are noted in the meeting minutes as 'with modifications made by IRB and shall be communicated to the investigator.

5.5.5. The Chairperson or designee calls for a separate vote on each element in review. The board votes to either:

5.5.5.1. Approve the study to start as presented with no modifications

5.5.5.2. Approve the study to start with board approved modifications to the consent (**Approved with recommendation**)

5.5.5.3. Require modifications to items noted at the convened meeting and follow-up by the Chairperson, after receipt of the requested modifications (**Approved with recommendation**)

5.5.5.4. Require modifications to the items and full board re-review or expedited review of the materials (**Approved with stipulation or Resubmission**)

5.5.5.5. Request further information regarding the item and full board re-review or expedited re-review of the material (**Approved with stipulation or Resubmission for re-review**)

5.5.5.6. Not approve the study, stating the reason for disapproval (**Disapproved**)

5.5.6. If the study is approved, the board determines the frequency of Continuing Review from each investigator.

5.6. Communicate the Decision to the investigator

5.6.1. If the study is approved, the Secretariat shall prepare an approval letter (AF/05-11/01) along with the approved documents to the investigator.

5.6.1.1. The letter includes, at a minimum, a listing of each document approved, the date set by the board for frequency of continuing review, and a review of other obligations and expectations from the investigator throughout the course of the study.

5.6.1.2. An approval and expiration date is placed on every page of each consent form approved by the IRB.

5.6.2. If the board requires modifications to any of the documents, the Secretariat shall prepare an Action Letter (AF/05-12/01**)** informing the investigator, the IRB's decision with clearly stated recommendations. Include following note clearly in the letter;

5.6.3. "If any of the documents listed above is either 'Approved with Recommendations' or 'solicited for Resubmission', you shall make revisions as per the recommendation(s) or provide the clarification(s), if any, and resubmit it for final Approval within 3 months from the issuance date of this review letter. If resubmission is not done within the given deadlines then the protocol file will be closed. Although resubmission of the revised documents or clarifications after the deadline is strongly discouraged, any such resubmission has to be submitted as a new protocol."

5.6.3 For the decision disapproval (AF/04-12/01), a notifying 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. If appeal is not done within 3 months from the issuance date of this review letter then the protocol file will be closed"

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

5.6.5 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.

5.7. Storage of the documents

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

5.7.2. Keep the completed Study Assessment Forms, Assessment Report Forms and the minutes of the meeting relevant to the protocol review in the protocol file.

5.7.3. If the protocol is approved, assign an approval number. Example: A protocol 002 of the year 2020 would be numbered as **IRB/Approval/2020/002**. Place the approval letter in the protocol file.

5.7.4. Store the file on an appropriate shelf in the designated cabinet.

6. GLOSSARY

Initial Review	The first time review of that protocol made by two or three individual reviewers (IRB members or non-members) in advance of the full board meeting, and comments of the reviewers shall be reported to the full board meeting.
Phase I studies	Initial introduction of an investigational new drug (IND) into humans, studies designed to determine the metabolism and pharmacological actions of drugs in humans, and studies designed to assess the side effects associated with increasing doses.
Phase II study	A Study of drug metabolism, structure-activity relationships, and mechanism of action in humans, as well as studies in which investigational drugs are used as research tools to explore biological phenomena or disease processes.
Phase III study	A Study expands controlled and uncontrolled trials performed after preliminary evidence suggesting effectiveness of the drug has been obtained. They are intended to gather the additional information about effectiveness and safety that is needed to evaluate the overall benefit-risk relationship of the drug and to provide an adequate basis for physician labeling.
Phase IV study	A study that seeks to expand an approved medication's use into a new population, new indication, or new dose.
Stipulation	Specify as terms of or condition for an agreement, contract, etc. state, put forward for a necessary condition.

7. REFERENCES

7.1. WHO. Standards and operational guidance for ethics review of health-related research with human participants (2011). (http://apps.who.int/iris/bitstream/10665/44783/1/9789241502948_eng.pdf - accessed 28 October 2017)

7.2. ICH HARMONISED GUIDELINE. INTEGRATED ADDENDUM TO ICH E6(R1): GUIDELINE FOR GOOD CLINICAL PRACTICE E6(R2) Current Step 4 version dated 9 November 2016 (https://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6/E6_R2__Step_4.pdf - accessed 28 October 2017)

7.3. Associated SOPs: SOP/012/01.

8. ANNEX

ANNEX 1 AF/02-010/01 Presentation templates for the Primary Reviewers during a protocol review

ANNEX 1
Form AF/01-010/01

Presentation template for the Primary Reviewers during a protocol review

Instruction: *Following items should be included for the presentation of protocol review by the Primary Reviewers. Please note that the reviewer/s should comment on each item on its adequacy, relevancy, appropriateness, etc.*

1.	Protocol Number :
2.	Protocol Title:
3.	Background of the study (precise and succinct):
4.	Objectives:
5.	Operational definitions:
6.	Methodology: 6.1 Study design 6.2 Sampling and sample size 6.3 Inclusion and exclusion criteria 6.4 Study plan/duration 6.5 Data analysis 6.6 Research instruments/data collection tools
7.	Involvement of vulnerable subjects:
8.	Study benefits and risks/compensation:
9.	Financial support/disclosure:
10.	Consent form:
11.	CVs of the investigator/s:
12.	References:
13.	Status of approval: