INSTITUTIONAL REVIEW BOARD (IRB)

Khesar Gyalpo University of Medical Sciences of Bhutan

STANDARD OPERATING PROCEDURES (SOPs)

Effective Date: October 01, 2021

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

TABLE OF CONTENTS

CHAPTER 1.1

WRITING, REVIEWING, DISTRIBUTING AND AMENDING STANDARD OPERATING PROCEDURES (SOP) FOR ETHICS BOARD

SOP NUMBER: SOP/001/01

INSTITUTIONAL REVIEW BOARD (IRB)

Khesar Gyalpo University of Medical Sciences of Bhutan

www.kgumsb.edu.bt

Effective Date: October 01, 2021
Supersedes: SOP/001/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

This Standard Operating Procedure (SOP) defines the process for writing, reviewing, distributing and amending SOPs within the Institutional Review Board (IRB). The SOPs shall provide clear and unambiguous instructions so that the related activities in the Ethics Board are conducted in accordance with the WHO Operating Guidelines for Ethical Review Committee that reviews Biomedical Research, *National Guideline for Ethics Committees*, ICH (International Conferences on Harmonization) and Good Clinical Practice (GCP).

2. SCOPE

This SOP covers the procedures of writing, reviewing, distributing and amending SOPs within the IRB.

3. RESPONSIBILITY

The secretariat of IRB shall be responsible for appointment of the SOP Team to formulate the SOPs by following the same procedures, format, and coding system when drafting or editing any SOP of the IRB.

3.1. Secretariat of IRB shall:

3.1.1. Co-ordinate activities of writing, reviewing, distributing and amending SOPs
3.1.2. Maintain in file all current SOPs and the list of SOPs
3.1.3. Maintain an up-to-date distribution list for each SOP distributed
3.1.4. Distribute the SOPs with a receipt to all users
3.1.5. Ensure all IRB members and Administrative staff involved have access to the SOPs
3.1.6. Ensure that all IRB members and involved staff are working according to current version of SOPs
3.1.7. Review the SOPs at least every *two years* and record the dates of review on the SOP Master file

3.2. SOP team shall:

3.2.1. Propose required SOPs
3.2.2. Select the format and coding system
3.2.3. Draft the SOP in consultation with IRB members and involved administrative staff
3.2.4. Assess the request(s) for SOP revision in consultation with the Secretariat and Chairperson

3.3. IRB members and involved administrative staff shall:

3.3.1. Propose revision of the SOP
3.3.2. Draft, discuss and review new SOP
3.3.3. Sign and date when they receive the approved SOPs
3.3.4. Maintain a file of all SOPs received
3.3.5. Return all out-of-date SOPs to the Secretariat

3.4. Chairperson of the IRB shall:

3.4.1. Approve the reviewed SOPs
3.4.2. Sign the approved SOPs and specifies the effective dates

4. FLOW CHART

No.	Activity	Responsibility
1	Appoint the SOP Team ↓	Secretariat
2	List all relevant SOPs ↓	SOP Team
3	Design a format and layout ↓	SOP Team
4	Draft a new/revise SOP ↓	SOP Team
5	Discuss the new/revise SOP ↓	IRB members Relevant administrative staff
6	Approve the new/revise SOP ↓	Chairperson
7	Implement, distribute and file all SOPs ↓	Secretariat
8	Review and request for a revision of existing SOPs ↓	SOP Team / IRB members/ administrative staff/chairperson
9	Manage and archive superseded SOPs	Administrative staff

5. DETAILED INSTRUCTIONS

5.1. Appoint the SOP Team

5.1.1. The secretariat shall appoint the appropriate IRB members who have a thorough understanding of ethical review process to form the SOP writing team.

5.2. List all relevant SOPs

5.2.1. Write down step by step all IRB procedures.

5.2.2. Organize, divide and name each process.

5.2.3. Make a list of SOPs with coding reference (*AF/01-001/01)*

5.3. Format and layout

5.3.1. Each SOP shall be given a number and a title that is self-explanatory and is easily understood. A unique code number with the format SOP/XXX/YY shall be assigned to each SOP item by the *Secretariat.* XXX is a three-digit number assigned specifically to the SOP. YY is a two-digit number identifying the version of the SOP, The number of version shall start from 01.

5.3.2. Each annex shall be given unique code number with the format *AF/BB-XXX/YY*. AF is the abbreviation for Annex Form. BB is a two-digit number identifying the number of the annex, for example AF/01-001/01 means Annex Form number one of the *SOP/001/01.*

5.3.3. Each SOP shall be prepared according to the standard template. Please refer to Annex 2 – *AF/02-001/01*.

5.4. Draft a new/revised SOP

5.4.1. If an SOP supersedes a previous version, indicate the previous SOP version and the main changes in the historical form (Annex 3 – *AF/03-001/01*).

5.4.2. When the need for a new SOP has been identified and agreed on, a draft shall be written by a designated member of the SOP team.

5.5. Discuss the new/revised SOP

5.5.1. The draft SOP shall be discussed with IRB members and all relevant administrative staff. The SOP shall be agreed upon by the people involved in that particular task.

5.6. Approve the new/revised SOP

5.6.1. The final version shall be passed to the Chairperson for review and approval. The Chair shall decide the effective date of the new SOP.

5.7. Implement, distribute and file all SOPs

5.7.1. The approved SOPs shall be implemented from the effective date.

5.7.2. The approved SOPs shall be distributed to the IRB members and the relevant staff by the Secretariat according to the distribution list. (Annex 4 – *AF/04-001/01*). When revised version is distributed, the old version shall be retrieved and destroyed.

5.7.3. One complete original set of current SOPs shall be filed centrally in the SOP Master file by the Secretariat. The Master file shall be kept in the office of the IRB.

5.8. Review and request for a revision of an existing SOP

5.8.1. Any member of the IRB or Secretariat who notices an inconsistency between two SOPs or has any suggestions on how to improve a procedure shall use the form in Annex 5 – *AF/05-001/01* to make a request.

5.8.2. If the Board agrees with the request, an appropriate team shall be designated to proceed with the revision process. If the Board does not agree, the chairperson shall inform the person who made the request of the decision.

5.8.3. Revision of the SOPs shall be reviewed and approved in the same manner as new SOPs (section 5.4-5.6)

5.8.4. The Secretariat is expected to review the SOPs at least every two years and record the dates of review in the SOP Master file.

5.9. Manage and archive superseded SOPs

5.9.1. One copy of the superseded SOPs shall be retained and clearly marked "superseded" and archived in the historical file by the Secretariat.

6. GLOSSARY

SOP (Standard Operating Procedure)	Detailed, written instructions, in a certain format, describe all activities and action undertaken by an organization to achieve uniformity of the performance of a specific function. The aim of the SOPs and their accompanying checklists and forms is to simplify the organization and documentation of operation, whilst maintaining high standards of Good Clinical Practice.
IRB members	Individuals serving as regular member of the IRB.
SOP Team	A selected team from the IRB members and other staff who will oversee the creation, preparation, review and periodic revision of the institute SOPs.
Master SOP files	An official collection of the institute Standard Operating Procedures (SOP) accessible to all staff, IRB members, auditors and government inspectors as a paper copy with an official stamp on each page and the approval signatures. Photocopies made from these official paper versions of the SOP cannot be considered current or official.
SOP historical files	A collection of previous official versions of a SOP, table of contents, relevant information regarding changes and all pre-planned deviations.

7. REFERENCES

1.1. 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)

1.2. 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)

8. ANNEX

ANNEX 1	AF 01-001/01	List of IRB SOPs
ANNEX 2	AF 02-001/01	Standard Operating Procedures Template
ANNEX 3	AF 03-001/01	Document History
ANNEX 4	AF 04-001/01	Log of SOP Recipients
ANNEX 5	AF 05-001/01	Request for Revision of an SOP

ANNEX 1
AF 01-001/01

List of IRB SOPs

Topic No.	Topics/ Standard Operating Procedures (SOPs)	Chapter/ SOP Code
	Glossary and Definition of Terms	
	Table of Contents	
1.	Preparing Standard Operating Procedures (SOPs) and Guidelines for Ethics Boards/ IRBs	Chapter 1
1.1.	Writing, Reviewing, Distributing and Amending Standard Operating Procedures for Ethics Boards/ IRBs	SOP/001/01
1.2.	Preparation of Guidelines	SOP/002/01
2	Constituting an Ethics Board/ Institutional Review Board (IRB)	Chapter 2
2.1.	Constituting an IRB	SOP/003/01
2.2.	Confidentiality /Conflict of Interest Agreements	SOP/004/01
2.3.	Training Personnel and IRB Members	SOP/005/01
2.4.	Selection of Independent Consultants	SOP/006/01
3.	Initial Review Procedures	Chapter 3
3.1.	Determination of Research Qualifying from Exemption of Ethics Review	SOP/007/01
3.2.	Management of Protocol Submissions	SOP/008/01
3.3.	Expedited Reviews	SOP/009/01
3.4.	Initial Review of Research/ Application Protocols	SOP/010/01
3.5.	Review of New Medical Devices Studies	SOP/011/01
3.6.	Use of Study Assessment Form	SOP/012/01
4	Protocol Amendments, Continuing Review, and End of Study	Chapter 4
4.1.	Review of Resubmitted Protocols	SOP/013/01
4.2.	Review of Protocol Amendments	SOP/014/01
4.3.	Management of Protocol Continuing Reviews	SOP/015/01
4.4.	Review of Final Reports	SOP/016/01
5	Monitoring Protocol Implementation	Chapter 5
5.1.	Intervention in Protocol Deviation/Non-Compliance/Violation	SOP/017/01
5.2.	Response to Research Participants' Request	SOP/018/01
5.3.	Management of Study Termination	SOP/019/01
6	Monitoring and Evaluation of Adverse Events	Chapter 6
6.1.	Review of Serious Adverse Events (SAE) Reports	SOP/020/01
7	Site Monitoring	Chapter 7
7.1.	Site Monitoring Visits	SOP/021/01
8	Preparation of Review Meeting Agenda and Communication Records	Chapter 8
8.1.	Agenda Preparation, Meeting Procedures and Minutes	SOP/022/01
8.2.	Emergency Meeting	SOP/023/01
8.3.	Communication Records	SOP/024/01
9	Managing Study Files	Chapter 9
9.1.	Maintenance of Active Study Files	SOP/025/01
9.2.	Archives and Retrieval of Documents	SOP/026/01
9.3.	Maintaining Confidentiality of IRB's Documents	SOP/027/01
10	Evaluating an IEC/IRB	Chapter 10
10.1	Audit and Inspection of the IRB	SOP/028/01

ANNEX 2
AF 02-001/01

Standard Operating Procedures Template

Name of Institution			
Title:	*Title which is self-explanatory and is easily understood*		
SOP No:	*SOP/xxx/yy*	Page:	of

TITLE *Title which is self-explanatory and is easily understood*

Effective Date: Supersedes:	
Author: *(Name).*	Date:
Approved by: *(Name)*	Date:

Table of CONTENTS

Main Text:

Purpose - *summarizes and explains the objectives of the procedure.*

Scope – *states the range of activities that the SOP applies to.*

Responsibility – *refers to person(s) assigned to perform the activities involved in the SOP*

Flow chart – *simplifies the procedures in step by step sequence and states clearly the responsible person(s) or position for each activity*

Detailed instructions – *describe procedures step by step in short and clear phrases or sentences. Split a long sentence into shorter ones.*

Glossary – *clarifies uncommon or ambiguous words or phases by explanation.*

Reference – *lists sources of the information given in the SOP.*

ANNEX - documents that explain further or clarify complex descriptions. "Description-by-example" is always recommended to avoid difficult texts which may be hard to understand.

ANNEX 3
(AF/03-001/01)

Document History

(The first draft 00 of the SOP History **shall** be produced as the output of the first circulation of the document and the final version is the version after the approval by the Chairperson which is 01)

Author	Version	Date	Amendment Number
SOP Team	00	*29-09-20*	First Draft
Dr. Karma Tenzin	01	*30-09-20*	Final Version
SOP Team	02	*dd-mm-yy*	Amendment 01
SOP Team	03	*dd-mm-yy*	Amendment 02
SOP Team	04	*dd-mm-yy*	Amendment 03
SOP Team	05	*dd-mm-yy*	Amendment 04
SOP Team	06	*dd-mm-yy*	Amendment 05
SOP Team	07	*dd-mm-yy*	Amendment 06

** For routine review without change, the SOP number and version shall remain same. However, the review date shall be minuted and documented in the SOP/001/01.

Summary of the Changes made in the SOP

A. Amendment 01, Month dd, yyyy

1. Chapter 1.1 SOP/001/01: Record what changes/amendments made ……
2. ……
3. ……
4. ……
5. ……
6. ……
7. ……

B. Amendment 02, Month dd, yyyy

1. Chapter 1.1 SOP/001/02: Record what changes/amendments made …….
2. ……..
3. ……..
4. ……..
5. ……..
6. ……..
7. ……..

C. Amendment 03, Month dd, yyyy

1. Chapter 1.3 SOP/001/03: Record what changes/amendments made …….
2. ……..
3. ……..
4. ……..
5. ……..
6. ……..
7. ……..

D. Amendment 04, Month dd, yyyy

1. Chapter 1.4 SOP/001/04: Record what changes/amendments made …….
2. ……..
3. ……..
4. ……..
5. ……..
6. ……..
7. ……..

ANNEX 4
(AF/04-001/01)

Log of SOP Recipients

No.	Name of Recipients	No. of Copies	Signature	Date
1	*Chairperson*			
2	*Dr. XXXX*			
3	Drg. YYYY			

ANNEX 5
AF/05-001/01

Request for Revision of an SOP

Please complete this form whenever a problem or a deficiency in an SOP is identified and maintained with the SOP until an authorized replacement is in place.

SOP/ / (Write the SOP number)	
Title:	
Details of problems or deficiency in the SOP:	
Identified by:	Date (D/M/Y): Click here to enter a date.
Discussed with:	
SOP revision required: ☐ Yes ☐ No	
If yes, to be carried out by whom?	
If no, why not?	
Date SOP re-finalized:	Click here to enter a date.
Date SOP approved:	Click here to enter a date.
Date SOP becomes effective:	Click here to enter a date.

CHAPTER 1.2

PREPARATION OF GUIDELINES

SOP NUMBER: SOP/002/01

Institutional Review Board
[IRB]

Khesar Gyalpo University of Medical Sciences of Bhutan

www.kgumsb.edu.bt

Effective Date: October 1, 2021 Supersedes: SOP/002/yy	
Author: SOP Team	Date: September 29, 2021
Approved by: Chairperson, IRB *Name:* ***Dr. Karma Tenzin***	Date: September 30, 2021

Table of Contents

1. PURPOSE

This procedure describes how to prepare a new guideline or update an existing one. It will also guide in developing the layout and format of each guideline.

2. SCOPE

This SOP applies to IRB guidelines and their amendment versions published and distributed by the IRB.

The IRB works according to internal rules that shall be described in the written SOPs. The SOPs are publicly available. In order to maintain a transparent relationship with non-members of the IRB, certain procedures shall form guidelines for use by investigators, scientific experts and by the Institute personnel.

3. RESPONSIBILITY

The IRB Secretariat or designated IRB members shall be responsible for the preparation or amendment of the guidelines as and when the need arises. The designated IRB members shall manage the preparation/amendment of the guidelines with the assistance of the Secretariat.

4. FLOW CHART

No.	Activity	Responsibility
1	Numbering of Guidelines ↓	IRB Secretariat
2	Numbering of the Version ↓	IRB Secretariat
3	Contents and Layout of A Guideline ↓	IRB Secretariat
4	Approval of New and Updated Guidelines ↓	IRB Chairperson
5	Information for Personnel ↓	IRB Members / Secretariat
6	Distribution of Guidelines	IRB Secretariat

5. DETAILED INSTRUCTIONS

5.1. Numbering of the Guidelines

5.1.1. SOP/001/01 lists all procedures used by the IRB in relation to preparing of guidelines.

5.1.2. When a new guideline is created, a subsequent number shall be allocated at the end of the list of existing guideline.

5.1.3. When a guideline is no longer used, its status is changed to “inactive”. It is not allowed to reuse the guideline number of an inactive guideline.

5.1.4. All guidelines are named and numbered in the following way :

GL 01 to GL 99

5.2. Numbering of the Version

5.2.1. Number guideline versions as follows:

5.2.1.1. Draft versions:

All draft versions are always indicated as “version 01" followed by the word “draft”.
For example: Version 01, draft

5.2.1.2. For any changes on a final version:
Version V, final to Version (V+1), final
For example, any changes on “version 01, final” shall be indicated as “version 02 final”.

5.3. Contents and Layout of a Guideline

1. Cover Page
2. A new or updated guideline has five sections:
3. Table of Contents
4. Main text
5. References
6. Appendices

Sections 1 to 4 are mandatory. The *“Appendices”* section is not mandatory.

5.3.1. Cover Page

The cover page shall have the following information:

5.3.1.1. Logo of the IRB/KGUMSB and related information (address, telephone number, fax number, email address).
5.3.1.2. Title and number of the guideline, date of implementation of the guideline
5.3.1.3. Date of the previous issues. If not applicable, the date of pervious issue is indicated by “N/A” (= not applicable).
5.3.1.4. Name (directory names and path included) of the corresponding computer document, if relevant.
5.3.1.5. Name of the editors and address of the contact office.
5.3.1.6. A copyright declaration.
5.3.1.7. Refer to *ANNEX 1 (AF/01-002/01)* for an example of a cover page.

5.3.2. Table of Contents

The table of contents lists all major headers and subheadings of the guideline, including the appendices and page numbers on which these appear in the guideline.

5.3.3. Main Text

5.3.3.1. Introduction

5.3.3.1.1. Summarize and explain the purpose of the guideline.
5.3.3.1.2. A short note on how the guideline was prepared.
5.3.3.1.3. A short note on how to use the guideline.

5.3.3.2. Detailed description

5.3.3.2.1. The final text shall be short and clear.
5.3.3.2.2. Long guidelines shall be split into shorter ones.
5.3.3.2.3. Wherever possible and relevant references shall be added
5.3.3.2.4. Limitation of the guidelines may be mentioned

5.3.4. Appendices

5.3.4.1.1. Replace long and complex descriptions.
5.3.4.1.2. “Descriptions-by-example” are always recommended to avoid writing difficult and hard to understand texts.
5.3.4.1.3. Glossary
5.3.4.1.4. Full form of abbreviations

5.4. Approval of New and Updated Guidelines

5.4.1. The members of the IRB shall prepare a new guideline or update an existing guideline.
5.4.2. The Chairperson of the IRB and the President of KGUMSB shall approve each new or updated guideline.
5.4.3. The final version is the one to be implemented.

5.5. Information for Personnel

5.5.1. All members of the IRB shall read and understand a new or updated guideline.
5.5.2. Each member shall sign a form indicating that they have read and understood each new or updated guideline.
5.5.3. Refer to *ANNEX 2 (AF/02-002/01)* for an example.
5.5.4. If the guideline is for investigators/students/institute personnel then they shall be given a copy of the guideline after taking their signature.

5.6. Distribution of Guidelines

5.6.1. Guidelines are not confidential and may be disclosed for use by investigators, scientific experts and IRB members.
5.6.1.1. A Log of Guideline Distribution shall be maintained for inventory records *ANNEX 3 (AF/03-002/01)*.

6. GLOSSARY

Guideline	Any suggestion, rules, etc., intended as a guide for specific practice
Head of the organization	President of KGUMSB, Thimphu, Bhutan

7. REFERENCE

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)

8. ANNEX

ANNEX 1	AF/01-002/01	Cover page of a Guideline (2 pages)
ANNEX 2	AF/02-002/01	Lists of Signatures
ANNEX 3	AF/03-002/01	Log of Guideline Distribution

ANNEX 1
AF/01-002/01

Cover page of a Guideline

Guideline for

…… ……

Version No……

Institutional Review Board

Address:

ANNEX 1
Form AF/01-002/01

Information on the Back of the Cover Page

Number of Copies Printed

Title of the Guideline

Version No.

Month/Year of Publication

ISBN:

Author:

Editor:

Publisher:

Computer Record

ANNEX 2
AF/02-002/01

LIST OF SIGNATURES

Title of the Guideline: ……..

Number of the Guideline: GL …….

The following listed persons with their signatures have read this guideline.

No.	Full Name of IRB members	Signature	Date

ANNEX 3
AF/03-002/01

Log of Guideline Distribution

#	Name of Recipients	Affiliation	Guideline#	No. of Copies	Date

CHAPTER 2.1

CONSTITUTING A INSTITUTIONAL REVIEW BOARD

SOP NUMBER: SOP/003/01

Institutional Review Board (IRB)

Khesar Gyalpo University of Medical Sciences Of Bhutan

www.kgumsb.edu.bt

Effective Date: October 1, 2021
Supersedes: SOP/003/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 IRB was established on 2nd July, 2021 with its formal ceremonial launch observed on the day, in order to provide independent guidance, advice, and decision (in the form of "approval/recommendation/stipulation/ disapproval") on health research or other specific research protocols involving human subjects.

The IRB is composed of both scientists and non-scientists. It is independent in its reflection, advice, and decision.

These Standard Operating Procedures (SOPs) describe the Terms of Reference (TOR) which provide the framework for constitution, responsibilities and activities of the IRB.

2. SCOPE

The SOP shall apply to all activities under the IRB.

3. RESPONSIBILITY

The IRB members & the Secretariat shall be responsible to read, understand and respect the rules set by the IRB.

4. FLOW CHART

No.	Activity	Responsibility
1	Ethical basis / Guidelines ↓	IRB Members, Secretariat
2	Composition of the IRB ↓	President KGUMSB and IRB Secretariat
3	Membership Requirements ↓	IRB Members and Secretariat
4	Roles and responsibilities of IRB members ↓	IRB Members
5	Resignation, Disqualification, Replacement of Members ↓	IRB Members and Secretariat
6	Independent Consultants ↓	President KGUMSB/ IRB Chairperson/ Members
7	Conditions of Appointment ↓	IRB Members & Secretariat
8	Officers ↓	IRB Chairperson and Vice-Chairperson
9	Secretariat ↓	IRB Member Secretary
10	Quorum Requirements ↓	IRB Members and Secretariat
11	Dissolving of the IRB	IRB Members and Secretariat

5. DETAILED INSTRUCTIONS

5.1. Ethical Basis

5.1.1. The IRB recognizes that the protocols it approves may also be approved by national and/or local ethics committees prior to their implementation in specific localities.

5.1.2. In evaluating protocols and ethical issues, the IRB is aware of the diversity of laws, cultures and practices governing research and medical practices in various countries around the world.

5.1.3. It attempts to inform itself, where possible, of the requirements and conditions of the various localities where proposed Health research is being considered.

5.1.4. The IRB also seeks to be informed, as appropriate, by national/local ethics committees and researchers of the impact of the research it has approved.

5.1.5. The IRB shall be guided in its reflection, advice, and decision by the ethical principles expressed in the Declaration of Helsinki (1964 and subsequent revisions).

5.1.6. It makes further reference to the National and International Ethical Guidelines for Biomedical Research Involving Human Subjects (CIOMS), the Belmont Report, and the European Convention on Human Rights and Biomedicine.

5.1.7. The IRB establishes its own SOPs based on the Operational Guidelines for Ethics Committees that review Biomedical Research (WHO), the WHO & ICH Guidelines for Good Clinical Practice and the local regulations *(Bhutan Health Research Guideline - to be developed)*.

5.1.8. The IRB shall seek to fulfil the requirements for international assurances and is established and functions in accordance with the national law and regulations.

5.2. Composition of the IRB

5.2.1. The IRB shall be composed of sixteen members excluding the IRB Member Secretary who shall not be the board member.

5.2.2. The composition of the IRB shall ensure diversity of background for complete and adequate review.

5.2.3. At least one member from non-medical/non-scientific area, one member from outside the health sector and one non-affiliated member.

5.2.4. Professional qualifications may include physician, pharmacist, nurse, behavioural or social scientist, lawyer, statistician, paramedic and/or layperson.

5.2.5. The IRB shall include representation from all genders.

5.2.6. The IRB shall include representation from the older and younger generations.

5.2.7. The IRB can have Alternate Member(s) in addition to the regular board members.

5.3. Membership requirements

5.3.1. The President of the KGUMSB shall be responsible for making the appointment of regular board members.

5.3.2. IRB Secretariat shall be responsible for seeking nominations of board members.

5.3.3. IRB Secretariat shall maintain a list of former IRB Board members as alternate members with their consent.

5.3.4. Members shall serve in their personal capacities, based on their interest, qualification, ethical and/or scientific knowledge and expertise, as well as on their commitment and willingness to volunteer the necessary time and effort for the IRB's work.

5.3.5. Members shall disclose, in writing, any interest or involvement – financial, professional or otherwise – in a project or proposal under consideration.

5.3.6. The IRB shall decide the extent to which members that might have a conflict of interest may participate in bringing out an advice/decision; refer to *SOP/004/01* – Confidentiality / Conflict of Interest Agreement.

5.3.7. Members shall be required to sign a confidentiality agreement at the start of their term.

5.3.8. The confidentiality agreement protects the privacy and confidentiality of all parties whose information may be disclosed to the IRB in the course of its work.
5.3.9. Members shall be appointed for a period of 4 years.
5.3.10. The Chairperson and the vice-chairperson shall be elected by the IRB members for two-year term. They may be re-elected but not for more than two consecutive terms. Should they resign or be disqualified, the IRB members elect a replacement until the completion of the normal term. If both the Chairperson and Vice Chairperson declare Conflict of Interests with any protocol then the board members shall nominate an acting Chairperson among themselves to manage the review of such protocols.
5.3.11. The members' appointments may be renewed by the President, KGUMSB, for up to two consecutive terms, upon recommendation by the Chairperson. The renewal of membership of the Chairperson (as a member of IRB) shall be recommended by the Vice Chairperson.

5.4. Roles and responsibilities of IRB members

5.4.1. Participate in the IRB meeting
5.4.2. Review, discuss and consider research proposals submitted for evaluation
5.4.3. Monitor serious adverse event reports and recommend appropriate action(s) *(SOP/020/01)*
5.4.4. Review the progress reports and monitor ongoing studies as appropriate
5.4.5. Evaluate final reports and outcomes
5.4.6. Review, develop and update guidelines on research and ethics
5.4.7. Maintain confidentiality of the documents and deliberations of IRB meetings *(SOP/027/01)*
5.4.8. Declare any conflict of interest
5.4.9. Participate in continuing education activities in biomedical ethics and biomedical research
5.4.10. Collaborate with the KGUMSB on all research-related activities

5.5. Resignation, Disqualification, Replacement of Members

5.5.1. Members may resign from their positions by submitting a letter of resignation to the Chairperson.
5.5.2. Members may also be disqualified from continuance should the Chairperson provide written arguments to the (other) members, according to IRB members' responsibilities listed in *Section 5.4*, and there is unanimous agreement.
5.5.3. Members that have resigned or have been disqualified may be replaced by the Head of the organization upon recommendation by the Chairperson.
5.5.4. Members may be disqualified if he/she fails to attend two consecutive meeting without proper leave of absence which is acceptable to the Chairperson.
5.5.5. An appropriate replacement for the disqualified member/resigned member shall be made by the President, KGUMSB upon recommendation by the Chairperson.

5.6. Independent Consultants

5.6.1. The IRB may be further supported in its reflections on specific protocols or requests for advice on specific ethical/ technical issues by Independent Consultants.
5.6.2. Independent Consultants are appointed by the Chairperson of the IRB.
5.6.3. Their professional qualifications may be in the areas of community and/or patient representation, medicine, statistics, social science, law, ethics, religion. Independent Consultants are appointed for the duration of the period sought *(see SOP/006/01)*.

5.7. Conditions of Appointment

5.7.1. Members and Independent Consultants are appointed to the IRB under the following conditions:

5.7.1.1. Willingness to publicize his/her full name, profession, and affiliation;

5.7.1.2. All financial accountability, reimbursement for work and expenses, if any, within or related to the IRB shall be recorded and made available to the public upon request;

5.7.1.3. All IRB Members, Alternate Members and Independent Consultants must sign Confidentiality / Conflict of Interest Agreements regarding meeting deliberations, applications, information on research participants, and related matters.

5.8. Officers

5.8.1. The following officers through their respective responsibilities contribute to the good functioning of the IRB:

Chairperson	Responsible to chair the meetings and liaise directly with the Head of the organization, report the meeting outcomes to the Head, and invite independent consultants to provide special expertise to the IRB on proposed research protocol. He/she shall also be a member of the National Health Research Board/Council,
Vice-Chairperson	Responsible to chair the meetings in the absence of the Chairperson and act as vice-chair during meetings with the Chairperson,
Secretariat	Responsible for the administrative aspect of the IRB *(see 5.9 – below)*

5.9. Secretariat

5.9.1. The Research and Innovation Unit of the Medical Education Centre for Research Innovation and Training (MECRIT), KGUMSB shall be the secretariat for the IRB.

5.9.2. The Research and Innovation Unit of the MECRIT shall appoint a member secretary to the IRB.

5.9.3. All Secretariat staff have to sign Confidentiality/Conflict of Interest Agreements.

5.9.4. The Secretariat shall have the following functions:

5.9.4.1. Organizing an effective and efficient tracking procedure for each proposal received *(see SOP/008/01, SOP/026/01)*.

5.9.4.2. Preparation, maintenance and distribution of study files *(see SOP/025/01)*

5.9.4.3. Organizing IRB meetings regularly *(SOP/022/01).*

5.9.4.4. Preparation and maintenance of meeting agenda and *minutes (see SOP/021/01)*

5.9.4.5. Maintaining the IRB's documentation and Archive *(See SOP/025/01 and SOP/026/01)*

5.9.4.6. Communicating with the IRB members and applicants *(SOP/023/01)*

5.9.4.7. Arrangement of training for personnel and IRB members *(see SOP/005/01)*

5.9.4.8. Organizing the preparation, review, revision and distribution of SOPs and guidelines *(see SOP/001/01 and SOP/026/01)*

5.9.4.9. Providing the necessary administrative support for IRB related activities to the Chairperson of the Board (e.g. communicating a decision to the applicant) – *(SOP/008/01 – SOP/022/01)*

5.9.4.10. Providing updates on relevant and contemporary issues related to ethics in health research, as well as relevant contemporary literature to the Board members.

5.9.4.11. Maintain budget for the regular meetings, and any other requirements.

5.10. DISSOLVING OF THE IRB

5.10.1. At any point in time, should the Organization cease to exist, the IRB shall be automatically dissolved.

5.10.2. The IRB may also be dissolved at any time by the **President, KGUMSB,** following written notification to each of the members.

6. GLOSSARY

Confidentiality	Prevention of disclosure, to other than authorized individuals, of IRB's information and documents
IRB	IRB is an independent body whose responsibility is to ensure the protection of the rights, safety and well-being of human subjects involved in a trial and to provide public assurance of that protection. The board shall review both technical and ethical issues related to the research proposal.
Scientists	Professionals with advanced training and expertise in the medical or non-medical areas related to the protocol being reviewed
Affiliated member	Members working under the **KGUMSB**
Non-affiliated member	Members from outside the **KGUMSB**
Scientific member	Members with masters or higher degrees; or members with sufficient research experience
Non-scientific member	Members with qualification below master degree
Alternate member	An individual appointed to the IRB to serve in the same capacity as the specific IRB member(s), who substitutes for members at convened meetings when the member is not in attendance.
Head of organization	President, KGUMSB, Thimphu, Bhutan
Secretariat	Research and Innovation Unit, MECRIT, KGUMSB
Member Secretary	A person nominated by the Secretariat and responsible for IRB activities.

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/001/01, SOP/004/01-005/01, SOP/008/01-011/01, and SOP/013/01-026/01.

CHAPTER 2.2

CONFIDENTIALITY/CONFLICT OF INTEREST AGREEMENT

SOP NUMBER: SOP/004/01

Institutional Review Board
(IRB)

Khesar Gyalpo University of Medical Sciences of Bhutan

www.kgumsb.edu.bt

Effective Date: October 1, 2021
Supersedes: SOP/004/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 section shall be to provide a form of Confidentiality/ Conflict of Interest Agreement and identify who shall read, understand, accept, keep in mind, sign and date the form. The procedures provide details when and where to sign as well as how the signed document shall be kept.

2. SCOPE

This SOP shall cover the Agreements on both Confidentiality and Conflict of Interest concerning information and procedures followed by the IRB.

3. RESPONSIBILITY

All newly-appointed IRB members shall be responsible to read, understand, accept and sign the agreement contained in the Confidentiality/ Conflict of Interest form before beginning their ethical review tasks with the KGUMSB to protect the rights of human study participants.

4. FLOW CHART

No.	Activity	Responsibility
1	Read the text carefully and thoroughly ↓	IRB members / guest attendees / observers
2	Ask questions, if any ↓	IRB members / guest attendees / observers
3	Sign to indicate consent ↓	IRB members / guest attendees / observers
4	Keep the Agreement in mind. ↓	IRB members / guest attendees / observers
5	Archive the signed forms	IRB Secretariat

5. DETAILED INSTRUCTIONS

5.1. Read the text carefully and thoroughly.

5.1.1. Newly appointed members obtain two copies of the Agreement Form *AF/01-004/01*.
5.1.2. Read through the text of the form very carefully.
5.1.3. The members fill in their names and their office on the blanks.

5.2. Ask questions, if any.

5.2.1. Direct questions to the Secretariat/Chairperson, if any part or sentences is not clear.
5.2.2. The Secretariat/Chairperson shall explain or clarify the contents of the document.

5.3. Sign with consent.

5.3.1. Sign and date both copies of the document in presence of a member of the Secretariat.
5.3.2. The members keep a copy as their records.

5.4. Keep the Agreement in mind.

5.4.1. The individual who sign the Confidentiality/ Conflict of Interest Agreement shall remember and comply with the requirements listed in the agreement.

5.5. Archive the signed forms of Confidentiality/Conflict of Interest Agreement.

5.5.1. The secretariat keeps a copy of the signed Agreement as the Institute's records.
5.5.2. Keep the copies in a Confidentiality/ Conflict of Interest Agreement file.
5.5.3. Store the file in a secure cabinet with limited key holders.

6. GLOSSARY

Confidentiality	The non-occurrence of unauthorized disclosure of information:
Confidentiality Agreement	*Sometimes called Secrecy or Nondisclosure agreements:* An agreement designed to protect trade secrets, information and expertise from being misused by those who have learned about them. The type of information that can be included under the umbrella of confidential information is virtually unlimited. Most confidentiality agreements exclude certain types of information from the definition of confidential information. It is very important that the recipient include these exceptions in the confidentiality agreement. An important point that must be covered in any confidentiality agreement is the standard by which the parties shall handle the confidential information. The agreement shall establish a time period during which disclosures shall be made and the period during which confidentiality of the information is to be maintained.
Conflict of Interest	A situation in which a person, such as a public official, an employee, or a professional, has a private or personal interest sufficient to appear to influence the objective exercise of his or her official duties. There are three key elements in this definition: financial interest; official duties; professional interest. A conflict of interest occurs when: • An individual's private interest differs from his or her professional obligations to the institute. • Professional actions or decisions occur that an independent observer might reasonably question. • A conflict depends upon situation and not on the character or actions of the individual. • Potential conflicts of interest shall be disclosed and managed as per policy.

7. REFERENCES

7.1. World Health Organization, Operational Guidelines for Ethics Committees that Review Biomedical Research, 2000.

7.2. International Conference on Harmonization, Guidance on Good Clinical Practice (ICH GCP) 2016.

8. ANNEX

ANNEX 1	AF/01-004/01	Confidentiality/ Conflict of Interest Agreement Form
ANNEX 2	AF/02-004/01	Confidentiality Agreement form for Guest/ Observer Attendees to IRB Meetings
ANNEX 3	AF/03-004/01	Confidentiality Agreement for Non-members Requesting Copy(S) of IRB Documents

ANNEX 1
AF/01-004/01

Confidentiality / Conflict of Interest Agreement Form

In recognition of the fact, that I…..*member's name, and his/her affiliation*……..herein referred to as the "Undersigned", has been appointed as a member of the IRB has been asked to assess research studies involving human subjects in order to ensure that they are conducted in a humane and ethical manner, with the highest standards of care according to the applied national, local regulations, institutional policies and guidelines;

Whereas, the appointment of the undersigned as a member of the *IRB* is based on individual merits and not as an advocate or representative of a particular district / community nor as the delegate of any organization or private interest;

Whereas, the fundamental duty of an IRB member is to **independently review both scientific and ethical aspects of research protocols** involving human subjects and make a determination and the best possible objective recommendations, based on the merits of the submissions under review;

Whereas, the IRB shall meet the highest ethical standards in order to merit the trust and confidence of the communities in the protection of the rights and well-being of human subjects;

The undersigned, as a member of the IRB, is expected to meet the same high standards of ethical behaviour to carry out its mandate.

This Agreement thus encompasses any information deemed Confidential or Proprietary provided to the Undersigned in conjunction with the duties as a member of the IRB. Any written information provided to the Undersigned that is of a Confidential, Proprietary, or Privileged nature shall be identified accordingly.

As such, the Undersigned agrees to hold all Confidential or Proprietary trade secrets ("information") in trust or confidence and agrees that it shall be used only for contemplated purposes, shall not be used for any other purpose or disclosed to any third party. Written Confidential information provided for review shall not be copied or retained. All Confidential information (and any copies and notes thereof) shall remain the sole property of the IRB.

The Undersigned agrees not to disclose or utilize, directly or indirectly, any Confidential or Proprietary information belonging to a third party in fulfilling this agreement. Furthermore, the Undersigned confirms that his/her performance of this agreement is consistent with the KGUMSB's policies, including Ministry of Health's policies and any contractual obligations they may have to third parties.

Any breach to this agreement shall be dealt as per the existing laws of the country.

Conflict of Interest

It is recognized that the potential for conflict of interest shall always exist but has faith in the IRB and its Chairperson to manage the conflict issues so that the ultimate outcome is the protection of human subjects.

It is the policy of the IRB that no member may participate in the review, comment or approval of any activity in which he/she has a conflict of interest except to provide information as requested by the IRB during the meeting.

The Undersigned shall immediately disclose to the Chairperson of the IRB, any actual or potential conflict of interest that he/she may have in relation to any particular proposal submitted for review by the Committee, and to abstain from any participation in discussions or recommendations in respect of such proposals.

If an applicant submitting a protocol believes that an IRB member has a potential conflict, the investigator may request that the member be excluded from the review of the protocol.

The request shall be in writing and addressed to the Chairperson. The request shall contain evidence that substantiates the claim that a conflict exists with the IRB member(s) in question. The Committee may elect to investigate the applicant's claim of the potential conflict. When a member has a conflict of interest, the member shall notify the Chairperson and may not participate in the IRB review or approval except to provide information requested by the Committee.

Examples of conflict of interest cases may be any of the following:

- A member is involved in a potentially competing research program.
- Access to funding or intellectual information may provide an unfair competitive advantage.
- A member's personal biases may interfere with his or her impartial judgment.

Agreement on Confidentiality and Conflict of Interest

Please sign and date this Agreement, if the Undersigned agrees with the terms and conditions set forth above. The original (signed and dated Agreement) shall be kept on file in the custody of the IRB. A copy shall be given to you for your records.

In the course of my activities as a member of the IRB, I may be provided with confidential information and documentation (which we shall refer to as the "Confidential Information"). I agree to take reasonable measures to protect the Confidential Information; subject to applicable legislation, including the Access to Information Act, not to disclose the Confidential Information to any person; not to use the Confidential Information for any purpose outside the Committee's mandate, and in particular, in a manner which would result in a benefit to myself or any third party; and to return all Confidential Information (including any minutes or notes I have made as part of my Committee duties) to the Chairperson upon termination of my functions as a Committee member.

Whenever I have a conflict of interest, I shall immediately inform the Chairperson not to count me toward a quorum for voting.

I, ……., have read and accept the aforementioned terms and conditions as explained in this Agreement.

_____	_____
Undersigned Signature	Date
_____	_____
President, KGUMSB	Date

(Please affix legal stamp)

ANNEX 2
AF/02-004/01

Confidentiality Agreement Form for Guest Attendees to IRB Meetings

I,……., understand that I am allowed to attend the IRB meeting as a guest or an observer. In the course of the meeting of the IRB, some confidential information may be disclosed or discussed. Upon signing this form, I agree to take reasonable measures to keep the information as Confidential.

Indicate the details (date and number) of the IRB Meeting attended:

……

……

……

_____ _____

Signature of the Guest or Observer Date

_____ _____

Chairperson of IRB Date

(Please affix legal stamp)

ANNEX 3
AF/03-004/01

Confidentiality Agreement Form for Non-members Requesting Copies of IRB's Documents

I,……....., as a non-member of IRB, understand that the copy(s) given to me by the IRB is (are) confidential. I shall use the information only for the indicated purpose as described to the IRB and shall not duplicate, give or distribute these documents to any person(s) without permission from the IRB. Upon signing this form, I agree to take reasonable measures and full responsibility to keep the information as Confidential.

I have received copies of the following IRB documents:

……

……

……

……

_____ _____
Signature of the recipient Date

_____ _____
Member Secretary Date

(Please affix legal stamp)

CHAPTER 2.3

TRAINING PERSONNEL AND IRB MEMBERS

SOP NUMBER: SOP/005/01

INSTITUTIONAL REVIEW BOARD
(IRB)

Khesar Gyalpo University of Medical Sciences of Bhutan

www.kgumsb.edu.bt

Effective Date: October 1, 2021
Supersedes: SOP/005/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 section shall be to inform the IRB personnel and members why training is necessary and how the members shall seek to occasionally attend training or workshop programs to up-date themselves on the progress of technology, information and ethics. Khesar Gyalpo University of Medical Sciences of Bhutan (KGUMSB) recognizes the importance of training and continuing professional development, therefore the University shall allocate an annual budget for specific training and study visits for IRB personnel and members. New IRB members shall possess adequate knowledge or undergo a training program prior to joining the Board.

2. SCOPE

The SOP shall apply to all personnel of the IRB.

3. RESPONSIBILITY

3.1. The University shall be responsible to provide training and education to the IRB members, whenever necessary.
3.2. The IRB members shall pursue for further training and education in the relevant fields as mandated.

4. FLOW CHART

No.	Activity	Responsibility
1	Topics for training ↓	KGUMSB/IRB members / Secretariat
2	How to get trained ↓	KGUMSB/IRB members / Secretariat
3	Keeping the training record.	KGUMSB/IRB members / Secretariat

5. DETAILED INSTRUCTIONS

5.1. Topics for training

IRB members shall maintain competence by ensuring currency of their knowledge of:

- Good Clinical Practice (GCP)
- CIOMS Guideline
- Declaration of Helsinki
- Ethical Issues
- Relevant laws
- Developments in relevant science, technical and environmental, health and safety aspects
- Relevant requirements of health, safety and environmental laws and regulations and related documents
- IRB Standard Operational Procedures
- Audit procedures
- Other relevant fields.

5.2. Training Procedures

5.2.1. The procedure for selection of candidates, identification of institute and training completion mandates shall be governed by the COS, KGUMSB and/or RGOB rules.

5.2.2. The secretariat shall initiate, propose and process for training of the IRB members.

5.2.3. The training shall be in the form of workshops, conferences, seminars, study visits, tailor-made courses, structured courses, etc.

5.3. Keeping the training records

5.3.1. Fill in the form *AF/01-005/01* to record the training/workshop/conference activities in chronological order.

5.3.2. Make a copy of the form.

5.3.3. Keep the original form as your record.

5.3.4. Give the copy to the secretariat to keep in the IRB file.

5.3.5. Submit a copy of evidence of training/workshop/conference activities (e.g., copy of attendance sheet or certificate) to the Secretariat for record.

5.4. Training Frequency

5.4.1. Minimum of 2 in-house training per year

5.4.2. Minimum of 1-3 full days training per year

6. GLOSSARY

Conference	A meeting of individuals or representatives of various organizations for the purpose of discussing and/or acting on topics of common interest.
Meeting	Deliberations between at least two (2) persons where such deliberations determine or result in the joint conduct or disposition of business.
Workshop	A group of people engaged in study or work on a creative project or subject
Study visit	A visit by an individual or a group of people to another site or country to update or gain knowledge in relevant fields.
COS	Condition of Services
RGOB	Royal Government of Bhutan

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)

8. ANNEX

ANNEX 1 *AF/01-005/01:* Training Record Form

ANNEX 1
AF/01-005/01

Training Record Form

Name:		
Staff / Membership since:		Gender:
Education Background:		
Work Experience:		

Training Experience:

No	Courses / Workshops / Conferences / Meetings Attended	Organized by:	Place	Duration	Source of Funding
1					
2					
3					
4					
5					
6					
7					
8					
9					

CHAPTER 2.4

SELECTION OF INDEPENDENT CONSULTANT

SOP NUMBER: SOP/006/01

INSTITUTIONAL REVIEW BOARD
(IRB)

Khesar Gyalpo University of Medical Sciences of Bhutan

www.kgumsb.edu.bt

Effective Date: October 1, 2021
Supersedes: SOP/006/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 SOP section shall be to provide procedures for engaging the expertise of a professional as a consultant to the IRB.

2. SCOPE

The SOP shall cover the process of selecting and appointing the independent consultant, and the requirement of the consultation service.

This SOP shall be applicable to the IRB and the selected independent consultant.

3. RESPONSIBILITY

Once a study involves procedures or information that is not within the area of expertise of the IRB members, it is the responsibility of the Chairperson or any IRB member to nominate a consultant with competence in special areas to assist in the review of issues that require expertise beyond or in addition to those available in the IRB. The qualification review shall be conducted by the IRB. The appointment shall be approved by the Chairperson.

4. FLOW CHART

No.	Activity	Responsibility
1	Selection of Independent Consultants ↓	IRB Members / Secretariat
2	Consultation Services ↓	IRB Secretariat / Consultant
3	Termination of the Services	Consultant / IRB

5. DETAILED INSTRUCTIONS

5.1. Selection of Independent Consultants

5.1.1. Identify the experts by the Chairperson/Secretariat/IRB members.
5.1.2. Conduct a qualification review of the prospective consultant
5.1.3. Recommend the identified consultants to the KGUMSB and seek approval
5.1.4. The consultant provides:
  5.1.4.1. A curriculum vitae
  5.1.4.2. A signed Professional Services Agreement
  5.1.4.3. A signed Confidentiality/Conflict of Interest Agreement (Form *AF/01-004/01*)
5.1.5. The Secretariat keeps the documents in a consultant's file and creates a roster of consultants with the areas of their expertise.
5.1.6. Fees, if any, shall be as per the COS and/or RGOB rules.

5.2. Consultation Services

5.2.1. The IRB Secretariat provides study protocol documents to the appropriate consultant for review.
5.2.2. The consultant shall complete a consultative report to be reviewed by the IRB at the time the study is reviewed.
5.2.3. The consultant may attend the IRB meeting, present the report and participate in the discussion but cannot vote.
5.2.4. The report becomes a permanent part of the study file.

5.3. Termination of the Services

5.3.1. Consultation services may be terminated by either the consultants themselves or by the IRB.

5.3.2. Upon termination of the consultant's services, a member of the Secretariat ensures that all the qualifying documentation and the reason for discontinuation of the services are filed with the administrative documents.

6. GLOSSARY

Independent consultant	An expert who gives advice, comments and suggestion upon review of the study protocols with no affiliation to the institutes or investigators proposing the research protocols.

CHAPTER 3.1

DETERMINATION OF RESEARCH QUALIFYING FOR EXEMPTION FROM ETHICS REVIEW

SOP NUMBER: SOP/007/01

INSTITUTIONAL REVIEW BOARD (IRB)

Khesar Gyalpo University of Medical Sciences of Bhutan

www.kgumsb.edu.bt

Effective Date: October 1, 2021
Supersedes: SOP/007a/yy

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

Table of Contents

5. PURPOSE

The purpose of this SOP shall be to provide guidance to IRB to decide if the proposed study qualifies for exemption from ethics review under the requirements of the National Health Policy, 2011.

6. SCOPE

This SOP shall apply to decide if the proposed study qualifies for exemption from ethics review.

7. RESPONSIBILITY

The IRB Secretariat and Chairperson shall be responsible to decide if the proposed study qualifies for exemption from ethics review.

8. FLOW CHART

No.	Activity	Responsibility
1.	Determination. ↓	IRB Member-Secretary /Chairperson
2.	Exemption Letter ↓	Chairperson
3.	Communicate the review result to the investigator. ↓	IRB Member-Secretary
4.	Report the exemption during the IRB meeting ↓	IRB Member-Secretary
5.	Storage of the documents	IRB Member-Secretary

9. DETAILED INSTRUCTIONS

9.1. Determine protocols for exemption from ethics review.

9.1.1. IRB Member-Secretary/IRB Chairperson determines if the proposed study qualifies for exemption from ethics review with the help of checklist (*AF/01-007/01*). Following are the criteria for exemptions;

9.1.1.1. The study does not involve human subjects.
9.1.1.2. Research about public behaviour (voting trends, opinion surveys, etc.)
9.1.1.3. Program evaluation of public programs
9.1.1.4. Surveillance functions of KGUMSB/ Faculties/ Affiliated Institutes
9.1.1.5. Public health practices
9.1.1.6. Historical and cultural events
9.1.1.7. Research involving large statistical data without identifiers
9.1.1.8. Research involving educational methods remain exempt, but only if the research is not likely to adversely affect classroom instruction time or student performance.
9.1.1.9. Curriculum development and educational testing remains exempt as long as;
9.1.1.9.1. any recorded information is completely de-identified
9.1.1.9.2. any disclosures of information would not place the subjects at risk of criminal or civil liability or financial or reputational harm
9.1.1.10. Secondary research involving identifiable private information, if
9.1.1.10.1. the identifiable information is already available to the public

9.1.1.10.2. the information is not re-identified, and the researcher does not attempt to re-identify it

9.1.1.11. The use of non-identifiable bio-specimens in research does not, on its own, require ethics review.

9.2. If the proposed study doesn't qualify for exemption from ethics review, such study has to be reviewed by IRB for ethical clearance. Follow *SOP/008/01* MANAGEMENT OF PROTOCOL SUBMISSION.

9.3. Exemption Letter

9.3.1. If a proposed study qualifies for exemption from ethics review then an **exemption** letter duly signed by the Chairperson shall be sent to the applicant/ Investigator within two working days after receiving the application.

9.4. Communicate the review result to the investigator

9.4.1. The Secretariat shall prepare the exemption letter and send it with the duly filled checklist (*AF/01-007/01*) to the Chairperson.

9.4.2. The Chairperson shall approve the exemption by signing on the letter (*AF/01-007/01*).

9.4.3. The Secretariat shall send the letter to the investigator.

9.5. Report the Exemption to the full board

9.5.1. Report the list of studies that are granted exemption of ethical approval to the full board during the board meeting.

9.6. Storage of the document

9.6.1. The checklist and the related meeting minutes shall be kept with the protocol file.

9.6.2. The copy of the exemption letter shall be kept in the protocol file.

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

10. GLOSSARY

Research	Research refers to a class of activity designed to develop or contribute to generalizable knowledge through a systematic investigation. Generalizable knowledge consists of theories, principles or relationships, or the accumulation of information on which they are based, that can be corroborated by accepted scientific methods of observation and inference.
Research involving human subjects	Research involving human subjects includes: 1. Studies of a physiological, biochemical or pathological process, or of the response to a specific intervention – whether physical, chemical or psychological – in healthy subjects or patients; 2. Controlled trials of diagnostic, preventive or therapeutic measures in larger groups of persons, designed to demonstrate a specific generalizable response to these measures against a background of individual biological variation; 3. Studies designed to determine the consequences for individuals and communities of specific preventive or therapeutic measures; 4. Studies concerning human health-related behaviour in a variety of circumstances and environments; 5. Research involving human subjects may employ either observation or physical, chemical or psychological intervention; it may also either generate records or make use of existing records containing biomedical or other private information about individuals who may or may not be identifiable from the records or information; and

	6. Definition of "human subject" does not include the use of non-identifiable biospecimens.

7. REFERENCES

7.1. CIOMS, International Ethical Guidelines for Biomedical Research Involving Human Subjects, 2002
7.2. CIOMS, International Ethical Guidelines for Epidemiological Studies, 2009
7.3. The Office for Human Research Protections (OHRP). Human Subject Regulations Decision Charts. https://www.hhs.gov/ohrp/sites/default/files/full-2016-decision-charts.pdf)
7.4. Associated SOPs: SOP/008/01

8. Annex

8.1. ANNEX 1 *AF/01-007/01* Checklist to determine whether the research is a biomedical research involving human subjects
8.2. ANNEX 2 *AF/02/007/01* Exemption Letter Templates
8.3. ANNEX 3 *AF/03-007/01* APPLICATION FORM for Exemption

ANNEX 1
AF/01-007/01

Checklist to determine if a proposed protocol qualifies for exemption from ethics review

STEP 1: Does the proposed study involve human participants[1]?

☐Yes ☐ No

STEP 2: Does the proposed study fulfils the criteria for exemptions specified under SOP/007/03 (9.1.1.1 to 9.1.1.11[2])

☐ Yes ☐ No

STEP 3: Decision making;

1. If 'No' for STEP 1 then the proposed study doesn't require ethical clearance from IRB.
2. If 'Yes' for STEP 1 and 'Yes' for STEP 2 then the proposed study doesn't require ethical clearance from IRB.
3. If 'Yes' for STEP 1 and 'No' for STEP 2 then the study has to be reviewed by IRB.

Recommendation: ☐ Exempt ☐ the study has to be reviewed by IRB for Clearance

Name and signature of the Reviewer/IRB Secretary:

DECISION TO BE MADE BY THE CHAIRPERSON
Decision: ☐ Exempt ☐ the study has to be reviewed by IRB for Clearance

Name and signature of the Chairperson:

[1] Research involving human subjects includes:

1. Studies of a physiological, biochemical or pathological process, or of the response to a specific intervention – whether physical, chemical or psychological – in healthy subjects or patients;
2. Controlled trials of diagnostic, preventive or therapeutic measures in larger groups of persons, designed to demonstrate a specific generalizable response to these measures against a background of individual biological variation;
3. Studies designed to determine the consequences for individuals and communities of specific preventive or therapeutic measures;
4. Studies concerning human health-related behaviour in a variety of circumstances and environments;
5. Research involving human subjects may employ either observation or physical, chemical or psychological intervention; it may also either generate records or make use of existing records containing biomedical or other information about individuals who may or may not be identifiable from the records or information; and
6. Definition of "human subject" does not include the use of non-identifiable biospecimens.

[2] Following are the criteria for exemptions:

1. 9.1.1.1. The study does not involve human subjects.
2. 9.1.1.2. Research about public behaviour (voting trends, opinion surveys, etc.)
3. 9.1.1.3. Program evaluation of public programs
4. 9.1.1.4. Surveillance functions of KGUMSB/ Affiliated Institutes/ Ministry of Health
5. 9.1.1.5. Public health practices
6. 9.1.1.6. Historical and cultural events
7. 9.1.1.7. Research involving large statistical data without identifiers
8. 9.1.1.8. Research involving educational methods remain exempt, but only if the research is not likely to adversely affect classroom instruction time or student performance.
9. 9.1.1.9. Curriculum development and educational testing remains exempt as long as;
10. 9.1.1.9.1. any recorded information is completely de-identified
11. 9.1.1.9.2. any disclosures of information would not place the subjects at risk of criminal or civil liability or financial or reputational harm
12. 9.1.1.10. Secondary research involving identifiable private information, if
13. 9.1.1.10.1. the identifiable information is already available to the public
14. 9.1.1.10.2. the information is not re-identified, and the researcher does not attempt to re-identify it
15. 9.1.1.11. The use of non-identifiable biospecimens in research does not, on its own, require ethics review.

ANNEX 2
Form AF/02-007/01 Exemption Letter Template

གཞི་སར་རྒྱལ་པོ་གསོ་རིག་གཙུག་ལག་སློབ་སྡེ།།

Khesar Gyalpo University of Medical Sciences of Bhutan
Royal Government of Bhutan

Ref. No. IRB/ / / Date:

EXEMPTION LETTER

Protocol No: PN/ /
Protocol Title:
Version Number: "...", dated: DD/MM/YYYY
Principal Investigator:
Institute:
Co-Investigators:

This is to state that Research Review board of Health (IRB) has determined that the above protocol, submitted to IRB for ethical approval, qualify for exemption from ethics review based on the criteria specified in the Standard Operating Procedures (SOP) of IRB - SOP/007 DETERMINATION OF RESEARCH QUALIFYING FOR EXEMPTION FROM ETHICS REVIEW and application form AF/03-007/01 APPLICATION FORM for Exemption.

Therefore, the need for IRB approval is exempted for the protocol. Nonetheless, the investigator(s) shall be responsible to;

1. Seek all other clearances/approvals required by law/policy including permission from the study sites before conducting the study/project,
2. Submit Final Report of the study/project, at the end of the study/project, for review and protocol file closure.
3.

Note: Technical and ethical soundness of protocols are not assessed by IRB for the protocols that qualify for exemptions of IRB review.

( )
Chairperson

For further information please contact: *.....@kgumsb.edu.bt; IRB Member-Secretary*

ANNEX 3
Form AF/03-007/01

APPLICATION FORM for EXEMPTION

Instructions: This form has 8 items. Follow the item specific instructions and fill all applicable items from 2 through 8. (To mark "✓" the given options double click on the first half of the box "☐")

1.	Protocol Number (*Protocol Number will be assigned by IRB Secretariat*):
2.	Protocol Title:
3.	Protocol Version Number:
4.	PARTICULARS OF THE PRINCIPAL INVESTIGATOR (PI) Name: …….. Address: ..... Contact Number: ..... Fax: ..... E-mail: …….....
5.	Proponent of the study: …….....

6. CO-INVESTIGATOR(S)

Name and Institution	BMHC No.	Role in the study	Does s/he meet or will meet authorship criteria* (Yes/ No)	Contact Number
1.				
2.				
3.				
4.				
5.				
6.				
7.				
8.				

* The ICMJE recommends that authorship be based on the following 4 criteria:
1. Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; AND
2. Drafting the work or revising it critically for important intellectual content; AND
3. Final approval of the version to be published; AND
4. Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

7.	Mark "✓" for the following sub-items 7.1 to 7.13 as appropriate 7.1. The study does not involve human subjects[3]. ☐Yes ☐ No Comments: ……

[3] Research involving human subjects includes:
1. Studies of a physiological, biochemical or pathological process, or of the response to a specific intervention – whether physical, chemical or psychological – in healthy subjects or patients;
2. Controlled trials of diagnostic, preventive or therapeutic measures in larger groups of persons, designed to demonstrate a specific generalizable response to these measures against a background of individual biological variation;
3. Studies designed to determine the consequences for individuals and communities of specific preventive or therapeutic measures;
4. Studies concerning human health-related behaviour in a variety of circumstances and environments;
5. Research involving human subjects may employ either observation or physical, chemical or psychological intervention; it may also either generate records or make use of existing records containing biomedical or other information about individuals who may or may not be identifiable from the records or information; and
6. Definition of "human subject" does not include the use of non-identifiable biospecimens.

	7.2. Research is about public behaviour (voting trends, opinion surveys, etc.) ☐Yes ☐ No Comments: …… 7.3. The project is a program evaluation of public programs ☐Yes ☐ No Comments: …… 7.4. The project is a surveillance functions of KGUMSB/ Affiliated Institutes/ Ministry of Health ☐Yes ☐ No Comments: …… 7.5. The project is a public health practices ☐Yes ☐ No Comments: …… 7.6. The project is about historical and cultural events ☐Yes ☐ No Comments: …… 7.7. The project is a research involving large statistical data without identifiers ☐Yes ☐ No Comments: …… 7.8. The project is a research involving educational methods and the research is not likely to adversely affect classroom instruction time or student performance. ☐Yes ☐ No Comments: …… 7.9. The project is a curriculum development and educational testing and any recorded information is completely de-identified ☐Yes ☐ No Comments: …… 7.10. The project is a curriculum development and educational testing and any disclosures of information would not place the subjects at risk of criminal or civil liability or financial or reputational harm ☐Yes ☐ No Comments: …… 7.11. The project is a secondary research involving identifiable private information and the identifiable information is already available to the public, the information is not re-identified, and the researcher does not attempt to re-identify it ☐Yes ☐ No Comments: …… 7.12. The project is a research involving use of non-identifiable bio-specimens. ☐Yes ☐ No Comments: ……
8.	**SIGNATURES:** _____ Date: …….. Principal Investigator _____ Date:…… Protocol Chairperson (if applicable)

CHAPTER 3.2

MANAGEMENT OF PROTOCOL SUBMISSION

SOP NUMBER: SOP/008/01

INSTITUTIONAL REVIEW BOARD
(IRB)

Khesar Gyalpo University of Medical Sciences of Bhutan

www.kgumsb.edu.bt

Effective Date: October 1, 2021
Supersedes: SOP/007b/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

This standard operating procedure is designed to describe how the Secretariat of the Research Ethics Board (IRB) manages protocol submissions to the IRB.

2. SCOPE

This SOP shall apply to the submission process including:

- Submission for Initial Review
- Resubmission of Protocols with Corrections
- Protocol Amendment
- Continuing Review of Approved Protocols
- Protocol Termination

3. RESPONSIBILITY

The IRB secretariat shall be responsible to receive and check the completeness of the submission package, and document the submitted protocol packages.

4. FLOW CHART

No.	Activity	Responsibility
1	Receive Submitted Packages ↓	IRB Secretariat
2	Check for submission items: ❑ Initial Review Application ❑ Resubmission of Protocols with Corrections ❑ Protocol Amendment ❑ Continuing Review of Approved Protocols ❑ Protocol Termination ↓	IRB Secretariat
3	Check the documents as per AF/01-008/01 ↓	IRB Secretariat
4 5	Fill the document receipt form ↓ Store the received packages	IRB Secretariat IRB Secretariat

5. DETAILED INSTRUCTIONS

5.1. Receive submitted packages

5.1.1. Initial Review Application

5.1.1.1. Go to 5.2.1.1

5.1.2. Resubmission of Protocols with Corrections

5.1.2.1. Retrieve the previous receipt form from the Secretariat's records.

5.1.2.2. Go to step 5.2.1.2

5.1.3. Protocol Amendment

5.1.3.1. Retrieve the previous receipt form from the Secretariat's records.

5.1.3.2. Go to step 5.2.1.2

5.1.4. Continuing Review of Approved Protocols

5.1.4.1. Retrieve the previous receipt form from the Secretariat's records.
5.1.4.2. Go to step 5.2.1.4

5.1.5. Protocol Termination

5.1.5.1. Retrieve the previous receipt form from the Secretariat's records.
5.1.5.2. Go to step 5.2.1.5

5.2. Check for submission items

5.2.1. Get relevant forms:

5.2.1.1. Initial Review Application

5.2.1.1.1. checklist for contents of a submitted package, ANNEX – AF/01-008/01
5.2.1.1.2. a document receipt form, ANNEX- AF/02-008/01
5.2.1.1.3. an application form for initial review, ANNEX – AF/03-008/01 or ANNEX – AF/05-008/01
5.2.1.1.4. Go to step 5.2.2.

5.2.1.2. Resubmission of Protocols with corrections

5.2.1.2.1. checklist for contents of a submitted package, ANNEX – AF/01-008/01
5.2.1.2.2. a document receipt form, ANNEX- AF/02-008/01
5.2.1.2.3. an application form for re-submitted protocol, AF/01-013/01
5.2.1.2.4. Go to step 5.2.2

5.2.1.3. Protocol Amendments

5.2.1.3.1. checklist for contents of a submitted package, ANNEX – AF/01-008/01
5.2.1.3.2. a document receipt form, ANNEX- AF/02-008/01
5.2.1.3.3. an application form for protocol amendment review, AF/01-014/01
5.2.1.3.4. Go to step 5.2.2

5.2.1.4. Annual Continuing Reviews of Approved Protocols

5.2.1.4.1. checklist for contents of a submitted package, ANNEX – AF/01-008/01
5.2.1.4.2. a document receipt form, ANNEX- AF/02-008/01
5.2.1.4.3. an application form for continuing review, AF/01-015/01
5.2.1.4.4. Go to step 5.2.2

5.2.1.5. Protocol Termination

5.2.1.5.1. checklist for contents of a submitted package, ANNEX – AF/01-008/01
5.2.1.5.2. a document receipt form, ANNEX- AF/02-008/01
5.2.1.5.3. an application form for continuing review, AF/01-015/01
5.2.1.5.4. Go to step 5.2.2

5.2.2. Fill in the forms:

5.2.2.1. Give the related application forms, applicants to fill up the relevant information.

5.2.3. Verify contents of Submitted Package

5.2.3.1. Use the checklist for contents of a submitted package, ANNEX- AF/01-008/01
5.2.3.2. Check the applicable documents to ensure that all required forms and materials are contained within the submitted package.
5.2.3.3. Verify contents of the protocol submitted package to include :
5.2.3.3.1. Original Application Form for Initial Review
5.2.3.3.2. Summary Sheet or Memorandum of the study Protocol
5.2.3.3.3. Study Protocol and Protocol-Related Documents

5.2.3.4. Check completeness of necessary information in the Application Form for Initial Review.

5.2.3.5. Ask the principal investigator for a Summary Sheet or Memorandum of the study protocol (AF/04-008/01) for inclusion of the followings:

5.2.3.5.1. Title of the Protocol
5.2.3.5.2. Principal Investigator
5.2.3.5.3. Sponsor(s)
5.2.3.5.4. Abstract
5.2.3.5.5. Type of Protocol (screening, survey, clinical trial and phase)
5.2.3.5.6. Objectives
5.2.3.5.7. Anticipated Outcome
5.2.3.5.8. Inclusion/Exclusion Criteria
5.2.3.5.9. Withdrawal or discontinuation Criteria
5.2.3.5.10. Modes of Treatment Studied
5.2.3.5.11. Methodology (synopsis of study design)
5.2.3.5.12. Analysis (methods)
5.2.3.5.13. Activity plan / Timeline
5.2.3.5.14. IND Number (if applicable)
5.2.3.5.15. Schedule and Duration of Treatment
5.2.3.5.16. Efficacy or Evaluation Criteria (Response/Outcome)
5.2.3.5.17. Safety Parameters Criteria (Toxicity)

5.2.3.6. Check the submitted Protocol and Related Documents for the following contents:

5.2.3.6.1. Subjects' information sheets
5.2.3.6.2. Informed Consent Form
5.2.3.6.3. Case Record Form (CRF)
5.2.3.6.4. Study budget and budget justification
5.2.3.6.5. Agreement of the study
5.2.3.6.6. Curriculum Vitae (CV) of investigators
5.2.3.6.7. Evidence of GCP training (Only in case of clinical trials)
5.2.3.6.8. Investigators' Brochure

5.2.3.7. See if changes made to the documents be underlined or highlighted.

5.2.4. Verify electronic documents (where applicable)

5.2.4.1. Place the electronic computer documents (protocol summary, protocol and protocol-related documents) on the IRB server (Database) or the Local Area Network at the time of submission for initial protocol review or protocol amendment packages in the following drive and folder:
D:\IRB_Database\Research protocol\Research proposal 2021\PN-001 (PN number)

5.2.4.2. Verify that the electronic version and the contents of the documents match the copy submitted by comparing a hard copy of the electronic document with the submitted one as follow;

5.2.4.2.1. Print out the protocol documents, if paper copies are not submitted.
5.2.4.2.2. Verify the correctness of the documents.
5.2.4.2.3. Check that all pages of the documents have been included and that the submitted protocol and protocol-related documents do not have missing pages.
5.2.4.2.4. Certify the printed hard copy in the same manner as the submitted document(s) with the dated signature.

5.2.4.2.5. Stamp and assign a protocol number to the received protocols, applying the system of PO for protocol followed by year and the last three digit indicating the protocol number
For example, PN/2021/001 means protocol number one of the year 2021

5.2.4.2.6. Count for correct numbers of copies.

5.2.4.2.7. Store the hard copy of the electronic document with the submitted documents.

5.2.4.2.8. Identify clearly as the hard copy of the electronic document.

5.2.5. Create a Protocol Specific File

5.2.5.1. Get the "PN/Year/Protocol Number" file. (PN/ 2021/01)

5.2.5.2. Record the name and the number of the submitted protocol.

5.2.5.3. Record the receiving date and the name of the receiver.

5.3. Complete the submission process

5.3.1. The study proposal shall reach to the IRB secretariat at least one month prior to the planned full board meeting.

5.3.2. Check the application form for completeness, sign and date the form.

5.3.3. Attach the application forms to the Research Protocol packages.

5.3.4. Complete the ANNEX-AF/02-008/01 and clearly state the missing items in the package, if any.

5.3.5. Stamp the receiving date on the letter and the first page of the documents.

5.3.6. Initial the receiver's name on the receiving documents.

5.3.7. Make a photocopy of the completed ANNEX- AF/02-008/01

5.3.8. Return the original copy of the ANNEX- AF/02-008/01 to the applicants for their records.

5.3.9. Attach the filled checklist ANNEX- AF/01-008/01 with the copy of the form ANNEX-AF/02-008/01.

5.3.10. Keep the copy of the document receipt form in the "PN/Year/Protocol Number" file.

5.3.11. Keep the copy of the submitted documents with original signatures in the "PN/Year/Protocol Number" file.

5.4. Store the received packages

5.4.1. Bind the packages together appropriately.

5.4.2. Store the dated and initial original protocol packages on the IRB submission shelf for review in FIFO sequence.

6. GLOSSARY

FIFO	First In First Out sequence

7. REFERENCE

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. The SPIRIT Statement (http://www.spirit-statement.org/spirit-statement/)

7.4. STROBE Statement (https://www.strobe-statement.org/?id=available-checklists)

7.5. The CONSORT Statement (http://www.consort-statement.org/)
7.6. Associated SOPs: 013, 014 and 015.

8. ANNEX

ANNEX 1	AF/01-008/01	Contents of a Submitted Package (Checklist)
ANNEX 2	AF/02-008/01	Document Receipt Form
ANNEX 3	AF/03-008/01	Application Form for Initial Review
ANNEX 4	AF/04-008/01	Protocol Summary Sheet/Memorandum
ANNEX 5	AF/05-008/01	Application Form for Case Study / Case Series

ANNEX 1
AF/01-008/01 **Contents of a Submitted Package**

Protocol Number:……..

☐ **Initial Review Submitted Package**

- ❑ Protocol Summary Sheet or Memorandum (ANNEX – AF/03-008/01)
- ❑ Application Form for Initial Review: ANNEX – AF/01-008/01
- ❑ Protocol and Protocol-Related Documents
  - ☐ PI's address and details
  - ☐ Study title
  - ☐ Objectives of the study
  - ☐ Information sheet of informed consent
  - ☐ Translated version of informed consent sheet
  - ☐ informed consent form (ICF)
  - ☐ Translated version of ICF
  - ☐ Study budget
  - ☐ CV of the PI
  - ☐ Evidence of GCP training (Only in case of clinical trials)
  - ☐ Research tools (Questionnaire/forms)
  - ☐ case report forms (CRF) if applicable
  - ☐ Investigator's brochure if applicable
  - ☐ Attachments (Pls. specify) .....
  - ☐ Others……

☐ Resubmission for Re-review Submitted Package

- ❑ Resubmission or "Correction" Memorandum
- ❑ Revised Protocol Summary Sheet (if submitted initially)
- ❑ Application Form for Initial Review: ANNEX – AF/01-008/01
- ❑ Protocol and Protocol-Related Documents
  - ☐ PI's address and details
  - ☐ Study title
  - ☐ Objectives of the study
  - ☐ Information sheet of informed consent
  - ☐ Translated version of informed consent sheet
  - ☐ informed consent form (ICF)
  - ☐ Translated version of ICF
  - ☐ study budget
  - ☐ CV of the PI
  - ☐ Research tools (Questionnaire/forms)
  - ☐ Evidence of GCP training (Only in case of clinical trials)
  - ☐ Case report forms (CRF) if applicable
  - ☐ investigator's brochure if applicable
  - ☐ Attachments (Pls. specify) .....
  - ☐ others……

Note: *Changes made to the protocol and protocol-related documents shall be clearly marked either with the underlining or highlighting feature of the document or the software package used to prepare the documents.*

☐ **Protocol Amendment Submitted Package**

- ❑ Request for Amendment Memorandum
- ❑ Amendment Submission Form: AF/01-014/01
- ❑ Protocol and Protocol-Related Documents

Note: *Changes made to the protocol and protocol-related documents shall be clearly marked either with the underlining or highlighting feature of the software package used to prepare the document.*

☐ **Annual Continuing Review Package**

- ❑ Request for Annual Continuing Review Memorandum
- ❑ Continuing Review Application Form: AF/01-015/01
- ❑ Current Informed Consent Document (last approved by the IRB)

☐ **Protocol Termination Package**

- ❑ Request for Termination Memorandum
- ❑ Continuing Review Application Form (Termination Submissions are contained on this form): AF/01-015/01

ANNEX 2
AF/02-008/01

Document Receipt Form

Protocol Number:		**Submitted date:**	
Protocol Version Number:			
Type of Submission:	☐ Initial Review ☐ Resubmission for re-review ☐ Protocol Amendments	☐ Continuing Review of Approved Protocols ☐ Protocol Termination	
Protocol Title:			
Principal Investigator:			
Telephone number:		**Fax :**	
E-mail:		**Preferred Contact**	☐ Phone ☐ Fax ☐ e-mail
Institute:			
Delivery route:	☐ Post ☐ E-submission ☐ in Person		
Documents submitted:	☐ Complete ☐ incomplete, will submit on……..		
Documents checklist :	**Documents submitted** ☐ PI address and details ☐ Study title ☐ Objectives of the study ☐ Information sheet of informed consent ☐ Translated version of informed consent sheet ☐ informed consent form (ICF) ☐ Translated version of ICF ☐ study budget ☐ CV of the PI ☐ Evidence of GCP training (Only in case of clinical trials) ☐ Research tools (Questionnaire/forms) ☐ case report forms (CRF) if applicable ☐ investigator's brochure if applicable ☐ Attachments (PIs specify) …… ☐others……..	**Documents to be submitted:** ☐ PI address and details ☐ Study title ☐ Objectives of the study ☐ Information sheet of informed consent ☐ Translated version of informed consent sheet ☐ informed consent form (ICF) ☐ Translated version of ICF ☐ study budget ☐ CV of the PI ☐ Evidence of GCP training (Only in case of clinical trials) ☐ Research tools (Questionnaire/forms) ☐ case report forms (CRF) if applicable ☐ investigator's brochure if applicable ☐ Attachments (PIs specify) …… ☐others……..	
Received by:			
Date received:			

Note: *Please bring this receipt with you when contacting the IRB.*

ANNEX 3
Form AF/03-008/01

APPLICATION FORM for INITIAL REVIEW

Instructions: This form has 30 items. Follow the item specific instructions and fill all applicable items from 2 through 30. (To mark "✓" the given options double click on the first half of the box "☐")

1.	Protocol Number (*Protocol Number will be assigned by IRB Secretariat*):
2.	Protocol Title:
3.	Protocol Version Number:
4.	PARTICULARS OF THE PRINCIPAL INVESTIGATOR (PI) Name: …… Address: ..... Contact Number: ..... Fax(optional): ..... E-mail: …….....
5.	Proponent of the study: …….....
6.	STUDY TYPE: (Mark "✓ "whichever apply to the study. Tick all that apply) ☐ Survey ☐ Retrospective ☐ Prospective ☐ Social ☐ Behavioral research ☐ Community based ☐ Individual based ☐ Screening ☐ Observational ☐ Epidemiology ☐ Intervention study ☐ Medical ☐ Research on stored biological samples ☐ Clinical Trial: ☐ Phase I ☐ Phase II ☐ Phase III ☐ Phase IV ☐ Genetic Study ☐ Others…….....
7.	CHARACTERISTICS of PARTICIPANTS: Age Range (Specify): Impaired: ☐ None ☐ Physically ☐ Cognitively ☐ Mentally Limitation: ☐ illiteracy ☐ Prisoners ☐ Hospitalized ☐ Nursing home ☐ Pregnancy ☐ Poor/uninsured ☐ Employees of study site ☐ Students or staff of the PI ☐ Military personnel ☐ Others vulnerable to coercion, specify…….
8.	REQUESTED EXCLUSION OF PARTICIPANTS: ☐ None ☐ Male ☐ Female ☐ Children ☐ Other (specify): .....
9.	SPECIAL RESOURCE REQUIREMENTS (Tick all that apply, ONLY if applicable): ☐ Intensive Care ☐ Isolation unit ☐ Surgery ☐ Psychiatric institution ☐ Paediatric Intensive Care ☐ Transfusion ☐ CAT scan ☐ EKG scam ☐ Gene therapy ☐ Controlled substances (Narcotics / Psychotropic) ☐ Prosthetics ☐ Gynaecological services ☐ Others (specify)…….. ☐ Organ transplantation, specify……..
10.	IONIZING RADIATION USE (X-rays, radioisotopes, etc): ☐ None or Not Applicable (NA) ☐ Medically indicated only ☐ All
11.	INVESTIGATIONAL NEW DRUG (IND) / DEVICE (IDE): ☐ None

	☐ IND DRA No.:……..... Name: …….. Sponsor: …….. Holder: ……	☐ IDE DRA No:…… Name: …… Sponsor: ……... Holder: ……...
12.	PROCEDURE USE: ☐ Invasive ☐ Non-invasive	
13.	MULTI-SITE COLLABORATION: ☐ YES, number of sites … ☐ NO	
14.	FINANCIAL DISCLOSURE: ☐ YES ☐ NO If NO why not?	

15. CO-INVESTIGATOR(S)

Name and Institution	BMHC No.	Role in the study	Does s/he meet or will meet authorship criteria* (Yes/ No)	Contact Number
1.				
2.				
3.				
4.				
5.				
6.				
7.				
8.				

* The ICMJE recommends that authorship be based on the following 4 criteria:
1. Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; AND
2. Drafting the work or revising it critically for important intellectual content; AND
3. Final approval of the version to be published; AND
4. Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

16.	Has the Principal Investigator (PI) ever been involved in or convicted of a crime, disciplined by a public or private medical organization, or by a licensing authority? ☐ No ☐ Yes, explain ……....
17.	Does the PI, the study colleagues or their families have any financial relationship with the sponsor other than payment for the conduct of the study? ☐ No ☐ Yes, If Yes describe the relationship ……..
18.	Does the PI, the study colleagues or their families have any other personal considerations that may compromise, or have the appearance of compromising a researcher's professional judgment in conducting or reporting research? ☐ No ☐ Yes, If Yes describe it …….
19.	For this study, how many of the following will the PI supervise? Sub-investigators……. Study sites ……. ☐ NA
20.	How many (in total) of the following does the PI currently supervise? Ongoing studies…… Sub-investigators…… ☐ NA

21.	Type of facility at the research site: ☐ Health facility ☐ University ☐ Community ☐ Others, specify: …….....
22.	Clinical Monitor Name, if applicable: …….. **Contact Number: ……..E-mail: ……..**
23.	**For genetic study only,** indicate whether it involves any form of gene transfer ☐ Yes ☐ No If YES has the study been reviewed by: ○ NA ○ None ○ Bio-safety ○ Recombinant DNA Advisory boards
24.	**For study that involves sending of biological samples outside the country;** is there a Material Transfer Agreement? ☐ Yes ☐ No ☐ NA
25.	How long will the research data be stored by the PI? …years after closing the study.

26	IS THERE A **REQUEST FOR INFORMED CONSENT WAIVER**? ☐ Yes (**GOTO 26.2**) ☐ No	
	26.1. Does the informed consent include the following? (Check 26.1.1 through 26.1.2)	
	26.1.1.	**Information sheet**: ☐ Yes ☐ No
	26.1.2.	26.1.2.1. For participants ≥ 18 years: ☐ NA (If NA **GOTO 26.1.2.2**) 26.1.2.1.1. Informed Consent: ☐ Yes ☐ No
		26.1.2.2. For participants 12 -18 years: ☐ NA (If NA **GOTO 26.1.2.3**) 26.1.2.2.1. Informed Consent from the parent(s) or legal guardian: ☐ Yes ☐ No 26.1.2.2.2. Informed Assent from the participant: ☐ Yes ☐ No
		26.1.2.3. For participants 7 to <12 years: ☐ NA (If NA **GOTO 26.1.2.4**) 26.1.2.3.1. Informed Consent from the parent(s) or legal guardian: ☐ Yes ☐ No 26.1.2.3.2. Verbal Informed Assent from the participant: ☐ Yes ☐ No
		26.1.2.4. For participants <7 years: ☐ NA (If NA **GOTO 26.1.2.5**) 26.1.2.4.1. Informed Consent from the parent(s) or legal guardian: ☐ Yes ☐ No
		26.1.2.5. For participants who are incompetent to give informed consent: ☐ NA (**GOTO 26.1.2.6**) 26.1.2.5.1. Informed Consent from the parent(s) or legal guardian: ☐ Yes ☐ No 26.1.2.5.2. Informed Assent from the participant: ☐ Yes ☐ No
		26.1.2.6. If participants are illiterate: ☐ NA (If NA **GOTO 26.1.2.7**) 26.1.2.6.1. Provision for thumb impression: ☐ Yes ☐ No 26.1.2.6.2. Provision for witness: ☐ Yes ☐ No
		26.1.2.7. Is there a statement by the researcher or person taking consent declaring that the informed consent is appropriately administered: ☐ Yes ☐ No
	26.1.3.	Dzongkha version of 26.1.3.1. information sheet: ☐ Yes ☐ No 26.1.3.2. informed consent form: ☐ Yes ☐ No

	26.2. If there is a request for informed consent waiver, provide justifications:

27.	What precautions will be used to maintain the confidentiality of identifiable health information? ☐ Records will be kept in a secured location and only accessible to personnel involved in the study. ☐ Computer based files will only be made available to personnel involved in the study through the use of access privileges and passwords. ☐ Before accessing to any study-related information, personnel have to sign statements agreeing to protect the security and confidentiality of identifiable health information. ☐ Whenever feasible, identifiers will be removed from study-related information. ☐ Other, specify……..
28.	What kind of means will be used to recruit subjects for the study? ☐ Personal contact ☐ Referrals ☐ from database other than the PI's list ☐ Advertising (All recruitment materials must be approved by IRB before use.) ☐ Other, specify……
29.	Has the research study been disapproved or terminated by any other Research Board? ☐ No ☐ Yes, explain…….....
30.	**SIGNATURES:** _____ Date: …….. Principal Investigator _____ Date:…… Protocol Chairperson (if applicable) **COMPLETION:** _____ Date:…… Member Secretary, IRB

ANNEX 4
Form AF/04-008/01

Protocol Summary Sheet (Checklist of items)

Guidelines for filling up the protocol summary sheet or checklist of items:

1. Indicate the page number(s) of the main protocol in the right hand column.
2. If any of the section is not applicable then write 'NA' instead of the page number(s).

Sl.No	Protocol Sections or Items	Specify the page numbers of the main protocol
1.	**Study Title**	
2.	**Names and institutional affiliations** of the principal investigator and other investigators	
3.	**Project summary:** (Like the abstract of a research paper, the project summary, should be no more than 300 words and at the most a page long (font size 12, single spacing). Provided preferably on a separate page, it should summarize all the central elements of the protocol, for example the rationale, objectives, methods, populations, time frame, and expected outcomes. It should stand on its own, and not refer the reader to points in the project description.)	
4.	**Background and rationale**: (A clear statement of the justification for the study, its significance in development and in meeting the needs of the country /population in which the research is carried out, including summary of relevant literatures)	
5.	**Objectives** : (State specific objectives, including any pre-specified hypotheses)	
6.	**Study Design**: (A detailed description of the design of the trial or study. In the case of controlled clinical trials the description should include, but not be limited to, whether assignment to treatment groups will be randomized (including the method of randomization), and whether the study will be blinded (single blind, double blind), or open)	
7.	**Study setting**: (A brief description of the site(s) where the research is to be conducted, including information about the adequacy of facilities for the safe and appropriate conduct of the research, and relevant demographic and epidemiological information about the country or region or site; and relevant dates, including periods of recruitment, exposure, follow-up, and data collection.)	
8.	**Study Participants /Eligibility criteria**: (The criteria for inclusion or exclusion of potential participants, and justification for the exclusion of any groups on the basis of age, sex, social or economic factors, or for other reasons. The justification for involving as research participants children or adolescents, persons who are unable to give informed consent or vulnerable persons or groups, and a description of special measures to minimize risks to such persons)	
9.	**Sample size**: (Estimated number of participants needed to achieve study objectives. Mention how the sample size was determined, including clinical and statistical assumptions supporting any sample size calculations.)	
10.	**Recruitment**: (Strategies for achieving adequate participant enrolment to reach target sample size. Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. The process of	

	recruitment, e.g. advertisements, and the steps to be taken to protect privacy and confidentiality during recruitment)	
11.	**Interventions and outcomes**, if applicable: (Interventions for each group with sufficient detail to allow replication, including how and when they will be administered; Criteria for discontinuing or modifying allocated interventions for a given trial participant (e.g., drug dose change in response to harms, participant request, or improving/worsening disease); Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (e.g., drug tablet return, laboratory tests); Relevant concomitant care and interventions that are permitted or prohibited during the trial; Primary, secondary, and other outcomes, including the specific measurement variable (e.g., systolic blood pressure), analysis metric (e.g., change from baseline, final value, time to event), method of aggregation (e.g., median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended; Assignment of interventions (for controlled trials)	
12.	**Data collection**: (Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (e.g., duplicate measurements, training of assessors) and a description of study instruments (e.g., questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols. Methods of recording and reporting adverse events or reactions, and provisions for dealing with complications.	
13.	**Variables**: (Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable)	
14.	**Data sources/ measurement**: (For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group)	
15.	**Data management**: (Plans for data entry, coding, security, and storage, including any related processes to promote data quality (e.g., double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol)	
16.	**Data Analysis**: Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol Methods for any additional analyses (e.g., subgroup and adjusted analyses) Definition of analysis population relating to protocol non-adherence (e.g., as randomised analysis), and any statistical methods to handle missing data (e.g., multiple imputation)	
17.	**Research ethics**: (Plans for seeking IRB or other research ethics committee/institutional review board approval. The known or foreseen risks of adverse reactions, including the risks attached to each proposed intervention and to any drug, vaccine or procedure to be tested. The potential individual benefits of the research to participants and to others. The expected benefits of the research to the population, including new knowledge that the study might generate. For research carrying more than minimal risk of physical injury, details	

	of plans, including insurance coverage, to provide treatment for such injury, including the funding of treatment, and to provide compensation for research-related disability or death. Provision for continued access to study interventions that have demonstrated significant benefit, indicating its modalities, the parties involved in continued care and the organization responsible for paying for it, and for how long it will continue. For research on pregnant women, a plan, if appropriate, for monitoring the outcome of the pregnancy with regard to both the health of the woman and the short-term and long-term health of the child.)	
18.	**Protocol amendments**: (Plans for communicating important protocol modifications to relevant parties (e.g., investigators, IRB or other REC/IRBs, trial participants, trial registries, journals, regulators)	
19.	**Informed Consent / Informed Assent Process**: (State who will obtain informed consent or assent from potential participants or legal guardians, and how. Additional consent provisions for collection and use of participant data and biological specimens in future studies, if applicable. An account of any economic or other inducements or incentives to prospective participants to participate, such as offers of cash payments, gifts, or free services or facilities, and of any financial obligations assumed by the participants, such as payment for medical services. Plans and procedures, and the persons responsible, for communicating to participants information arising from the study (on harm or benefit, for example), or from other research on the same topic, that could affect participants' willingness to continue in the study. Plans to inform participants about the results of the study)	
20.	**Confidentiality**: (How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the study)	
21.	**Declaration of interests**: (State any financial and other competing interests for principal investigators for the overall study and each study site. Even if there is no COIs state that there is no COIs)	
22.	**Access to data**: (Statement of who will have access to the final study dataset, and disclosure of contractual agreements that limit such access for investigators)	
23.	**Ancillary and post-trial care**: (Provisions, if any, for ancillary and post-study care, and for compensation to those who suffer harm from study participation)	
24.	**Sponsor(s)/ Funding**: (Sources and types of financial, material, and other support. Provide the itemized budget details as well)	
25.	**Trial registration**, if applicable: Trial identifier and registry name. If not yet registered, name of intended registry.	
26.	**Appendixes**: (Provided the list of all appendixes, if applicable)	
27.	**Facilities**: (Provide the important facilities required/available for the study namely computers, laboratories, special equipment, etc.)	
28.	**Study Timeline**: (Gantt Chart showing major activities from proposal development to report dissemination phases of a research project)	
29.	**References**: List bibliographic references included in the proposal.	

Note: *Please don't forget to write dated version number in the protocol and all relevant documents to ensure that everyone refers to the same version of a given document as well as to ensure that what is approved is what is eventually put to use.*

ANNEX 5
Form AF/05-008/01

APPLICATION FORM for Initial Review of CASE STUDY / CASE SERIES

1. Protocol Number (*To be assigned by IRB Secretariat):*
2. Title: ……
3. Version No.: ……
4. Total number of cases: ……
5. PARTICULARS OF THE PRINCIPAL INVESTIGATOR (PI)

   Name: ……

   Address: ……

   Contact Number: …… Fax: ……

   E-mail: ……
6. CHARACTERISTICS of CASES:

   Age Range (Specify):

   Impaired: ☐ None ☐ Physically ☐ Cognitively ☐ Mentally

   Limitation: ☐ illiteracy ☐ Prisoners ☐ Hospitalized ☐ Nursing home

   ☐ Pregnancy ☐ Poor/uninsured ☐ Employees of study site

   ☐ Students or staff of the PI ☐ Military personnel

   ☐ Others vulnerable to coercion, specify……
7. Specify the site(s) of cases (Institution, Place and Country): .....
8. FINANCIAL DISCLOSURE: ☐ YES ☐ NO, why not? ...

   .....

   .....
9. **CO-INVESTIGATOR(S)**:

Name and Institution	Role in the study	Contact Number
1.		
2.		
3.		
4.		
5.		
6.		
7.		
8.		

10. Has the Principal Investigator (PI) ever been involved in or convicted of a crime, disciplined by a public or private medical organization, or by a licensing authority?

    ☐ No ☐ Yes, explain……

11. Does the PI, the study colleagues or their families have any financial relationship with the sponsor other than payment for the conduct of the study?
    ☐ No ☐ Yes, If Yes describe the relationship……..

12. Does the PI, the study colleagues or their families have any other personal considerations that may compromise, or have the appearance of compromising a researcher's professional judgment in reporting case(s)?
    ☐ No ☐ Yes, If Yes describe it ……

13. How long will the research data be stored by the PI? …….years after closing the study.
14. Is there a written permission to use the patient information for research from the patient or their parent(s)/legal guardian?
    ☐ Yes ☐ No
15. Is the identifiers removed from study-related information or report? ☐ Yes ☐ No
16. Has the case study been disapproved or terminated by any other Research Board?

    ☐ No ☐ Yes, explain…….....

SIGNATURES:

_____ Date: ……..
Principal Investigator

_____ Date:……
Protocol Chairperson (if applicable)

COMPLETION:

_____ Date:……
Member Secretary, IRB

CHAPTER 3.3

EXPEDITED REVIEW

SOP NUMBER: SOP/009/01

INSTITUTIONAL REVIEW BOARD
(IRB)

Khesar Gyalpo University of Medical Sciences of Bhutan

www.kgumsb.edu.bt

Effective Date: October 1, 2021
Supersedes: SOP/008/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 SOP shall be to provide criteria for determination of which study protocols can be reviewed through expedited process as well as instructions on management, review and approval of the **expedited** review

2. SCOPE

This SOP shall apply to the review and approval of study proposals with minimum risk to participants, protocol amendments or informed consent with minor changes of currently approved studies.

3. RESPONSIBILITY

The IRB Secretariat shall be responsible to define which study protocols shall be reviewed and approved through expedited channel. The Chairperson shall nominate two or more IRB members as the expedited reviewers to conduct the review.

4. FLOW CHART

No.	Activity	Responsibility
1.	Determine protocols for expedited review. ↓	IRB Member Secretary/ Chairperson
2	Nominate the expedited reviewers ↓	Chairperson
3.	Distribute the protocol packages to the reviewers ↓	IRB Member Secretary
4	Review the assigned protocols ↓	Reviewers
5. 6.	Communicate the review result to the investigator. ↓ Report the expedited review during the IRB meeting ↓	IRB Member Secretary IRB Member Secretary
7	Storage of the documents	IRB Member Secretary

5. DETAILED INSTRUCTIONS

5.1. Determine protocols for expedited review.

IRB Chairperson determines the expedited review for non–significant risk and IRB secretary determines the administrative issues for the study to be qualified for expedited review according to the following criteria:

5.1.1. Initial review

5.1.1.1. Proposals involve interviewing of a non-confidential nature (not of a private e.g. relate to sexual preference etc.), not likely to harm the status or interests of the individual and not likely to offend the sensibilities of the people involved.

5.1.1.2. Those that involve collection of small amounts of blood samples (and not too frequent) e.g. by finger, heel or ear stick except with sensitive issues which involves social risk and/or vulnerable population.

5.1.1.3. Those that involve collection of biological specimens for research purposes by non-invasive means (e.g. collection of body fluids or excreta non-invasively, collection of hair or nail clippings in a non-disfiguring or non-threatening manner) except with sensitive issues which involves social risk and/or vulnerable population

5.1.1.4. Collection of data for research purposes through non-invasive procedures (not involving general anaesthesia or sedation) routinely employed in clinical practice and using medical devices which have been already approved for use. Examples of such procedures include collection of data through application of EEG or ECG electrodes, acoustic testing, tests using the Doppler principle, non-invasive blood pressure and other routine clinical measurements, exercise tolerance etc except with sensitive issues which involves social risk and/or vulnerable population. However procedures involving the use of x-rays or microwaves are NOT Recommended for expedited review.

5.1.1.5. Research involving data, documents or specimens that have been already collected or shall be collected for ongoing medical treatment or diagnosis except with sensitive issues which involves social risk and/or vulnerable population

5.1.2. Minor modification /amendment of protocol

5.1.2.1. Administrative revisions such as correction of typing errors; addition or deletion of non-procedural items such as the addition of study personnel names, laboratories, etc.; non-significant risk research activity; and when the research activity includes only minor changes from previously approved protocol. In such cases the Chairperson can review and approve it.

5.1.3. Continuing review of protocol

5.1.3.1. Continuing review of the study may not be conducted through an expedited review procedure, unless:

1. The study was eligible for, and initially reviewed by, an expedited review procedure; or
2. The study has changed such that only the activities that are eligible for expedited review are remaining; or
3. Continuing review with no modifications /amendment to the original protocol and no additional risks has been identified. In the third condition, the Chairperson can review the report and approve the continuation of the study for appropriate time except with sensitive issues which involves social risk and/or vulnerable population.

5.1.4. Review of previously reviewed protocol

5.1.4.1. Review of protocols that have previously gone through Full Board Review can be expedited unless otherwise specified in the minutes of the meeting. In such cases the IRB Secretary can directly send the revised protocol and related documents to the Primary Reviewer(s) for review.

5.1.4.2. Review of protocols approved with recommendations in previous submission can be expedited only with minor modifications of the protocol. In such cases the Chairperson can review and approve it unless otherwise specified in the minutes of the meeting.

5.1.4.3. If the protocol satisfied any of the criteria for **expedited** review, the secretariat shall send the protocol to the Chairperson.

5.2. Nominate the expedited reviewers

5.2.1. Chairperson nominates 2 or more IRB members with related expertise to review the protocol.

5.2.2. The selected members are normally those who reviewed and recommended the previous version of that protocol, if it is not submitted for the first time.

5.3. Send the protocol packages to the reviewers

5.3.1. The secretariat shall send the protocol packages (study protocol with all the attached documents) and the study assessment form (*AF/01-012/01*) to the selected members.

5.4. Review the assigned protocols

5.4.1. Carry out the expedited review on the complete protocol package.

5.4.2. The review may be made either by circulation of comments, telephone discussion or meeting.

5.4.3. THE EXPEDITED REVIEW SHALL NOT TAKE LONGER THAN TWO WEEKS

5.4.3.1. The reviewers shall submit the review forms within five working days.

5.4.4. The reviewers forward their comments to the Secretariat.

5.4.5. If consensus cannot be reached among the expedited reviewers, the chairperson can either take the final call or refer the proposal for a full board review.

5.5. Communicate the review result to the investigator

5.5.1. The Secretariat prepares an action letter according to the review report and sends it with the protocol package to the Chairperson.

5.5.2. The Chairperson approves the expedited review by signing on the letter

5.5.3. The Secretariat sends the letter to the investigator

5.6. Report the expedited review to the full board

5.6.1. List the expedited review items in the meeting agenda and report the review results to the full board during the meeting.

5.6.2. If any board member raises concern about any of the proposals presented to it as expedited review, then that proposal shall undergo a regular review. The previous review decision shall be recalled.

5.7. Storage of the document

5.7.1. The review report and the related meeting minutes are kept with the protocol file.

5.7.2. The copy of the action letter is kept in the Correspondence File.

5.7.3. If the protocol is approved, assign an approval number in sequential order.

Example: A protocol, submitted in November of the year 2021 and it is the 12th protocol approved by the IRB in that year, would be numbered as 012/11-21.

5.7.4. Fill in the number of the Application Review Form (*AF/01-008/01*). Place the original documents of the Application Review and the Assessment Forms in sequence of approval number in the Approved file.

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

6. GLOSSARY

Administrative Documents	Documents include official minutes of board meetings as described in Standard Operating Procedures, both historical and Master Files as described in SOP/027/01
Expedited approval	An IRB approval granted only by the Chairperson of IRB for minor changes to current IRB approved research activities and for research which involves no more than minimal risk.
Expedited review	A review process by only two or more designated IRB members who then report the decision to the full board meeting. An expedited review is a *speedy* one for minor *changes to the approved protocol* and for *research proposal* with *minimal risk in nature*.

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. Code of Federal Regulation (CFR) 21.

7.4. Associated SOPs: SOP/008/01 and SOP/028/01

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

www.kgumsb.edu.bt

Effective Date: October 1, 2021
Supersedes: SOP/010/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

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:

CHAPTER 3.5

REVIEW OF MEDICAL DEVICE STUDY

SOP NUMBER: SOP/011/01

INSTITUTIONAL REVIEW BOARD
(IRB)

Khesar Gyalpo University of Medical Sciences of Bhutan

www.kgumsb.edu.bt

Effective Date: October 1, 2021	
Supersedes: SOP/010/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 provide instructions for review and approval of medical device studies submitted to the IRB.

2. SCOPE

This SOP shall apply to the submission and the review processes of protocols involving the study of new medical devices in human subjects.

3. RESPONSIBILITY

During the review of medical device studies, the IRB may make some different decision than those made during the review of drug studies. The IRB shall determine if the proposed investigation has *Significant Risk (SR)* or *Non-significant Risk (NSR)*, and then the IRB shall decide if the investigation is approved or not. In determining *SR* or *NSR*, the IRB shall review all information submitted by the sponsor.

The IRB shall consider the nature of the harm that may result from the use of the device. If a device being investigated might cause significant harm to any one of the participants, the study shall be considered *SR*. In deciding if a device presents significant or non-significant risks, the IRB shall consider the device's total risks, not those compared with the risks of alternative devices or procedures. If the device is used in conjunction with a procedure involving risk, the IRB shall consider the risks of the procedure in conjunction with the risks of the device. The IRB may also consult with the regulatory agency to form its opinion.

The IRB may agree or disagree with the sponsor's initial *NSR* assessment. If the IRB agrees with the sponsor's initial *NSR* assessment and approves the study, the study may begin without submission of an IDE (Investigational Device Exemption) application to the regulatory agency. If the IRB disagrees, the sponsor shall notify the regulatory agency that an *SR* determination has been made. The study can be conducted as an *SR* investigation following regulatory approval of an IDE application.

4. FLOW CHART

No.	Activity	Responsibility
1	Submission of documents ↓	Applicant/IRB Secretariat
2	Activities before a committee meeting ↓	IRB Secretariat / members / Reviewers
3	Activities during a committee meeting ↓	IRB members / Secretariat / Chairperson
4	Activities after the meeting ↓	IRB Secretariat
5	Notify the investigators ↓	IRB Secretariat
6	Storage of the documents	IRB Secretariat

5. DETAILED INSTRUCTIONS

5.1. Submission of documents

5.1.1. Receive a new medical device study.

5.1.2. Check the submitted package for completeness.

5.1.3. Document the checking procedure by completing a checklist form (AF/01-008/01 Contents of a submitted package).

5.1.4. At a minimum, the IRB shall receive the following documents prior to review/approval of a medical device study:

- 5.1.4.1. Proposed investigational plan
- 5.1.4.2. Informed consent form
- 5.1.4.3. Description of the device
- 5.1.4.4. Description of participant selection criteria
- 5.1.4.5. Monitoring procedures
- 5.1.4.6. Reports of prior investigations conducted with the device
- 5.1.4.7. Investigator's Curriculum Vitae
- 5.1.4.8. Investigator's professional license(s)
- 5.1.4.9. Risk assessment data / information
- 5.1.4.10. Statistics used in making the risk determination.
- 5.1.4.11. Application for Review (AF/01-008/01)
- 5.1.4.12. Document Received Form (AF/02-008/01
- 5.1.4.13. Copies of all labelling for investigational use only

5.1.5. The sponsor shall inform the IRB whether other EC have reviewed the proposed study and what determination was made.

5.1.6. The sponsor shall inform the IRB of the Agency's assessment of the device's risk if such an assessment has been made.

5.1.7. If the Sponsor believes the study is NSR, supporting information shall be submitted.

5.1.8. Contact the applicant to submit additional information or documents, if the application is complete.

5.2. Before the Committee meeting

5.2.1. The Chairperson nominates and assigns two to three reviewers to review the study. The reviewers shall review the study according to the assessment form (AF/01-012/01).

5.2.2. IRB Member Secretary shall prepare the documents for distribution to each IRB member.

5.2.3. IRB Member Secretary shall send the documents to each IRB member.

5.2.4. Place the new medical device study on the meeting agenda.

5.3. During the Committee meeting

5.3.1. Reviewers present a brief oral or written summary of the study design.

5.3.2. The Chairperson shall open discussion about whether the study is SR or NSR (see examples in ANNEX 1, *AF/01-008/01*).

5.3.3. The Chairperson shall lead discussion about each document under consideration (e.g. protocol, informed consent, investigators and site qualifications, advertisements).

5.3.4. Decide the degree of risk.

5.3.5. Consider whether or not the study shall be approved.

5.3.6. The Chairperson shall call for a separate vote on each element in review. The IRB votes to either:

- 5.3.6.1. Approve the study to start as presented with no modifications
- 5.3.6.2. Approve the study to start with minor modifications to item(s) noted at the convened meeting and to be followed-up by the Secretariat and Chairperson, after receiving the requested modifications

5.3.6.3. Require major modifications and/or request further information to be resubmitted and subjected to review in the next full Board meeting.

5.3.6.4. Disapprove the study and state the reason.

5.3.7. Record the vote of risk assessment in the decision form (*AF/04-012/01*) and the meeting minutes (*AF/03-022/01*).

5.3.8. Note the recommendations for changes to the protocol and/or informed consent recommended by IRB members in the minutes as 'with modifications made by IRB' and shall be communicated to the investigator.

5.3.9. Determine the frequency of Continuing Review for the approved study.

5.4. After the meeting

5.4.1. Prepare meeting minutes

5.4.1.1. Follow the procedure in SOP/022/01

5.4.2. Notify the investigators

5.4.2.1. The Secretariat shall send an action letter along with the approved documents to the investigator. The letter contains, at a minimum, a listing of each document approved, the date set by the IRB for frequency of continuing review, and a review of other obligations and expectations from the investigator throughout the course of the study.

5.4.2.2. If the committee votes not to approve the study, the Chairperson or Secretariat shall immediately notify the investigator in writing of the decision and the reason for disapproving the study. If the investigator wishes to appeal this decision, he or she may do so by contacting the IRB. This process is stated in the action letter provided to the investigator.

5.4.2.3. If the IRB votes to require modifications to any of the documents, the Secretariat shall either generate the revisions to the documents, or send a written request of the specific changes to the investigator asking him or her to make the necessary changes and resubmit the documents to the IRB.

5.4.3. Storage of the documents

5.4.3.1. Prepare an appropriate label.

5.4.3.2. Store the document packages in the shelf for active files.

6. GLOSSARY

Medical Device	Any health care product that does not achieve any of its intended purposes by chemical action or by being metabolized. Medical devices include items such as diagnostic test kits, crutches, electrodes, prescribed beds, pacemakers, arterial grafts, intra-ocular lenses, and orthopaedic pins. Medical devices also include diagnostic aids such as reagents and test kits for in vitro diagnosis of disease and other conditions (for example, pregnancy).
Investigational Medical Device	A medical device which is the object of clinical research to determine its safety or effectiveness.
Investigational Device Exemption (IDE)	Investigational Device Exemption allows the investigational device to be used in a clinical study in order to collect safety and effectiveness data required to support a Pre-market Approval (PMA) application or a Pre-market Notification submission to the Drug Regulatory Authority. Clinical

	studies are most often conducted to support a PMA. Only a small percentage of studies require clinical data to support the application. Investigational use also includes clinical evaluation of certain modifications or new intended uses of legally marketed devices. All clinical evaluations of investigational devices, unless exempt, shall have an approved IDE before the study is initiated. An IDE is approved by an IRB. If the study involves a significant risk device, the IDE shall also be approved by the Drug Regulatory Authority. An approved IDE permits a device to be shipped lawfully for the purpose of conducting investigations of the device without complying with other requirements that would apply to devices in commercial distribution. Sponsors need not submit a PMA (Pre-Market Approval) or Pre-market Notification, register their establishment, or lists the device while the device is under investigation. Sponsors of IDE's are also exempt from the Quality System (QS) Regulation except for the requirements for design control.
New Study	A study protocol including the informed consent, investigator qualifications, and advertisements presented to the IRB for approval for the first time. This includes re-application for those studies denied approval by IRB.
Non-significant Risk Device (NSR)	An investigational device that does not pose a significant risk. A list of examples is found in ANNEX 1.
Risk	The probability of harm or discomfort to study participants. Acceptable risk differs depending on the conditions for which the product is being tested. A product for sore throat, for example, shall be expected to have a low incidence of side effects. However, unpleasant side effects may be an acceptable risk when testing a promising treatment for a life-threatening illness.
Significant Risk Device (SR)	An investigational device that: (1) is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of the participant, (2) is purported or represented to be for a use in supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of the participant, (3) is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety, or welfare of the participant, or (4) Otherwise presents a potential for serious risk to the health, safety, or welfare of the participant. A list of examples is found in ANNEX 2.

7. REFERENCES

7.1. Code of Federal Regulation (CFR) 21, Volume 8, Part 812, April 2003, Food and Drug Administration, U.S. Government Printing Office via GPO Access

7.2. Associated SOP: SOP/008/01-SOP/010/01 and SOP/022/01

8. ANNEX

ANNEX 1 AF/01-011/01 Examples of Non-significant Risk Device Studies

ANNEX 2 AF/02-011/01 Examples of Significant Risk Device Studies

ANNEX 1
AF/01-011/01

NON-SIGNIFICANT RISK DEVICE STUDIES

EXAMPLES:

- Bio-stimulation Lasers for treatment of pain
- Caries Removal Solution
- Daily Wear Contact Lenses and Associated Cleaners and Solutions
- Dental Filling Materials, Cushions or Pads made from traditional materials and designs
- Denture Repair Kits and Re-aligners
- Gynecologic Laparoscope and Accessories at power levels established prior to May 28, 1976 (excluding use in female sterilization)
- Externally worn Monitor for Insulin Reactions
- Jaundice Monitor for Infants
- Magnetic Resonance Imaging (MRI) Devices within specified physical parameters
- Menstrual Pads
- Menstrual Tampons of “old” materials (used prior to May 28, 1976)
- Non-implantable Male Reproductive Aids
- Ob/Gyn Diagnostic Ultrasound (within specified parameters)
- Transcutaneous Electric Nerve Stimulation (TENS) Devices for treatment of pain
- Wound Dressings, excluding absorbable hemostatic devices and dressings

ANNEX 2
AF/02-011/01

SIGNIFICANT RISK DEVICE STUDIES

General Medical Use

Catheters:

- Cardiology – diagnostic, treatment, transluminal coronary angioplasty, intra-aortic ballloon with control system
- Gastroenterology and Urology – biliary and urologic
- General Hospital – long-term percutaneous, implanted, subcutaneous and intravascular
- Neurology – cerebrovascular, occlusion balloon
- Collagen Implant Material for use in ear, nose and throat, orthopedics and plastic surgery
- Lasers for use in Ob/Gyn, cardiology, gastro-enterology, urology, pulmonary, ophthalmology and neurology
- Tissue Adhesives for use in neurology, gastro-enterology, ophthalmology, general and plastic surgery, and cardiology

Anesthesiology

- Respiratory Ventilators
- Electro-anesthesia Apparatus
- Gas Machines for Anesthesia or Analgesia
- High Frequency Jet Ventilators greater than 150 BPM

Cardiovascular

- Arterial Embolization Device
- Artificial Heart, permanent implant and short term use
- Cardiac Bypass Systems: oxygenator, cardiopulmonary blood pump, ventricular assist devices
- Cardiac Pacemaker/Pulse Generator: implantable, external transcutaneous, antitachycardia, esophageal
- Cardiovascular/Intravascular Filters
- Coronary Artery Retroperfusion System
- DC-Defibrillators
- Implantable Cardioverters
- Laser Coronary Angioplasty Device
- Pacemaker Programmer
- Percutaneous Conduction Tissue Ablation Electrode
- Replacement Heart Valve
- Vascular and Arterial Graft Prostheses

Dental

- Endosseous Implant

Ear, Nose and Throat

- Cochlear Implant
- Total Ossicular Prosthesis Replacement
- Gastroenterology and Urology
- Anastomosis Device
- Endoscope and/or Accessories

- Extracorporeal Hyperthermia System
- Extrocorporeal Photophersis System
- Extracorporeal Shock-Wave Lithotriptor
- Kidney Perfusion System
- Mechanical/Hydraulic Impotence and Incontinence Devices
- Implantable Penile Prosthesis
- Peritoneal Shunt

General and Plastic Surgery

- Absorbable Hemostatic Agents
- Artificial Skin
- Injectable Silicone
- Implantable Prostheses: chin, nose, cheek, ear
- Sutures

General Hospital

- Infusion Pumps: Implantable and closed-loop, depending on infused drug
- Implantable Vascular Access Devices

Neurology

- Hydrocephalus Shunts
- Implanted Intracerebral/Subcortical Stimulator
- Implanted Intracranial Pressure Monitor
- Impalnted Spinal Cord and Nerve Stimulators and Electrodes

Obstetrics and Gynecology

- Cervical Dilator
- Chorionic Villus Sampling Catheter, phase II (pregnancy continued to term)
- Contraceptive Devices: tubal occlusion, cervical cap, diaphragm, intrauterine device (IUD) and introducer, and sponge

Ophthalmics

- Extended Wear Contacts Lens
- Intraocular Lens (investigations subject to 21 CFR 813)
- Eye Valve Implant
- Retinal Reattachment Systems: sulfur hexafluoride, silicone oil, tacks, perfluoropropane

Orthopedics

- Implantable Prostheses: ligament, tendon, hip, knee, finger
- Bone Growth Stimulator
- Calcium Tri-Phosphate/Hydroxyapatite Ceramics
- Xenografts

Radiology

- Hyperthermia Systems and Applicators

CHAPTER 3.6

USE OF STUDY ASSESSMENT FORM

SOP NUMBER: SOP/012/01

INSTITUTIONAL REVIEW BOARD
(IRB)

Khesar Gyalpo University of Medical Sciences of Bhutan

www.kgumsb.edu.bt

Effective Date: October 1, 2021
Supersedes: SOP/011/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

This SOP describes how the IRB members shall use the assessment forms when reviewing the study protocols initially submitted for approval. The Assessment Form (AF/01-012/01) is designed to standardize the review process and to facilitate reporting, recommendation and comments given to each individual protocol.

2. SCOPE

This SOP shall apply to the review and assessment of all protocols submitted for initial review and approval from the IRB. The specific questions in the Assessment Form shall be adequately addressed in the protocol itself and/or protocol-related documents under review.
Relevant points made during discussion and deliberation about a specific protocol shall be recorded on the form.

The decision reached by the board and the reasons for its decision is recorded on the Decision Form (AF/04-012/01).

3. RESPONSIBILITY

The reviewers shall be responsible to fill the assessment form along with decision and comments they might have after reviewing each study protocol. The IRB Secretariat shall be responsible for recording and filing the decision made by the IRB, relevant points and deliberation about a specific protocol, including the reasons for that decision on the decision from, ANNEX – AF/04-012/01. The Chairperson of the IRB shall sign and date to approve the decision in the form.

4. FLOW CHART

No.	Activity	Responsibility
1	Summarize the protocol in an Assessment Form ↓	IRB Secretariat
2	Use the Assessment Form to guide the review ↓	IRB members / Reviewers
3	Record the review decision on the Assessment Report ↓	IRB members / Reviewers
4	Gather Assessment Reports	IRB Secretariat
5	Record the IRB Decision on the Decision Form	IRB Secretariat

5. DETAILED INSTRUCTIONS

5.1. Summarize the protocol in an Assessment Form.

Record general information about the protocol in the form, Annex- AF/01-012/01 such as:

5.1.1. Title of the protocol
5.1.2. Protocol number and date
5.1.3. Principal Investigators, license & contact number
5.1.4. Co-investigators & contact number
5.1.5. Funding agency & contact number
5.1.6. Study types
5.1.7. Duration of the study
5.1.8. Status of the protocol – New / Revised / Amended
5.1.9. Review status – Regular / Expedited / Emergency
5.1.10. Reviewer's name

5.1.11. Objective and description of the Study

5.2. Use the Assessment Form to guide the review

Use the Assessment Form to review the protocol and the study related documents, and make the comments on the form.

5.2.1. Review the study protocol (see details in Annex 3).

5.2.1.1. Need for human participants for study
5.2.1.2. Objectives of the study
5.2.1.3. Review of literature
5.2.1.4. Sample size
5.2.1.5. Methodology and data management
5.2.1.6. Inclusion/exclusion criteria
5.2.1.7. Control arms (placebo, if any)
5.2.1.8. Withdrawal or discontinuation criteria

5.2.2. Examine the qualification of investigators and of study sites.

5.2.2.1. Consider whether study and training background of the participating investigators relate to the study.
5.2.2.2. Examine disclosure or declaration of potential conflicts of interest
5.2.2.3. Availability of facilities and infrastructure at study sites to accommodate the study.
5.2.2.4. Non-physician principal investigators (PI) shall be advised by a physician when necessary.

5.2.3. Review study participation (see guidance on ANNEX 7).

5.2.3.1. Voluntary, non-coercive recruitment/participation/withdrawal
5.2.3.2. Procedures for obtaining informed consent
5.2.3.3. Contents of the patient information sheet - title, objective, study design and procedures
5.2.3.4. Contents and language of the informed consent document
5.2.3.5. Translation of the informed consent document in the local language used – simple and easy to understand by general public
5.2.3.6. Contact persons with address and phone numbers for questions about subject's rights and study or injury
5.2.3.7. Privacy and confidentiality
5.2.3.8. Risks and discomforts – physical / mental / social
5.2.3.9. Alternative treatment
5.2.3.10. Benefits – to participants and to others
5.2.3.11. Compensation for participation / for injury– reasonable / unreasonable
5.2.3.12. Involvement of vulnerable participants
5.2.3.13. Provisions for medical/psychosocial support
5.2.3.14. Treatment for study related injuries
5.2.3.15. Use of biological materials
5.2.3.16. New Findings / information
5.2.3.17. No waiver of rights statement
5.2.3.18. Authorization or Release of information
5.2.3.19. Copy of signed and dated consent form
5.2.3.20. Signatures with dates of participant, person conducting informed consent discussion, investigator and witness

5.2.4. Examine community involvement and impact.

5.2.4.1. Community consultation

5.2.4.2. Involvement of local researchers and institutions in the protocol design, analysis and publication of the results

5.2.4.3. Contribution to development of local capacity for research and treatment

5.2.4.4. Benefit to local communities

5.2.4.5. Availability of study results

5.3. Record the review decision on the Assessment Report

5.3.1. Get the assessment report form, Annex- AF/03-012/01

5.3.2. Record the decision by marking in the desired block any of the following: "Approved, Approved with recommendation, Solicited for Resubmission, or Disapproved."

5.3.3. Include comments, suggestion and reason for disapproval.

5.3.4. Check the completeness and correctness of the assessment form.

5.3.5. Sign and date the decision form.

5.3.6. Give or send the complete forms to the IRB Secretariat *2 days* before the board meeting.

5.4. Gather the assessment reports.

5.4.1. Collect the assessment forms and the review result from each reviewer.

5.4.2. Organize the forms in order.

5.4.3. Summarize the comments, suggestions, and opinions of each study in the meeting agenda.

5.4.4. Follow SOP/021/01 Preparation of meeting agenda and minutes.

5.5. Record the IRB decision on the decision form

5.5.1. Get the IRB's decision from, ANNEX – AF/04-012/01

5.5.2. Complete the information. (by the Secretariat)

5.5.3. List participating members and their votes.

5.5.4. Summarize the guidance, advice and decision reached by the IRB members.

5.5.5. Sign and date the document by the Chairperson of the IRB.

5.5.6. Make a copy of the completed decision form.

5.5.7. Keep the original copy in the file labelled "IRB's decision".

5.5.8. Keep the copy of the decision form with the study protocol

5.5.9. Return the file and the protocol to the appropriate shelves.

6. GLOSSARY

Study Assessment Form	An official record that documents the protocol review process.
Document	Document may be of any forms, e.g., paper, electronic mail (e-mail), faxes, audio or video tape, etc.
Pre-clinical study	Animal and *in vitro* studies provide information on possible toxicities and mechanisms of action, and starting doses for human studies.
Vulnerable subjects	A vulnerable category of subjects includes children, prisoners, pregnant women, handicapped or mentally disabled persons, refugees, displaced persons and economically or educationally

	disadvantaged persons, who are likely to be vulnerable to coercion or undue influence.	
Categories of Risk	Type of risk	Definition/description
	Less than minimal risk (Level I)	Probability of harm or discomfort anticipated in the research is nil or not expected. For example, research on anonymous or non-identified data/samples, data available in the public domain, meta-analysis, etc.
	Minimal risk (Level II)	Probability of harm or discomfort anticipated in the research is not greater than that ordinarily encountered in routine daily life activities of an average healthy individual or general population or during the performance of routine tests where occurrence of serious harm or an adverse event (AE) is unlikely. Examples include research involving routine questioning or history taking, observing, physical examination, chest X-ray, obtaining body fluids without invasive intervention, such as hair, saliva or urine samples, etc.
	Minor increase over minimal risk or Low risk (Level III)	Increment in probability of harm or discomfort is only a little more than the minimal risk threshold. This may present in situations such as routine research on children and adolescents; research on persons incapable of giving consent; delaying or withholding a proven intervention or standard of care in a control or placebo group during randomized trials; use of minimally invasive procedures that might cause no more than brief pain or tenderness, small bruises or scars, or very slight, temporary distress, such as drawing a small sample of blood for testing; trying a new diagnostic technique in pregnant and breastfeeding women, etc. Such research should have a social value. Use of personal identifiable data in research also imposes indirect risks. Social risks, psychological harm and discomfort may also fall in this category.
	More than minimal risk or High risk (Level IV)	Probability of harm or discomfort anticipated in the research is invasive and greater than minimal risk. Examples include research involving any interventional study using a drug, device or invasive procedure such as lumbar puncture, lung or liver biopsy, endoscopic procedure, intravenous sedation for diagnostic procedures, etc.

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. Ethical Guidelines for Biomedical research on Human Subjects, 2000.

7.4. Cavazos N., Forster D., and Bowen A.J., Ethical Concerns in Placebo-controlled studies: An Analytical Approach, Drug Information Journal 36(2) 2002: pgs 249-259, via WIRB documents

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8. ANNEX

ANNEX 1	AF/01-012/01	Study Assessment Form (5 pages)
ANNEX 2	AF/02-012/01	Study Assessment Form for case studies and case series
ANNEX 3	AF/03-012/01	Informed Consent Assessment Form
ANNEX 4	AF/03-012/01	Assessment Report Form
ANNEX 5	AF/04-012/01	IRB's Decision
ANNEX 6	AF/05-012/01	Action letter templates
ANNEX 7	AF/06-012/01	Approval Letter Templates
ANNEX 8		Guidance for reviewing a study protocol
ANNEX 9		Informed Consent Process
ANNEX 10		Informed consent Form (ADAPTED FROM WHO-GUIDELINE)
ANNEX 11		Guides to Placebo Justification
ANNEX 12		Criteria for Research Protocol Approval

ANNEX 1

AF/01-012/01 **Study Assessment Form**

Protocol Number:	
Protocol Title :	
Protocol: Version No.... Dated.....	**Informed Consent:** Version No..... Dated.....
Principal Investigators: **Institute**:	
Co-investigator(s):	
Funding Agency:	
Duration of the Study: (From protocol development to report dissemination)	
Start Date of Data Collection:	**Completion Date** of Data Collection:

Type of the Study (Tick all relevant):

☐ Intervention ☐ Epidemiology ☐ Observation
☐ Document based ☐ Individual based ☐ Genetic
☐ Social Survey ☐ Others, specify…….

Description of the Study in brief: (Mark all that applicable to the study)

☐ Randomized ☐ Stratified Randomized ☐ Open-labeled
☐ Double blinded ☐ Placebo controlled ☐ Treatment controlled
☐ Cross-over ☐ Parallel ☐ Interim Analysis
☐ Use of Tissue samples ☐ Use of Blood samples ☐ Use of genetic materials
☐ Multicenter study ☐ Screening ☐ Descriptive
☐ Others, specify …….

Study Objectives: ……
……
……
……
……
……
……

Review Status: ☐ Full board ☐ Expedited ☐ Emergency

Mark and comment on whatever items applicable to the study.		
Study Protocol – Scientific issues		
1.	Objectives of the Study ☐ clear ☐ unclear	What should be improved?
2.	Need for Human Subjects. ☐ Yes ☐ No (Note: Refer SOP/007/03 for more details on the definition of human subject)	
3.	Methodology: (Study design, sampling methodology, Data collection and analysis plan) ☐ clear ☐ unclear	
4.	Background Information and Data ☐ sufficient ☐ insufficient	
5.	Sufficient number of participants? ☐ Yes ☐ No (Note: For quantitative study, is sample size calculation details provided?)	
6.	Inclusion Criteria ☐ appropriate ☐ inappropriate ☐ Not provided	
7.	Exclusion Criteria ☐ appropriate ☐ inappropriate ☐ Not provided	
8.	Discontinuation and Withdrawal Criteria ☐ appropriate ☐ inappropriate ☐ Not provided (Note: The intervention(s) has to be discontinued and withdrawn if there is SAE/AE and there has to be clear criteria for such discontinuation and withdrawal of the intervention(s).	
9.	Data collection tools (such as Questionnaire, Guidelines, Manuals, Forms) ☐ appropriate ☐ inappropriate ☐ Not provided	
Qualifications of Investigators and study sites		

10.	a. Are Qualification and experience of the Participating Investigators appropriate? ☐ Yes ☐ No ☐ CV not attached	
	b. For Clinical Trails only, does the PI and/or Co-PI has proof of GCP training ☐ Yes ☐ No ☐ Proof not attached ☐ NA (Note: Usually the GCP training certificates are valid for only 2-3 years. Check the validity of the certificate)	
11.	Facilities and infrastructure of Participating Sites ☐ Appropriate ☐ Inappropriate ☐ Site not mentioned	
12.	Disclosure or Declaration of Potential Conflicts of Interest ☐ Yes ☐ No (Note: Refer serial number 17 of the "AF/01-009/05 APPLICATION FORM for INITIAL REVIEW")	
13.	Is there a Physician if the PI is non Physician ☐ Yes ☐ No ☐ Not applicable	
Study Participation- Ethical Issues		
14.	Categories of Risk ☐ Less than minimal risk (Level I) ☐ Minimal risk (Level II) ☐ Minor increase over minimal risk or Low risk (Level III) ☐ More than minimal risk or High risk (Level IV) (Note: Level I - Probability of harm or discomfort anticipated in the research is nil or not expected. Level II - Probability of harm or discomfort anticipated in the research is not greater than that ordinarily encountered in routine daily life activities of an average healthy individual or general population or during the performance of routine tests where occurrence of serious harm or an adverse event (AE) is unlikely. Level III - Increment in probability of harm or discomfort is only a little more than the minimal risk threshold. Level IV - Probability of harm or discomfort anticipated in the research is invasive and greater than minimal risk. Refer SOP/12 for definition/description of Categories of Risk)	

15.	Risks and Benefits Assessment ☐ acceptable ☐ unacceptable (Note: The reviewers shall assess the risks and benefits of the study. Comment on how to protect vulnerable subjects, level of risks, identification of types of risks (e.g. placebo, clinical or social risk, etc.), benefits: benefits to participants, benefits to society, risk/benefit ratio)	
16.	Involvement of Vulnerable Participants ☐ Yes ☐ No (Note: Refer Glossary in the SOP/12 or section 5.1.10 of Chapter 11 for the definition of vulnerable participants.)	
17.	Voluntary, Non-Coercive Recruitment of Participants ☐ Yes ☐ No ☐ NA	
18.	Are blood/tissue samples sent abroad? ☐ Yes ☐ No (Note: If 'Yes', review the Material Transport Agreement. For details refer SOP/)	
19.	Privacy & Confidentiality ☐ Yes ☐ No (Note: Privacy refers to persons and their interest in controlling access to themselves. Confidentiality refers to agreements with the participant about how data are to be handled.)	
20.	Inducement for Participation ☐ Unlikely ☐ Likely (Note: Among other things like information sheet and examine the budget details)	
21.	Provision for Medical / Psychosocial Support ☐ appropriate ☐ inappropriate ☐ Not mentioned ☐ NA	
22.	Provision for Treatment of Study-Related Injuries ☐ appropriate ☐ inappropriate ☐ Not mentioned ☐ NA	
23.	Provision for Compensation ☐ appropriate ☐ inappropriate ☐ NA	
Community involvement and Impact		

24.	Community Consultation ☐ Yes ☐ No ☐ NA (Note: Community is a group of people living in the same place or having a particular characteristic in common. E.g., epilepsy population, Bhutanese community in Australia, etc.)	
25.	Involvement of Local Researchers and Institution in the Protocol Design, Analysis and Publication of Results ☐ Yes ☐ No	
26.	Contribution to Development of Local Capacity for Research and Treatment ☐ Yes ☐ No	
27.	Benefit to Local Communities ☐ Yes ☐ No	
28.	Availability of similar Study / Results ☐ Yes ☐ No (Note: Refer the list of protocols approved by IRB besides doing literature search online)	

Reviewer's Name and Signature: _____

Date: _____

ANNEX 2
AF/02-012/01 Study Assessment Form for Case Study and Case Series

Protocol Number:
Study Title :
Draft Report or Protocol: Version No... Dated
Principal Investigator(s): **Institute**:
Co – investigator(s):
Funding Agency:
Description of the Case Study in brief:
Review Status: ☐ Full board ☐ Expedited ☐ Emergency

Mark and comment on whatever items are applicable to the study.		
Scientific issues		
1	Is the case or case series report or protocol scientifically sound ☐ Yes ☐ No	
Qualifications of Investigator(s) or Author(s)		
2	Are Qualification and experience of the Participating Investigators appropriate? ☐ Yes ☐ No ☐ CV not attached	
3	Disclosure or Declaration of Potential Conflict of Interests ☐ Yes ☐ No (**Note:** Refer serial number 11 and 12 of the "AF/05-008 APPLICATION FORM for Initial Review of CASE STUDY / CASE SERIES")	
Privacy and Confidentiality		

4	Is the personal identifiers removed from study-related information or report? ☐ Yes ☐ No ☐ NA	
5	(For prospective case or case series studies only) Is the issues of Privacy & Confidentiality adequately addressed in the protocol? ☐ Yes ☐ No ☐ NA (Note: Privacy refers to persons and their interest in controlling access to themselves. Confidentiality refers to agreements with the participant about how data are to be handled.)	
Informed Consent and/or Informed Assent		
6	Is there a written permission to use the patient information for research from the patient or their parent(s)/legal guardian? ☐ Yes ☐ No ☐ NA	
7	(For prospective case or case series studies only) Is there an Informed Consent documents submitted for review? ☐ Yes ☐ No ☐ NA (Note: For prospective case or case series studies, use AF/03-012 Informed Consent Assessment Form to assess the Informed Consent documents)	

Reviewer's Name and Signature: _____

Date: _____

ANNEX 3

AF/03-012/01 **Informed Consent Assessment Form**

Protocol Number:		
Protocol Title :		
Protocol: Version No.... Dated.....	**Informed Consent:** Version No..... Dated.....	
Principal Investigators: **Institute**:		
Co-investigator(s):		
Sl.No	Informed Consent Information	Comments
1.	Are procedures for obtaining Informed Consent appropriate? ☐ Yes ☐ No	
2.	Is there an informed consent information to be provided for the participants ☐ Yes ☐ No	
3.	Contents of the Informed Consent clear ☐ clear ☐ unclear	
4.	Language of the Informed Consent ☐ clear ☐ unclear	
5.	Information contents for the informed consent adequate ☐ Adequate ☐ Inadequate	
6.	Is the informed consent information translated into local language ☐ Yes ☐ No ☐ NA	
7.	Form for signature to ensure the administration of informed consent form, witness and person conducting informed consent form ☐ appropriate ☐ inappropriate ☐ Not available ☐ NA	
8.	Contact Persons for Participants ☐ Yes ☐ No (**Note:** Name and contact number of the investigator(s) and IRB shall be there in the information sheet)	

Reviewer's Name and Signature: _____

Date: _____

Annex 4
AF/04-012/01 Assessment Report Form

Review Date (DD/MM/YYYY): **.....**
Protocol number: …… Version No.: .....Dated: .....

Protocol Title :		
Elements Reviewed (AF/01-012/01)	☐ Attached	☐ Not attached
Review of Revised Application ☐ Yes ☐ No	Date of Previous review:	
DECISION : (**Note:** Refer "ANNEX 9 of SOP/012/01" for the criteria)	Protocol (Version No._____): ☐ Approved ☐ Approved with Recommendation ☐ Solicited for Resubmission (Expedited ☐ Full Board ☐) ☐ Disapproved If approved, the frequency for continuing review: _____	
	Informed Consent Form (Version No._____): ☐ Approved ☐ Approved with Recommendation ☐ Solicited for Resubmission (Expedited ☐ Full Board ☐) ☐ Disapproved	
	Tools (Version No._____): ☐ Approved ☐ Approved with Recommendation ☐ Solicited for Resubmission (Expedited ☐ Full Board ☐) ☐ Disapproved	
	Other related documents (ex. Advertisement), Yes ☐ No ☐ If Yes, specify: _____ ☐ Approved ☐ Approved with Recommendation ☐ Solicited for Resubmission (Expedited ☐ Full Board ☐) ☐ Disapproved	
Comment (**Note:** Mention recommendations/clarification to be sought from the assessment form AF/01or2-012/01 and any other additional comments here):		
Signature :		Date:

ANNEX 5
AF/05-012/01 **IRB Decision Form**

Meeting No.: ……../…….. Date (D/M/Y):

Protocol number…… Version No.: …… Dated: .....

Protocol Title :		
Principal Investigators:		
Institute:		
Elements Reviewed (AF/ 01-012) :	☐ Attached ☐ Not attached	
Review of Revised Application ☐ Yes ☐ No	Date of Previous review:	
Decision of the meeting: (Note: Refer "ANNEX 12 of SOP/012/05" for the criteria)	☐ Approved ☐ Approved with Recommendation ☐ Disapproved ☐ Resubmission (Expedited ☐ Full Board ☐) If approved, the frequency for continuing review:	

No.	Voting IRB members	Decision			
		AP	AR	RES	DA

Note: AP - Approved; AR – Approved with recommendation;

RES – Resubmission for re-review; DA – Disapproved

Signature: ……

Chairperson
Date:

ANNEX 6
- AF/06-012/01 **Action letter template**

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Khesar Gyalpo University of Medical Sciences of Bhutan
Royal Government of Bhutan

Ref. No. / / / Date:

IRB REVIEW LETTER (This is not an approval letter)

Protocol No: .....
Principal Investigator: .....
Institute: .....
Co-Investigator(s): .....
Proponent of the study: .....

Dear .....,
Please find the review summary of your protocol titled "....." version "..." dated "DD/MM/YYYY" submitted to IRB on "DD/MM/YYYY". The protocol was reviewed by ...th IRB full board meeting (or The protocol was reviewed through expedited review process by IRB).

Upon review of the protocol and/or other document(s) the board made the following decision:	
LIST OF DOCUMENTS	DECISION
Protocol	Approved/Approved with recommendations/Solicited for resubmission/Disapproved
Informed Consent Form	Approved/Approved with recommendations/Solicited for resubmission/Disapproved
Tools (Questionnaire/forms/guides/etc)	Approved/Approved with recommendations/Solicited for resubmission/Disapproved
Advertisements (Recruitment materials)	Approved/Approved with recommendations/Solicited for resubmission/Disapproved
Others (Specify).....	Approved/Approved with recommendations/Solicited for resubmission/Disapproved
Recommendation(s)/clarification(s):	

PLEASE NOTE THAT:

a. 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.
b. The study can be conducted **ONLY after obtaining Final Approval** from the IRB.

If disapproved, please include the following lines;
"If you wish to appeal to this decision, please contact the IRB and submit your appeal in writing within 3 months from the issuance date of this review letter, addressed to the IRB Chairperson with justification as to why the appeal shall be granted. If appeal is not done within the given deadlines then the protocol file will be closed."

Signature
(Name)
Chairperson

For further information please contact: *...@kgumsb.edu.bt; IRB Member Secretary*

ANNEX 7

- AF/07-012/01 Approval Letter Template

ཀོ་སར་རྒྱལ་པོ་གསོ་རིག་གཙུག་ལག་སློབ་སྡེ།།

Khesar Gyalpo University of Medical Sciences of Bhutan
Royal Government of Bhutan

Ref. No. **IRB/Approval/YYYY/002** **Approval Date: DD/MM/YYYY**

IRB APPROVAL LETTER (valid through DD/MM/YYYY)

PI: **Institute:**	**Study Title**:
Co-Investigator(s): **Proponent of the study:**	
Mode of Review: Initial Review: ☐ *Full Board Review (Meeting No. X/YYYY-XXth)* ☐ *Expedited review* Resubmission (1): ☐ *Full Board Review (Meeting No. X/YYYY-XXth)* ☐ *Expedited review* Resubmission (n): ☐ *Full Board Review (Meeting No. X/YYYY-XXth)* ☐ *Expedited review*	
Date of continuing review: DD/MM/YYYY Note: *Please submit continuing review report along with application form AF/01/015/05 at least seven days before the date of continuing review. If the study is completed then please submit final report of the study.*	
List of document(s) approved: Protocol : Version No. ... Dated: ..... Informed Consent Form : Version No. ... Dated: ..... Tools (Questionnaire/forms/guides/etc) : Version No. ... Dated: ..... Others (Specify) ..... : Version No. ... Dated:	
Conditions for Approval: 1. *This approval is granted for the scientific and ethical soundness of the study. The PI shall be responsible to seek all other clearances/approvals required by law/policy including permission from the study sites before conducting the study.* 2. *Report serious adverse events to IRB within 10 working days after the incident and unexpected events should be included in the continuing review report or the final report.* 3. *No biological material shall be used for other research purpose beyond which is specified in this protocol.* 4. *Any new research study with stored biological material from this study will need a new approval from the IRB before study begins.* 5. *Any changes to the proposal or to the attachments (informed consent and research tools such as forms) shall be approved by IRB before implementation.* 6. *Final report of the study shall be submitted to IRB at the end of the study for review and protocol file closure.*	

Signature
(Name)
Chairperson

For further information please contact: *IRB Member Secretary:*
Tel: +975-
E-mail:

ANNEX 8

Guidance for reviewing a study protocol

Reviewers shall think about and try to find answers to the following questions:

1. How will the knowledge, result or outcome of the study contribute to human well-being?
   - ❑ Knowledge from the basic research may possibly benefit.
   - ❑ A new choice of method, drug or device that benefits the subject during the study and others in the future.
   - ❑ Provide safety data or more competitive choices.

2. Does the study design give answers to the objectives? Whether
   - ❑ The endpoints are appropriately selected.
   - ❑ The participating duration of a study participant is adequate to allow sufficient change in the endpoints.
   - ❑ The control arm is appropriately selected for best comparison.
   - ❑ The placebo is justified.
   - ❑ The number of study participants in non-treatment (or placebo) arm is minimized.
   - ❑ Unbiased assignment (e.g. Randomization, etc.) Is in practice.
   - ❑ Inclusion and exclusion criteria are carefully selected to eliminate confounding factors as much as possible.
   - ❑ The sample group size appropriate with the given statistical assumptions.
   - ❑ Predictable risks are minimized.
   - ❑ The tests and procedures that are more than minimal risk are cautiously used.
   - ❑ Subject deception is avoided.
   - ❑ Instruction and counselling for study participants are included (if needed) when deception is integral to the study design.
   - ❑ The study participants are adequately assessed and provided follow-up care, if needed.

3. Who will be the participants in the study? Whether
   - ❑ The described population is appropriate for the study.
   - ❑ Predictable vulnerabilities are considered.
   - ❑ It is completely necessary to conduct the study in a vulnerable population. If not, is there any other way to get the study answers?
   - ❑ There will be secondary participants.

4. Do the inclusion and exclusion criteria
   - ❑ Selectively include participants most likely to serve the objective of the study?
   - ❑ Equitably include participants?
   - ❑ Properly exclude participants who can predictably confound the results?
   - ❑ Properly exclude participants who may predictably be at increased risk in the study due to coexisting conditions or circumstances?

5. Does the study design have adequate built-in safeguards for risks?
   - ❑ Appropriate screening of potential participants?
   - ❑ Use of a stepwise dose escalation with analysis of the results before proceeding?
   - ❑ Does the frequency of visits and biological samplings reasonably monitor the expected effects?
   - ❑ Are there defined stopping (discontinuation) /withdrawal criteria for participants with worsening condition?
   - ❑ Is there minimized use of medication withdrawal and placebo whenever possible?
   - ❑ Will rescue medications and procedures be allowed when appropriate?

- Is there a defined safety committee to perform interim assessments, when appropriate?
- Is appropriate follow-up designed into the study? For instance, gene transfer research may require following the participants for years or for their entire lifetime after they receive the gene transfer agent.

6. Is pre-clinical and/or early clinical studies sufficiently performed before this study?

- The animal study and *in vitro* testing results?
- Previous clinical results, if done?
- Whether the proposed study is appropriately built on the pre-clinical and/or early clinical results.
  - The selected dose based on adequate prior results?
  - Monitoring tests designed to detect expected possible risks and side effects?

7. Does the study and the informed consent process include issues of special concern, such as:

- Waiver or alteration of consent?
- Delayed consent (e.g., emergency treatment, etc.)?
- Deception?
- Sensitive information of participants that may require a confidentiality statement?

ANNEX 9

Informed Consent Process

The actual **process of informed consent** shall:

- Give the participants significant **information** about the study.
- Make sure the participants have **enough time** to carefully read and consider all options.
- **Answer all questions** of the participants before making decision to participate.
- Explain **risks or concerns** to the participants**.**
- Make sure that all information is **understood and satisfied by the participants**.
- Make sure the participants understand the study and the consent process.
- Obtain **voluntary** informed **consent** to participate.
- Make sure the participants can **freely consent without coercion, pressure or other undue influences.**
- Consent shall be **informally verified on a continuing basis.**
- **Continue to inform** the participants throughout the study.
- **Continue to re-affirm** the **consent** to participate throughout the study.

Procedures or methods used in the informed consent process for recruitment of study participants include:

- A consent form-See template below
- Brochures, Pamphlets or other reading materials (i.e., letters to participants, phone pre-screening questionnaires, phone hold messages)
- Internet information
- Instruction sheets
- Audio-visual presentations
- Charts, diagrams or posters
- Discussions
- Consultation with others

For participants ≥ 18 years

- Informed Consent

For participants 12 years through <18years

- Informed Consent from the parent(s) or legal guardian
- Informed Assent from the participant

For participants 7 years through <12 years

- Informed Consent from the parent(s) or legal guardian
- Verbal Informed Assent from the participant

For participants <7 years

- Informed Consent from the parent(s) or legal guardian
- Any obvious signs or indication of denial by the minors shall be respected.

Techniques to improve the readability of consent forms:

- Use short sentences and paragraphs
- Limit to one thought or topic in a sentence, avoid run-on sentence
- Use simple words, less syllables in a word.
- Use common words, remove technical jargon and medical terms.

- Try to use correct basic grammar and form.
- Use "gene **transfer**" instead of "gene **therapy**" (less implied effectiveness).
- Use "**agent**" instead of "**drug**" or "**medicine**" (less implied effectiveness).
- Try to avoid the use of "**treatment**", "**therapy**" or "**therapeutic**" in studies involving gene transfer (because these words imply effectiveness)

Waiver/alteration of Informed Consent

In certain situations, the IRB may approve a consent procedure that does not include, or which alters (e.g. deferral), some or all of the elements of informed consent, or waive the requirement to obtain informed consent. The Examples of such studies may include but not limited to:

- The research involves no more than minimal risk to the participants ,
- The waivered or altered consent does not involve a therapeutic intervention,
- The waiver or alteration is unlikely to adversely affect the rights and welfare of the participant,
- The research could not practicably be carried out without the waiver or alteration,
- The information is used in a manner that will ensure its confidentiality,
- The public interest in conducting the research exceeds the public interest in protecting the privacy of the individuals,

Waiver of signature in informed consent (Verbal Consent)

In certain situation when obtaining ICF is required but obtaining written informed consent is not feasible or verbal consent is more appropriate then IRB may approve waiver of signature in informed consent (verbal consent).

ANNEX 10

Informed consent Form (ADAPTED FROM WHO-GUIDELINE)

Notes to Researchers:

1. This informed consent contents different sections. Please chose the section which is relevant to your study
2. Language used throughout form shall be at the level of a local student of class 6th/8th standard
3. Please note that this is a template developed by the IRB to assist the Principal Investigator in the design of their informed consent forms (ICF). It is important that Principal Investigators adapt their own ICFs to the outline and requirements of their particular study.
4. Each section of the informed consent form consists of two parts: the information sheet and the consent certificate.
5. Do not be concerned by the length of this template. It is long only because it contains guidance and explanations which are for you and which you will not include in the informed consent forms that you develop and provide to participants in your research.
6. This template includes examples of key questions that may be asked at the end of each section that could ensure the understanding of the information being provided, especially if the research study is complex. These are just examples, and suggestions, and the investigators will have to modify the questions depending upon their study.
7. In this template:
   - square brackets indicate where specific information is to be inserted
   - bold lettering indicates sections or wording which shall be included
   - Standard lettering is used for explanations to researchers only and shall not be included in your consent forms. The explanation is provided in black, and examples are provided in red in italics. Suggested questions to elucidate understanding are given in black in italics.

Annex 10.1:

Informed Parental Consent Form Template for Research Involving Children (Clinical Studies)

) (This template is for either clinical trials or clinical research)

Name of Principle Investigator:

[Informed Consent Form for _____]

Name the group of individuals for whom this consent is written. Because research for a single project is often carried out with a number of different groups of individuals - for example healthcare workers, patients, and parents of patients - it is important that you identify which group this particular consent is for.

(This informed consent form is for the parents of children between the ages of 1 and 4 years of age who attend clinic Z, and who we are asking to participate in research X)

[Name of Principal Investigator]
[Name of Organization]
[Name of Sponsor]
[Name of Proposal and version]

PART I: Information Sheet
Introduction

Briefly state who you are and explain that you are inviting them to have their child participate in research which you are doing. Inform them that may talk to anyone they feel comfortable talking with about the research and that they can take time to reflect on whether they want their child to participate or not. Assure the parent that if they do not understand some of the words or concepts, that you will take time to explain them as you go along and that they can ask questions now or later.

(I am X, working for the Y Research Institute. We are doing research on Z disease, which is very common in this country.

I am going to give you information and invite you to have your child participate in this research. You do not have to decide today whether or not you agree that your child may participate in the research. Before you decide, you can talk to anyone you feel comfortable with.

There may be some words that you do not understand. Please ask me to stop as we go through the information and I will take time to explain. If you have questions later, you can ask them of me, the study doctor or the staff.)

Purpose

Explain the problem/research question in lay terms which will clarify rather than confuse. Use local and simplified terms for a disease, e.g. local name of disease instead of malaria, mosquito instead of anopheles, "mosquitoes help in spreading the disease" rather than "mosquitoes are the vectors". Avoid using terms like pathogenesis, indicators, determinants, equitable etc. There are guides on the internet to help you find substitutes for words which are overly scientific or are professional jargon.

Recognize that parents' feelings about involving their children in research can be complicated. The desire and feeling of responsibility to protect their child from risk or discomfort may exist alongside the hope that the study drug will help either their child or others. It is, therefore, important to provide clear and understandable explanations, and to give parents time to reflect on whether they will consent to have their child participate.

(Malaria is one of the most common and dangerous diseases in this region. The vaccine that is currently being used is not as good as we would like it to be but there is a new vaccine which may work better. The purpose of this research is to test the new vaccine to see if it protects young children better than the current vaccine).

Type of Research Intervention
Briefly state the intervention if you have not already done so. This will be expanded upon in the procedures section.

(An injection OR a series of three injections OR taking a vaccine orally, a biopsy).

Participant selection
State clearly why you have chosen their child to participate in this study. Parents may wonder why their child has been chosen for a study and may be fearful, confused or concerned. Include a brief statement on why children, rather than adults, are being studied.

(The vaccine has been found to be effective with adults and older children. Because of how young children grow and develop, we can't assume that the vaccine will be as effective on young children unless we test it on children

We are inviting you to take part in this research because it is important that we test a new vaccine on children who do not have malaria but who live in an area where malaria is a serious problem. Because you and your child live in this area and your child does not have malaria, we are asking if you would allow your child to participate.)

- ***Example of question to elucidate understanding:*** *Do you know why your child has been identified as a potential research participant? Do you know what the study is about?*

Voluntary Participation
Indicate clearly that they can choose to have their child participate or not. State, if it is applicable, that they will still receive all the services they usually do if they decide not to participate. This can be repeated and expanded upon later in the form as well. It is important to state clearly at the beginning of the form that participation is voluntary so that the other information can be heard in this context.

(Your decision to have your child participate in this study is entirely voluntary. It is your choice whether to have your child participate or not. If you choose not to consent, all the services you and your child receive at this clinic will continue and nothing will change. You may also choose to change your mind later and stop participating, even if you agreed earlier, and the services you and/or your child receives at the clinic will continue.)

- ***Examples of question to elucidate understanding:*** *If you decide that you do not want your child to take part in this research study, do you know what your options for him/her are? Do you*

know that you do not have to accept that your child takes part in this research study? Do you have any questions?

Include the following section only if the protocol is for a clinical trial:

Information on the Trial Drug [Name of Drug]

1) give the phase of the trial and explain what that means. Explain to the parent why you are comparing or testing the drugs.
2) provide as much information as is appropriate and understandable about the drug such as its manufacturer or location of manufacture and the reason for its development.
3) explain the known experience with this drug
4) explain comprehensively all the known side-effects/toxicity of this drug, as well as the adverse effects of all the other medicines that are being used in the trial

(The ABX vaccine has been tested twice before but only with older children and adults. In both studies, the vaccine worked better than the vaccine that currently exist. While the current vaccine protects only 60% of people who take the vaccine the new one protected more than 80% of the people the new vaccine also protected for a longer time period. We want to compare those two vaccines - the current one and the new one - in a younger age group, and that is why we are doing this research.

The drug is made by Company AB, who is working with a local hospital to have it tested. It's called a _____type of drug because it helps part of the blood to_____. The new vaccine that we are studying has no known side effects. The current vaccine that is being used in the study also has no known side effects.)

Procedures and Protocol

It is important that the parents know what to expect and what is expected of them and their child. Describe or explain the exact procedures that will be followed on a step-by-step basis, the tests that will be done, and the drugs that will be given. It is also important to explain from the outset what some of the more unfamiliar procedures involve (placebo, randomization, biopsy, etc.) Describe very clearly which procedure is routine and which is experimental or research. Explain that the parent may stay with the child during the procedures. If the researchers are to have access to the child's medical records, this shall be stated.

Use active, rather than conditional, language. Write "we will ask you to…." instead of "we would like to ask you to…."

In this template, this section has been divided into two: firstly, an explanation of unfamiliar procedures and, secondly, a description of process.

A. Unfamiliar Procedures

If the protocol is for a clinical trial:
1) involving randomization or blinding, the participants shall be told what that means and what chance they have of getting which drug (i.e. one in four chances of getting the test drug). A very minimal statement is provided below to give you an example. You may need to be more explicit about what is exactly involved.

(Because we do not know if the new vaccine is better than the currently available vaccine for treating this disease, we need to make comparisons. Children taking part in this research will be put into groups which are selected by chance, as if by tossing a coin.

One group will get the vaccine we are testing, and the other group will get the malaria vaccine which is currently used in this region. It is important that neither you nor we know which of the two vaccines your child was given. This information will be in our files, but we will not look at these files until after the research is finished. This is the best way we have for testing vaccines without being influenced by what we think or hope might happen. We will then compare which of the two has the best results.

The healthcare workers will be looking after you and the other participants very carefully during the study. If we are concerned about what the medicines or treatment is doing, we will find out which vaccine your child is getting and make changes.)

2) While Involving a placebo, it is important to ensure that the participants understand what is meant by a placebo. An example for a placebo is given below.

(A placebo or inactive medicine looks like real medicine but it is not. It is a dummy or pretend medicine. It has no effect on a person because it has no real medicine in it. Sometimes when we want to know whether a new medicine is good, we give some people the new medicine and some people the pretend or dummy medicine. For the research to be good, it is important that you and your child do not know whether the real medicine or the pretend or dummy medicine was given. This is one of the best ways we have for knowing what the medicine we are testing really does.)

3) which may necessitate a rescue medicine, then provide information about the rescue medicine or treatment such as what it is and the criterion for its use. For example, in pain trials, if the test drug does not control pain, then intravenous morphine may be used as a rescue medicine

(If we find that the medicine that is being used does not have the desired effect, or not to the extent that we wish it to have, we will use what is called a "rescue medicine.".)

B. Description of the Process

Describe the process on a step-by-step basis.

(You may stay with your child during each of the visits and during the procedures. In the first visit, a small amount of blood, equal to about a teaspoon will be taken from your child's arm. This will be tested for the presence of substances that help your child's body to fight infections. Your child will feel some discomfort when the needle stick goes into her/his arm but this will go away very quickly. There may be slight bruising but this will disappear in a few days.

In the next visit, your child will be given either the test vaccine or the vaccine that is currently being used for malaria in this region. Neither you nor we will know, until later in the study, which vaccine your child was given. The vaccine will be given by a trained healthcare worker. After the vaccine, we ask that you and your child stay at the clinic for 30 minutes so that the healthcare worker can observe any immediate changes in the child's mood, and if swelling occurs around the injection site. We will give you and your child juice and something small to eat.

We will ask your child's physician to give us the details of your child's health and illness related information. If you do not wish us to do that, please let us know. However, because your child's health records are very important for the study, if we cannot look at the health records, we will not be able to include your child in the study.

At the end of the study, we will contact you by letter to tell you which of the two vaccines your child was given….)

In case of a clinical research:
Explain that there are standards/guidelines that must be followed. If a biopsy will be taken, then explain whether it will be under local anesthesia, sedation or general anesthesia, and what sort of symptoms and side effects the participant should expect under each category.

(Your child will receive the treatment for his/her condition according to national guidelines, etc. The sample will be taken using a local anesthesia which means that only the part of your child that we are taking the sample from, and a small surrounding area, will lose feeling for a short time. Your child shouldn't feel pain, etc.)

For any clinical study (if relevant):
If blood samples are to be taken explain how many times and how much in a language that the person understands. It may, for example, be inappropriate to tell a tribal villager that blood equal to a table-spoon full will be taken.

If the tissues/blood samples or any other human biological material will be stored for a duration longer than the research purpose, or is likely to be used for a purpose other than mentioned in the research proposal, then provide information about this and obtain consent specifically for such storage and use in addition to consent for participation in the study - (see last section)

If not, then explicitly mention here that the biological samples obtained during this research procedure will be used only for this research, and will be destroyed after ___ years, when the research is completed.

Duration
Include a statement about the time commitments of the research for the participant and for the parent including both the duration of the research and follow-up, if relevant.

(The research takes place over ___ (number of) days/ or ___ (number of) months in total. During that time, it will be necessary for you to come to the clinic/hospital/health facility _____ (number of) days, for ____ (number of) hours each day. We would like to meet with you six months after your last visit for a final check-up. Altogether, we will see you and your child 4 times over a year).

- ***Examples of question to elucidate understanding:*** *Can you tell me if you remember the number of times that we are asking you to come to the hospital to complete the treatment? The research project? How many injections will you be given? How many tablets? How much blood will be taken from your veins, using a syringe and needle? Over how many weeks? Etc. Do you have any other questions? Do you want me to go through the procedures again?*

Side Effects
Parents should be told if there are any known or anticipated side effects and what will happen in the event of a side effect or an unexpected event.

(These vaccines can have some unwanted effects or some effects that we are not currently aware of. However, we will follow your child closely and keep track of these unwanted effects or any problems.

We will give you a telephone number to call if you notice anything out of the ordinary, or if you have concerns or questions. You can also bring your child to this health facility at anytime and ask to see [Name of nurse, doctor, researcher].

We may use some other medicines to decrease the symptoms of the side effects or reactions. Or we may stop the use of one or more drugs. If this is necessary we will discuss it together with you and you will always be consulted before we move to the next step.)

Risks

A risk can be thought of as being the possibility that harm may occur. Explain and describe any such possible or anticipated risks. Provide enough information about the risks that the parent can make an informed decision. Describe the level of care that will be available in the event that harm does occur, who will provide it, and who will pay for it.

(By participating in this research it is possible that your child will be at greater risk than he/she would otherwise be. There is a possibility that _____may happen as a result of taking this drug. While the possibility of this happening is very low, you should still be aware of the possibility. If something unexpected happens and harm does occur, we will provide your child with_____. [Explain the level of care that will be available, who will provide it, and who will pay for it. Inform the parent if there is a particular insurance in place.])

Discomforts

Explain and describe the type and source of any anticipated discomforts that are in addition to the side effects and risks discussed above.

(By participating in this research it is possible that your child may experience some discomfort such as the discomfort of the injections. There may be a slight hardening and/or swelling where the needle stick goes into the skin. This should disappear in one day. Your child may also be fussier than usual or more tired. These behaviors usually stop within one day but if you are concerned, please call me or come to the clinic.)

- ***Examples of question to elucidate understanding:*** *Do you understand that, while the research study is on-going, no-one may know which medicine your child is receiving? Do you know that the medicine that we are testing is a new medicine, and we do not know everything about it? Do you understand that your child may have some unwanted side-effects from the medicines? Do you understand that these side-effects can happen whether or not your child is in the research study? Etc. Do you have any questions?*

Benefits

Benefits may be divided into benefits to the individual, benefits to the community in which the individual resides, and benefits to society as a whole as a result of finding an answer to the research question. Mention only those activities that will be actual benefits and not those to which they are entitled regardless of participation.

(If your child participates in this research, he/she will have the following benefits: any interim illnesses will be treated at no charge to you. If your child falls sick during this period he/she will be treated free of charge. There may not be any other benefit for your child but his/her participation is likely to help us find the answer to the research question. There may not be any benefit to the society at this stage of the research, but future generations are likely to benefit.)

Reimbursements
State clearly what you will provide the participants with as a result of their participation. IRB does not encourage incentives beyond reimbursements for expenses incurred as a result of participation in research. The expenses may include, for example, travel expenses and reimbursement for time lost. The amount should be determined within the host country context.

(You will not be provided any incentive to take part in this research. However, you will be reimbursed with - provide a figure if money is involved - for your lost time and travel expense.)

- ***Examples of question to elucidate understanding:*** *Can you tell me if you have understood correctly the benefits that your child will have if you allow him/her to take part in the study? Do you know if the study will pay for your and your child's travel costs and your time lost, and do you know how much you will be re-imbrued? Do you have any other questions?*

Confidentiality
Explain how the research team will maintain the confidentiality of data, especially with respect to the information about the participant, which would otherwise be known only to the physician but would now be available to the entire research team. Because something out of the ordinary is being done through research, any individual taking part in the research is likely to be more easily identified by members of the community and is therefore more likely to be stigmatized.

(The information that we collect from this research project will be kept confidential. Information about your child that will be collected from the research will be put away and no-one but the researchers will be able to see it. Any information about your child will have a number on it instead of his/her name. Only the researchers will know what his/her number is and we will lock that information up with a lock and key. It will not be shared with or given to anyone except [name who will have access to the information, such as research sponsors, DSMB board, your clinician, etc].)

- ***Example of question to elucidate understanding:*** *Did you understand the procedures that we will be using to make sure that any information that we as researchers collect about you and/or your child will remain confidential? Do you have any questions about them?*

Sharing of the results
Your plan for sharing the information with the participants and their parents should be provided.
If you have a plan and a timeline for the sharing of information, include the details. Also inform the parent that the research findings will be shared more broadly, for example, through publications and conferences.

(The knowledge that we get from this study will be shared with you before it is made widely available to the public. Confidential information will not be shared. There will be small meetings in the community and these will be announced. Afterwards, we will publish the results in order that other interested people may learn from our research).

Right to Refuse or Withdraw
This is a reconfirmation that participation is voluntary and includes the right to withdraw. Tailor this section well to ensure that it fits for the group for whom you are seeking consent. The example used here is for a parent of an infant at a clinic.

(You do not have to agree to your child taking part in this research if you do not wish to do so and refusing to allow your child to participate will not affect your treatment or your child's treatment at this

Centre in any way. You and your child will still have all the benefits that you would otherwise have at this Centre. You may stop your child from participating in the research at any time that you wish without either you or your child losing any of your rights as a patient here. Neither your treatment nor your child's treatment at this Centre will be affected in any way.)

Alternatives to participating

Include this section only if the study involves administration of investigational drugs or use of new therapeutic procedures. It is important to explain and describe the established standard treatment.

(If you do not wish your child to take part in the research, your child will be provided with the established standard treatment available at the centre/institute/hospital. People who have malaria are given….)

Who to Contact

Provide the name and contact information of someone who is involved, informed and accessible (a local person who can actually be contacted.) State also that the proposal has been approved and how.

(If you have any questions you may ask them now or later, even after the study has started. If you wish to ask questions later, you may contact any of the following: [name, address/telephone number/e-mail] This proposal has been reviewed and approved by [name of the IRB e.g. IRB], which is a committee whose task it is to make sure that research participants are protected from harm. If you wish to find about more about the IRB, contact [name, address, and telephone number.])

PART II: Certificate of Consent

Certificate of Consent

…This section should be written in the first person and have a statement similar to the one in bold below. If the participant is illiterate but gives oral consent, a witness must sign. A researcher or the person going over the informed consent must sign all consent. The certificate of consent should avoid statements that have "I understand…." phrases. The understanding should perhaps be better tested through targeted questions during the reading of the information sheet (some examples of questions are given above), or through the questions being asked at the end of the reading of the information sheet, if the potential participant is reading the information sheet him/herself…

(I have been invited to have my child participate in research of a new malaria vaccine). **I have read the foregoing information, or it has been read to me. I have had the opportunity to ask questions about it and any questions that I have asked have been answered to my satisfaction. I consent voluntarily for my child to participate as a participant in this study.**

Print Name of Participant_____

Print Name of Parent or Guardian_____

Signature of Parent or Guardian _____

Date _____

Day/month/year

If illiterate

A literate witness must sign (if possible, this person should be selected by the participant and should have no connection to the research team). Participants who are illiterate should include their thumb print as well.

I have witnessed the accurate reading of the consent form to the parent of the potential participant, and the individual has had the opportunity to ask questions. I confirm that the individual has given consent freely.

Print name of witness*_____ *AND* *Thumb print of parent

Signature of witness _____

Date _____
Day/month/year

Statement by the researcher/person taking consent
I have accurately read out the information sheet to the parent of the potential participant, and to the best of my ability made sure that the person understands that the following will be done:
1.
2.
3.
I confirm that the parent was given an opportunity to ask questions about the study, and all the questions asked by the parent have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.

A copy of this ICF has been provided to the participant.

Print Name of Researcher/person taking the consent_____

Signature of Researcher /person taking the consent_____

Date _____
Day/month/year

An Informed Assent Form will_____ OR will not _____ be completed.

ANNEX 10.2
Informed Parental Consent Template for Research Involving Children (Qualitative Studies)

L C
(For use with Participant Observation, Focus Group Discussions, Interviews, and Surveys)

[Informed Consent Form for _____]
Name the group of individuals for whom this consent is written. Because research for a single project is often carried out with a number of different groups of individuals - for example healthcare workers, patients, and parents of patients - it is important that you identify which group this particular consent is for.

(E.g. This informed consent form is for parents of adolescent girls and boys participating in the research titled. "What do we want: Adolescents and health systems "?)

[Name of Principle Investigator]
[Name of Organization]
[Name of Sponsor]
[Name of Project and Version]

This Informed Consent Form has two parts:

- **Information Sheet (to share information about the study with you)**
- **Certificate of Consent (for signatures if you agree that your child may participate)**

You will be given a copy of the full Informed Consent Form

Part I: Information Sheet
Introduction
Briefly state who you are and explain that you are inviting them to have their child participate in research which you are doing. Inform them that may talk to anyone they feel comfortable talking with about the research and that they can take time to reflect on whether they want their child to participate or not. Assure the parent that if they do not understand some of the words or concepts, that you will take time to explain them as you go along and that they may ask questions now or later.

(Example: I am X, and I work at Y organization in _____. I am doing some research which might help your clinic/hospital do more to help teenagers become and stay healthier. In our research we will talk to many teenagers, both girls and boys, and ask them a number of questions. Whenever researchers study children, we talk to the parents and ask them for their permission. After you have heard more about the study, and if you agree, then the next thing I will do is ask your daughter/son for their agreement as well. Both of you have to agree independently before I can begin.

You do not have to decide today whether or not you agree to have your child participate in this research. Before you decide, you can talk to anyone you feel comfortable with.

There may be some words that you do not understand. Please ask me to stop as we go through the information and I will take time to explain. If you have questions later, you can ask them of me or of another researcher.)

Purpose
Explain in lay terms why the research is being done and what is expected from the results. Explain why you need to conduct the research with children.

(Example: It is possible that the clinics and the hospital in this region are not providing some of the services that are important for teenagers. In this study we will talk to teenage girls and boys about what they know about caring for their bodies in a healthy way including sexual and reproductive health. We will invite them to share their knowledge and understanding with us so that we can find ways of meeting their needs at the local clinics and hospital.)

Type of Research Intervention
Briefly state the intervention. This will be expanded upon in the procedures section.

(Example: A questionnaire OR a focus group OR an interview)

Selection of Participants
State clearly why you have chosen their child to participate in this study. Parents may wonder why their children have been chosen for a study and may be fearful, confused or concerned.

(Example: We want to talk to many teenagers about their health and what information or services they want for themselves. One part of health that we want to talk to them about is sexuality. We would like to ask your daughter/son to participate because she/he is a teenager and lives in this region.)

- ***Example of question to elucidate understanding:*** *Do you know why we are asking your child to take part in this study? Do you know what the study is about?*

Voluntary Participation
Indicate clearly that they can choose for their child to participate or not and reassure they will still receive all the services they usually do if they choose not to participate. Also inform them that their child will also have input into the decision. This can be repeated and expanded upon later in the form as well. It is important to state clearly at the beginning of the form that participation is voluntary so that the other information can be heard in this context. Participants may also be more alert at the beginning.

(Example: You do not have to agree that your daughter/son can talk to us. You can choose to say no and any services that you and your family receive at this centre will not change. We know that the decision can be difficult when it involves your children. And it can be especially hard when the research includes sensitive topics like sexuality. You can ask as many questions as you like and we take the time to answer them. You don't have to decide today. You can think about it and tell me what you decide later.)

- ***Examples of question to elucidate understanding:*** *If you decide not to allow your child to take part in this research study, do you know what the options for him are? Do you know that your child does not have to take part in this research study, if you do not wish so? Do you have any questions?*

Procedure

Explain what each of the steps or procedures involve. Indicate when the research will take place and where. If there are surveys, indicate where and how the surveys will be collected and distributed.

(Examples:
1) The following applies only to focus group discussions*:*
Your daughter/son will take *part in a discussion with 7-8 other teenagers, or a mix of teenagers and social service workers from the community. The girls and boys will be in separate groups. This discussion will be guided by [give name of moderator] or me.*

2) The following applies only to interviews*:*
Your daughter/son will participate in an interview with [name of interviewer] or myself.

3) The following applies only to questionnaire surveys*:*
*Your daughter/son will fill out a questionnaire which will be provided by [name of distributor of blank questionnaires] and collected by [name of collector of completed questionnaires].**OR** the questionnaire can be read aloud and she/he can give me the answer which she/he wants me to write.)*

Explain the type of questions that the participants are likely to be asked in the focus group discussion, interview or in the questionnaire. If the questions are sensitive, acknowledge this, try to anticipate parents' concerns and protective responses, and address these. Parents may be concerned that if researchers talk to their children about sexuality it may encourage them to explore sexual activities with their peers. Other concerns may include disbelief that their child is ready to talk about sexuality, or parents may be personally embarrassed.

(Examples:
1) The following applies only to focus group discussions:
The group discussion will start with me, or the focus group guide (use the local word for group discussion leader), making sure that the participants are comfortable. We will also answer questions about the research that they might have. Then we will ask questions about the health system in this community. We will talk about where they go for information about health, and whether they get the information and services they need and want. We will encourage them to talk about sexual and reproductive health as well as other important health topics such as food and nutrition. These are the types of questions we will ask. We will not ask them to share personal stories or anything that they are not comfortable sharing.

The discussion will take place in [location of the FGD], and no one else but the people who take part in the discussion and the guide or I will be present during this discussion. The entire discussion will be tape-recorded, but no-one will be identified by name on the tape. The tape will be kept [explain how the tape will be stored]. The information recorded is confidential, and no one else except [name of person(s) with access to the tapes] will be allowed to listen to the tapes. [The tapes will be destroyed after ____period of time.]

2) The following applies only to interviews:
If your daughter does not wish to answer any of the questions during the interview, she may say so and the interviewer will move on to the next question. The interview will take place in [location of the interview], and no one else but the interviewer will be present unless your child asks for someone else to be there. The information recorded is confidential, and no one else except [name of person(s) with access to the information] will have access to the information documented during your interview.) [The tapes will be destroyed after _____period of time.]

3) The following applies only to questionnaires and surveys:
If your daughter/son does not wish to answer some of the questions included in the questionnaire, she/he may skip them and move on to the next question. The information recorded is confidential, and no one else except [name of person(s) with access to the information] will have access to her questionnaire. [The questionnaires will be destroyed after _____period of time.])

Duration
Include a statement about the time commitments of the study for the child and any time commitments on the part of the parent(s). Include both the duration of the study and follow-up, if relevant.

*(Example: We are asking your child to participate in an interview which will take about 1 hour of her/his time. We can do this outside of school/work hours. There is also a questionnaire that we will either provide to your child or which we will do together with her/him. This also takes about an hour. Altogether, we are asking for about 2 hours of your child's time.***)**

- ***Examples of question to elucidate understanding:*** *If you decide that your child can take part in the study, do you know how much time will the interview take? Where will it take place? Do you know that we will be sending a transport to pick up your child from your home? Do you know how much time will the discussion with other people take? If you agree that your child can take part, do you know if he/she can stop participating? Do you know that your child may not respond to the questions that he/she does not wish to respond to? Etc. Do you have any more questions?*

Risks and Discomforts
Explain any risks or discomforts including any limits to confidentiality.

(If the discussion is on sensitive and personal issues e.g. reproductive and sexual health, personal habits etc. then an example of text could be something like "We are asking your son/daughter to share with us some very personal and confidential information, and he/she may feel uncomfortable talking about some of the topics. You must know that he/she does not have to answer any question or take part in the discussion/interview/survey if he/she doesn't wish to do so, and that is also fine. He/she does not have to give us any reason for not responding to any question, or for refusing to take part in the interview"

OR If for example, the discussion is on opinions on government policies and community beliefs, and in general no personal information is sought, then the text under risks could read something like "There is a risk that your son/daughter may share some personal or confidential information by chance, or that he/she may feel uncomfortable talking about some of the topics. However, we do not wish for this to happen. You must know that he/she does not have to answer any question or take part in the discussion/interview/survey if he/she feels the question(s) are too personal or if talking about them makes him/her uncomfortable.)
Your daughter/son may choose to tell you about the interview and the questionnaire but she/he does not have to do this. We will not be sharing with you either the questions we ask or the responses given to us by your child.)

Benefits
Describe any benefits to their child, to the community, or any benefits which are expected in the future as a result of the research.

(Example: There will be no immediate and direct benefit to your child or to you, but your child's participation is likely to help us find out more about the health needs of teenage girls and boys and we hope that these will help the local clinics and hospitals to meet those needs better in the future.)

Reimbursements
State clearly what you will provide the participants with as a result of their participation. IRB does not encourage incentives beyond reimbursements for expenses incurred as a result of participation in research. The expenses may include, for example, travel expenses and reimbursement for time lost. The amount should be determined within the host country context.

(Example: Your daughter/son will not be provided with any payment to take part in the research. However, she/he will be given with [provide a figure, if money is involved] for her/his time, and travel expense (if applicable).)

- ***Examples of question to elucidate understanding:*** *Can you tell me if you have understood correctly the benefits that your child will have if you allow him/her to take part in the study? Do you know if the study will pay for your travel costs and time lost, and do you know how much you will be re-imbrued? Do you have any other questions?*

Confidentiality:
Explain how the research team will maintain the confidentiality of data, especially with respect to the information about the participant. Outline any limits there are to confidentiality. Note that with focus groups confidentiality cannot be guaranteed because what is said within the group becomes common knowledge. Participants can be asked not to share outside of the group but this does not guarantee confidentiality.

(Examples:
Because something out of the ordinary is being done through research in your community, it will draw attention. If your daughter/son participates, she and you may be asked questions by other people in the community.

We will not be sharing information about your son or daughter outside of the research team. The information that we collect from this research project will be kept confidential. Information about your child that will be collected from the research will be put away and no-one but the researchers will be able to see it. Any information about your child will have a number on it instead of his/her name. Only the researchers will know what his/her number is and we will lock that information up with a lock and key. It will not be shared with or given to anyone except [name who will have access to the information, such as research sponsors, DSMB board, your clinician, etc].

The following applies to focus groups*:*
We will ask your child and others in the group not to talk to people outside the group about what was said in the group. We will, in other words, ask each participant to keep what was said in the group confidential. You should know, however, that we cannot stop or prevent participants who were in the group from sharing things that should be confidential.)

- ***Example of question to elucidate understanding:*** *Did you understand the procedures that we will be using to make sure that any information that we as researchers collect about your child will remain confidential? Do you understand that the we cannot guarantee complete*

confidentiality of information that your child shares with us in a group discussion Do you have any more questions?

Sharing of Research Findings
Include a statement indicating that the research findings will be shared in a timely fashion but that confidential information will remain confidential. If you have a plan and timeline for the sharing of information, include the details. Also inform the parent that the research findings will be shared more broadly, for examples, through publications and conferences.

(Example: At the end of the study, we will be sharing what we have learnt with the participants and with the community. We will do this by meeting first with the participants and then with the larger community. Nothing that your child will tell us today will be shared with anybody outside the research team, and nothing will be attributed to him/her by name. A written report will also be given to the participants which they can share with their families. We will also publish the results in order that other interested people may learn from our research.)

Right to refuse or withdraw
Explain again the voluntary nature of consent. Also explain that their child will be asked to agree - or assent - and that the child's concerns and wishes will be taken very seriously.

(Example: You may choose not to have your child participate in this study and your child does not have to take part in this research if she/he does not wish to do so. Choosing to participate or not will not affect either your own or your child's future treatment at the Centre here in any way. You and your child will still have all the benefits that would otherwise be available at this Centre. Your child may stop participating in the discussion/interview at any time that you or she/he wish without either of you losing any of your rights here.)

Who to Contact
Provide the name and contact information of someone who is involved, informed and accessible (a local person who can actually be contacted. State also that the proposal has been approved and how.

(Example: If you have any questions you may ask them now or later, even after the study has started. If you wish to ask questions later, you may contact any of the following: [name, address/telephone number/e-mail]
This proposal has been reviewed and approved by [name of the IRB], which is a committee whose task it is to make sure that research participants are protected from harm. If you wish to find about more about the IRB, contact [name, address, and telephone number.])

- *<u>Example of question to elucidate understanding:</u> Do you know that you do not have to allow your child take part in this study if you do not wish to? You can say No if you wish to? Do you know that you can ask me questions later, if you wish to? Do you know that I have given the contact details of the person who can give you more information about the study? Etc.*

PART II: Certificate of Consent
Certificate of Consent
This section can be written in the first person. It should include a few brief statements about the research and be followed by a statement similar to the one in bold below. If the participant is illiterate but gives oral consent a witness must sign. A researcher or the person going over the informed consent must sign each consent. Because the certificate is an integral part of the information sheet and not a stand-alone document, the layout or design of the form should reflect this.

I have been asked to give consent for my daughter/son to participate in this research study which will involve her completing one interview and one questionnaire **I have read the foregoing information, or it has been read to me. I have had the opportunity to ask questions about it and any questions that I have asked have been answered to my satisfaction. I consent voluntarily for my child to participate as a participant in this study.**

Print Name of Parent or Guardian _____

Signature of Parent of Guardian_____

Date _____
Day/month/year

If illiterate
A literate witness must sign (if possible, this person should be selected by the participant and should have no connection to the research team). Participants who are illiterate should include their thumb print as well.

I have witnessed the accurate reading of the consent form to the parent of the potential participant, and the individual has had the opportunity to ask questions. I confirm that the individual has given consent freely.

Print name of witness_____ ***AND*** ***Thumb print of participant***

Signature of witness **_____**

Date _____
Day/month/year

Statement by the researcher/person taking consent
I have accurately read out the information sheet to the parent of the potential participant, and to the best of my ability made sure that the person understands that the following will be done:
1.
2.
3.
I confirm that the parent was given an opportunity to ask questions about the study, and all the questions asked by him/her have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.

A copy of this Informed Consent Form has been provided to the parent or guardian of the participant ____

Print Name of Researcher/person taking the consent_____

ANNEX 10.3

Informed Consent Form Template for Consent for Storage and Future Use of Unused Samples

Additional Consent to [Name of Project]

Include the following section if the research protocol calls for storage and future use of samples

This Statement of Consent consists of two parts:

- **Information Sheet (to share information about unused samples with you)**
- **Certificate of Consent (to record your agreement)**

You will be given a copy of the full Statement of Consent

Part 1. Information Sheet

Explain that you are seeking permission to store their unused samples for possible future use in either your own research or someone else's research. State that they need to make some decisions about their blood/tissue/sperm/sputum sample because they gave you permission only to use it for the current research.

Explain that sometimes people don't want their samples used for research into areas they might not agree with, for example, research into birth control or reproductive technology. Use lay terms to explain research possibilities. If genetic research is a possibility, explain what this is and any implications for them. State that they can tell you if there is something they don't want their sample used for, or if they don't want their sample used at all.

Inform the participant that at present, the researchers can trace which blood/tissue/sperm/sputum sample belongs to the participant. In most cases, the participant must decide whether they want to let the researchers keep the sample but get rid of all identifying information, or whether they are comfortable with the researchers knowing whose sample it is. Explain the risks and benefits of each of these options. Inform the participant of researcher obligations in cases where the sample remains linked. These obligations include informing the participant of results which have immediate clinical relevance.

Inform participants that their sample will not be sold for profit and that any research which uses their sample will have been approved.

Right to Refuse and Withdraw

Explain that the participant may refuse to allow samples to be kept or put restrictions on those samples with no loss of benefits and that the current research study will not be affected in any way. Inform the participant that they may withdraw permission at anytime and provide them with the name, address, and number of the person and sponsoring institution to contact.

Confidentiality

Briefly explain how confidentiality will be maintained including any limitations.

You can ask me any more questions about any part of the information provided above, if you wish to. Do you have any questions?

Part II. Certificate of Consent

If any of the (TYPE OF SAMPLE i.e. blood, tissue) I have provided for this research project is unused or leftover when the project is completed (Tick **one** choice from each of the following boxes)

☐ I wish my [TYPE OF SAMPLE] sample to be destroyed immediately.

☐ I want my [TYPE OF SAMPLE] sample to be destroyed after ____ years.

☐ I give permission for my [TYPE OF SAMPLE] sample to be stored indefinitely

AND (if the sample is to be stored)

☐ I give permission for my (TYPE OF SAMPLE) sample to be stored and used in future research but only on the same subject as the current research project : [give name of current research]

☐ I give my permission for my [TYPE OF SAMPLE] sample to be stored and used in future research of any type which has been properly approved

☐ I give permission for my [TYPE OF SAMPLE] sample to be stored and used in future research except for research about [NAME TYPE OF RESEARCH]

AND

☐ I want my identity to be removed from my (TYPE OF SAMPLE) sample.

☐ I want my identity to be kept with my (TYPE OF SAMPLE) sample.

I have read the information, or it has been read to me. I have had the opportunity to ask questions about it and my questions have been answered to my satisfaction. I consent voluntarily to have my samples stored in the manner and for the purpose indicated above.

Print Name of Participant_____

Signature of Participant _____

Date _____
Day/month/year

If illiterate

A literate witness must sign (if possible, this person should be selected by the participant and should have no connection to the research team). Participants who are illiterate should include their thumb-print as well.

I have witnessed the accurate reading of the consent form to the potential participant, and the individual has had the opportunity to ask questions. I confirm that the individual has given consent freely.

Print name of witness_____ ***AND*** ***Thumb print of participant***

Signature of witness _____

Date _____
Day/month/year

Statement by the researcher/person taking consent

I have accurately read out the information sheet to the potential participant, and to the best of my ability made sure that the participant understands that the following will be done:

1.

2.

3.

I confirm that the participant was given an opportunity to ask questions about the nature and manner of storage of the samples, and all the questions asked by the participant have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.

A copy of this ICF has been provided to the participant.

Print Name of Researcher/person taking the consent_____

Signature of Researcher /person taking the consent_____

Date _____

Day/month/year

ANNEX 10.4

Informed Assent Form Template for Children/Minors

An Informed Assent Form does not replace a consent form signed by parents or guardians. The assent is in addition to the consent and signals the child's willing cooperation in the study.

[Informed Assent Form for _____]

Name the group of individuals for whom this assent is written. Because research for a single project is often carried out on a number of different groups of individuals - for example children with malaria, children without malaria, students - it is important that you identify which group particular assent is for.

(This informed assent form is for children between the ages of 12 - 18 who attend clinic X and who we are inviting to participate in research Y.)

[Name of Principle Investigator]
[Name of Organization]
[Name of Sponsor]
[Name of Project and Version]

This Informed Assent Form has two parts:

- **Information Sheet (gives you information about the study)**
- **Certificate of Assent (this is where you sign if you agree to participate)**

You will be given a copy of the full Informed Assent Form

Part I: Information Sheet
Introduction
This is a brief introduction to ensure the child knows who you are and that this is a research study. Give your name, say what you do and clearly state that you are doing research. Inform the child that you have spoken to their parents and that parental consent is also necessary. Let them know that they can speak to anyone they choose about the research before they make up their mind.

(Example: My name is ____and my job is to research and test vaccines to see which work best to stop malaria before it makes someone sick .We want to know if this new vaccine will stop children from getting sick and we think this research could help tell us that.

I am going to give you information and invite you to be part of a research study. You can choose whether or not you want to participate. We have discussed this research with your parent(s)/guardian and they know that we are also asking you for your agreement. If you are going to participate in the research, your parent(s)/guardian also have to agree. But if you do not wish to take part in the research, you do not have to, even if your parents have agreed.

You may discuss anything in this form with your parents or friends or anyone else you feel comfortable talking to. You can decide whether to participate or not after you have talked it over. You do not have to decide immediately.

There may be some words you don't understand or things that you want me to explain more about because you are interested or concerned. Please ask me to stop at anytime and I will take time to explain).

Purpose: Why are you doing this research?
Explain the purpose of the research in clear simple terms.
(Example: We want to find better ways to prevent malaria before it makes children sick. We have a new vaccine to prevent malaria which we are hoping might be better than the one that is currently being used. In order to find out if it is better we have to test it.)

Choice of participants: Why are you asking me?
Children, like adults, like to know why they are being invited to be in the research. It is important to address any fears they may have about why they were chosen.

(Example: We are testing this vaccine on children who are your age - between 12 and 18 years old - who live in a place where there is malaria. We are only testing the vaccine on children who do not have malaria.)

Participation is voluntary: Do I have to do this?
State clearly and in child-friendly language that the choice to participate is theirs. If there is a possibility that their decision not to participate might be over-ridden by parental consent, this should be stated clearly and simply.

(Example: You don't have to be in this research if you don't want to be. It's up to you. If you decide not to be in the research, it's okay and nothing changes. This is still your clinic, everything stays the same as before. Even if you say "yes" now, you can change your mind later and it's still okay.

If applicable: If anything changes and we want you to stay in the research study even if you want to stop, we will talk to you first .)

- ***Examples of question to elucidate understanding:*** *If you decide not to take part in this research study, do you know what your options are? Do you know that you do not have to take part in this research study, if you do not wish to? Do you have any questions?*

I have checked with the child and they understand that participation is voluntary __ (initial)

Information on the Trial Drug [Name of Drug]: What is this drug and what do you know about it?
Include the following section only if the protocol is for a clinical trial:

1) Give the phase of the trial and explain what that means. Explain to the participant why you are comparing or testing the drugs.
2) Provide as much information as is appropriate and understandable about the drug such as its manufacturer or location of manufacture and the reason for its development.
3) Explain the known experience with this drug
4) Explain comprehensively all the known side-effects/toxicity of this drug, as well as the adverse effects of all the other medicines that are being used in the trial

(Example: The vaccine we are testing in this research is called ABX. It has been tested twice before with adults who do not have malaria but who live in areas where malaria is common. We now want to test the vaccine on teenagers who do not have malaria. This second research is called a "phase 2" trial.

The vaccine ABX is made by Company C. It has very few side effects. It can make you feel tired for the first 24 hours after being given the drug. Also, 20% of the people who tried the drug in previous research experienced temporary swelling where the injection entered the skin. We know of no greater risk or other side effects. Some participants in the research will not be given the drug which we are testing. Instead, they will be given the drug XYZ, the drug which is most commonly used in this region to treat malaria. There is no risk associated with that drug and no known side effects.)

Procedures: What is going to happen to me?
Explain the procedures and any medical terminology in simple language. Focus on what is expected of the child. Describe which part of the research is experimental.

(Example: We are going to test the vaccine by giving some of the children in the research study the new vaccine and the others are going to get the vaccine that is already being used to prevent malaria. Neither you nor the researchers will know which vaccine you were given until after the study is over. By doing the research like this, we can compare which of the vaccines is better without being influenced by what we think or hope the research will show.

If you decide that you want to do this, there will be three things that happen.
1. In about ten days, you will come to the clinic with your parents and you will get an injection/shot in your arm. This is either the vaccine that we are testing or the vaccine that is usually used to prevent malaria.

2... At the clinic we will also give you a mosquito net to take home and sleep under. Maybe you have seen these before. They stop mosquitoes from biting you during the night when you sleep.

3. Once a month for six months after that, you will come to the clinic and the nurse will take your temperature. She will also take a little bit of your blood, about three or four drops, from your finger with a finger prick. This might hurt a little but the hurt will go away before very long.

Altogether you will come to the clinic 7 times over 7 months. At the end of seven months, the research will be finished.

I have a picture here to show you what will happen. You can ask me to stop and explain again at any time and I will explain more about the process).

- ***Examples of question to elucidate understanding:*** *Can you tell me if you remember the number of times that we are asking you to come to the hospital to complete the treatment? How many times extra will you have to come if you decide to take part in the research study? How many injections will you be given? How many tablets? How much blood will be taken from your veins, using a syringe and needle? Over how many weeks? Etc. Do you have any other questions? Do you want me to go through the procedures again?*

I have checked with the child and they understand the procedures _____ (initial))

Risks: Is this bad or dangerous for me?

Explain any risks using simple, clear language.

(Example: The vaccine is considered safe. It has already been tested on adults and on other children. There has been nothing that has worried us at all. If anything unusual happens to you, however, we need to know and you should feel free you to call us anytime with your concerns or questions. Another way of us knowing how you are is by having you come to the clinic every month for a check-up. If you get sick or have concerns or questions in-between the scheduled visits to clinic, you should let me or the staff nurse know. You don't have to wait for a scheduled visit.)

Discomforts: Will it hurt?
If there will be any discomforts state these clearly and simply. State that they should tell you and/or their parents if they are sick, experience discomfort or pain. Address what may be some of the child's worries, for example, missing school or extra expense to parents.

(Example: There are a few other things that I want you to know.

The injection might hurt for just a second when it goes into your arm. It might get a little bit red and hard around the place where the injection/needle goes in. That should go away in a day. If it hurts longer than that, or if it stays hard for longer or swells up, tell your parents or me. If you feel bad or strange, tell us.

Sleeping under a mosquito net can be uncomfortable because it can be hot and stuffy.

Sometimes you may not want to come to the clinic to get your blood checked or have your temperature taken. It's important that you try to come. It won't take very long. You will miss a little bit of school - about an hour every month - and we will tell your teacher about that so that she knows its okay.)

- ***Examples of question to elucidate understanding:*** *Do you understand that, while the research study is on-going, no-one may know which medicine you re receiving? Do you know that the medicine that we are testing is a new medicine, and we do not know everything about it? Do you understand that you may have some unwanted side-effects from the medicines? Do you understand that these side-effects can happen whether or not you are in the research study? Etc. Do you have any other questions?*

I have checked with the child and they understand the risks and discomforts ____ (initial)

Benefits: Is there anything good that happens to me?
Describe any benefits to the child.

(Example: Nothing really good might happen to you. The vaccine may not stop you from getting malaria. But this research might help us to find a vaccine now or later that could help other children. There are a couple of good things if you do decide that you want to do this. You do get regular check-ups with the nurse so that if you are sick, we will know very soon and this can be important. And you will keep the mosquito net which will help keep mosquitoes away from you. Because mosquitoes cause malaria, this is important.)

I have checked with the child and they understand the benefits_____ (initial)

Reimbursements: Do I get anything for being in the research?

Mention any reimbursements or forms of appreciation that will be provided. Any gifts given to children should be small enough to not be an inducement or reason for participating. WHO does not encourage incentives beyond reimbursements for expenses incurred as a result of participation in the research? These expenses may include, for example, travel expenses and reimbursement for time lost. The amount should be determined within the host country context.

(Example: Because you live quite far from the clinic, we will give your parents enough money to pay for the trip here and (whatever other expense is reasonable).

- ***Examples of question to elucidate understanding:*** *Can you tell me if you have understood correctly the benefits that you will have if you take part in the study? Do you know if the study will pay for your travel costs and time lost, and do you know how much you will be re-imbursed? Do you have any other questions?*

Confidentiality: Is everybody going to know about this?
Explain what confidentiality means in simple terms. State any limits to confidentiality. Indicate what their parents will or will not be told.

(Example: We will not tell other people that you are in this research and we won't share information about you to anyone who does not work in the research study. After the research is over, you and your parents will be told which of the two injections you received and the results.

Information about you that will be collected from the research will be put away and no-one but the researchers will be able to see it. Any information about you will have a number on it instead of your name. Only the researchers will know what your number is and we will lock that information up with a lock and key. It will not be shared with or given to anyone except [name who will have access to the information, such as research sponsors, DSMB board, your clinician, etc].)

- ***Example of question to elucidate understanding:*** *Did you understand the procedures that we will be using to make sure that any information that we as researchers collect about you will remain confidential? Do you have any questions about them?*

Compensation: What happens if I get hurt?
Describe to the ability of the child to understand and explain that parents have been given more information.

(Example: If you become sick during the research, we will look after you. We have given your parents information about what to do if you are hurt or get sick during the research.)

Sharing the Findings: Will you tell me the results?
Describe to the ability of the child to understand that the research findings will be shared in a timely fashion but that confidential information will remain confidential. If you have a plan and a timeline for the sharing of information, include the details. Also tell the child that the research will be shared more broadly, i.e. in a book, journal, conferences, etc.

(Example: When we are finished the research, I will sit down with you and your parent and I will tell you about what we learnt. I will also give you a paper with the results written down. Afterwards, we will be telling more people, scientists and others, about the research and what we found. We will do this by writing and sharing reports and by going to meetings with people who are interested in the work we do.)

Right to Refuse or Withdraw: Can I choose not to be in the research? Can I change my mind?
You may want to re-emphasize that participation is voluntary and any limits to this.

(Example: You do not have to be in this research. No one will be mad or disappointed with you if you say no. It's your choice. You can think about it and tell us later if you want. You can say "yes" now and change your mind later and it will still be okay.)

Who to Contact: Who can I talk to or ask questions to?
List and give contact information for those people who the child can contact easily (a local person who can actually be contacted). Tell the child that they can also talk to anyone they want to about this (their own doctor, a family friend, a teacher).

(Example: You can ask me questions now or later. You can ask the nurse questions. I have written a number and address where you can reach us or, if you are nearby, you can come and see us. If you want to talk to someone else that you know like your teacher or doctor or auntie, that's okay too.)

If you choose to be part of this research I will also give you a copy of this paper to keep for yourself. You can ask your parents to look after it if you want.

- *Example of question to elucidate understanding:* ***Do you know that you do not have to take part in this study if you do not wish to? You can say No if you wish to? Do you know that you can ask me questions later, if you wish to? Do you know that I have given the contact details of the person who can give you more information about the study? Etc.***

You can ask me any more questions about any part of the research study, if you wish to. Do you have any questions?

PART 2: Certificate of Assent
This section can be written in the first person. It should include a few brief statements about the research and be followed by a statement similar to the one identified as 'suggested wording' below. If the child is illiterate but gives oral assent, a witness must sign instead. A researcher or the person going over the informed assent with the child must sign all assents.

(Example: I understand the research is about testing a new vaccine for malaria and that I might get either the new vaccine which is being tested or the vaccine which is currently being used. I understand that I will get an injection and that I will come for regular monthly check-ups at the clinic where I will give a blood sample with a finger prick.)

I have read this information (or had the information read to me). I have had my questions answered and know that I can ask questions later if I have them. I agree to take part in the research.

OR

I do not wish to take part in the research and I have not signed the assent below._____ (initialled by child/minor)

Only if child assents:

Print name of child _____

For child 12 years through <18 years: Signature of child: _____

For child 7 years through <12 years: Verbal assent provided: ☐Yes ☐No

Date: _____
Day/month/year

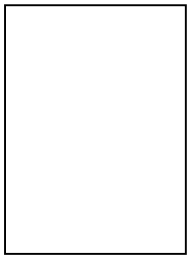
If illiterate:
A literate witness must sign (if possible, this person should be selected by the participant, not be a parent, and should have no connection to the research team). Participants who are illiterate should include their thumb print as well.

I have witnessed the accurate reading of the assent form to the child, and the individual has had the opportunity to ask questions. I confirm that the individual has given consent freely.

Print name of witness (not a parent) _____ AND Thumb print of participant

Signature of witness _____

Date _____
Day/month/year



I have accurately read or witnessed the accurate reading of the assent form to the potential participant, and the individual has had the opportunity to ask questions. I confirm that the individual has given assent freely.

Print name of researcher_____

Signature of researcher_____

Date_____
Day/month/year

Statement by the researcher/person taking consent
I have accurately read out the information sheet to the potential participant, and to the best of my ability made sure that the child understands that the following will be done:
1.
2.
3.
I confirm that the child was given an opportunity to ask questions about the study, and all the questions asked by him/her have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.

A copy of this assent form has been provided to the participant.

Print Name of Researcher/person taking the assent_____

Signature of Researcher /person taking the assent _____

Date _____
Day/month/year

Copy provided to the participant _____ (initialed by researcher/assistant)

Parent/Guardian has signed an informed consent ___Yes ___No _____ (initialed by researcher/assistant

Annex 10.5:

Informed Consent Form Template for Qualitative Studies

(This template is for research interventions that use questionnaires, in-depth interviews or focus group discussions)

[Informed Consent Form for _____]

Name the group of individuals for whom this consent is written. Because research for a single project is often carried out with a number of different groups of individuals - for example counselors, community members, clients of services - it is important that you identify which group this particular consent is for.

(Example: This informed consent form is for social service providers in the community X and who we are inviting to participate in research Y, titled "The Community Response to Malaria Project".)

You may provide the following information either as a running paragraph or under headings as shown below.

[Name of Principle Investigator]
[Name of Organization]
[Name of Sponsor]
[Name of Project and Version]

This Informed Consent Form has two parts:

- **Information Sheet (to share information about the study with you)**
- **Certificate of Consent (for signatures if you choose to participate)**

You will be given a copy of the full Informed Consent Form

Part I: Information Sheet

Introduction

Briefly state who you are and that you are inviting them to participate in research which you are doing. Inform them that they may talk to anyone they feel comfortable talking with about the research and that they can take time to reflect on whether they want to participate or not. Assure the participant that if they do not understand some of the words or concepts, that you will take time to explain them as you go along and that they can ask questions at anytime.

(Example: I am X, working for the Y organization. I am doing research on the disease malaria which is very common in this country and in this region. I am going to give you information and invite you to be part of this research. You do not have to decide today whether or not you will participate in the research. Before you decide, you can talk to anyone you feel comfortable with about the research.
This consent form may contain words that you do not understand. Please ask me to stop as we go through the information and I will take time to explain. If you have questions later, you can ask them of me or of another researcher.)

Purpose of the research
Explain the research question in lay terms which will clarify rather than confuse. Use local and simplified words rather than scientific terms and professional jargon. In your explanation, consider local beliefs and knowledge when deciding how best to provide the information. Investigators however need to be careful not to mislead participants, by suggesting research interests that they do not have. For example, if the study wants to find out about treatments provided by local practitioners, wording should not suggest that they want to find out about how the practitioners are advertising themselves. Misleading participants may be essential and justified in certain circumstances, but that needs to be carefully argued, and approved by an ethics committee.

(Example: Malaria is making many people sick in your community. We want to find ways to stop this from happening. We believe that you can help us by telling us what you know both about malaria and about local health practices in general. We want to learn what people who live or work here know about the causes of malaria and why some people get it. We want to learn about the different ways that people try to stop malaria before someone gets it or before it comes to the community, and how people know when someone has it. We also want to know more about local health practices because this knowledge might help us to learn how to better control malaria in this community.)

Type of Research Intervention
Briefly state the type of intervention that will be undertaken. This will be expanded upon in the procedures section but it may be helpful and less confusing to the participant if they know from the very beginning whether, for example, the research involves a vaccine, an interview, a questionnaire, or a series of finger pricks.

(Example: This research will involve your participation in a group discussion that will take about one and a half hour, and a one hour interview).

Participant Selection
Indicate why you have chosen this person to participate in this research. People wonder why they have been chosen and may be fearful, confused or concerned.

(Example: You are being invited to take part in this research because we feel that your experience as a social worker (or as a mother, or as a responsible citizen) can contribute much to our understanding and knowledge of local health practices.)

- ***Example of question to elucidate understanding:*** *Do you know why we are asking you to take part in this study? Do you know what the study is about?*

Voluntary Participation
Indicate clearly that they can choose to participate or not. State, only if it is applicable, that they will still receive all the services they usually do if they choose not to participate. Explanation: It may be more applicable to assure them that their choosing to participate or not will not have any bearing on their job or job-related evaluations. This can be repeated and expanded upon later in the form as well. It is important to state clearly at the beginning of the form that participation is voluntary so that the other information can be heard in this context. Although, if the interview or group discussion has already taken place, the person cannot 'stop participation' but request that the information provided by them not be used in the research study.

(Example: Your participation in this research is entirely voluntary. It is your choice whether to participate or not. If you choose not to participate all the services you receive at this Centre will continue and nothing will change.
OR
The choice that you make will have no bearing on your job or on any work-related evaluations or reports. You may change your mind later and stop participating even if you agreed earlier.)

- ***Examples of question to elucidate understanding:*** *If you decide not to take part in this research study, do you know what your options are? Do you know that you do not have to take part in this research study, if you do not wish to? Do you have any questions?*

Procedures
A. Provide a brief introduction to the format of the research study.

(Example: We are asking you to help us learn more about malaria in your community. We are inviting you to take part in this research project. If you accept, you will be asked to…. :)

B. Explain the type of questions that the participants are likely to be asked in the focus group, the interviews, or the survey. If the research involves questions or discussion which may be sensitive or potentially cause embarrassment, inform the participant of this.

(Example 1 (for focus group discussions)
Take part in a discussion with 7-8 other persons with similar experiences. This discussion will be guided by [name of moderator/guider] or myself.
The group discussion will start with me, or the focus group guide or moderator (use the local word for group discussion leader), making sure that you are comfortable. We can also answer questions about the research that you might have. Then we will ask you questions about the malaria and give you time to share your knowledge. The questions will be about malaria in your community, how is it recognized, what people do to stop it from spreading to other people, who people go to for help and what happens when people become sick with it.
We will also talk about community practices more generally because this will give us a chance to understand more about malaria but in a different way. These are the types of questions we will ask…... ***We will not ask you to share personal beliefs, practices or stories and you do not have to share any knowledge that you are not comfortable sharing.***
The discussion will take place in [location of the FGD], and no one else but the people who take part in the discussion and guide or myself will be present during this discussion. The entire discussion will be tape-recorded, but no-one will be identified by name on the tape. The tape will be kept [explain how the tape will be stored]. The information recorded is confidential, and no one else except [name of person(s)] will have access to the tapes. The tapes will be destroyed after _____number of days/weeks.

Example 2 (for interviews)
Participate in an interview with [name of interviewer] or myself.
During the interview, I or another interviewer will sit down with you in a comfortable place at the Centre. If it is better for you, the interview can take place in your home or a friend's home. If you do not wish to answer any of the questions during the interview, you may say so and the interviewer will move on to the next question. No one else but the interviewer will be present unless you would like someone else to be there. The information recorded is confidential, and no one else except [name of person(s)] will access to the information documented during your interview. The entire interview will be tape-recorded, but no-one will be identified by name on the tape. The tape will be kept [explain how the tape will be stored]. The information recorded is confidential, and no one else except [name of person(s)] will have access to the tapes. The tapes will be destroyed after _____number of days/weeks.

Example 3 (for questionnaire surveys)
Fill out a survey which will be provided by [name of distributor of blank surveys] and collected by [name of collector of completed surveys].OR you may answer the questionnaire yourself, or it can be read to you and you can say out loud the answer you want me to write down.
If you do not wish to answer any of the questions included in the survey, you may skip them and move on to the next question. [Describe how the survey will be distributed and collected]. The information recorded is confidential, your name is not being included on the forms, only a number will identify you, and no one else except [name of person(s) with access to the information] will have access to your survey.)

Duration
Include a statement about the time commitments of the research for the participant including both the duration of the research and follow-up, if relevant.

(Example: The research takes place over ___ (number of) days/ or ___ (number of) months in total. During that time, we will visit you three times for interviewing you at one month interval and each interview will last for about one hour each. The group discussion will be held once and will take about one and a half hour.)

- ***Examples of question to elucidate understanding:*** *If you decide to take part in the study, do you know how much time will the interview take? Where will it take place? Do you know that we will be sending you transport to pick you up from your home? Do you know how much time will the discussion with other people take? If you agree to take part, do you know if you can stop participating? Do you know that you may not respond to the questions that you do not wish to respond to? Etc. Do you have any more questions?*

Risks

Explain and describe any risks that you anticipate or that are possible. The risks depend upon the nature and type of qualitative intervention, and should be, as usual, tailored to the specific issue and situation.

(If the discussion is on sensitive and personal issues e.g. reproductive and sexual health, personal habits etc. then an example of text could be something like "We are asking you to share with us some very personal and confidential information, and you may feel uncomfortable talking about some of the topics. You do not have to answer any question or take part in the discussion/interview/survey if you don't wish to do so, and that is also fine. You do not have to give us any reason for not responding to any question, or for refusing to take part in the interview"
OR If for example, the discussion is on opinions on government policies and community beliefs, and in general no personal information is sought, then the text under risks could read something like "There is a risk that you may share some personal or confidential information by chance, or that you may feel uncomfortable talking about some of the topics. However, we do not wish for this to happen. You do not have to answer any question or take part in the discussion/interview/survey if you feel the question(s) are too personal or if talking about them makes you uncomfortable.)

Benefits

Benefits may be divided into benefits to the individual, benefits to the community in which the individual resides, and benefits to society as a whole as a result of finding an answer to the research question. Mention only those activities that will be actual benefits and not those to which they are entitled regardless of participation.

(Example: There will be no direct benefit to you, but your participation is likely to help us find out more about how to prevent and treat malaria in your community).

Reimbursements

State clearly what you will provide the participants with as a result of their participation. IRB does not encourage incentives beyond reimbursements for expenses incurred as a result of participation in the research. These may include, for example, travel costs and reimbursement for time lost. The amount should be determined within the host country context.

Example: You will not be provided any incentive to take part in the research. However, we will give you [provide a figure, if money is involved] for your time, and travel expense (if applicable).

- ***Examples of question to elucidate understanding:*** *Can you tell me if you have understood correctly the benefits that you will have if you take part in the study? Do you know if the study will pay for your travel costs and time lost, and do you know how much you will be re-imbursed? Do you have any other questions?*

Confidentiality

Explain how the research team will maintain the confidentiality of data with respect to both information about the participant and information that the participant shares. Outline any limits to confidentiality. Inform the participant that because something out of the ordinary is being done through research, any individual taking part in the research is likely to be more easily identified by members of the community and therefore more likely to be stigmatized. If the research is sensitive and/or involves participants who are highly vulnerable - research concerning violence against women for example - explain to the participant any extra precautions you will take to ensure safety and anonymity.

(Example: The research being done in the community may draw attention and if you participate you may be asked questions by other people in the community. We will not be sharing information about you to anyone outside of the research team. The information that we collect from this research project will be kept private. Any information about you will have a number on it instead of your name. Only the researchers will know what your number is and we will lock that information up with a lock and key. It will not be shared with or given to anyone except [name who will have access to the information, such as research sponsors, DSMB board, your clinician, etc])

The following applies to focus groups:
Focus groups provide a particular challenge to confidentiality because once something is said in the group it becomes common knowledge. Explain to the participant that you will encourage group participants to respect confidentiality, but that you cannot guarantee it.

(Example: We will ask you and others in the group not to talk to people outside the group about what was said in the group. We will, in other words, ask each of you to keep what was said in the group confidential. You should know, however, that we cannot stop or prevent participants who were in the group from sharing things that should be confidential.)

- ***Example of question to elucidate understanding:*** *Did you understand the procedures that we will be using to make sure that any information that we as researchers collect about you will remain confidential? Do you understand that we cannot guarantee complete confidentiality of information that you share with us in a group discussion Do you have any more questions?*

Sharing the Results
Your plan for sharing the findings with the participants should be provided. If you have a plan and a timeline for the sharing of information, include the details. You may also inform the participant that the research findings will be shared more broadly, for example, through publications and conferences.

(Example: Nothing that you tell us today will be shared with anybody outside the research team, and nothing will be attributed to you by name. The knowledge that we get from this research will be shared with you and your community before it is made widely available to the public. Each participant will receive a summary of the results. There will also be small meetings in the community and these will be announced. Following the meetings, we will publish the results so that other interested people may learn from the research.)

Right to Refuse or Withdraw
This is a reconfirmation that participation is voluntary and includes the right to withdraw. Tailor this section to ensure that it fits for the group for whom you are seeking consent. The example used here is for a community social worker. Participants should have an opportunity to review their remarks in individual interviews and erase part or all of the recording or note.

(Example: You do not have to take part in this research if you do not wish to do so, and choosing to participate will not affect your job or job-related evaluations in any way. You may stop participating in the [discussion/interview] at any time that you wish without your job being affected. I will give you an opportunity at the end of the interview/discussion to review your remarks, and you can ask to modify or remove portions of those, if you do not agree with my notes or if I did not understand you correctly.)

Who to Contact

Provide the name and contact information of someone who is involved, informed and accessible - **a** local person who can actually be contacted. State also the name (and contact details) of the local IRB that has approved the proposal. State also that the proposal has also been approved by the IRB.

(Example: If you have any questions, you can ask them now or later. If you wish to ask questions later, you may contact any of the following: [name, address/telephone number/e-mail]
This proposal has been reviewed and approved by [name of the local IRB], which is a committee whose task it is to make sure that research participants are protected from harm. If you wish to find about more about the IRB, contact _____.)

This proposal has been reviewed and approved by [name of the local IRB], which is a committee whose task it is to make sure that research participants are protected from harm. If you wish to find about more about the IRB, contact [name, address, and telephone number.]).
Example of question to elucidate understanding: *Do you know that you do not have to take part in this study if you do not wish to? You can say No if you wish to? Do you know that you can ask me questions later, if you wish to? Do you know that I have given the contact details of the person who can give you more information about the study? Etc.*

You can ask me any more questions about any part of the research study, if you wish to. Do you have any questions?

Part II: Certificate of Consent

This section must be written in the first person. It should include a few brief statements about the research and be followed by a statement similar the one in bold below. If the participant is illiterate but gives oral consent, a witness must sign. A researcher or the person going over the informed consent must sign each consent. Because the certificate is an integral part of the informed consent and not a stand-alone document, the layout or design of the form should reflect this. The certificate of consent should avoid statements that have "I understand…." phrases. The understanding should perhaps be better tested through targeted questions during the reading of the information sheet (some examples of questions are given above), or through the questions being asked at the end of the reading of the information sheet, if the potential participant is reading the information sheet him/herself.

Example: I have been invited to participate in research about malaria and local health practices.

(This section is mandatory)
I have read the foregoing information, or it has been read to me. I have had the opportunity to ask questions about it and any questions I have been asked have been answered to my satisfaction. I consent voluntarily to be a participant in this study

Print Name of Participant_____
Signature of Participant _____
Date _____
Day/month/year

If illiterate [1]

[1] A literate witness must sign (if possible, this person should be selected by the participant and should have no connection to the research team). Participants who are illiterate should include their thumb print as well.

I have witnessed the accurate reading of the consent form to the potential participant, and the individual has had the opportunity to ask questions. I confirm that the individual has given consent freely.

Print name of witness_____ **Thumb print of participant**

Signature of witness _____

Date _____
Day/month/year

Statement by the researcher/person taking consent

I have accurately read out the information sheet to the potential participant, and to the best of my ability made sure that the participant understands that the following will be done:

1.
2.
3.

I confirm that the participant was given an opportunity to ask questions about the study, and all the questions asked by the participant have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.

A copy of this ICF has been provided to the participant.
Print Name of Researcher/person taking the consent_____

Signature of Researcher /person taking the consent_____

Date _____
Day/month/year

Annex 10.6

Informed Consent Form Template for Clinical Studies

L C

(This template is for either clinical trials or clinical research)

[Informed Consent form for _____ _____]

Name the group of individuals for whom this informed consent form is written. Because research for a single project is often carried out with a number of different groups of individuals - for example healthcare workers, patients, and parents of patients - it is important that you identify which group this particular consent is for.

(Example: This Informed Consent Form is for men and women who attend clinic Z, and who we are inviting to participate in research on X. The title of our research project is "……..")

You may provide the following information either as a running paragraph or under headings as shown below.

[Name of Principal Investigator]
[Name of Organization]
[Name of Sponsor]
[Name of Proposal and version]

This Informed Consent Form has two parts:

- **Information Sheet (to share information about the research with you)**
- **Certificate of Consent (for signatures if you agree to take part)**

You will be given a copy of the full Informed Consent Form

PART I: Information Sheet

Introduction

Briefly state who you are and explain that you are inviting them to participate in the research you are doing. Inform them that they may talk to anyone they feel comfortable talking with about the research and that they can take time to reflect on whether they want to participate or not. Assure the participant that if they do not understand some of the words or concepts, that you will take time to explain them as you go along and that they can ask questions now or later.

(Example: I am X, working for the Y Research Institute. We are doing research on Z disease, which is very common in this country. I am going to give you information and invite you to be part of this research. You do not have to decide today whether or not you will participate in the research. Before you decide, you can talk to anyone you feel comfortable with about the research.

There may be some words that you do not understand. Please ask me to stop as we go through the information and I will take time to explain. If you have questions later, you can ask them of me, the study doctor or the staff.)

Purpose of the research
Explain in lay terms why you are doing the research. The language used should clarify rather than confuse. Use local and simplified terms for a disease, e.g. local name of disease instead of malaria, mosquito instead of anopheles, "mosquitoes help in spreading the disease" rather than "mosquitoes are the vectors". Avoid using terms like pathogenesis, indicators, determinants, equitable etc. There are guides on the internet to help you find substitutes for words which are overly scientific or are professional jargon.

(Example: Malaria is one of the most common and dangerous diseases in this region. The drugs that are currently used to help people with malaria are not as good as we would like them to be. In fact, only 40 out of every 100 people given the malaria drug XYZ are completely cured. There is a new drug which may work better. The reason we are doing this research is to find out if the new drug ABX is better than drug XYZ which is currently being used.)

Type of Research Intervention
Briefly state the type of intervention that will be undertaken. This will be expanded upon in the procedures section but it may be helpful and less confusing to the participant if they know from the very beginning whether, for example, the research involves a vaccine, an interview, a biopsy or a series of finger pricks.

(Example: This research will involve a single injection in your arm as well as four follow-up visits to the clinic.)

Participant selection
State why this participant has been chosen for this research. People often wonder why they have been chosen to participate and may be fearful, confused or concerned.

(Example: We are inviting all adults with malaria who attend clinic Z to participate in the research on the new malaria drug.)

- ***Example of question to elucidate understanding:*** *Do you know why we are asking you to take part in this study? Do you know what the study is about?*

Voluntary Participation
Indicate clearly that they can choose to participate or not. State, what the alternative - in terms of the treatment offered by the clinic - will be, if they decide not to participate. State, only if it is applicable, that they will still receive all the services they usually do whether they choose to participate or not. This can be repeated and expanded upon later in the form as well, but it is important to state clearly at the beginning of the form that participation is voluntary so that the other information can be heard in this context.

(Example: Your participation in this research is entirely voluntary. It is your choice whether to participate or not. Whether you choose to participate or not, all the services you receive at this clinic will continue and nothing will change. If you choose not to participate in this research project, you will offered the treatment that is routinely offered in this clinic/hospital for disease Z, and we will tell you more about it later. You may change your mind later and stop participating even if you agreed earlier.)

- ***Examples of question to elucidate understanding:*** *If you decide not to take part in this research study, do you know what your options are? Do you know that you do not have to take part in this research study, if you do not wish to? Do you have any questions?*

Include the following section only if the protocol is for a clinical trial:

Information on the Trial Drug [Name of Drug]
1) give the phase of the trial and explain what that means. Explain to the participant why you are comparing or testing the drugs.
2) provide as much information as is appropriate and understandable about the drug such as its manufacturer or location of manufacture and the reason for its development.
3) explain the known experience with this drug
4) explain comprehensively all the known side-effects/toxicity of this drug, as well as the adverse effects of all the other medicines that are being used in the trial

(Example: The drug we are testing in this research is called ABX. It has been tested before with people who do not have malaria but who live in areas where malaria is common. We now want to test the drug on people who have malaria. This second research is called a "phase 2" trial.

The drug ABX is made by Company C. You should know that it has a few side effects. One of the side effects, or problems, is that you may feel tired for the first day after being given the drug. Also, 20% of the people who tried the drug in previous research experienced temporary swelling where the injection entered the skin. We know of no other problem or risks.

Some participants in the research will not be given the drug which we are testing. Instead, they will be given the drug XYZ, the drug which is most commonly used in this region to treat malaria. There is no risk associated with that drug and no known problems. It does not, however, cure malaria as often as we would like.)

Procedures and Protocol
Describe or explain the exact procedures that will be followed on a step-by-step basis, the tests that will be done, and any drugs that will be given. Explain from the outset what some of the more unfamiliar procedures involve (placebo, randomization, biopsy, etc.) Indicate which procedure is routine and which is experimental or research.Participants should know what to expect and what is expected of them. Use active, rather than conditional, language. Write "we will ask you to…." instead of "we would like to ask you to…."

In this template, this section has been divided into two: firstly, an explanation of unfamiliar procedures and, secondly, a description of process.

A. Unfamiliar Procedures
This section should be included if there may be procedures which are not familiar to the participant.

If the protocol is for a clinical trial:
1) Involving randomization or blinding, the participants should be told what that means and what chance they have of getting which drug (i.e. one in four chances of getting the test drug).

(Example: Because we do not know if the new malaria drug is better than the currently available drug for treating malaria, we need to compare the two. To do this, we will put people taking part in this research into two groups. The groups are selected by chance, as if by tossing a coin.

Participants in one group will be given the test drug while participants in the other group will be given the drug that is currently being used for malaria. It is important that neither you nor we know which of the two drugs you are given. This information will be in our files, but we will not look at these files until after the research is finished. This is the best way we have for testing without being influenced by what we think or hope might happen. We will then compare which of the two has the best results.

The healthcare workers will be looking after you and the other participants very carefully during the study. If we are concerned about what the drug is doing, we will find out which drug you are getting and make changes. If there is anything you are concerned about or that is bothering you about the research please talk to me or one of the other researchers)

2) Involving an inactive drug or placebo, it is important to ensure that the participants understand what is meant by a placebo or inactive drug.

(Example: A placebo or inactive medicine looks like real medicine but it is not. It is a dummy or pretend medicine. It has no effect on a person because it has no real medicine in it. Sometimes when we want to know whether a new medicine is good, we give some people the new medicine and some people the pretend or dummy medicine. For the research to be good, it is important that you do not know whether you have been given the real medicine or the pretend or dummy medicine. This is one of the best ways we have for knowing what the medicine we are testing really does.)

3) Which may necessitate a rescue medicine, then provide information about the rescue medicine or treatment such as what it is and the criterion for its use. For example, in pain trials, if the test drug does not control pain, then intravenous morphine may be used as a rescue medicine.

(Example: If we find that the medicine that is being used does not have the desired effect, or not to the extent that we wish it to have, we will use what is called a "rescue medicine." The medicine that we will use is called QRS and it has been proven to control pain. If you find that the drug we are testing does not stop your pain and it is very uncomfortable for you, we can use the rescue medicine to make you more comfortable.)

If the protocol is for clinical research:
Firstly, explain that there are standards/guidelines that will be followed for the treatment of their condition. Secondly, if as part of the research a biopsy will be taken, then explain whether it will be under local anesthesia, sedation or general anesthesia, and what sort of symptoms and side effects the participant should expect under each category.

(Example: You will receive the treatment of your condition according to national guidelines. This means that you will be (explain the treatment). To confirm the cause of your swelling, a small sample of your skin will be taken. The guidelines say that the sample must be taken using a local anesthesia which means that we will give you an injection close to the area where we will take the sample from. This will make the area numb so that you will not feel any pain when we take the sample.)

For any clinical study (if relevant):
If blood samples are to be taken explain how many times and how much in a language that the person understands. It may, for example, be inappropriate to tell a tribal villager that blood equal to a wine-glass full will be taken but it may be very appropriate to use pictures or other props to illustrate the procedure if it is unfamiliar.

If the samples are to be used only for this research, then explicitly mention here that the biological samples obtained during this research procedure will be used only for this research, and will be destroyed after ____ years, when the research is completed. If the tissues/blood samples or any other human biological material will be stored for a duration longer than the research purpose, or is likely to be used for a purpose other than mentioned in the research proposal, then provide information about this and obtain consent specifically for such storage and use in addition to consent for participation in the study - (see last section)

(Example: We will take blood from your arm using a syringe and needle. Each time we will take about this much blood (show a spoon, vial or other small container with a small amount of water in it. In total, we will take about ……..this much blood in x number of weeks/months. At the end of the research, in 1 year, any leftover blood sample will be destroyed.)

B. Description of the Process

Describe to the participant what will happen on a step-by-step basis. It may be helpful to the participant if you use drawings or props to better illustrate the procedures. A small vial or container with a little water in it is one way of showing how much blood will be withdrawn.

(Example: During the research you make five visits to the clinic.

- *In the first visit, a small amount of blood, equal to about a teaspoon, will be taken from your arm with a syringe. This blood will be tested for the presence of substances that help your body to fight infections. We will also ask you a few questions about your general health and measure how tall you are and how much you weigh.*
- *At the next visit, which will be two weeks later, you will again be asked some questions about your health and then you will be given either the test drug or the drug that is currently used for malaria. As explained before, neither you nor we will know whether you have received the test or the dummy/pretend drug.*
- *After one week, you will come back to the clinic for a blood test. This will involve….)*

Duration

Include a statement about the time commitments of the research for the participant including both the duration of the research and follow-up, if relevant.

(Example: The research takes place over ___ (number of) days/ or ___ (number of) months in total. During that time, it will be necessary for you to come to the clinic/hospital/health facility _____ (number of) days, for ____ (number of) hours each day. We would like to meet with you three months after your last clinic visit for a final check-up.

In total, you will be asked to come 5 times to the clinic in 6 months. At the end of six months, the research will be finished.)

- ***Examples of question to elucidate understanding:*** *Can you tell me if you remember the number of times that we are asking you to come to the hospital to complete the treatment? The research project? How many injections will you be given? How many tablets? How much blood will be taken from your veins, using a syringe and needle? Over how many weeks? Etc. Do you have any other questions? Do you want me to go through the procedures again?*

Side Effects

Potential participants should be told if there are any known or anticipated side effects and what will happen in the event of a side effect or an unexpected event.

(Example: As already mentioned, this drug can have some unwanted effects. It can make you tired and it can cause some temporary swelling around the place where the injection goes into your arm. It is possible that it may also cause some problems that we are not aware of. However, we will follow you closely and keep track of any unwanted effects or any problems. We may use some other medicines to decrease the symptoms of the side effects or reactions. Or we may stop the use of one or more drugs. If this is necessary we will discuss it together with you and you will always be consulted before we move to the next step.)

Risks

Explain and describe any possible or anticipated risks. Describe the level of care that will be available in the event that harm does occur, who will provide it, and who will pay for it. A risk can be thought of as being the possibility that harm may occur. Provide enough information about the risks that the participant can make an informed decision.

(Example: By participating in this research it is possible that you will be at greater risk than you would otherwise be. There is, for example, a risk that your disease will not get better and that the new medicine doesn't work even as well as the old one. If, however, the medicine is not working and your fever does not go down in 48 hours we will give you quinine injections which will bring your fever down and make you more comfortable.

While the possibility of this happening is very low, you should still be aware of the possibility. We will try to decrease the chances of this event occurring, but if something unexpected happens, we will provide you with_____.)

- ***Examples of question to elucidate understanding:*** *Do you understand that, while the research study is on-going, no-one may know which medicine you re receiving? Do you know that the medicine that we are testing is a new medicine, and we do not know everything about it? Do you understand that you may have some unwanted side-effects from the medicines? Do you understand that these side-effects can happen whether or not you are in the research study? Etc. Do you have any other questions?*

Benefits
Mention only those activities that will be actual benefits and not those to which they are entitled regardless of participation. Benefits may be divided into benefits to the individual, benefits to the community in which the individual resides, and benefits to society as a whole as a result of finding an answer to the research question.

(Example: If you participate in this research, you will have the following benefits: any interim illnesses will be treated at no charge to you. If your child falls sick during this period he/she will be treated free of charge. There may not be any benefit for you but your participation is likely to help us find the answer to the research question. There may not be any benefit to the society at this stage of the research, but future generations are likely to benefit.)

Reimbursements
State clearly what you will provide the participants with as a result of their participation. WHO does not encourage incentives. However, it recommends that reimbursements for expenses incurred as a result of participation in the research be provided. These may include, for example, travel costs and money for wages lost due to visits to health facilities. The amount should be determined within the host country context.

(Example: We will give you [amount of money] to pay for your travel to the clinic/parking and we will give you [amount] for lost work time. You will not be given any other money or gifts to take part in this research.)

- ***Examples of question to elucidate understanding:*** *Can you tell me if you have understood correctly the benefits that you will have if you take part in the study? Do you know if the study will pay for your travel costs and time lost, and do you know how much you will be re-imbursed? Do you have any other questions?*

Confidentiality
Explain how the research team will maintain the confidentiality of data, especially with respect to the information about the participant which would otherwise be known only to the physician but would now be available to the entire research team. Note that because something out of the ordinary is being done through research, any individual taking part in the research is likely to be more easily identified by members of the community and is therefore more likely to be stigmatized.

(Example: With this research, something out of the ordinary is being done in your community. It is possible that if others in the community are aware that you are participating, they may ask you questions. We will not be sharing the identity of those participating in the research.

The information that we collect from this research project will be kept confidential. Information about you that will be collected during the research will be put away and no-one but the researchers will be able to see it. Any information about you will have a number on it instead of your name. Only the researchers will know what your number is and we will lock that information up with a lock and key. It will not be shared with or given to anyone except [name who will have access to the information, such as research sponsors, DSMB board, your clinician, etc].)

- ***Example of question to elucidate understanding:*** *Did you understand the procedures that we will be using to make sure that any information that we as researchers collect about you will remain confidential? Do you have any questions about them?*

Sharing the Results
Where it is relevant, your plan for sharing the information with the participants should be provided. If you have a plan and a timeline for the sharing of information, include the details. You should also inform the participant that the research findings will be shared more broadly, for example, through publications and conferences.

(Example: The knowledge that we get from doing this research will be shared with you through community meetings before it is made widely available to the public. Confidential information will not be shared. There will be small meetings in the community and these will be announced. After these meetings, we will publish the results in order that other interested people may learn from our research.)

Right to Refuse or Withdraw
This is a reconfirmation that participation is voluntary and includes the right to withdraw. Tailor this section to ensure that it fits for the group for whom you are seeking consent. The example used here is for a patient at a clinic.

(Example: You do not have to take part in this research if you do not wish to do so and refusing to participate will not affect your treatment at this clinic in any way. You will still have all the benefits that you would otherwise have at this clinic. You may stop participating in the research at any time that you wish without losing any of your rights as a patient here. Your treatment at this clinic will not be affected in any way.)
OR
(Example: You do not have to take part in this research if you do not wish to do so. You may also stop participating in the research at any time you choose. It is your choice and all of your rights will still be respected.)

Alternatives to Participating
Include this section only if the study involves administration of investigational drugs or use of new therapeutic procedures. It is important to explain and describe the <u>established</u> standard treatment.

(Example: If you do not wish to take part in the research, you will be provided with the established standard treatment available at the centre/institute/hospital. People who have malaria are given….)

Who to Contact
Provide the name and contact information of someone who is involved, informed and accessible (a local person who can actually be contacted. State also that the proposal has been approved and how.

(Example: If you have any questions you may ask them now or later, even after the study has started. If you wish to ask questions later, you may contact any of the following: [name, address/telephone number/e-mail])

This proposal has been reviewed and approved by [name of the local IRB], which is a committee whose task it is to make sure that research participants are protected from harm. If you wish to find about more about the IRB, contact [name, address, and telephone number.]). It has also been reviewed by the Ethics Review Committee of the World Health Organization (WHO), which is funding/sponsoring/supporting the study.

- *<u>Example of question to elucidate understanding:</u>* ***Do you know that you do not have to take part in this study if you do not wish to? You can say No if you wish to? Do you know***

that you can ask me questions later, if you wish to? Do you know that I have given the contact details of the person who can give you more information about the study? Etc.

You can ask me any more questions about any part of the research study, if you wish to. Do you have any questions?

PART II: Certificate of Consent

This section should be written in the first person and have a statement similar to the one in bold below. If the participant is illiterate but gives oral consent, a witness must sign. A researcher or the person going over the informed consent must sign each consent. The certificate of consent should avoid statements that have "I understand…." phrases. The understanding should perhaps be better tested through targeted questions during the reading of the information sheet (some examples of questions are given above), or through the questions being asked at the end of the reading of the information sheet, if the potential participant is reading the information sheet him/herself.

I have read the foregoing information, or it has been read to me. I have had the opportunity to ask questions about it and any questions that I have asked have been answered to my satisfaction. I consent voluntarily to participate as a participant in this research.

Print Name of Participant_____

Signature of Participant _____

Date _____

Day/month/year

If illiterate

A literate witness must sign (if possible, this person should be selected by the participant and should have no connection to the research team). Participants who are illiterate should include their thumb-print as well.

I have witnessed the accurate reading of the consent form to the potential participant, and the individual has had the opportunity to ask questions. I confirm that the individual has given consent freely.

Print name of witness_____ ***AND*** ***Thumb print of participant***

Signature of witness _____

Date _____
Day/month/year

Statement by the researcher/person taking consent

I have accurately read out the information sheet to the potential participant, and to the best of my ability made sure that the participant understands that the following will be done:

1.
2.
3.

I confirm that the participant was given an opportunity to ask questions about the study, and all the questions asked by the participant have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.

A copy of this ICF has been provided to the participant.

Print Name of Researcher/person taking the consent_____

Signature of Researcher /person taking the consent_____

Date _____
Day/month/year

ANNEX 11

Guide to Placebo Justification

Background conditions, such as benefits of standard treatment, risk of using placebo, risk management and disclosure should be considered. The followings are some guides to ease committee decision.

I. Benefits of standard treatment

1) Is there a standard treatment?
2) Is the standard treatment widely accepted?
3) Has efficacy of the treatment been consistently proven?
4) Are all newly diagnosed patients with this condition put in standard treatment (versus observed or other)?
5) Does the treatment act on the basic mechanism of the disease (vs. symptoms)?
6) Are most (≥85%) of the patients with this condition responsive to standard treatment alternatives (vs. resistant or refractory)?

If the answer of* (1) *to* (6) *are "yes", placebo is not recommended.
If any one or more answers are "no", placebo may be possible.

7) Are the side effects of the standard treatment severe?
8) Does standard treatment have many uncomfortable side effects?
9) Does standard treatment have contraindications that prevent some subjects from being treated?
10) Is there substantial (≤25%) placebo response in this disease or symptom?

If the answer of* (7) *to* (10) *are "no", placebo is not recommended.
If any one or more answers are "yes", placebo may be possible.

II. Risks of placebo

1) Is the risk of using placebo instead of treatment life threatening?

If yes, placebo is not acceptable.

2) Is the use of placebo instead of treatment likely to lead to permanent damage?

If yes, placebo is not acceptable.

3) Is the risk of using placebo instead of treatment likely to cause irreversible disease progression?

If yes, placebo is not acceptable.

4) Can the use of placebo instead of treatment lead to an acute emergency?
5) Is the risk of using placebo instead of treatment not relieve the distressing symptoms?

If the answer of* (4) *to* (5) *are "yes", placebo is not acceptable unless risk management is adequate.

III. Risk management

1) Is there benefit in the overall management of the subject?

☐ *Yes, consider placebo*
☐ *No, placebo not recommended*.

2) Will the discontinuation of previous treatment put the participant in danger of acute relapse when transferred to placebo?

☐ *No, consider placebo*
☐ *Yes, placebo not recommended*.

3) Are subjects at high risk for the use of placebo excluded?

☐ *Yes, consider placebo*
☐ *No, placebo not recommended*.

4) Is the duration of the study, the minimum necessary in relation to the duration of the action of the study drug?

☐ *Yes, consider placebo*
☐ *No, placebo not recommended*.

5) Are there clearly defined stopping provision to withdraw the subject in case he/she does not improve?

☐ *Yes, consider placebo*
☐ *No, placebo not recommended*.

6) Is risk monitoring adequate to identify progression of the disease before the subject experience severe consequences?

☐ *Not applicable.*
☐ *Yes, consider placebo*
☐ *No, placebo not recommended*.

7) Are there clearly defined stopping rules to withdraw the subject before the advent of severe disease progression?

☐ *Yes, consider placebo*
☐ *No, placebo not recommended*.

8) If the risk of placebo is an acute emergency, are rescue medication and emergency treatment available?

☐ *Not applicable.*
☐ *Yes, consider placebo*
☐ *No, placebo not recommended*.

9) If the risk of placebo is the persistence of distressing symptoms, is concurrent medication to control them allowed?

☐ *Not applicable.*
☐ *Yes, consider placebo.*
☐ *No, placebos not recommend*.

10) If the risk of placebo is severe physical discomfort or pain, is there rescue medication?

☐ *Not applicable.*
☐ *Yes, consider placebo.*
☐ *No, placebos not recommend*.

IV. Risk disclosure in the consent form

1) Are the risks of getting placebo instead of active treatment fully disclosed?
   ☐ *Yes, consider placebo.*
2) Are the risks of the test drug disclosed?
   ☐ *Yes, consider placebo.*
3) Are the advantages of alternative treatments explained?
   ☐ *Yes, consider placebo.*

Conclusions:

1. The use of placebo is ethically acceptable because:
   - ☐ Subjects are not exposed to severe or permanent harm by the use of placebo.
   - ☐ Subjects under placebo will benefit from the overall treatment of the disease.
   - ☐ Risks of the use of placebo are minimized.
   - ☐ Risks are adequately disclosed in the consent form.

2. The use of placebo in this study could be reconsidered if the following conditions are met:

   ……
   ……
   ……
   …
   .

3. The use of placebo in this study is ethically unacceptable because:
   - ☐ Subjects are exposed to severe or permanent harm by the use of placebo instead of active treatment.
   - ☐ Due to the nature of the disease, the risks of placebo can not be minimized.

ANNEX 12

Criteria for Research Protocol Approval

In order to **approve** research, IRB shall determine that all of the following requirements are satisfied:

1. Risks to subjects are minimized (i) by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and (ii) whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes;
2. Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result. In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research). The IRB should not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.
3. Selection of subjects is equitable. In making this assessment the IRB should take into account the purposes of the research and the setting in which the research will be conducted and should be particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons.
4. Informed consent will be sought from each prospective subject or the subject's legally authorized representative.
5. Informed consent will be appropriately documented.
6. When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.
7. When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.
8. When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects
9. Protocol is technically sound (background, objectives, methodology and data collection tools)

Approved with recommendations

The protocols will be "approved with recommendations" when all the criteria for approval are satisfied. However, the following conditions needs to be fulfilled:

1. Obtain administrative clearances as required by law/policy including permission from the study sites before conducting the study.
2. Minor modification(s) such as typographical errors, grammar, references

The protocols "approved with recommendation" can be reviewed by the Chairperson, after receipt of the requested modifications.

Solicited for Resubmission

If the criteria for approval are not satisfied then the protocol will be "solicited for resubmission".

The review of the resubmitted protocol will be guided by the decision of the preceding review and/or "SOP/008/05 Expedited Review".

Disapproval

The protocols will be “disapproved” under following conditions, but not limited to:

1. Major violation of ethical principles.
2. If the plagiarism is identified.
3. Any other reason as decided by the board.

CHAPTER 4.1

REVIEW OF RESUBMITTED PROTOCOLS

SOP NUMBER: SOP/013/01

INSTITUTIONAL REVIEW BOARD
(IRB)

Khesar Gyalpo University of Medical Sciences of Bhutan

www.kgumsb.edu.bt

Effective Date: October 1, 2021
Supersedes: SOP/012/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

This procedure describes how resubmitted study protocols shall be managed, re-reviewed and approved by the IRB.

2. SCOPE

This SOP shall apply to study protocols that have been reviewed earlier with recommendations from IRB for some corrections in the initial review process requested to be resubmitted for review.

3. RESPONSIBILITY

The IRB Secretariat shall be responsible to ensure the completeness of the resubmitted documents and to notify the Chairperson that a protocol previously approved with conditions for revision has been resubmitted to the IRB for reconsideration.

A re-submitted protocol may be reviewed and approved by either the Chairperson or some IRB members/reviewers, or full Board. How the protocol shall be reviewed should have been determined by the IRB at the time of the initial review. This information can be found on the Decision Form (AF 04-012/01).

4. FLOW CHART

No.	Activity	Responsibility
1	Receive protocol resubmitted package and distribute to the primary reviewers ↓	IRB Member Secretary
2	Review the revised protocol ↓	Primary Reviewers
3	Include in the IRB meeting agenda ↓	IRB Member Secretary
4	IRB Meeting ↓	IRB Members / Reviewers
5	Communicate the IRB decision to the investigator ↓	IRB Secretariat / Chairperson
6	Storage of the documents	IRB Secretariat

5. DETAILED INSTRUCTIONS

5.1. Receive protocol resubmitted package and distribute to the reviewers.

5.1.1. Check the submitted packages and complete the submission process (refers to SOP/008/01 – Management of Protocol Submission, section 5.3). The package includes:

5.1.1.1. Memorandum addressing the corrections,

5.1.1.2. Revised version of protocol and related documents such as the informed consent document, data collection or case report forms, diary sheets, etc are included as part of the package.

5.1.1.3. Changes made to the documents should be underlined or highlighted.

5.1.2. Distribute the protocol package to the reviewers.

5.1.2.1. Referring to the information on the decision form of the previous meeting whether the resubmitted protocol is for expedited or full board review.

5.1.2.1.1. If for Expedited Review, refer to SOP 009 – Expedited Review

5.1.2.1.2. If for full board review, distribute the package to the previous primary reviewers.

5.1.2.2. The protocol package includes the submitted documents listed in 5.1.1, along with previous review meeting minutes, the decision form of the previous meeting, Resubmitted Protocol Review Form (AF/01-013/01), and the due date for the review.

5.2. Review the revised protocol.

5.2.1. Refer to the meeting minutes and/or the action letter as guidance for the review.

5.2.2. Consider whether the recommendation of the IRB has been followed.

5.2.3. Complete the Resubmitted Protocol Review Form (AF/01-013/01).

5.2.4. Notify the IRB Secretariat by the due date.

5.3. IRB meeting

5.3.1. The Secretariat receives the review report and informs the Chairperson.

5.3.2. If no IRB meeting is necessary, then go to step 5.4.

5.3.3. If the IRB previously decided to see the new revision, then proceed with the following steps:

5.3.3.1. The primary reviewer shall present a brief oral or written summary of the study design and his/her comments to the IRB members.

5.3.3.2. The Chairperson shall entertain discussion on the protocol revision.

5.3.3.3. Further 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.

5.3.3.4. The Chairperson shall call for a vote on the revision to either:

5.3.3.4.1. Approve the study to start as presented with no modifications (**Approved**)

5.3.3.4.2. Approve the study to start with Board approved modifications to the consent (**Approved with minor modification**)

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

5.3.3.4.4. **Not Approved**.

5.3.3.5. The IRB Member Secretary shall record the Board's decision on the Decision Form and the Chairperson shall sign for the approval.

5.4 Communicate the IRB decision to the investigator (Refer to SOP/010/01 – Initial Review, section 5.6)

5.5 Storage of the documents (Refer to SOP/010/01– Initial Review, section 5.7)

6. GLOSSARY

Document	All kinds of evidence to include paper documents, electronic mail (e-mail), fax, audio or video tape.
Completed Assessment Form	An official record of the review decision along with comments and dated signature of the reviewer.

7. REFERENCES

7.1. International Conference on Harmonization, Guidance on Good Clinical Practice (ICH GCP) 2016.
7.2. World Health Organization, Operational Guidelines for Ethics Committees that Review Biomedical Research, 2000.
7.3. World Health Organisation, Standards and operational guidance for ethics review of health-related research with human participants, 2011
7.4. Associated SOPs: SOP/010/01.

8. ANNEX

ANNEX 1 AF/01-013/01 Re-submitted Protocol Review Form
ANNEX 2 AF/02-013/01 Application Form for Resubmitted Protocol Review

ANNEX 1
AF 01-013/01

Resubmitted Protocol Review Form

Protocol No.:	Version No.: dated DD/MM/YYYY
Protocol Title:	
Principal Investigator:	
Proponent of the study:	
☐ 2nd Review ☐ 3rd Review ☐ 4th Review ☐ ...th Review *(**NB**: Consider Initial review to be the 1st review)*	
Initial Review Date:	Last Review Date:
Previous Decision of IRB: ☐ Approved with Recommendations ☐ Resubmission ☐ Disapproved	
✧ Recommendations/clarifications sought in previous review	
1.	☐ Addressed ☐ Not Addressed
2.	☐ Addressed ☐ Not Addressed
3.	☐ Addressed ☐ Not Addressed
4.	☐ Addressed ☐ Not Addressed
✧ Other revisions, is any:	
1.	
2.	
✧ What need to be further revised, if required:	

Decision of the reviewer ☐ Approve ☐ Approve with Recommendations ☐ Solicit for Resubmission ☐ Disapprove

If approved, frequencies for continuing review (CR): ... *(**NB**: Default schedule for CR is one month before the approval expiry date)*

SIGNATURES:

_____ Date: ……

Protocol Reviewer

ANNEX 2
Form AF/02-013/01

APPLICATION FORM for RESUBMITTED PROTOCOL REVIEW

1. Protocol Number (*To be assigned by IRB Secretariat*): ...

2. Protocol Title: ...

2.1. Protocol Version No.: ... Dated: ...

3. PARTICULARS OF THE PRINCIPAL INVESTIGATOR (PI)

Name: ……

Address: ……

Telephone: …… Fax(optional): ……..

E-mail: …….....

3.1 Proponent of the study: …….....

4.	Recommendations/clarifications sought in previous review:	Clarification/Action Taken
	1.	
	2.	
	3.	
	4.	
	5.	
	6.	
	7.	
	8.	

5.	Other revisions, is any:
	1.
	2.
	3.
	4.

SIGNATURES:

_____ Date: ……..

Principal Investigator

_____ Date:……

Protocol Chairperson (if applicable)

COMPLETION:

_____ Date: ……

Member Secretary, IRB

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	

CHAPTER 4.3

MANAGEMENT OF PROTOCOL CONTINUING REVIEWS

SOP NUMBER: SOP/015/01

INSTITUTIONAL REVIEW BOARD
(IRB)

Khesar Gyalpo University of Medical Sciences of Bhutan

www.kgumsb.edu.bt

Effective Date: October 01, 2021 Supersedes: SOP/001/yy	
Author: SOP Team	Date: September 29, 2021
Approved by: Chairperson, IRB *Name:* ***Dr. Karma Tenzin***	Date: September 30, 2021

Table of Contents

1. PURPOSE

This procedure describes how continuing reviews of previously approved *IRB* protocols shall be managed by the Ethics Board.

The purpose of the continuing review shall be to monitor the progress of the entire study, not just the changes in it, to ensure continuous protection of the rights and welfare of research participants. Continuing review of the study may not be conducted through an expedited review procedure, unless (1) the study was eligible for, and initially reviewed by, an expedited review procedure; or (2) the study has changed such that only the activities that are eligible for expedited review are remaining; or (3) Continuing review with no modifications /amendment to the original protocol and no additional risks have been identified.

2. SCOPE

This SOP shall apply to conducting any continuing review of study protocols involving human subjects at intervals appropriate to the degree of risk but *not less than once a year.* Depending upon the degree of risk to the participants, the nature of the studies, and the vulnerability of the study participants and duration of the study, the IRB may choose to review or monitor the protocols more frequently.

3. RESPONSIBILITY

The IRB Secretariat shall be responsible to remind the IRB and the principal investigators regarding study protocols that shall be continuously reviewed. *The frequency of continuing review is based on the IRB decision during the approval of the study protocol.*

The IRB shall be responsible for reviewing the progress made in the protocol, the occurrence of unexpected events or problems, and the rate of accrual of participants. The protocol informed consent documents and assent documents shall be examined to ensure that the information remains accurate and unchanged from the original approved protocol.

The IRB has the same options for decision making on a continuing review package as for an initial review package. The decision shall be made as *approved; approved with recommendations; resubmission and disapproved.*

4. FLOW CHART

No.	Activity	Responsibility
1	Determine the date of continuing review ↓	Members and Chairperson
2	Notify the study team ↓	IRB Secretariat
3	Manage continuing review package upon receipt ↓	IRB Secretariat

No.	Activity	Responsibility
4	Notify the members of the IRB ↓	IRB Secretariat
5	Continuing review process ↓	IRB Secretariat, Members and Chairperson
6	Communicate the decision to the investigator ↓	IRB Secretariat
7	Storage of the Documents	IRB Secretariat

5. DETAILED INSTRUCTIONS

5.1 Determine the date of continuing review.

5.1.1 The Members and Chairperson shall be responsible for determining the date of continuing review.

5.1.2 Once the date of continuing review is determined, add it to the "database tracking system" under the column 'continuing review date'.

5.1.3 Look through the approval letter and/or database tracking system for the due date of continuing reviews. Plan for continuing review at least two months ahead and as close as possible to the due date of continuing reviews or in the first quarter of the study period.

5.2 Notify the principal investigator or the study team

5.2.1 Inform the Study Team at least two months in advance of the due date for the continuing review by fax, post, e-mail or other appropriate means.

5.2.2 Fax, mail or e-mail also a Continuing Review Application Form, ANNEX - AF/01-015/01 to the Study Team to fill up.

5.2.3 Keep the informed notice in the protocol file.

5.2.4 Allow the Study Team sufficient time to collate the information and to prepare a report package required for the continuing review.

5.3 Manage continuing review package upon receipt.

5.3.1 Receive a package of continuing review for each protocol prepared and submitted by the Study Team.

5.3.2 Upon receipt of the package, the Secretariat of the IRB shall perform the following:

5.3.2.1 Initial and date the submission package

5.3.2.1.1 See SOP/008/01 for procedures on receipt of submitted packages.

5.3.2.2 Verify the contents of the package.

5.3.2.2.1 Make sure that the contents of the package include:

5.3.2.2.1.1 Continuing Review Application Form

5.3.2.2.1.1.1 Check for complete information and for the presence of the required signatures (investigator and the chairperson of IRB).

5.3.2.2.1.1.2 See the Continuing Review Application Form, ANNEX - AF/01-015/01.

5.3.2.3 Continuing Review Memorandum with progress report

5.3.2.3.1 Summarize the progress of the protocol since the time of the last review.

5.3.2.3.2 Include information about the number of participants enrolled to date and since the time of the last review, an explanation for any "yes" answers on the application form

and a discussion of scientific development, either through the conduct of this study or similar research that may alter risks to research participants.

5.3.2.4 Current Informed Consent Document

5.3.2.4.1 - Ensure that the version of the informed consent document is the most recently approved informed consent document.

5.3.3 Photocopy the package.

5.3.3.1 Make sufficient copies (for both members and reviewers) of the original continuing review package in accordance with IRB SOP/ Procedures for Maintaining Confidentiality of IRB Documents.

5.3.4 Store the continuing review package.

5.3.4.1 Store the original package in the protocol specific file.

5.4 Notify the Members of the IRB.

5.4.1 Distribute the protocol progress report and the informed consent document to the IRB members.

5.5 Prepare meeting agenda.

5.5.1 See SOP/022/01 for procedures on the preparation of meeting agenda.

5.5.2 Place the review on the agenda for the meeting of the IRB which coincides with the first quarter of the study period or nearest next regular IRB scheduled meeting.

5.5.3 Distribute the materials to the IRB members by electronic mail (e-mail), or fax or by post, according to SOP/027/01 (Procedures for Maintaining Confidentiality of IRB Documents) at least one and a half to two weeks in advance of the scheduled meeting.

5.5.4 Keep copies of "sent" e-mail, fax cover memos and/or letter accompanying posted materials in the Correspondence Section of the protocol specific file.

5.5.5 Record and keep the IRB members' response upon receipt of the agenda in the member correspondence file.

5.6 Continuing Review Process

Continuing Review Application Form

5.6.1 Use the Continuing Review Application Form, ANNEX - AF/01-015/01 to guide the review and deliberation process.

5.6.2 If there are amendments or changes then "Review of Protocol Amendments" SOP/014 applies.

5.6.3 Sign and date the Continuing Review Application Form by the Chairperson of the IRB after a decision has been reached.

5.6.3.1 The completed Continuing Review Applications Form is the official record of the decision reached by the IRB for the protocol.

5.6.4 Maintain and keep the form and minutes of the meeting relevant to the continuing review as part of the official record of the review process.

5.7 Communicate the decision to the investigator

5.7.1 Send the action letter to the Principal Investigator within *5 working days*

5.8 Store original documents.

5.8.1 Place the original completed documents with the other documents in the Continuing Review Package in the protocol file.

6 GLOSSARY

Approved Protocols	Protocols that have been *approved without stipulations* or *approved with recommendations* by the IRB may proceed. Protocols that have been *approved with stipulations* by the IRB may not proceed until the conditions set by the IRB in the decision have been met. Protocols shall be amended and submitted to the IRB within *one* month for re-review.

7 REFERENCES

7.1 World Health Organization, Operational Guidelines for Ethics Boards that Review Biomedical Research, 2000.

7.2 World Health Organization, Standards and operational guidance for ethics review of health-related research with human participants, 2011.

7.3 International Conference on Harmonization, Guidance on Good Clinical Practice (ICH GCP) 2016.

7.4 Associated SOP/008/01, SOP/022/01 and SOP/027/01.

8 ANNEX

ANNEX1 AF/01-015/01 Continuing Review Application Form (2 pages)

ANNEX – 1
AF/01-015/01

Continuing Review Application Form

PROTOCOL No.:	PROTOCOL TITLE:
Principal Investigator:	Site……

Action Requested:
- ❑ Renew - New Participant Accrual To Continue
- ❑ Renew - Enrolled Participant Follow Up Only
- ❑ Terminate - Protocol Discontinued

Have There Been Any Amendments Since The Last Review?
- ❑ No
- ❑ Yes (Describe Briefly In Attached Narrative)

Summary of Protocol Participants:
- _____ Accrual Ceiling Set By IRB
- _____ New Participants Accrued Since Last Review
- _____ Total Participants Accrued since Protocol Began

Accrual Exclusions
- ❑ None
- ❑ Male
- ❑ Female
- ❑ Other (Specify: _____)

Impaired Participants
- ❑ None
- ❑ Physically
- ❑ Cognitively
- ❑ Both

Have There Been Any Changes In The Participant Population, Recruitment Or Selection Criteria Since The Last Review?
- ❑ No
- ❑ Yes (Explain Changes In Attached Narrative)

Have There Been Any Changes In The Informed Consent Process Or Documentation Since The Last Review?
- ❑ No
- ❑ Yes (Explain Changes In Attached Narrative)

Has Any Information Appeared In The Literature, Or Evolved From This Or Similar Research That Might Affect The IRB's Evaluation Of The Risk/Benefit Analysis Of Human Subjects Involved In This Protocol?
- ❑ No
- ❑ Yes (Discuss In The Attached Narrative)

Have Any Unexpected Complications Or Side Effects Been Noted Since Last Review?
- ❑ No
- ❑ Yes (Discuss In The Attached Narrative)

Have Any Participants Withdrawn From This Study Since The Last IRB Approval?
- ❑ No
- ❑ Yes (Discuss In The Attached Narrative)

Investigational New Drug/Device
☐ None ☐ Ind ☐ Ide
Dra No. ……..
Name: ……
Sponsor: ……
Holder: ……

Ionizing Radiation Use (X-Rays, Radioisotopes, Etc)
- ❑ None
- ❑ Medically Indicated Only

Have Any Participating Investigators Been Added Or Deleted Since Last Review?
- ❑ No
- ❑ Yes (Identify all changes in the attached narrative and submit the CV of the new investigator(s)

Have Any New Collaborating Sites (Institutions) Been Added Or Deleted Since The Last Review?
- ❑ No
- ❑ Yes (Identify All Changes And Provide An Explanation Of Changes In The Attached Narrative)

HAVE THERE BEEN ANY CHANGES IN SUPERVISOR / INVESTIGATOR? ❑ NONE ❑ DELETE:…… ❑ ADD: ……..	HAVE ANY INVESTIGATORS DEVELOPED AN EQUITY OR CONSULTATIVE RELATIONSHIP WITH A SOURCE RELATED TO THIS PROTOCOL WHICH MIGHT BE CONSIDERED A CONFLICT OF INTEREST? ❑ NO ❑ YES (Append A Statement Of Disclosure)

SIGNATURES:

_____Date: ……

Protocol Chairperson (if applicable)

_____ Date: ……

INSTITUTE.... SUPERVISOR

_____ Date: ……

INSTITUTE.... Director

_____

(For use by IRB)

COMPLETION

_____ Date:……

Member Secretary, IRB

(For IRB use)

Complete the following section if there are no changes or amendments. If there are changes or amendments refer "Review of Protocol Amendments" SOP/013.

Member's Recommendation:

☐ Approved ☐ Approved with Recommendation

☐ Resubmission ☐ Disapproved

Comments, if any: .....

.....

FINAL DECISION of IRB:

A. By Chairperson

☐ Approved ☐ Approved with Recommendation

☐ Resubmission ☐ Disapproved

Comments, if any: .....

.....

B. By Full Board

☐ Approved ☐ Approved with Recommendation

☐ Resubmission ☐ Disapproved

Comments, if any: .....

.....

CHAPTER 4.4

REVIEW OF FINAL REPORT

SOP NUMBER: SOP/016/01

INSTITUTIONAL REVIEW BOARD
(IRB)

Khesar Gyalpo University of Medical Sciences of Bhutan

www.kgumsb.edu.bt

Effective Date: October 1, 2021
Supersedes: SOP/016/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 SOP shall be to provide instructions on the review and follow-up, if appropriate, of Final Reports for any study previously approved by IRB.

2. SCOPE

This SOP shall apply to the review and follow-up of the Final Report which is an obligatory review of each investigator's activities presented as a written report of studies completed to the IRB.

Although IRB provides a Study Report Form, ANNEX - AF/01-016/01 to the investigator, any mechanism (letter format, form provided by the Sponsor, etc.) may be used, provided that the information submitted is sufficient.

3. RESPONSIBILITY

The IRB secretariat shall be responsible to review the report for completeness before sharing with the Primary Reviewers and Chairperson. The IRB shall be responsible to review the final report and decide whether any further information or follow-up is required.

4. FLOW CHART

No.	Activity	Responsibility
1	Receive final report ↓	IRB Secretariat
2	Send to Primary reviewers for comments/approval ↓	IRB Member Secretary
3	Include in the agenda for next meeting ↓	IRB Member Secretary
4	Activities during meeting ↓	IRB Secretariat / Members / Chairperson
5	Activities after the board meeting	IRB Secretariat

5. DETAILED INSTRUCTIONS

5.1. Receive Final report

5.1.1. See SOP/008/01 (Management of Protocol Submission) for receiving and checking the report packages.

5.1.2. The IRB Member Secretary shall review the submitted report for completeness and brief the Chairperson.

5.2. Sends to Primary reviewers

5.2.1. IRB Member Secretary shall send the report to the primary reviewers for comments and approval

5.2.2. Primary reviewer(s) shall review the report using Format for Review of Research Report, ANNEX - AF/02-016/01, and approves or provides comments on the report

5.2.3. If primary reviewers consent to same decision then the IRB Member Secretary shall prepare the review/approval letter and send it to the Chairperson along with the copies of the review forms for endorsement.

5.2.4. If there is no consensus in the decision between the primary reviewers then the Chairperson may either take the final call or forward the report to full board.

5.3. During the meeting

5.3.1. The primary reviewers shall present the reports to the Board member

5.3.2. The Chairman shall entertain any discussion of the study.

5.3.3. If appropriate to the discussions, an IRB member may call for consensus on whether to request further information or to take other action with the investigator.

5.3.4. Summarize what action shall be taken.

5.4. After the meeting

5.4.1. Note the decision in the meeting minutes

5.4.2. Communicate the decision to the investigator

5.4.3. If no further action from the IRB,

5.4.3.1. Send an acknowledged letter to the investigator.

5.4.3.2. Get a copy of the final report signed by the Chairperson.

5.4.4. If any follow-up actions required by the Board,

5.4.4.1. Send a letter with the signature of the Chairperson to the investigator informing the Board's decision within five working days of the meeting.

5.4.5. Refer to SOP 025 – Achieves and Retrieval of the Documents, Section 5.1 "After Receiving the Final Report", if the study is considered closed.

6. ANNEX

ANNEX 1	AF/01-016/01	Study Report Form
ANNEX 2	AF/02-016/01	Format for Review of Research Report
ANNEX 3	AF/03-016/01	Report Review Letter Template

7. REFERENCES

7.1. World Health Organization, Operational Guidelines for Ethics Committees that Review Biomedical Research, 2000.

7.2. International Conference on Harmonization, Guidance on Good Clinical Practice (ICH GCP) 2016.

7.3. World Health Organization, Standards and operational guidance for ethics review of health-related research with human participants Guidance document, 2011

7.4. Related SOP/008/01

ANNEX 1
AF/01-016/01

Study Report Form

Protocol No.:		**Protocol Title :**
Principal Investigator:		
Phone number:		E-mail address :
Sponsor's Name		
Address:		
Phone :		E-mail :
Study site(s):		
Total Number of study participants :		No. of Study Arms:
Number of participants who received the test articles:		
Study materials:		
Treatment form:		
Study dose(s): (if applicable).		
Duration of the study		
Objectives:		
Results: (Use extra blank paper, if more space is required.)		
Signature of P.I.:		Date:

ANNEX 2
AF/02-016/01

Format for Review of Research Report

I. Protocol No:					
Protocol Title:					
Principal Investigator:					
II. Elements of Review					
Sl No.	**Protocol parameters**	**Reviewer's observation** *(Please mark 'X' in relevant cages)*			
		Same as approved by IRB	**Minor diversion from that IRB by approved**	**Major diversion from that approved by IRB**	**Remarks**
1	Protocol Title				
2	Type of study				
3	Principal investigator(s)				
4	Co-investigator(s)				
5	Objectives				
6	Sample size				
7	Sampling method				
8	Inclusion criteria				
9	Exclusion criteria				
10	Recruitment of subjects				
11	Discontinuation & withdrawal criteria				
12	Voluntary, non-coercive recruitment of subjects				
13	Involvement of vulnerable subjects				
14	Informed consent procedures				
15	Data collection tools				
16	Data analysis				
17	Privacy & Confidentiality				
18	Risk-Benefit assessment / management				
Any other comments:					

IV. Reviewer's Recommendation on Closure of Research project

I certify that I have made the foregoing observations on the basis of my objective assessment of the protocol and the final report and I confirm that I have complied with the IRB policies and guidelines in reviewing this report.

I, therefore, recommend that the report shall be;

- ☐ Approved and the protocol file shall be closed as the PI has adhered with the approved protocol and the report is technically sound.
- ☐ Approved and the protocol file shall be closed; however, the PI shall be reprimand for minor violation(s) (specify violations/comments).....
- ☐ Either resubmitted with revision or justifications shall be provided for the major violations (specify the violations/comments).....

Signature of Reviewer: …….

Name of Reviewer: ……

III. IRB Endorsement

The recommendation of the reviewer of research report is endorsed/approved by:

A. By Board Members

1. Unanimous decision ☐
2. By Voting : ☐

i. For: …….....
ii. Against: …….....
iii. Total voting members: ……

B. By Chairperson

1. Approved: ☐
2. Not approved: ☐

Signature: ……
Office seal:

ANNEX 3
AF/03-016/01 REPORT REVIEW LETTER TEMPLATE

གེ་སར་རྒྱལ་པོ་གསོ་རིག་གཙུག་ལག་སློབ་སྡེ།།

Khesar Gyalpo University of Medical Sciences of Bhutan
Royal Government of Bhutan

Ref. No. IRB/PN/2021/008 Date:

REPORT REVIEW LETTER

The

……..

……..

Subject: Closing letter for PN/2021/008 "**……..**"

Dear Doctor,

The Report of protocol No PO/2021/008 titled "**……..**"submitted to IRB was reviewed by the IRB and the report is;

☐ Approved and the protocol file is closed.

☐ Approved and the protocol file is closed; however, the PI is reprimanded for the following minor violation(s) (specify violations/comments)……

……

☐ Called for resubmission with revision or justifications for the following major violations shall be provided for review by IRB (specify the violations/comments)……..

Congratulation for the successful completion of the study! And thank you for complying with the conditions of approval.

Or

Specify violations/comments:
1
2
3

Yours sincerely

( )

Chairperson

For further information please contact: *…@kgumsb.edu.bt; Member Secretary*

CHAPTER 5.1

INTERVENTION IN PROTOCOL DEVIATION/NON-COMPLIANCE/VIOLATION

SOP NUMBER: SOP/017/01

INSTITUTIONAL REVIEW BOARD (IRB)

Khesar Gyalpo University of Medical Sciences of Bhutan

www.kgumsb.edu.bt

Effective Date: October 1, 2021
Supersedes: SOP/016/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 SOP shall be to provide instructions for taking action and maintaining records that identify investigators/institutes who fail to follow the procedures written in the approved protocol or to comply with national / international guidelines for the conduct of human research, including those who fail to respond to the IRB's requests.

2. SCOPE

This SOP shall apply to all IRB approved research protocols involving human subjects.

3. RESPONSIBILITY

The designated member of the Secretariat shall be responsible for collecting and recording the deviation / non-compliance / violation list, ANNEX - AF/01-017/01. It shall be the responsibility of the IRB to review the issues and make decisions.

4. FLOW CHART

No.	Activity	Responsibility
1	Note Protocol deviation / non-compliance / violation. ↓	Primary Reviewers and Chairperson
2	Board discussion and decision ↓	IRB members and Chairperson
3	Notify the investigator ↓	IRB Secretariat, members and Chairperson
4	Keep records and follow up	IRB Secretariat

5. DETAILED INSTRUCTIONS

5.1. Whenever protocol deviation / non-compliance / violation has been observed:

5.1.1. Ensure that the issues as well as the details of non-compliance involving research investigators as commented by the primary reviewers shall be included in the agenda of the IRB meeting.

5.1.2. Maintain a file that identifies investigators who are found to be non-compliant with national/international regulations or who fail to follow protocol approval stipulations or fail to respond to the IRB's request for information/action.

5.2. The IRB's Decision

5.2.1. The Board shall discuss and make the decision during the meeting. Such decisions shall be recorded in the minutes.

5.2.2. The chairperson shall notify the investigator of the IRB's decision in writing, when the Board

5.2.2.1. suspends further enrolment of research participants,

5.2.2.2. terminates approval of a current approved study,

5.2.2.3. request for additional information, or

5.3. Notify the investigator

5.3.1. The IRB Secretariat members shall record the IRB's decision.
5.3.2. Draft and type a notification letter.
5.3.3. Get the dated signature of the Chairperson on the letter.
5.3.4. Make adequate copies of the notification letter.
5.3.5. Send the original copy of the notification to the principal investigator.
5.3.6. Send a copy of the notification to the relevant national authorities and institutes.
5.3.7. Send a copy to the sponsor or the sponsor's representative of the study, if applicable.

5.4. Keep records and follow up

5.4.1. Keep a copy of the notification letter in the "deviation / non-compliance / violation" file.
5.4.2. Store the file in the shelf with an appropriate label.
5.4.3. Follow up with the PI after a reasonable time from the issuance of the notification.

6. GLOSSARY

Deviation / Non-compliance / Violation	The Principal Investigator/s do not perform the study in compliance with the originally approved protocol, ICH GCP, DRA, FDA regulations and/or fails to respond to the IRB's request for information/action.

7. REFERENCES

7.1. World Health Organization, Operational Guidelines for Ethics Committees that Review Biomedical Research, 2000.
7.2. International Conference on Harmonization, Guidance on Good Clinical Practice (ICH GCP) 2016.
7.3. World Health Organization, Standards and operational guidance for ethics review of health-related research with human participants Guidance document, 2011

8. ANNEX

ANNEX 1 AF/01-017/01 Deviation/Non Compliance/Violation Record

ANNEX 1
AF/01-017/01

Deviation / Non-Compliance / Violation Record

Protocol Number:	Date:……
Study Title:	
Investigator	Contact No.:
Institution:	Contact No.:
Sponsor:	Contact No.:

☐ Deviation from protocol ○ Major ○ Minor	☐ Non-Compliance ☐ Violation
Description:	
IRB's Decision:	
Actions taken:	Outcome:

Found by:…… Date:……	Reported by:…… Date:……

CHAPTER 5.2

RESPONSE TO RESEARCH PARTICIPANTS' REQUEST

SOP NUMBER: SOP/018/01

INSTITUTIONAL REVIEW BOARD
(IRB)

Khesar Gyalpo University of Medical Sciences of Bhutan

www.kgumsb.edu.bt

Effective Date: October 1, 2021 Supersedes: SOP/0017/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 KGUMSB considers protection of the rights and welfare of the human subjects participating in a clinical investigation/research approved by the IRB as its primary responsibility. Therefore, the IRB should make sure that the Informed Consent documents reviewed by the IRB should contain the statement, "Questions regarding the rights of a participant/patient may be addressed to the IRB Chairperson" and should also make sure to provide with the contact name and phone number of the responsible official of the IRB.

This procedure provides guidelines for dealing with and accommodating requests by participants/patients regarding their rights as a participant in any approved research study.

2. SCOPE

This SOP shall apply to all requests concerning the rights and well-being of the research participants participating in studies approved by the IRB.

3. RESPONSIBILITY

The KGUMSB's policy designates the Chairperson of the IRB as the person responsible for communicating with participants/patients regarding their rights as study participants. Delegation of this responsibility to another IRB member or IRB Member Secretary shall be acceptable as long as the delegation is documented (in writing). Delegation to non-IRB members shall not be permitted.

All Staff and IRB members acting on behalf of the IRB shall be responsible to facilitate participant/patient requests within the scope of their responsibilities.

4. FLOW CHART

No.	Activity	Responsibility
1	Receive the request ↓	IRB Members and Secretariat
2	Take action ↓	IRB Members and Chairperson
3	File the request document	IRB Secretariat

5. DETAILED INSTRUCTIONS

5.1. Receive the request.

5.1.1. The IRB secretariat or member shall receive the inquiry or request from research participants/patients.

5.1.2. Record the request and information in the request record form, ANNEX - AF/01-018/01

5.1.3. Refer the inquiry to the IRB Chairperson in writing.

5.1.4. The Chairperson shall:

5.1.4.1. document the communication for the IRB study file,

5.1.4.2. request follow-up information,

5.1.4.3. provide advice as required,

5.1.4.4. inform the other IRB members about the inquiry,
5.1.4.5. Follow-up at the next IRB meeting, or
5.1.4.6. Delegate these tasks to IRB Secretariat or members.

5.2. Take Action

5.2.1. Investigate the fact.
5.2.2. Record information and any action or follow-up taken in the form, ANNEX - AF/01-018/01
5.2.3. Sign and date the form.
5.2.4. Report to the IRB about the action taken and the outcomes.

5.3. File the request document

5.3.1. Keep the record form in the "response" file.
5.3.2. Keep a copy in the study file.
5.3.3. Store the file in the appropriately labelled shelf.

6. GLOSSARY

Participants' rights	Any study participants has the right not to participate in any study, withdraw at any point of time from the study and to receive standard care if she/he withdraws from a study.

7. ANNEX

ANNEX 1 AF/01-018/01 Request Record Form

8. REFERENCES

8.1. World Health Organization, Operational Guidelines for Ethics Committees that Review Biomedical Research, 2000.
8.2. International Conference on Harmonization, Guidance on Good Clinical Practice (ICH GCP) 2016.
8.3. World Health Organization, Standards and operational guidance for ethics review of health-related research with human participants, 2011.

ANNEX 1
AF/01-018/01

Request Record Form

Date Received:	
Received by :	
Request from :	❑ Telephone call No……... ❑ Fax No……..… ❑ Mailed letter / Date…… ……. ❑ E-mail / Date…… ❑ Walk-in / Date / Time…….. ❑ Other, specify …….
Participant's Name:	
Contact Address: Phone:	
Title of the Participating Study	
Starting date of participation:	
What is requested?	
Action taken: Outcome:	

Signature

_____
Member Secretary, IRB

CHAPTER 5.3

MANAGEMENT OF STUDY TERMINATION

SOP NUMBER: SOP/019/01

INSTITUTIONAL REVIEW BOARD
(IRB)

Khesar Gyalpo University of Medical Sciences of Bhutan

www.kgumsb.edu.bt

Effective Date: October 1, 2021
Supersedes: SOP/018/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

This procedure describes how an IRB shall proceed and manage the termination of an approved research study. Protocols are usually terminated at the recommendation of the IRB members, institute heads, sponsor, PI, DSMB or other authorized bodies when subject enrolment and subject follow-up are discontinued before the scheduled end of the study, **when the IRB has observed gross violation of the approved terms and condition of the study**, when it is certain that the approved study can no longer be feasible to carry on due to changes in legal, political or economic circumstances, or when the safety or benefit of the study participants is doubtful or at risk.

2. SCOPE

This SOP shall apply to any study approved by IRB that is being recommended for termination before its scheduled completion.

3. RESPONSIBILITY

The IRB shall be responsible to terminate any study that the IRB has previously approved when subject enrolment and subject follow-up are discontinued before the scheduled end of the study, when the IRB has observed gross violation of the approved terms and condition of the study, when it is certain that the approved study can no longer be feasible to carry on due to changes in legal, political or economic circumstances, or when the safety or benefit of the study participants is doubtful or at risk. The Secretariat is responsible for management of the termination process.

4. FLOW CHART

No.	Activity	Responsibility
1	Receive recommendation for study termination ↓	Investigator and IRB Secretariat
2	Review and Discuss the Termination Package ↓	Secretariat and IRB
3	Notify the Principal Investigator ↓	IRB Secretariat
4	Store the Protocol Documents ↓	IRB Secretariat
5	Inactivate the Protocol Document	IRB Secretariat

5. DETAILED INSTRUCTIONS

5.1. Receive recommendation for study termination.

5.1.1. Receive recommendation and comments from IRB members, institute heads, sponsor, PI, DSMB or other authorized bodies for approved study protocol termination.

5.1.2. Inform the principal investigator or the study office to prepare and submit a protocol termination package.

5.1.3. Receive the study protocol termination package prepared and submitted by the principal investigator or the study office.

5.1.4. Verify the contents of the package for inclusion of:

5.1.4.1. Request for Termination Memorandum, ANNEX- AF/01-019/01

5.1.4.2. The request for termination memorandum should contain a brief written summary of the protocol, its results, and actual data.

5.1.4.3. Original Continuing Review Application Form, ANNEX – AF/01-015/01

5.1.4.4. Termination is indicated under “Action Request”.

5.1.4.5. Completeness of the information, including actual data since the time of the last continuing review.

5.1.4.6. Presence of the required signatures (Principal Investigator).
5.1.4.7. Initial and date the package upon receipt.

5.2. Review and discuss the Termination Package.

5.2.1. Notify the Chairperson regarding the recommendation for study protocol termination.
5.2.2. Send a copy of the termination package to the Primary Reviewers within one working day upon receipt.
5.2.3. The Chairperson shall review the results, reasons and accrual data.
5.2.4. The Chairperson shall call for an emergency meeting to discuss about the recommendation.
5.2.5. The Chairperson shall sign and date the Continuing Review Application Form in acknowledgment and approval of the termination.
5.2.6. The Chairperson shall return the form back to the Secretariat within 5 working days of receipt of the package.
5.2.7. The Secretariat shall review, sign, and date the Continuing Review Application Form indicating that the termination process is complete.

5.3. Notify the Principal Investigator.

5.3.1. Make a copy of the completed Continuing Review Application Form
5.3.2. Send the copy to the principal investigator for their records within 7 working days.

5.4. Store the protocol documents.

5.4.1. Keep the original version of the request memorandum for termination and the original version of the Continuing Review Application Form in the Protocol file.
5.4.2. Send the file to archive.
5.4.3. Store the protocol documents indefinitely.

5.5. Inactivate the protocol documents.

5.5.1. Place the study protocol into the inactive protocol folder in the computer records under the following directory:
5.5.2. F:\studyfiles\inactive protocols

6. GLOSSARY

DSMB	Data Safety Monitoring Board constitutes a group of scientific people formed for every major study that is done to monitor the data handling.

7. REFERENCES

7.1. World Health Organization, Operational Guidelines for Ethics Committees that Review Biomedical Research, 2000.
7.2. International Conference on Harmonization, Guidance on Good Clinical Practice (ICH GCP) 2016.
7.3. World Health Organization, Standards and operational guidance for ethics review of health-related research with human participants Guidance document, 2011
7.4. Associated SOP: SOP/015/01

8. ANNEX

ANNEX 1 AF/01-019/01 Termination Memorandum

ANNEX 1
AF/01-019/01

Study Termination Memorandum

PROTOCOL NUMBER:		PROTOCOL TITLE:	
PRINCIPAL INVESTIGATOR:			
PHONE :		E-MAIL:	
INSTITUTE:			
SPONSOR:			
IRB APPROVAL DATE:		DATE OF LAST REPORT:	
STARTING DATE:		TERMINATION DATE:	
NO. OF PARTICIPANTS:		NO. ENROLLED:	
REASON FOR TERMINATION			
SUMMARY OF RESULTS			
ACCRUAL DATA:			
P.I.SIGNATURE:		DATE:	

CHAPTER 6

REVIEW OF SERIOUS ADVERSE EVENT REPORTS

SOP NUMBER: SOP/020/01

INSTITUTIONAL REVIEW BOARD
(IRB)

Khesar Gyalpo University of Medical Sciences of Bhutan

www.kgumsb.edu.bt

Effective Date: October 1, 2021
Supersedes: SOP/019/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 SOP shall be to provide instructions on the review and follow-up reports of serious adverse experience and unexpected events for any active study approved by the IRB. The SAE shall be reported by the investigators or sponsors within 10 working days after the incident occurred and in the event of deaths it should be reported within 24 hours and unexpected events shall be included in the continuing review report submitted to IRB.

Unanticipated risks are sometimes discovered during the course of studies. Information that may impact on the risk/benefit ratio shall be promptly reported to and reviewed by the IRB to ensure adequate protection of the welfare of the study participants.

The unanticipated risks may as well include any event that in the investigator's opinion, may adversely affect the rights, welfare or safety of subjects in the study.

2. SCOPE

This SOP shall apply to the review of SAE and unexpected events reports submitted by investigators, Data Safety Monitoring Board (DSMB), sponsor, local safety monitor, IRB members or other concerned parties.

3. RESPONSIBILITY

The IRB shall be responsible to review and address SAE and unexpected events involving risks to subjects or others as well as ethics complaints. In addition, the Committee is authorized to offer mediation under appropriate circumstances.

IRB shall also make sure that researchers are made aware of the policies and procedures concerning reporting and continuing review requirements.

The IRB Member Secretary in consultation with the Chairperson shall be responsible for first screening the assessment of the reports and seeing whether they need a review by the Chairperson, other qualified IRB members or full IRB meeting, or external consultants/experts or by the National Health Research Board (NHRB).

4. FLOW CHART

No.	Activity	Responsibility
1	Review and determine the review channel ↓	IRB Member Secretary, Chairperson, members
2	Safety Report Review Process ↓	IRB members and Chairperson
3	Communicate the decision to investigator or clinical trial office. ↓	IRB Secretariat and Chairperson
4.	Storage of the documents	IRB Secretariat and Chairperson

5. DETAILED INSTRUCTIONS

5.1. Review and determine the review channel

5.1.1. IRB Member Secretary or members shall review the safety report and determine whether the report requires review by full Board of IRB or by the Chairperson or other qualified/relevant IRB member(s).

5.1.2. Criteria for the review. The **review criteria** are as follows:

5.1.2.1. Assessment of adverse experience is unknown or unlikely

5.1.2.1.1. Report is forwarded to the Chairperson for review and determination if report shall be reviewed at the convened meeting by full Board of IRB.

5.1.2.2. Assessment of adverse experience is possibly caused by, or probably caused by the investigational product.

5.1.2.2.1. The report is added to the agenda for review at a convened meeting by full Board of IRB.

5.1.2.3. An adverse experience/IND Safety Report has been previously seen by full Board but being resubmitted by another investigator participating in the multi-study site (as part of a multi-centre /site study).

5.1.2.3.1. This notification does not require full Board review.

5.1.2.3.2. To be reviewed by the Chairperson or other qualified IRB members and secretariat

5.1.3. Complete the general information on the Safety Report Review Form

5.2. Safety report review process

5.2.1. Expedited Review process

5.2.1.1. Distribute the review package to the expedited reviewer. The package includes:

5.2.1.1.1. Safety Report

5.2.1.1.2. Safety Report Review Form (AF/03-019/01)

5.2.1.1.3. Protocol, ICF, and related documents

5.2.1.2. The reviewer records the review decision and recommendations on the Safety Report Review From

5.2.1.3. Refer to SOP 008 – Expedited Review

5.2.2. Full Board Review Process

5.2.2.1. After reading and reviewing the report, the Chairperson or designee entertains discussion on the study and similar adverse experiences or advisories.

5.2.2.2. If appropriate to the discussions, the Chairperson or another IRB member may call for a consensus on whether to:

5.2.2.2.1. Request an amendment of the protocol

5.2.2.2.2. Request an amendment of the consent form.

5.2.2.2.3. Request further information.

5.2.2.2.4. Suspend the enrolment

5.2.2.2.5. Terminate the study.

5.2.2.2.6. No action

5.2.2.3. The IRB Secretariat records the decision and recommendations on the Safety Report Review Form.

5.3. Communicate the decision to the investigator and the clinical trial officer

5.3.1. The IRB secretariat drafts a formal letter to the investigators or the clinical trial office to notify them of the IRB decision and recommendations and if any action they shall take accordingly.

5.3.2. Get the Chairperson to approve, sign and date the letter.

5.3.3. Send the letter to the investigator or the clinical trial office within 5 working days.

5.4. Store the document

5.4.1. Keep the letter in the “Correspondence File”

5.4.2. Keep the SAE reports, review forms along with the related review minutes in the protocol file.

6. GLOSSARY

Adverse Event	Any untoward medical occurrence in a patient or clinical investigation participant administered an investigational product and which does not necessarily have a causal relationship with this treatment. The adverse event can therefore be any unfavourable or unintended sign or experience associated with the use of the investigational product, whether or not related to the product.
Adverse Drug Reaction	In the pre-clinical experience with a new medicinal product or its new usages, particularly as the therapeutic dose(s) may not have been established all noxious or unintended responses to the product related to any dose shall be considered adverse drug reactions. The phrase "responses to a medicinal product" means that a causal relationship between the product and the adverse event is at least a reasonable possibility, i.e., the relationship can not be ruled out. Regarding marketed products, a response to a product which is noxious and unintended and which occurs at doses normally used in man for prophylaxis, diagnosis or therapy of diseases or for modification of physiological function.
IND	Investigational New Drugs means substances with potential therapeutic actions during the process of scientific studies in human in order to verify their potential effects and safety for human use and to get approval for marketing.
SAE	The adverse event is SERIOUS and shall be reported when the patient outcome is: **Death** - Report if the patient's death is suspected as being a direct outcome of the adverse event. **Life-Threatening** - Report if the patient was at substantial risk of dying at the time of the adverse event or it is suspected that the use or continued use of the product would result in the patient's death. *Examples: Pacemaker failure; gastrointestinal hemorrhage; bone marrow suppression; infusion pump failure which permits uncontrolled free flow resulting in excessive drug dosing.* **Hospitalization** (initial or prolonged) - Report if admission to the hospital or prolongation of a hospital stay results because of the adverse event. *Examples: Anaphylaxis; pseudomembranous colitis; or bleeding causing or prolonging hospitalization.* **Disability** - Report if the adverse event resulted in a significant, persistent, or permanent change, impairment, damage or disruption in the patient's body function/structure, physical activities or quality of life. *Examples: Cerebrovascular accident due to drug-induced hypercoagulability; toxicity; peripheral neuropathy.* **Congenital Anomaly** - Report if there are suspicions that exposure to a medical product prior to conception or during pregnancy resulted in an adverse outcome in the child. *Examples: Vaginal cancer in female offspring from diethylstilbestrol during pregnancy; malformation in the offspring caused by thalidomide.* **Requires Intervention to Prevent Permanent Impairment or Damage** – Report if suspect that the use of a medical product may result in a condition which required medical or surgical intervention to preclude permanent

	impairment or damage to a patient. *Examples: Acetaminophen(paracetamol) overdose-induced hepatotoxicity requiring treatment with acetylcysteine to prevent permanent damage; burns from radiation equipment requiring drug therapy; breakage of a screw requiring replacement of hardware to prevent mal-union of a fractured long bone.*
Unexpected ADR	Unexpected Adverse Drug Reaction is an adverse reaction, the nature or severity of which is not consistent with the informed consent / information sheets or the applicable product information (e.g., investigator's brochure for the unapproved investigational product or package insert / summary of product characteristics for an approved product.
NHRB DSMB	Highest decision making body in Bhutan in terms of health research.

7. REFERENCES

7.1. World Health Organization, Operational Guidelines for Ethics Committees that Review Biomedical Research, 2000.

7.2. International Conference on Harmonization, Guidance on Good Clinical Practice (ICH GCP) 2016.

8. ANNEX

ANNEX 1	AF/01-020/01	Serious Adverse Event Report
ANNEX 2	AF/02-020/01	Unexpected Adverse Drug Reaction Report
ANNEX 3	AF/03-020/01	Safety Report Review Form

ANNEX 1
AF/01-020/01

Serious Adverse Event Report

Principal Investigator: …….. Study Site:

Protocol Title: …… Protocol No.:

Sponsor (if applicable)……

Name of the study drug / medical device:

Report Type
☐ Initial ☐ follow-up
☐ Final

Report Source:
☐ Investigator ☐ Sponsor
☐ DSMB ☐ IRB member
☐ Others, specify:

Subject's initial/number:	Age:	☐ Male ☐ Female

Describe Reactions (onset date, signs, symptoms, including relevant tests/ lab data)
Medical treatment
Progression of the SAE

Seriousness:	Relation to ○ Drug ○ Device ○ study
☐ Death	☐ Not related
☐ Life Threatening	☐ Possibly
☐ Hospitalization –○ initial ○ prolong	☐ Probably
☐ Disability / Incapacity	☐ Definitely related
☐ Congenital Anomaly	☐ Unknown
☐ Other……	

Changes to the protocol recommended?	☐ No ☐ Yes , attach proposal
Changes to the informed consent form recommended?	☐ No ☐ Yes , attach proposal

Reported by: ……

Report Date:

ANNEX 2
AF/02-020/01

Unexpected Adverse Event Summary Report

Principal Investigator: ……

Study Title: ……... **Protocol No.:**

Name of the studied medicine/device……..…….. **This report covers the period :**

Sponsor: ……... **From……To…….**

#	Description of Unexpected Adverse Events	Date of Event (D/M/Y)	Date start and end of Tx (D/M/Y)	F or M	Age (Y)	SERIOUS Yes No	RELATED TO STUDY Yes No	Concomitant medication	Intervention
						☐ ☐	☐ ☐		
						☐ ☐	☐ ☐		
						☐ ☐	☐ ☐		
						☐ ☐	☐ ☐		

Comment:

Reviewed by: …… **Date** (D/M/Y): ……

ANNEX 3
AF/03-020/01

Safety Report Review Form

General Information	
Protocol Title:	
Protocol No.:	**Report received date:**
Review Channel:	
☐ Full Board Review Review Date:	☐ Expedited Review Reviewer Name:
Completed by: (Signature) Date:	
Review Decision:	
☐ Terminate the study	☐ Suspend the enrolment
☐ Request protocol amendment	☐ Request ICF amendment
☐ Request further information	☐ No Action
Recommendation:	
Reviewer Signature: (For Expedited Review) Date:	IRB Secretariat Signature: (For Full Board Review) Date:
IRB Chairperson Sign: Date:	

CHAPTER 7

SITE MONITORING VISITS

SOP NUMBER: SOP/021/01

INSTITUTIONAL REVIEW BOARD
(IRB)

Khesar Gyalpo University of Medical Sciences of Bhutan

www.kgumsb.edu.bt

Effective Date: October 1, 2021
Supersedes: SOP/020/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 SOP is to provide procedures as to when and how a study site shall be visited and monitored of its performance or compliance to GCP.

2. SCOPE

This SOP shall apply to any visit and/or monitoring of any study sites as stated in the IRB approved study protocols that identify the place(s) where the study and/or laboratory procedures are being carried out or performed.

3. RESPONSIBILITY

The IRB shall be responsible to perform or designate some qualified agents to perform on its behalf on-site inspection of the research projects it has approved.

The IRB members or Secretariat in consultation with the Chairperson may initiate an on-site evaluation of a study site for cause or for a routine audit.

4. FLOW CHART

No.	Activity	Responsibility
1	Selection of study sites ↓	IRB members and Chairperson
2	Procedures before the visit ↓	IRB members and/or representative
3	Procedures during the visit ↓	IRB members and/or representative
4	Procedures after the visit ↓	IRB members and/or representative
5	Review and approve the site visit report during the IRB meeting ↓	IRB members and/or representative
6	Notify the study site ↓	IRB secretariat
7	Storage of the document	IRB secretariat

5. DETAILED INSTRUCTIONS

5.1. Selection of study sites

5.1.1. Review periodically the database files of the submitted/approved study protocols.

5.1.2. Select study sites needed to be monitored based on the following criteria:

5.1.2.1. Reports of remarkable serious adverse events

5.1.2.2. Non-compliance or suspicious conduct

5.1.2.3. Research involving clinical drug trials

5.1.2.4. Not submitting information/reports on time

5.2. Before the visit

The IRB representatives shall

5.2.1. Contact the site to notify them that they shall be visiting them. At that time, the monitor and the site shall coordinate a time for the site evaluation visit.
5.2.2. Make the appropriate travel arrangements.
5.2.3. Review the IRB files for the study and site,
5.2.4. Make appropriate notes, or
5.2.5. Copy and take some parts of the files for comparison with the site files.

5.3. During the visit

5.3.1. Bring the Site Monitoring Report (AF/01-021/01) form as a checklist for the site visit.
5.3.2. The IRB representatives shall
5.3.2.1. Review the informed consent document to make sure that the site is using the most recent approved version,
5.3.2.2. Review randomly the subject files to ensure that subjects are signing the correct informed consent,
5.3.2.3. Observe the informed consent process, if possible,
5.3.2.4. Observe laboratory and other facilities necessary for the study at the site.
5.3.2.5. Review the IRB files for the study to ensure that documentation is filed appropriately.
5.3.2.6. Collect views of the study participants.
5.3.2.7. Debrief the visit report/comments.
5.3.2.8. Get immediate feedback.

5.4. After the visit

The IRB representative shall:
5.4.1. Write a report/comment (use the ANNEX - AF/01-021/01) within 2 weeks describing the findings during the audit
5.4.2. Send the site visit report to the IRB Secretariat for Full Board review.

5.5. Review and approve the site visit report during the IRB meeting

5.5.1. The IRB Secretariat shall schedule the presentation in the meeting agenda.
5.5.2. The IRB representative shall present the results of on-site inspections to the Full Board.
5.5.3. The full board review & discuss the findings and comments of the report
5.5.4. The IRB Secretariat shall record the discussion and decision in the meeting minutes.

5.6. Notify the study site

5.6.1. The IRB Secretariat shall prepare a letter to inform the site of the Committee's decision and recommendation.
5.6.2. The Chairperson shall sign and date the letter.
5.6.3. The IRB Secretariat shall send the letter to the study site within 5 working days of the meeting.

5.7. Storage of the documents

5.7.1. Keep the site visit report with the related review meeting minutes in the site files.
5.7.2. Keep the copy of the letter in the Correspondence File.

6. GLOSSARY

IRB representative/s	Many IRB members rarely find time to perform monitoring visit themselves. They may ask outside experts or the staff of Ethics Committees of local institution to perform the tasks on their behalf and later report their findings to IRB.
Monitoring visit	An action that IRB or its representatives visit study sites to assess how well the selected investigators and the institutes are conducting researches, taking care of subjects, recording data and reporting their observations, especially serious adverse events found during the studies. Normally monitoring visit shall be arranged in advance with the principal investigators.

7. REFERENCES

7.1. World Health Organization, Operational Guidelines for Ethics Committees that Review Biomedical Research, 2000.
7.2. International Conference on Harmonization, Guidance on Good Clinical Practice (ICH GCP) 2016.

8. ANNEX

ANNEX 1 AF/01-021/01: Site Monitoring Visit Report

ANNEX 1
AF/01-021/01

Site Monitoring Visit Report

Protocol Number:	Date of the Visit:	
Study Title:		
Principal Investigators:		Phone:
Institute:	Address:	
Sponsor:	Address:	
Total number of expected subjects:	Total subjects enrolled:	
Are site facilities appropriate? ☐ Yes ☐ No	Comment:	
Are Informed Consents of approved version? ☐ Yes ☐ No	Comment:	
Any adverse events found? ☐ Yes ☐ No	Comment:	
Any protocol non-compliance /violation? ☐ Yes ☐ No	Comment:	
Are all Case Record Forms up to date? ☐ Yes ☐ No	Comment:	
Are storage of data and investigating products locked? ☐ Yes ☐ No	Comment:	
How well are participants protected? ☐ Good ☐ Fair ☐ Not good	Comment:	
Any outstanding tasks or results of visit? ☐ Yes ☐ No	Give details:	
Duration of visit: …….hours	Starting from:	Finish:
Name of IRB member/ representatives and accompanier:		
Completed by:		Date:

CHAPTER 8.1

AGENDA PREPARATION, MEETING PROCEDURES AND MINUTES

SOP NUMBER: SOP/022/01

INSTITUTIONAL REVIEW BOARD (IRB)

Khesar Gyalpo University of Medical Sciences of Bhutan

www.kgumsb.edu.bt

Effective Date: October 1,2021
Supersedes: SOP/021/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 identify the administrative process and provide instructions for the preparation, review, approval and distribution of meeting agenda, minutes and action, invitation, and notification letters of IRB.

2. SCOPE

This SOP shall apply to administrative processes concerning the preparation of the agenda for all regular IRB meetings, divided into three stages: before, during and after the meeting.

3. RESPONSIBILITY

The IRB Secretariat staff shall be responsible to prepare the agenda for the IRB meeting and to ensure the quality and validity of the minutes after the meeting is over. The Chairperson shall review and approve the agenda and the minutes sent to him/her.

4. FLOW CHART

No.	Activity	Responsibility
1	Before each Board Meeting ↓	IRB Secretariat / Chairperson
2	During the Meeting ↓	IRB Secretariat, Members and Chairperson
3	Voting ↓	IRB Members without conflict of interest / Chairperson
4	After the Board Meeting ↓	IRB Secretariat / Chairperson
5	Storage of the documents	IRB Secretariat staff

5. DETAILED INSTRUCTIONS

5.1. Before each Board meeting

5.1.1. Check for filled up forms for completeness.

5.1.1.1. The Secretariat shall:

5.1.1.1.1. Review the new study application for completeness.

5.1.1.1.2. Document the review by completing the appropriate checklist. If incomplete, the staff member attempts to obtain the information from the person who submitted the application package.

5.1.2. Consider the appropriate review channel of each protocol

5.1.2.1. Use the criteria and the procedures as described in the corresponding SOPs when deciding the review channel.

5.1.2.1.1. SOP/009/01 for Expedited Review

5.1.2.1.2. SOP/010/01 for Initial Review of Submitted Protocols

5.1.2.1.3. SOP/013/01 for Review of Resubmitted Protocols

5.1.2.1.4. SOP/014/01 for Review of Protocol Amendments

5.1.2.1.5. SOP/015/01 for Management of protocol continuing Reviews

5.1.2.1.6. SOP/016/01 for Review of Final Reports

5.1.2.1.7. SOP/019/01 for Management of study termination.
5.1.2.1.8. SOP/020/01 for Review of Serious Adverse Event Reports

5.1.3. Assign protocol reviewers

5.1.3.1. Assign at least two to three reviewers (for technical and ethical reviews) for initial review of each submitted protocol by the IRB Chairperson.
5.1.3.1.1. The technical reviewer shall prepare a brief protocol summary, including a statement of the purposes, the evaluation parameters, and the methodology of the protocol. The ethical reviewer examines the consent form for completeness of information and protection of human subjects.
5.1.3.1.2. The assignment shall be based on the information provided in SOP/005/01 and SOP/006/01

5.1.4. Prepare meeting agenda

5.1.4.1. Schedule the review as soon as possible after submission, either at the time of the next scheduled meeting or within 4 weeks after submission.
5.1.4.1.1. Arrange extra IRB meetings to accommodate protocol reviews.
5.1.4.2. Consult the Chairperson to schedule the meeting date.
5.1.4.3. Prepare the meeting agenda, according to the ANNEX - AF/01-021/01
5.1.4.4. Schedule protocols in the agenda on a first-come first-serve basis.
5.1.4.5. Include "request to appeal" items in the agenda, upon receipt of the correspondence, preferably during the next convened Board meeting.
5.1.4.6. Prepare invitation letters to the reviewers and the members.
5.1.4.6.1. Allow at least 3 weeks for the review process.
5.1.4.7. Specify the due date for the return of comments.
5.1.4.7.1. Allow at least 5 working days to the IRB Member Secretary to process the documents
5.1.4.8. Include an Application form for Initial Review, ANNEX - AF/01-008/01 with the protocol package along with the invitation letter, a response form and the meeting agenda.
5.1.4.9. Prepare the package for delivery.
5.1.4.10. Record the name of the assigned reviewers in the appropriate database or the review assignment file.

5.1.5. Distribution of Protocol Packages to the IRB Members

5.1.5.1. Keep in mind Procedure for Maintaining Confidentiality of IRB documents (SOP/027/01) when preparing and distributing documents.
5.1.5.2. Distribute copies of the protocol submission packages to the assigned reviewers and IRB members by either electronic mail (if electronic submission protocols), telefax, or by post *one week* in advance of the scheduled meeting.
5.1.5.3. Keep copies of "sent" e-mail, fax cover memos and/or letters accompanying posted materials in the Correspondence section of the respective protocol file.
5.1.5.4. Verify (verbally, by e-mail, by fax or by mail) with the members whether the protocol packages are received.

5.1.6. Prepare for the meeting

5.1.6.1. Make a room reservation on the schedule meeting date and time.
5.1.6.2. Make sure that the room, equipment and facilities are available in good running condition and cleaned for the meeting day.

5.2. During the meeting

5.2.1. The IRB may allow investigators, project managers, sponsors, etc., to attend the portion of the Board meeting related to their studies.

5.2.2. At the discretion of the Chairman, guests may be allowed to observe the Board meetings.
5.2.3. These guests may include a potential client, students, etc.
5.2.4. Guests shall be required to sign a confidentiality agreement form, ANNEX- AF/02-004/01
5.2.5. The Secretariat shall report on the minutes of the previous meeting and presents the agenda for discussion.
5.2.6. The Secretariat shall record the discussions and the decisions made during the meeting.
5.2.7. The Chairperson may inform members and attendees of the rules being followed during meetings. .
5.2.8. The meeting proceeds in the order organized in the agenda; however, the Chairperson in discussion with the IRB may allow some amendments.
5.2.9. The approval process starts when one of the reviewers gives a brief about the study and presents his/her observations and comments.
5.2.10. In case the reviewer cannot be present during the meeting, a member of the Secretariat or an IRB member may give the briefing about the study by reading the comments and evaluation of the reviewers.
5.2.11. The other members shall give their comments right after the presentation and the discussion about the study takes place.
5.2.12. Investigators may be allowed to present their projects in brief and clarify any questions the IRB members may have.

5.2.13. Quorum Requirements

5.2.13.1. A minimum of ***"50%+1"*** of the members must be present at a meeting in order to issue a valid advice and/or decision.

5.2.13.2. Professional qualifications of the quorum requirements shall consist of at least one member whose primary area of expertise is in a non-scientific area, one medical scientist and at least one member who is independent of the institution/research site.

5.2.13.3. A provision for a maximum of 3 alternate members is kept for each board meeting.

5.2.14. Frequency of the meeting

5.2.14.1. The IRB shall meet at least 2 times a year in July and January.

5.2.14.2. Emergency meeting may be convened if required, wherein the secretariat shall notify the members upon approval from the Chairperson.

5.3. Voting

5.3.1. In order to avoid conflict of interest, only those Board members and alternate members who are independent of the investigator and the sponsor of the trial will vote on the research-related matters.
5.3.2. All voting will take place after the observers / presenters / Board members with a conflict of interest leave the meeting room.
5.3.3. The Chair shall determine if the number of voting Board members is sufficient to constitute a quorum (refer 5.2.13) and proceeds accordingly.
5.3.4. A board member shall make a motion to recommend action on a protocol or issue being discussed.
5.3.5. The motion is seconded and voting takes place.
5.3.6. A motion is carried out once the majority of IRB members vote in favour of the motion.

5.4. After the Board meeting,

5.4.1. Preparing the Minutes and the Decision Forms

5.4.1.1. Assembling the meeting minutes and the decision form

5.4.1.1.1. Use the format as shown in ANNEX - AF/02-022/01to write a minute.

5.4.1.1.2. Compose the summary of each meeting discussion and decision in a concise and easy-to-read style.

5.4.1.1.3. Make sure to cover all contents in each particular category.

5.4.1.1.4. Check spelling, grammar and context of the written minutes.

5.4.1.1.5. Finish the minutes within five working days after the meeting.

5.4.1.2. Contents of the IRB Meeting Minutes

5.4.1.2.1. The official minutes of the Board meeting consist of, but are not limited to, the following:

5.4.1.2.1.1. Name of person preparing the minutes

5.4.1.2.1.2. Location where the meeting was held (city, state)

5.4.1.2.1.3. Meeting date

5.4.1.2.1.4. Attending Board members and guests

5.4.1.2.1.5. Agenda items

5.4.1.2.1.6. Individual serving as Chairperson of the meeting

5.4.1.2.1.7. Determination of a duly constituted quorum by the Chairperson to proceed with the meeting

5.4.1.2.2. Requirements for each study or activity requesting Approval:

5.4.1.2.2.1. Sponsor's name;

5.4.1.2.2.2. Protocol number/date/version of protocol, when available;

5.4.1.2.2.3. Investigator's name;

5.4.1.2.2.4. Advertisements;

5.4.1.2.2.5. Name of Board member presenting study materials;

5.4.1.2.2.6. Discussion as deemed appropriate by the Chairperson

5.4.1.2.2.7. Number of members voting 'yes', 'no', or 'abstention'

5.4.1.2.2.8. Number of abstentions and the reason for the abstention;

5.4.1.2.2.9. Reference to the investigator approval letter that lists all changes requested by the Board;

5.4.1.2.2.10. Determination of the next requested continuing review.

5.4.1.2.3. Requirements for each study or activity requesting Expedited Review:

5.4.1.2.3.1. Sponsor's name;

5.4.1.2.3.2. Protocol number, if applicable;

5.4.1.2.3.3. Investigator's name;

5.4.1.2.3.4. Lists of expedited approval requests and outcomes.

5.4.1.2.4. Required for each Continuing Review Report:

5.4.1.2.4.1. Sponsor's name;

5.4.1.2.4.2. Protocol number, if applicable;

5.4.1.2.4.3. Investigator's name;

5.4.1.2.4.4. Indication of the Board's determination to continue, terminate, or amend the study;

5.4.1.2.4.5. Lists of recommendations or actions to be taken up with the investigator, if applicable.

5.4.1.2.5. Required for each Adverse Event notification and Final Report:

5.4.1.2.5.1. Sponsor's name;

5.4.1.2.5.2. Protocol number, if applicable;

5.4.1.2.5.3. Investigator's name;

5.4.1.2.5.4. Actions deemed appropriate by the Board's review.

5.4.1.2.6. Required for Termination of Approval:

5.4.1.2.6.1. Sponsor name's;

5.4.1.2.6.2. Protocol number, if applicable;

5.4.1.2.6.3. Investigator's name; reason for termination

5.4.2. Approval of the minutes and the decision

5.4.2.1. Circulate the draft minutes to all IRB Board Members, Chairperson, Vice Chairperson, IRB Member Secretary and Secretariat within three working days after each meeting for review and comments.

5.4.2.1.1. As soon as possible after each meeting, a copy of the minutes is sent to a senior administrative staff member for quality control and review Allow up to two working days for review and comments.

5.4.2.2. The IRB Member Secretary shall check the correctness and completeness of the minutes, indicating review by signing and dating the minutes.

5.4.2.3. Following review, the minutes shall be given to the Chairperson or designee for review and approval.

5.4.2.4. The Chairperson shall indicate approval by signing and dating the minutes.

5.4.3. Distribute the Decision and the minutes

5.4.3.1. Send the approved Action Letter to the applicants informing them of the IRB's decisions and recommendations.

5.4.3.2. Record the receiver and the delivery date of the Action Letter

5.4.3.3. Send the approved minutes to the IRB members.

5.4.4. Storage of the documents

5.4.4.1. Place the original version of the minutes and the signed decision form in the IRB files for the specific protocol.

5.4.4.2. Place all correspondence in the appropriate file.

5.4.4.3. Place a copy of the approval letter in the "minutes" file to inform the Board Members of the Expedited approval.

5.4.4.4. Document the appeal requests in the meeting minutes.

6. GLOSSARY

Agenda	A list of things to be done; a program of business at a meeting
Minutes	An official record of the business discussed and transacted at a meeting, conference, etc.
Quorum	Number of IRB members required to act on any motion presented to the Board for action.
Majority vote	A motion is carried out if one half plus one member of the required quorum vote in its favour.

7. REFERENCES

7.1. World Health Organization, Operational Guidelines for Ethics Boards that Review Biomedical Research, 2000

7.2. International Conference on Harmonization, Guidance on Good Clinical Practice (ICH GCP) 2016.

7.3. World Health Organization, Standards and operational guidance for ethics review of health-related research with human participants Guidance document, 2011

7.4. Associated SOP/004/01-SOP/006/01, SOP/008/01, SOP/010/01-SOP/016/01, SOP/012/01, and SOP/027/01.

8. ANNEX

ANNEX 1	AF/01-022/01	Agenda format
ANNEX 2	AF/02-022/01	Form of IRB Meeting Minutes
ANNEX 3	AF/03-022/01	IRB Meeting Minutes Template

ANNEX 1
AF/01-022/01

Format of an Agenda

Tentative agenda for xth IRB Full Board Meeting
dth Month, 2021

Sl. No.	AGENDA	TIME	PRESENTER
DD/MM/YYYY			
1	Opening remarks	9:00 am	Chairperson
2	Agenda adoption and quorum determination		
3	Review and endorsement of minutes of wth IRB Board meeting		IRB Member Secretary
4	Updates by IRB Member Secretary		IRB Member Secretary
Initial Full Board Review			
5	PN/YYYY/VVV xxxx _ Mr AZ		Primary Reviewers
6	PN/YYYY/VVV xxxx _ Mr AZ		Primary Reviewers
Expedited Review, Continuing Review & Resubmitted Review			
14	PN/YYYY/VVV xxxx _ Mr AZ		Primary Reviewers
15	PN/YYYY/VVV xxxx _ Mr AZ		Primary Reviewers
Reports for closure			
17	PN/YYYY/VVV xxxx _ Mr AZ		Primary Reviewers
18	PN/YYYY/VVV xxxx _ Mr AZ		Primary Reviewers
	Next Board Meeting date		IRB Member Secretary
	Any other issues		
	Closing Remarks		Chairperson

ANNEX 2
AF/02-022/01

Form of IRB Meeting Minutes

Meeting No.:	Meeting date:
☐ Regular meeting	☐ Emergency meeting
Venue of meeting:	
Agenda items:	
Starting time:	Adjourned time :

Attending board members and guests:

1. 10.
2. 11.
3. 12.
4. 13.
5. 14.
6. 15.
7. 16.
8. 17.
9. 18.

Chairperson/Vice Chairperson:

Was there sufficient voting member representative for the session met?

☐ Yes ☐ No

Prepared by:…… Reviewed by:……..

Date: …… Date: ……..

Approved by: ……

Date: ……..

ANNEX 3
AF/03-022/01 IRB Meeting Minutes Template

Agenda Item 1: Opening Remarks
Agenda Item 2: Adoption of Agenda
Agenda Item 3: Updates by IRB Member Secretary on the status of Protocols
Agenda Item 4: Declaration of Conflict of Interest (CoI)
Protocols for Initial Full Board Review
Agenda Item 5:
Protocol Number: Title: PI: Primary Reviewer 1: Primary Reviewer 2: Discussion: Decision: Recommendations/Clarifications:
Protocols for Resubmission Agenda Item 6: Protocol Number: Title: PI: Primary Reviewer 1: Primary Reviewer 2: Discussion: Decision: Recommendations/Clarifications:
Protocols for Final Report Review Agenda Item 7: Protocol Number: Title: PI: Primary Reviewer 1: Primary Reviewer 2: Discussion: Decision: Recommendations/Clarifications:
Agenda Item 8: Any other Issues
Agenda Item 9: Next Board Meeting Date
Agenda Item 10: Closing Remarks

CHAPTER 8.2

EMERGENCY MEETING

SOP NUMBER: SOP/023/01

INSTITUTIONAL REVIEW BOARD
(IRB)

Khesar Gyalpo University of Medical Sciences of Bhutan

www.kgumsb.edu.bt

Effective Date: October 1, 2021
Supersedes: SOP/022/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 SOP shall be:

1.1. to identify the administrative process for preparing for an emergency meeting;

1.2. To provide instructions on the review and approval of study activities using the Emergency Meeting Procedure.

2. SCOPE

This SOP shall apply to emergency IRB meetings. Emergency meetings may be scheduled to review/approve safety / life threatening issues, new studies, and additional investigators, continuing review, protocol amendments and other study activities that require full Committee review. An independent consultant may be requested to attend the meeting to provide expert information on the relevant topics. E.g. For certain dental studies, it may be necessary to invite a dentist to attend the meeting as well.

3. RESPONSIBILITY

The IRB Chairperson may call for an emergency meeting as appropriate.

4. FLOW CHART

No.	Activity	Responsibility
1	Before the Committee meeting ↓	IRB Secretariat IRB Chairperson
2	During the meeting ↓	IRB Members and Chairperson
3	After the meeting	IRB Secretariat

5. DETAILED INSTRUCTIONS

5.1. Before the Committee meeting

5.1.1. The IRB Chairperson shall decide to call an emergency meeting based on the following criteria:

5.1.1.1. Urgent issues (if delay will affect or have impact to the public benefit, national interest, etc.)

5.1.1.2. Occurrence of unexpected serious adverse events.

5.1.1.3. A matter of life and death

5.1.2. The IRB Secretariat shall contact and inform IRB members and the following representatives must be present within the quorum to conduct the Emergency meeting

5.1.2.1. At least one scientific member

5.1.2.2. A non-scientific member

5.1.2.3. A member with expertise on the item to discussed

- *E.g. for routine medical research studies, a physician may be invited.*

5.1.3. The IRB Secretariat shall prepare packets for distribution to the members.

5.1.3.1. Attach a separate sheet with information about meeting date, time, phone numbers, the meeting ID number and an attendant confirmation form to the packets.

5.1.4. Refer to the relevant SOPs (SOP/011/01 - Initial Review of Application Protocol, SOP/010/01- Expedited Review, SOP/015/01 - Review of Protocol Amendments)

5.2. During the meeting

5.2.1. Determine if there is a quorum.

5.2.2. Follow the related SOPs:

- 5.2.2.1. SOP/003/01 – Constituting an Ethics Committee
- 5.2.2.2. SOP/008/01 – Management of Protocol Submission
- 5.2.2.3. SOP/012/01 – Use of Study Assessment Form
- 5.2.2.4. SOP/009/01 – Expedited Review
- 5.2.2.5. SOP/010/01 – Initial Review of Application Protocol
- 5.2.2.6. SOP/011/01 – Review of New Medical Device Studies
- 5.2.2.7. SOP/014/01 – Review of Protocol Amendments
- 5.2.2.8. SOP/015/01 – Management of protocol continuing Reviews
- 5.2.2.9. SOP/022/01 – Preparation of Meeting, agenda, minutes & action letters

5.3. After the meeting

5.3.1. Follow the related SOPs in 5.2.

6. GLOSSARY

Emergency meeting	An IRB meeting that is scheduled outside of a normally scheduled meeting to review study activities that require full IRB review and approval. In order to hold an emergency meeting, a quorum shall be maintained throughout the entire discussion and voting portions of the meeting. Emergency meetings may be held via teleconference, if applicable.

7. REFERENCES

7.1. World Health Organization, Operational Guidelines for Ethics Committees that Review Biomedical Research, 2000.

7.2. International Conference on Harmonization, Guidance on Good Clinical Practice (ICH GCP) 1996 & 2016.

7.3. World Health Organization, Standards and operational guidance for ethics review of health-related research with human participants, 2011.

7.4. Associated SOPs: SOP/003/01, SOP/009/01, SOP/012/01, SOP/013/01, SOP/015/01, SOP/016/01, and SOP/023/01.

CHAPTER 8.3

COMMUNICATION RECORDS

SOP NUMBER: SOP/024/01

INSTITUTIONAL REVIEW BOARD
(IRB)

Khesar Gyalpo University of Medical Sciences of Bhutan

www.kgumsb.edu.bt

Effective Date: October 1, 2021
Supersedes: SOP/023/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 SOP shall be to ensure proper completion, distribution and filing of verbal and written communication and other study-related or process-related information done with investigators, sponsors, volunteer subjects, institutes and/or relevant government agencies.

2. SCOPE

This SOP shall apply to all communicating activities related to the studies under the approval of the IRB.

3. RESPONSIBILITY

All IRB administrative staff, committee members, member secretary and chairperson shall be responsible to conduct of activities with IRB to complete a written communication record for telephone or interpersonal discussions related to past, present and/or future studies and/or processes involving the IRB.

4. FLOW CHART

No.	Activity	Responsibility
1	Communication recording mechanism ↓	IRB secretariat / members / Chairperson
2	Contents of a written record ↓	IRB secretariat / members / Chairperson
3	Distribution of the record	IRB secretariat / members / Chairperson

5. DETAILED INSTRUCTIONS

5.1. Communication recording mechanism

5.1.1. Individuals may utilize different communication recording mechanisms that may be handwritten, typed or computer-generated.

5.2. Contents of a written record

5.2.1. The record shall contain, but is not limited to, the following information:

- 5.2.1.1. Date of communication
- 5.2.1.2. Study information, i.e., sponsor, protocol number, investigator, etc.
- 5.2.1.3. Name of person contacted
- 5.2.1.4. Contact address, telephone number, and e-mail
- 5.2.1.5. Summary of the communication made
- 5.2.1.6. Notation of any follow-up necessary
- 5.2.1.7. Signature of individual completing record

5.3. Distribution of the record

5.3.1. Upon completion of the records, the individual distributes copies to:

- 5.3.1.1. The study file
- 5.3.1.2. Others, as appropriate
- 5.3.1.3. Secretariat or administrative staff for filing

6. ANNEX

Annex 1 AF/01-024/01 Communication Record Form

ANNEX 1
AF/01-024/01

Communication Record Form

Date:			
Means of Contact	☐ Telephone ☐ Fax ☐ e-mail ☐ In Person		
Person contacted:	☐ Reviewer ☐ IRB/REC member ☐ Media ☐ Chairperson ☐ Secretariat ☐ Regulatory ☐ Sponsor ☐ Investigator ☐ Others (specify) ☐ Subject ☐ Institute ……		
Name:			
Telephone No.		Fax No.	
e-mail			
Protocol No.			
Title :			
Communication Issues / Reason for making contact:			
Follow-up Action :	☐ Return call ☐ will call again ☐ None ☐ See notes ☐ Circulation ☐ Confidential		
Summary of Communication:			
Recorded by:			

CHAPTER 9.1

MAINTENANCE OF ACTIVE STUDY FILES

SOP NUMBER: SOP/025/01

INSTITUTIONAL REVIEW BOARD
(IRB)

Khesar Gyalpo University of Medical Sciences of Bhutan

www.kgumsb.edu.bt

Effective Date: October 1, 2021
Supersedes: SOP/024/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 SOP is to provide instructions for preparation, circulation and maintenance of active study files and other related documents approved by the IRB.

2. SCOPE

This SOP shall apply to all active study files and their related documents that are maintained in the IRB office.

3. RESPONSIBILITY

The IRB Secretariat shall be responsible to ensure that all study files are prepared, maintained, circulated and kept securely for the specified period of time under a proper system that ensures confidentiality and facilitates retrieval at any time.

4. FLOW CHART

No.	Activity	Responsibility
1	Organize the contents of the active study files ↓	IRB Secretariat
2	Maintain the active study files	IRB Secretariat

5. DETAILED INSTRUCTIONS

5.1. Organize the contents of the active study files

5.1.1. Get the master copy of the study files.

5.1.2. Gather, classify and combine all related documents together.

5.1.3. Check if a study file contains, at a minimum, the following documents:

- 5.1.3.1. Original applications and any updates received during the study.
- 5.1.3.2. Investigator's brochures or similar documents
- 5.1.3.3. Approval letters and other correspondence sent to the investigator.
- 5.1.3.4. Approved documents (protocols, amendment, informed consent form, advertising materials, etc.)
- 5.1.3.5. Adverse experience reports or IND safety reports received
- 5.1.3.6. Continuing review reports

5.1.4. Use a folder with the following on the cover:

- 5.1.4.1. The name of the sponsor, if applicable
- 5.1.4.2. The protocol number
- 5.1.4.3. The number assigned by the IRB Secretariat
- 5.1.4.4. Put the following into each folder with the following information:
  - 5.1.4.4.1. Sponsor with address and contact phone/e-mail id of contact person, protocol number, investigator name (with address, e-mail, telephone and fax) and title
  - 5.1.4.4.2. Application form of the IRB Protocol, Case Report Form, Investigator's Brochure (drug studies), Informed consent documents with translations in the relevant languages, advertising material and recruitment procedures, investigator bio data, any other material submitted by the investigator
    - 5.1.4.4.2.1. Correspondence
    - 5.1.4.4.2.2. Initial Approval with the final version of all above documents (protocol, ICD, CRF etc.)
    - 5.1.4.4.2.3. Revisions/Amendments
    - 5.1.4.4.2.4. Adverse Events

5.1.4.4.2.5. Continuing Review, if applicable
5.1.4.4.2.6. Final report

5.2. Maintain the active study files

5.2.1. Assign the approved study files with unique identifiers (on a sheet of paper) established by a member of the IRB Secretariat
5.2.2. Combine related documents of the approved study files appropriately.
5.2.3. Attach an identity Label to the package.
5.2.4. Keep all active and potential study packages in a secure file cabinet.
5.2.5. Maintain the study files in an easily accessible and secure place until the final report is reviewed and accepted by the IRB.
5.2.6. Send all closed study files to archive.
5.2.7. Store the closed study files for at least 5 years after the study closure.

Note: For studies with multiple study sites, a member Secretariat should maintain the files to allow cross-referencing without unnecessary duplications.

6. GLOSSARY

Active Study File	Any approved protocol, supporting documents, records containing communications and reports that correspond to each currently approved study.
CRF	Case Record Form or Case Report Form is a printed, optical or electronic document designed to record all of the protocol required information to be reported to the sponsor on each trial participant.
IND	Investigational New Drug is a drug that has never been seen in the market because it is under investigation of its efficacy and safety and not yet been approved for marketing by the local authorities. The drug is therefore approved for used only at some certain study sites.
ICD	Informed Consent Document is a written, signed and dated paper confirming participant's willingness to voluntarily participate in a particular trial, after having been informed of all aspects of the trial that are relevant to the participant's decision to participate.
Master file	A file for storage of the originally signed and dated documents

CHAPTER 9.2

ARCHIVES AND RETRIEVAL OF DOCUMENTS

SOP NUMBER: SOP/026/01

INSTITUTIONAL REVIEW BOARD
(IRB)

Khesar Gyalpo University of Medical Sciences of Bhutan

www.kgumsb.edu.bt

Effective Date: October 1, 2021
Supersedes: SOP/025/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 SOP shall be to provide instructions for storing *inactive* study files and administrative documents in a secure manner while maintaining access for review by auditors and inspectors.

2. SCOPE

This SOP shall apply to archiving the study files and administrative documents that are retained for **at least five years** (or more for some particular cases) after completion of the research so that the records are accessible for future reference. Copying files and documents for or by authorized representatives of the national authority is allowed when required.

3. RESPONSIBILITY

The IRB Secretariat shall be responsible for maintaining inactive study files and administrative documents.

4. FLOW CHART

No.	Activity	Responsibility
1	After receiving the final report ↓	IRB members, secretariat
2	When archiving administrative documents ↓	IRB secretariat
3	Retrieving Documents	IRB secretariat

5. DETAILED INSTRUCTION

5.1. After receiving the final report

5.1.1. IRB Secretariat and Members shall review the Final Report of the study.

5.1.2. A member of the Secretariat shall:

- 5.1.2.1. Remove the contents of the entire file from the active study filing area.
- 5.1.2.2. Verify that all documents are present in an organized manner.
- 5.1.2.3. Assign an archive number
- 5.1.2.4. Enter the number into the file and the data base.
- 5.1.2.5. place the file in a storage container
- 5.1.2.6. Send to the archives.

5.1.3. Hold the files of multi-centre studies, until all the study sites are closed.

5.1.4. Place in a storage container together.

5.1.5. Send to the archive.

5.2. When archiving administrative documents

5.2.1. A staff of the IRB Secretariat shall:

- 5.2.1.1. perform inventories of miscellaneous administrative documents
- 5.2.1.2. place the documents in the appropriate storage container, and
- 5.2.1.3. Send it to the appropriate storage facility so that it may be easily retrieved.

Note: The IRB Secretariat shall maintain past committee membership information as well as the active administrative documents.

5.3. Retrieving Documents

5.3.1. Keep in mind the SOP/026/01 (Maintaining Confidentiality of IRB documents)

5.3.2. Retrieval of documents can only be done with a request form (AF/01-026/01, see ANNEX 1) signed and dated by the IRB Chairperson or the Secretariat.
5.3.3. The requestor shall also sign and date the log of request, ANNEX - AF/02-026/01
5.3.4. The Secretariat shall retrieve archived documents in compliance with the procedures of the IRB.
5.3.5. Return the file back to its place.
5.3.6. Record, sign and date when the document has been returned and kept.

6. GLOSSARY

Administrative Documents	Documents include official minutes of committee meetings (as described in SOP/022/01) and the Standard Operating Procedures, both historical files and Master Files as described in SOP/001/01.
Inactive Study Files	Approved and supporting documents (protocols, protocol amendments, informed consents, advertisements, investigator and site information), records containing communications and correspondence with the investigator, and reports (including but not limited to Continuing Review Reports, IND Safety Reports, reports of injuries to subjects, scientific evaluations) that correspond to each study approved by the IRB for which a final report has been reviewed and accepted.

7. REFERENCES

7.1. World Health Organization, Operational Guidelines for Ethics Committees that Review Biomedical Research, 2000.
7.2. International Conference on Harmonization, Guidance on Good Clinical Practice (ICH GCP) 2016
7.3. World Health Organization, Standards and operational guidance for ethics review of health-related research with human participants, 2011.
7.4. Associated SOPs: SOP/026/01.

8. ANNEX

ANNEX 1	AF/01-026/01	Document Request Form
ANNEX 2	AF/02-026/01	Logs of Requested IRB Documents

ANNEX 1
AF/01-026/01

Document Request Form

Name of Document requested:	Archive No:
Requested by:	Date:
☐ Chairperson ☐ Secretariat ☐ IRB Member	
☐ Secretariat staff ☐ Authority ☐ Others……..	
Purpose of the request:	
Approved by:	Date:
Retrieved by:	Date:
Returned by:	Date:
Archived by:	Date:

ANNEX 2
AF/02-026/01

Log of Requested IRB Documents

No	Document	Requester	Date Requested	Retrieved by	Archived by	Returned Date

Page No…….

CHAPTER 9.3

MAINTAINING CONFIDENTIALITY OF IRB'S DOCUMENTS

SOP NUMBER: SOP/027/01

INSTITUTIONAL REVIEW BOARD
(IRB)

Khesar Gyalpo University of Medical Sciences of Bhutan

www.kgumsb.edu.bt

Effective Date: October 1, 2021
Supersedes: SOP/026/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 sources of violation of confidentiality are usually found in the day-to-day use of copies of original documents. This SOP therefore describes how to handle original documents and copies of documents in order to protect confidentiality of documents.

2. SCOPE

This SOP shall apply to all kinds of handling, distribution and storage of submitted study protocols, IRB documents, and correspondence with experts, auditors and the general public.

3. RESPONSIBILITY

Confidentiality of study protocols, IRB documents, and correspondence with experts and auditors is mandatory. IRB members and staff shall be required to sign confidentiality agreements with the KGUMSB.

If non-members of the IRB need copies of documents, the IRB member/staff requesting a copy on behalf of the non-members shall be responsible to maintain confidentiality of documents.

4. FLOW CHART

No.	Activity	Responsibility
1	Access to IRB documents ↓	IRB members and Secretariat
2	Classify confidential documents ↓	IRB members and Secretariat
3	Copy confidential documents ↓	IRB Secretariat
4	File Log of Copies	IRB Secretariat

5. DETAILED INSTRUCTIONS

5.1. Access to IRB Documents

The IRB members and the staff of the Secretariat of the IRB shall **read, understand and agree to the following:**

5.1.1. Members of the IRB shall:

5.1.1.1. Sign a confidentiality agreement (AF/01-004/01) with the IRB at the KGUMSB before the start of any activity of the IRB.

5.1.1.2. Have access to all IRB documents.

5.1.1.3. Be free to request and to use original documents or copies of original documents.

5.1.2. Secretariat of the IRB

5.1.2.1. The member secretary of the IRB is a staff member of the MECRIT, KGUMSB

5.1.2.2. Sign a confidentiality agreement with the IRB, KGUMSB

5.1.2.3. Have access to any document issued by or to the IRB, according to SOP/027/01 (Maintaining Confidentiality of IRB's Documents).

5.2. Classify confidential documents.

5.2.1. Types of documents

The types of documents reviewed by IRB members include:

5.2.1.1. Study protocols and related documents (case report forms, informed consent documents, diary forms, scientific documents, expert opinions or reviews)

5.2.1.2. IRB documents (meeting minutes, advice and decisions)

5.2.1.3. Correspondence (experts, auditors, study participants, etc.)

Note: Copies of all versions of documents, including draft and sequential definitive versions are to be kept private and confidential with the exception of those made according to the following sections.

5.3. Copy of confidential documents

Copies of documents, including draft and sequential versions, shall be considered to be confidential and shall not be permitted to be brought out *except when a document is needed for day-to-day operations.*

5.3.1. Copy Authorization

5.3.1.1. Only members of the IRB shall be allowed to ask for copies.

5.3.1.2. Only staff members of the Secretariat of the IRB shall be allowed to make such copies.

5.3.1.3. The Member Secretary of the IRB may ask for help, but shall be responsible for maintaining confidentiality of all documents.

5.3.2. Log of Copies

5.3.2.1. A Log of Copies (see ANNEX 1 Form AF/01-027/01) shall be kept by the Secretariat.

5.3.2.2. The log should include: the name and signature of the individual receiving the copy; the initial of the IRB Member Secretary who made the copy; the number of copies made and the date that the copies were made.

5.3.3. Copies requested by non-members of the IRB

5.3.3.1. Copies of IRB's documents requested by non-members of the IRB (including the Member Secretary) shall be given upon prior permission from the Chairperson of the IRB and the person requesting for the document signs a confidentiality agreement form (AF/01-004/01).

5.3.3.2. Copies made for non-members of the IRB shall be recorded in both the Log of Requests for Copies of IRB's documents (AF/01-027/01) and the log of Copies of the Original Documents (AF/02-027/01).

5.4. File Log of Copies.

5.4.1. The Log of Copies of Original Documents shall be stored with the original documents.

5.4.2. The Log of Copies of Original Documents shall not be a confidential document and shall be reviewed upon request.

5.4.3. A Log of Copies of Original Documents shall be maintained.

6. GLOSSARY

Document	Documents mean the followings: - Study Protocols and related documents (such as case report forms, informed consents, diary forms, scientific documents, reports, records, expert opinions or reviews) - IRB documents (SOPs, meeting minutes, advice and decisions) - Correspondance (experts, auditors, study participants, etc.) of any forms, such as printed or written papers, hard copies, electronic mails (e-mail), faxes, audio or video tapes, etc.
Non-members of the IRB	Any relevant person/persons who presently is/are not a member/members of the IRB such as authorities, monitors, auditors, subjects, etc.

7. REFERENCES

7.1. World Health Organization, Operational Guidelines for Ethics Committees that Review Biomedical Research, 2000.

7.2. International Conference on Harmonization, Guidance on Good Clinical Practice (ICH GCP) 2016

7.3. World Health Organization, Standards and operational guidance for ethics review of health-related research with human participants, 2011.

7.4. Associated SOPs : SOP/004/01

8. ANNEX

ANNEX 1 AF/01-027/01 Log of Requests for Copies of IRB documents
ANNEX 2 AF/02-027/01 Logs of Copies of Original Documents

ANNEX 1
Form AF/01-027/01

Log of Requests for Copies of IRB Documents

No	Documents requested	# of Copies	Name of Recipient	Signature of Recipient	Secretariat Initials	Date

ANNEX 2
Form AF/02-027/01

Log of Copies of Original Documents

Title of the Document:……

No	Name of Recipient	# of Copies	Reasons of the Request	Signature of Recipient	Secretariat Initials	Date

Note: *This log should be attached to the original documents.*

CHAPTER 10

AUDITING AND INSPECTION OF THE IRB

SOP NUMBER: SOP/028/01

INSTITUTIONAL REVIEW BOARD
(IRB)

Khesar Gyalpo University of Medical Sciences of Bhutan

www.kgumsb.edu.bt

Effective Date: October 1, 2021 Supersedes: SOP/027/yy	
Author: SOP Team Approved by: Chairperson, IRB *Name:* ***Dr. Karma Tenzin***	Date: September 29, 2021 Date: September 30, 2021

Table of Contents

1. PURPOSE

The purpose of this procedure shall be to guide how to prepare for an audit or inspection of the IRB processes.

2. SCOPE

This SOP shall apply to every unit of the IRB

3. RESPONSIBILITY

The Secretariat, the Members, and the Chairperson of the IRB shall be responsible to perform all tasks according to the SOPs and shall be accountable during evaluation, audit or inspection visits of authorities and guests.

4. FLOW CHART

No.	Activity	Responsibility
1	Call for an Audit / Inspection ↓	IRB Chairperson / Head of Organization
2	Prepare for the visit ↓	IRB Secretariat / Members and Chairperson
3	Receive Auditor / Inspector ↓	IRB Secretariat / Members and Chairperson
4	Correct the mistakes ↓	IRB Secretariat / Members and Chairperson
5	Record the Event	IRB Secretariat

5. DETAILED INSTRUCTIONS

5.1. Call for an Audit / Inspection

5.1.1. Receive a notice of inspection visit
5.1.2. The Chairperson informs the Secretariat /Head of Organization.
5.1.3. The Chairperson alerts every unit to get ready.

5.2. Prepare for the visit

5.2.1. Get a checklist form, ANNEX – AF/01-028/01.
5.2.2. Go through all steps on the list.
5.2.3. Note and comment on each part.
5.2.4. Emphasize on the studies with problems.
5.2.5. Check if all documents are labeled and kept in the right order for easy and quick search.
5.2.6. Check for any missing or disorganized records.
5.2.6.1. Background and training records of IRB members

5.2.6.2. Application Submission Records
5.2.6.3. Protocol Assessment Records
5.2.6.4. Communication Records
5.2.6.5. Amendment Approval
5.2.6.6. Meeting Agenda, Minutes, Action letters
5.2.6.7. Active files
5.2.6.8. Continuing and Final reports

5.2.7. Reserve a meeting room and all necessary facilities.
5.2.8. Review the IRB SOPs.
5.2.9. Make sure that no omission or deviation exists.
5.2.10. Make sure to have good reasons for any omission or deviation.
5.2.11. Inform IRB members about the inspection date if they are able to attend the audit/inspection meeting.

5.3. Receive Auditor / Inspector

5.3.1. The Chairperson or the Secretariat shall receive and accompany the auditors/inspectors to the reserved meeting room.
5.3.2. Members and some key staff shall also be present in the meeting room.
5.3.3. The conversation starts with the auditor/inspector stating the purpose of the visit and what kind of information and data are needed.
5.3.4. Answer questions of the auditors/inspectors clearly, politely and truthfully with confidence and straight to the point.
5.3.5. Find and get all information and files requested by the auditors/inspectors.
5.3.6. Take note of the comments, recommendation of the auditors/inspectors.

5.4. Correct the mistakes

5.4.1. Review comments and recommendations of the auditors/inspectors.
5.4.2. Write a report and have it approved by the Chairperson.
5.4.3. The Chairperson calls for the correction.
5.4.4. Allow appropriate time for correction and improvement process.
5.4.5. Carry an internal follow-up audit.
5.4.6. Evaluate the outcome.
5.4.7. Report the outcome to the IRB.

5.5. Record the Audit/Inspection Event

5.5.1. Keep record of the report on the audit/inspection meeting in the audit/inspection file.
5.5.2. Record also the findings from the internal follow-up audit in the internal audit file.

6. GLOSSARY

Audit	A systematic and independent examination of research trial approval activities and documents to determine whether the review and approval activities were conducted and data were recorded and accurately reported according to the SOPs, GCP, Declaration of Helsinki and applicable regulatory requirements
Inspection	The act by a regulatory authorities of conducting an official review of documents, facilities, records, and any other resources that are deemed by the authorities to be related to the clinical trial and that may be located at the site of the trial, at the sponsor's and/or contract research organization (CRO) facilities, Office of Ethics Committees, or at other establishments deemed appropriate by the regulatory authorities

7. REFERENCES

7.1.1. World Health Organization, Operational Guidelines for Ethics Committees that Review Biomedical Research, 2000.

7.1.2. International Conference on Harmonization, Guidance on Good Clinical Practice (ICH GCP) 2016.

7.1.3. World Health Organization, Surveying and Evaluating Ethical Review Practices, Feb. 2002.

7.2. World Health Organization, Standards and operational guidance for ethics review of health-related research with human participants, 2011.

7.3. Associated SOPs: SOP/001/01, SOP/028/01

8. ANNEX

ANNEX 1 AF/01-028/01 Audit and Inspection Checklist

ANNEX 1
AF/01-027/01

Audit and Inspection Checklist

Internal Audit External Audit Inspection		Date:
The date(s) which the audit/inspection has been agreed for:		
Will an interpreter be required? If yes, what arrangement has been made?		☐ Yes…… ☐ No
Review the SOPs and note details of any omissions or deviations, with reasons		
Check the files for the presence of all signed documents. Note any that are missing and actions taken. ☐ Background and training records of IRB members ☐ Application Submission Records ☐ Protocol Assessment Records ☐ Communication Records ☐ Amendment Approval ☐ Meeting Agenda, Minutes, Action letters ☐ Active files ☐ Continuing and Final reports		
Are any documents known to be missing from the study master file?		
Which personnel and members will be available? Give details of times and dates.		
What arrangements are there in the event the auditor/inspector needs to make copies of documents?		
Completed by:		Date:

CHAPTER 11

GLOSSARY

INSTITUTIONAL REVIEW BOARD
(IRB)

Khesar Gyalpo University of Medical Sciences of Bhutan

www.kgumsb.edu.bt

Table of Contents

1. PURPOSE

This SOP shall provide guidance regarding definition of terms, abbreviations and titles used by the *IRB* and its administrators to facilitate use and understanding of the *IRB* Standard Operating Procedures and activities

The definitions are divided into two sections:
1.1. Description/definition of individual roles as used in the *IRB* SOPs
1.2. Description/definition of terms and abbreviation used in the *IRB* SOPs

2. SCOPE

This section shall apply to all *IRB* SOPs and activities in addition to persons preparing and/or using the SOPs.

3. RESPONSIBILITY

The *IRB* members shall be responsible to define or determine and approve the appropriateness of the description.

4. FLOW CHART

No.	Activity	Responsibility
1	Description of individual titles and roles	*IRB* members and Secretariat
2	Definition of terms	*IRB* members and Secretariat
3	Addition / Correction of new titles and terms	*IRB* members and Secretariat
4	Approval of the new addendum	*IRB* members / Chairperson

5. DETAILED INSTRUCTIONS

5.1. Description of individual roles

5.1.1. KGUMSB

The Khesar Gyalpo University of Medical Sciences Of Bhutan.

5.1.2. Chairperson

A member of the *IRB* who presides over a board meeting He/she is responsible for expedited approvals on behalf of the Board.

5.1.3. Vice Chairperson

A member of the *IRB* who assist the Chairperson or presides over a board meeting in absence of the chairperson. He/she is responsible for expedited approvals on behalf of the Board.

5.1.4. Supervisor

The person at the study site who is responsible for managing the study. Sometimes, the Principal Investigator is also the site coordinator and manager.

5.1.5. IRB

The *IRB* is a body established to review and monitor health research involving human subjects. The primary purpose of such a review is the protection of the rights and welfare of the human subjects. In accordance with applicable national/international regulations, the *IRB* has the authority to approve, require modifications to, or disapprove research.

The *IRB* consists of at least five voting members in addition to the other members during the session. The composition of the membership must reflect a diversity of backgrounds sufficient to assure:

5.1.5.1. expertise and experience to provide adequate review of research activities
5.1.5.2. consideration of race, gender, and cultural backgrounds
5.1.5.3. sensitivity to attitudes and concerns of the community and the patient population
5.1.5.4. knowledge of applicable regulation, laws and standards of professional conduct and practice
5.1.5.5. no member participates in the review process of any study project in which he/she has a conflicting interest
5.1.5.6. no gender discrimination

5.1.6. IRB Members

Individuals who have agreed to become a member of the *IRB* after being nominated by the *KGUMSB*.

5.1.7. Investigational New Drug (IND)

Investigational new drug means a new substance/medicine or biological product that is used in a clinical investigation. The term also includes a biological product that is used in vitro for diagnostic purposes. The terms “investigational drug” and “investigational new drug” are deemed to be synonymous for purposes of this part.

Principal Investigator

Individual responsible for implementing and coordinating an investigational study

5.1.8. Secretariat

The *IRB* staff who are responsible for the day-to-day administrative functions and duties which support the activities and responsibilities of the *IRB* members.

5.1.9. SOP Team

A selected group of *individuals* and administrative staff who oversee the preparation, review and periodic revision of the *IRB* SOPs

5.1.10. Vulnerable subjects

A category of research participants that includes children, prisoners, pregnant women, handicapped or mentally disabled persons and economically or educationally disadvantaged persons who are likely inclined to coercion or undue influence

5.2. Definition of Terms

5.2.1. Active study files

Supporting and approved documents, records containing communications, and reports that correspond to each active (current) study approved by the *IRB.*

5.2.2. Administrative documents

Documents include official minutes of Board meetings as described in SOP... *IRB* meeting minutes and voting records and the standard operating procedures, both historical files and Master Files as described in the SOP, SOP distribution, implementation and file maintenance.

5.2.3. Deviation

Any instance in which the current approved *IRB* SOP has not been followed.

5.2.4. Expedited approval

An *IRB* approval granted only by the Chairperson of the *IRB* or a designated *individual or IRB* member (not the full Board) for "minor" changes to current *IRB*-approved research activities and for research which involves no more than minimal risk

5.2.5. Final report

An obligatory review of study activities presented as a written report to the *IRB* after the last subject has completed all visits and all adverse experiences have been brought to appropriate resolution.

Complete, comprehensive written description of a completed trial that describes the experimental materials and statistical design, presentation and evaluation of the trial results and statistical analyses.

5.2.6. Historical file

A document file which was effectively used in the past and presently became obsolete or expired, but still had to be kept in a file for reference purposes.

5.2.7. Inactive study files

Supporting and approved documents (protocols, protocol amendments, informed consents, advertisements, investigator and site information), records containing communication and correspondence with the investigator, and reports (including but not limited to progress reports, IND Safety Reports, reports of injuries to subjects, scientific evaluations) that correspond to each study approved by the *IRB* for which a final report has been reviewed and accepted Inactive study files are archived for a minimum of five years following the completion of the study. These files can be retrieved as needed.

5.2.8. Investigational medical device

A medical device which is the object of clinical research to determine its safety or effectiveness.

5.2.9. Master files

Original copies of documents such as SOPs, guidelines, instruction, manual with real signatures of preparers, reviewers and authorized persons are systematically stored in secured cabinets with limited access.

5.2.10. Medical Device

A medical device is any health care product that does not achieve any of its intended purposes by chemical action or by being metabolized. Medical devices include items such as diagnostic test kits, crutches, electrodes, prescribed beds, pacemakers, arterial grafts, intra-occular lenses, and orthopedic pins. Medical devices also include diagnostic aids such as reagents and test kids for *in vitro* diagnosis of disease and other conditions, (for example, pregnancy).

5.2.11. Minutes

The official record of events, activities, and actions taken on agenda items presented to a duly constituted (quorum present) independent board review meeting. The minutes identify fully each protocol and/ or activity and record the outcomes of each voting action. The board votes separately on each collective set or each item submitted for review: protocol, consent form, investigator, and advertisement(s). The record notes the number for, number against, the number of abstaining votes, and the reason for the abstention(s), without identifying the individual member's names.

5.2.12. New Study

A study protocol including the informed consent, investigator's qualifications, information on the drug or device and advertisements (if applicable) presented to *IRB* for approval for the first time and not previously approved by this board. This includes re-application for those studies denied approval by *IRB*.

5.2.13. Non-compliance record

A list containing the identity of investigators who are considered by the *IRB* to be non-compliant with national/international regulations or who fail to respond to the committee's requests, and the incident(s) justifying the reason for the determination of non-compliance.

5.2.14. Non-significant Risk Device (NSR)

A non-significant risk device is an investigational device that does not pose a significant risk.

5.2.15. Progress Report

An ongoing review of each investigator's study activities presented as a written report to obtain extended approval for the study from the *IRB*. Generally, these reports are due annually with the *IRB* sending a written notification reminding the investigator of this obligation. More frequent reports may be requested at the discretion of the *IRB*.

5.2.16. Protocol Amendment

A change to the study protocol during the planning or course of the trial or the amendment is a foreseen change to the study plan that requires formal approval by the sponsor.

5.2.17. Quorum

Attendance required arriving at a decision at any convened meeting of the board i.e. 50% of the members including the five voting members.

5.2.18. Significant Risk Device (SR)

A significant risk device is an investigational device that: (1) is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of the subject, (2) is purported or represented to be for a use in supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of the subject, (3) is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety, or welfare of the subject, or (4) otherwise presents a potential for serious risk to the health, safety, or welfare of the participants.

5.3. Addition / Correction of terms

5.3.1. Members are encouraged to propose any additional terms or make correction of any terms defined in this SOP at any time, if he/she feels clarification should be made.

5.3.2. Write your proposal.

5.3.3. Submit your proposal to the *IRB* secretariat.

5.4. Approval of the addendum

5.4.1. *IRB* secretariat shall bring the proposal to a meeting.

5.4.2. The proposal shall be discussed for further opinion.

5.4.3. Agreement and approval shall be made at the meeting.

6. REFERENCES

6.1. World Health Organization, Operational Guidelines for Ethics Committees that Review Biomedical Research, 2000.

6.2. International Conference on Harmonization, Guidance on Good Clinical Practice (ICH GCP) 1996.