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

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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