NIGERIAN INSTITUTE OF MEDICAL RESEACH

**INSTITUTIONAL REVIEW BOARD**

# STANDARD OPERATING PROCEDURES

# TABLE OF CONTENTS


| S/N | TOPIC | PAGE |
|---|---|---|
| 1. | Constituting An Institutional Review Board | 1 – 14 |
| 2. | Management of Protocol Submission | 15 - 21 |
| 3. | Initial Review of Application Protocol | 22 – 38 |
| 4. | Idemnity for Research | 39 – 42 |
| 5. | Adverse Event Reporting Procedures | 43 – 47 |
| 6. | Clinical Trial | 48 – 56 |
| 7. | Review of Medical Device Study | 57 – 65 |
| 8. | Report of Monitoring Visit | 66 – 80 |
| 9. | Training and Continuing Education of Ethics Members and Personnel | 81 – 87 |

NIMR - INSTITUTIONAL REVIEW BOARD

STANDARD OPERATING PROCEDURE

# CONSTITUTING AN INSTITUTIONAL REVIEW BOARD

## 1. Purpose

The IRB was effectively constituted on October 2004 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 non-scientists and community members. It is independent in its reflection, advice, and decision. These Standard Operating Procedures (SOP) describe the Terms of Reference (TOR) which provide the framework for constitution, responsibilities and activities of the Institutional Review Board (IRB).

**2. Scope** The SOP applies to all activities under the auspice of the institutional Review Board of NIMR, Yaba, Lagos.

**3. Responsibility** It is the responsibility of the IRB members, secretariat to read understand and respect the rules set by the IRB

## 4. Flow chart

| № | Activity | Responsibility |
|---|---|---|
| 1 | Ethical basis / Guidelines | IRB Members, Secretariat |
| 2 | Composition of the IRB | IRB Members and Secretariat |
| 3 | Membership Requirements | IRB Members and Secretariat |
| 4 | Resignation, Disqualification, Replacement of Members | Chief Executive Officer |
| 5 | Independent Consultants | IRB Member |
| 6 | Conditions of Appointment | IRB Members and Secretariat |
| 7 | Officers | IRB Members |
| 8 | Secretariat | IRB Secretary |
| 9 | Quorum Requirements | IRB Members and Secretariat |
| 10 | Dissolving of the IRB | IRB Members and Secretariat |

## 5.0 IRB OFFICE

### 5.1 Physical Location and security

5.1.1 The IRB should have a dedicated office located at the NIMR

5.1.2 The IRB secretariat only should be authorized to have access to the IRB office

5.1.3 IRB documents should be kept secure in locked cabinets accessed by authorized IRB secretariat only.

5.2 **Operations**

5.2.1 The operations of the IRB office should be spearheaded by the IRB Administrator/Secretary as per instructions from the IRB through the chairperson

5.2.2 The operations of the IRB office should be separate from and independent from the administration of the institution but strictly as per the decisions of the IRB implemented through the chairperson and the secretariat

5.2.3 Applications to the IRB must be channeled through the IRB secretariat

5.2.4 All decisions and communication from the IRB to the applicants must be conveyed by the secretariat

## 6. Detailed Instructions

### 6.1 Ethical basis

6.1.1. 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.

6.1.2. 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 (especially in Nigeria).

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

6.1.4. 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.

6.1.5. The IRB is guided in its reflection, advice, and decision by the ethic principles expressed in the various international and national ethical guideline and declaration and their revisions

6.1.6. The IRB establishes its own standard operating procedures 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.

6.1.7 The IRB seeks to fulfill the requirements for international assurances and its establishment and functions are in accordance with the national law and regulations.

## 6.2 Composition of the IRB

6.2.1. The IRB is composed of at least 5 members

6.2.2. The members shall include at least one member whose primary concerns are in medical science, at least one member whose primary concerns are in non- medical/nonscientific areas, and at least a member from outside the institute.

6.2.3. The members should have various backgrounds to promote complete and adequate review of research activities commonly conducted by the institute.

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

6.2.5. The IRB cannot consist entirely of men or entirely of women It must be gender sensitive.

6.2.6 ERC should be multidisciplinary and multi-sectoral in composition, including persons with relevant but diverse scientific expertise, balanced age and gender distribution, who have the qualifications and experience to review and evaluate scientific and medical ethics aspects of research protocol.

## 6.3 Membership requirements

6.3.1. The head of the institution is responsible for making the appointment of Board members. The Head of the Institution will liaise or consult with department/institution in the appointment process

6.3.2. Members are selected in their personal capacities, based on their interest, 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.

6.3.3. Members should be able to read and understand the official language in which the proposals are written

6.3.4. The appointing authority should write an appointment letter to the prospective member inviting him/her to be a member of the IRB.

6.3.5. IRB members ought to be given a sitting allowance to compensate for their time spent on IRB work and costs of travel on ERC business.

6.3.6. Members must disclose in writing any interest or involvement -financial, professional or otherwise -in a project or proposal under consideration.

6.3.7. The IRB will decide the extent to which members that might have a conflict of interest may participate in bringing out an advice/decision.

6.3.8. Members will be required to sign a confidentiality agreement at the start of their term.

6.3.9. 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.

6.3.10. A member may be appointed up to three terms (maximum of 9 years) subject to competence, meeting attendance records and willingness to serve on the ERC.

6.3.11. Their appointments may be renewed by the Director-General of the institute for up to two consecutive terms. Their appointment will be for 3 terms.

6.3.12. Appointment of IRB members may represent all divisions and not necessarily having heads of divisions as members.

## 6.4 Independence of the IRB

6.4.1 The IRB must be independent from the appointing authority, hosting institution, researchers, sponsors and any other stakeholders in its review and decision-making processes

6.4.2 If there is any conflict of interest regarding a particular proposal, IRB members must declare their conflict of interest and recuse themselves from the review process of that particular proposal. This is critical to ensure objective assessment of submitted proposal.

6.4.2.1 Conflict of interest (COI) can be declared at the time research proposals are submitted, upon receiving the IRB agenda prior to the meeting and at the beginning of each meeting

6.4.2.2 IRB members who have a COI related to any research protocol must refrain from participating in any discussion of the protocol or related matters except to the extent necessary to provide relevant, factual information requested by the IRB, and should not deliberate or vote on those protocols or related matters

6.4.2.3 Unless requested by the IRB to provide information to the IRB, the IRB member or expert with a COI will be required to leave the room for the final discussion and vote. An IRB member assigned to carry out an expedited review for a protocol or related matters with respect to which a COI has been identified, must notify the IRB chair or administrator using the official COI form so that the protocol may be reassigned

6.4.3 Members should not share or give their personal opinions about submitted proposals and review decisions outside ERC meetings

## 7.0 ROLES AND MANDATES OF THE IRB

7.1.1 To safeguard the dignity, rights, safety, and well being of all actual or potential research participants and/or communities

7.1.2 To review protocols submitted by researchers from NIMR proposing to conduct health research involving participation of humans or affecting humans directly or indirectly.

7.1.3 To act in the full interest of actual or potential research participants and concerned communities, taking into account the interests and needs of researchers, and having due regard for the requirements of relevant regulatory agencies and applicable laws

7.1.4 To ensure that only qualified investigators are allowed to conduct proposed studies. (The investigators and study teams should be qualified by training and experience).

7.1.5 To provide ethical oversight through passive and active monitoring of approved projects

7.1.6 To suspend, withdraw approval or stop health research projects that the IRB approved but are proved to be harming participants to an extent that makes the risk/benefit ratio ethically unacceptable.

7.1.7 To ensure that research results have potential benefit to the participating individuals/communities and are disseminated to policy makers to enable translation into policy and/or interventions.

7.1.8 To provide initial review, continuing review and review of amendments of health research proposals as detailed in the relevant SOPs

7.1.9 To give ethical support and advice to researchers, policy makers and any other stakeholders.

7.1.10 To make efforts to conduct community outreach activities so as to sensitize communities about health research and health research ethics.

7.1.11 To charge administrative fees for services rendered. The payments should be made within the financial institutional framework of the organization but fully allocated to the activities of the IRB

## 7.2 Resignation, Disqualification, Replacement of Members

7.2.1. Members may resign their positions by submitting a letter of resignation to the Chairperson.

7.2.2. Members may also be disqualified from continuance should the Chairperson provide written arguments to the (other) members and there is unanimous agreement.

7.2.3. Members that have resigned or have been disqualified may be replaced by appointing authorities.

## 7.3. Independent Consultants

7.3.1. The IRB may be further supported in its reflections on specific protocols or requests for advice on specific ethical issues by Independent Consultants.

7.3.2. Independent Consultants are appointed by the members of the IRB.

7.3.3. 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

## 7.4 Conditions of Appointment

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

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

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

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

### 7.5.1 Secretariat

7.5.1.1 The Secretariat is composed of the IRB secretary, assistant secretary (who are IRB members) and the administrative support staff.

7.5.1.2 The secretariat should be made up of full-time employees of the institution where the IRB is based

7.5.1.3 The secretariat should be headed by an Administrator who should be knowledgeable about Health Research Ethics and is a full member of the IRB with voting power. The Administrator may have authority to counter-sign IRB official documents signed by either the chairperson or vice chairperson of the IRB

7.5.1.4 A deputy Administrator may be appointed so as to run the IRB office in the event that the Administrator is absent

7.5.1.5 The deputy Administrator should have authority to countersign IRB official documents signed by either the chairperson or vice chairperson only when the Administrator is not available.

7.5.1.6 The secretariat may have support staff who are not members of the IRB but help with clerical work as assigned by the IRB Administrator

7.5.1.7 Secretariat support staff must not review proposals or offer any advice to applicants regarding the contents of submitted applications.

7.5.1.8 Secretariat support staff should keep information that they are exposed to in the IRB office private and confidential and should sign private & confidentiality forms as well as conflict of interest forms upon joining the IRB office.

### 7.5.2 Members

7.5.2.1 Membership becomes effective upon accepting an invitation from the appointing authority. Acceptance must be indicated by the member's dated signature.

7.5.2.2 A member should be willing to have his/her full name, profession and affiliation (s) published in the public domain

7.5.2.3 Members are responsible for reviewing protocols to safeguard the rights, dignity and welfare of study participants

7.5.2.4 Members are responsible for reviewing progress reports

7.5.2.5 Members are responsible for oversight visits in order to monitor ongoing studies approved by the IRB

7.5.2.6 Members are obliged to read IRB documents such as protocols, project reports and SAE reports given to them by the IRB secretariat in advance preparation of IRB meetings.

7.5.2.7 Members are obliged to keep IRB documents given to them secure, private and confidential

7.5.2.8 Members should attend meetings regularly and participate fully and actively in deliberations during IRB meetings

7.5.2.9 Members must declare any conflict of interest for any protocol, and withdraw from the reviewing process of that particular protocol

7.5.2.10 An updated list of current members should be kept in a file in the IRB office. Previous lists of members with dates of their tenure of office should be filed.

7.5.2.11 Members should be able to read and write so that they can read protocols and other IRB documents

7.5.2.12 New members should undergo an orientation exercise upon joining the IRB in order for them to familiarize with the SOPs and train them on basic Health Research Ethics. Such training should be organized by the IRB secretariat, the host institutions and/or any other players involved in such training.

7.5.2.13 Continuous training of IRB members on Health Research Ethics and other relevant areas such as Good Clinical Practice (GCP) and experimental designs should be organized as frequently as possible or as is necessary.

7.5.2.14 Updated CVs of all the members should be kept on file by the IRB secretariat in the IRB office.

7.5.2.15 Membership may be renewed only twice, however; at least one-third of the old members should be retained at every point in time. The maximum tenure of office of IRB members is nine (9) years.

7.5.2.16 The chairperson may resign by sending his/her resignation letter to the appointing authority after duly informing the Board in a meeting

7.5.2.17 For any voluntary resignation a prior notice of at least one month should be given

7.5.2.18 Membership should be terminated by the appointing authority on The advice of the IRB if a member is going to be away for more than one year

7.5.2.19 Membership should be terminated by the appointing authority upon advice by the IRB if a member has been absent from three consecutive meetings without sending any apologies

7.5.2.20 Membership could be terminated by the appointing authority upon advice by the IRB if a member has been absent from six consecutive meetings with or without apologies.

7.5.2.21 Membership should be terminated by the appointing authority for misconduct that tarnishes the credibility of the IRB as determined and advised by the IRB

7.5.2.22 Membership should be terminated if a member is convicted by a court of law for a criminal offence

7.5.2.23 Membership should be terminated by the appointing authority in consultation with the IRB if a member is suffering from chronic incapacitating illness that significantly reduces the ability to process information and make rational independent decisions

7.5.2.24 Membership should automatically terminate when a member dies

### 7.5.3 Roles and responsibilities of IRB members

7.5.3.1 Participate in the IRB meeting(s)

7.5.3.2 Review, discuss and consider research proposals submitted for evaluation

7.5.3.3 Monitor serious adverse event reports and recommend appropriate action(s)

7.5.3.4 Review the progress reports and monitor ongoing studies as appropriate (site visits).

7.5.3.5 Evaluate final reports and outcomes

7.5.3.6 Maintain confidentiality of the documents and deliberations of IRB meetings

7.5.3.7 Declare any conflict of interest

7.5.3.8 Participate in continuing education activities in biomedical ethics and biomedical research and contribute to deliberations, and be punctual at meetings.

7.5.3.9 Sourcing grants for the activities of the IRB

## 7.6 Officers

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

**Chairman:** In order to enhance independence of the committee, the chairperson should not be affiliated with the institution where the IRB is based

Responsible to chair the meetings and liaise directly with the Director General of the institute, report the meeting outcomes to the Director General in consultation with IRB members, invite independent consultants in consultation with IRB members to provide special expertise to the IRB on specialized research protocol.

The chairperson should have authority to sign IRB official

documents such as the approval certificate

Should the chairperson decide to step down as chairperson of the IRB, he/she should inform the Board in writing at least one month in advance; and the Board is obliged to inform the appointing authority

**Vice-Chairperson:** The Vice chairperson should be selected using the same process as for the chairperson

Responsible to chair the meetings in the absence of the Chairperson and act as vice-chair during meetings with the Chairperson.

In the absence of both the chairperson and Vice chairperson, the IRB members should select an acting chairperson to chair the current meeting provided a quorum is satisfied.

The selected acting chairperson should sign minutes of previous meeting confirmed during his/her chairpersonship.

Acting chairperson should not have authority to sign IRB official documents such as approval certificates but may sign minutes confirmed during his/her chairpersonship

The process of resignation should be the same as that for the chairperson. The Vice chairperson may resign by sending his/her resignation letter to the appointing authority after duly informing the Board in a meeting

**Secretary:** Responsible for all the administrative protocols of the IRB.

Organizing an effective and efficient tracking procedure for each proposal received.

Preparation, maintenance and distribution of study files and Organizing IRB meetings regularly.

Preparation and maintenance of meeting agenda and minutes,

Maintaining the IRB's documentation and archive,

Communicating with the IRB members and applicants,

Arrangement of training for personnel and IRB members.

Organizing the preparation, review, revision and distribution of SOPs and guidelines.

Providing the necessary administrative support for IRB related activities to the chairperson of the committee (e.g. communicating a decision to the applicant).

Providing updates on relevant and contemporary issues related to ethics in health research, as well as relevant contemporary literature to the IRB members. This is implied in the effective day to day running of the IRB Secretariat.

For continuity and smooth running of the IRB office, IRB Secretary should serve up to a maximum of five (5) terms, which translates to a maximum of fifteen (15) years.

This time limit for IRB Secretary should be reviewed after every three years so as to reduce it if the availability of personnel trained in Health Research Ethics employed by the institution improves.

**Asst Secretary:** Secretary to assist the secretary in administrative Secretary protocols.

7.6.2. The officers are appointed by the Appointing Authority for three-year terms. They may be re-elected but not for more than two consecutive terms. Should they resign or be disqualified, the Appointing Authority appoints a replacement until the completion of the normal term.

## 8.0 Quorum Requirements

8.1 A minimum of 50% (to the nearest whole number) of the members must be present at a meeting in order to issue a valid advice and/or decision.

8.2 Professional qualifications of the quorum requirements should 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.

## 9.0 DISOLVING THE IRB

The IRB should automatically cease to exist when the institution at which it is based ceases to exist.

## 10.0 GLOSSARY

| | |
|---|---|
| **Confidentiality** | Prevention of disclosure, to other than authorized individuals, of IRB's information and documents |
| **IRB** | Institutional Review Board is an independent body (either a review board or committee) 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. |
| **Scientists** | Professionals with advanced training and expertise in the medical or non-medical areas related to the protocol being reviewed |
| **Lay Persons:** | Members appointed to represent the community's interest |
| **SAE :** | Severe Adverse Effect |

## 11.0 REFERENCES

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

10.2 International Conference on Harmonization, Guidance on Good Clinical Practice (ICH GCP) 1996.

NIMR - INSTITUTIONAL REVIEW BOARD
STANDARD OPERATING PROCEDURE

# MANAGEMENT OF PROTOCOL SUBMISSION

## 1. Purpose

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

## 2. Scope

Protocol submissions include:

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

## 3. Responsibility

It is the responsibility of the IRB secretariat to receive, record, distribute for review and get the submission packages approved by the IRB, as well as to deliver the review results to the protocol applicants.

## 4. Flow chart

| No. | Activity | Responsibility |
|---|---|---|
| 1. | Receive Submitted Packages | IRB Secretariat |
| 2. | Check for submission items:<br>• Initial Review Application<br>• Resubmission of Protocols with Corrections<br>• Protocol Amendment<br>• Continuing Review of Approved Protocols<br>• Protocol Termination | IRB Secretariat |
| 3. | Complete the submission process | IRB Secretariat |
| 4. | Store the received packages | IRB Secretariat |

## 5. Detailed instructions

### 5.1 Check for submission items

#### 5.1.1 Get relevant forms: Abridged and full protocol forms

* A checklist for contents of a submitted package
* A document receipt for payment for review process.
* An application form for initial review

*Material Transfer Agreement (MTA) if applicable
*Data Sharing Agreement (DSA) if applicable
* Evidence of electronic submission of abridged format to nimr_irb@yahoo.com
* A document receipt form
*Four (4) hard copies of the protocol

**5.1.2. Resubmission o f Protocols with corrections (Annex 1)**

* A checklist form
* a review form

**5.1.3. Protocol Amendments**

* A checklist for contents of a submitted package
* A document receipt form. (Annex 1)
* A re-review report form,

**5 1.4. Annual Continuing Reviews of Approved Protocols**

* A checklist for contents of a submitted package
* A document receipt form
* A re-review report form

**5.1.5. Protocol Termination**

* A checklist for contents of a submitted package
* A document receipt form
* A re-review report form

*Any protocol with three (3) consecutive appearances in statutory meeting without response from the PI should be expunged.

**5.1.6. Verify Contents of Submitted Package**

* Use the checklist for contents of a submitted package
* Check the applicable documents to ensure that all required forms and materials are contained within the submitted package.
* Verify contents of the protocol submitted package to include:
    - Original Application Form for Initial Review
    - Summary Sheet or Memorandum of the study Protocol
    - Study Protocol and Protocol-Related Documents
* Check completeness of necessary information in the Application Form for Initial Review.
* Check the Summary Sheet or Memorandum of the study protocol for inclusion of the following:
    - Title of the Protocol
    - Principal Investigator
    - Sponsor
    - Abstract
    - Type of Protocol (screening, survey, clinical trial and phase)
    - Objectives
    - Anticipated Outcome
    - Inclusion/Exclusion Criteria
    - Withdrawal or discontinuation Criteria
    - Modes of Treatment Studied

- Methodology (synopsis of study design)
- Analysis (methods)
- Activity plan / Timeline
- IND Number (if applicable)
- Schedule and Duration of Treatment
- Efficacy or Evaluation Criteria (Response/Outcome)
- Safety Parameters Criteria (Toxicity)

* Check the submitted **Protocol and Related Documents** for the following contents:
  - Subjects' information sheets
  - Informed Consent Form
  - Case Record Form (CRF)
  - Study budget and budget justification
  - Agreement of the study
  - Curriculum Vitae (CV) of investigators
  - Investigators' Brochure
* See if changes made to the documents be underlined or highlighted.

### 5.1.7. Verify electronic documents (abridged format of submission)

* Check the IRB e-mail box for confirmation
* Print out the protocol documents.
* Verify the correctness of the documents.
* Check that all pages of the documents have been included and that the submitted protocol and protocol-related documents do not have missing pages.
* Certify the printed hard copy in the same manner as the submitted document(s) with the dated signature Stamp and assign a running number to the received protocols, applying the system as shown below
  IRB/year
  /serial number of protocol
* Count for correct numbers of copies.
* Store the hard copy of the electronic document with the submitted documents.
* Use the assigned running number of the protocol as the labeled name.
* Identify clearly as the hard copy of the electronic document.

### 5.1.8. Create a Protocol Specific File (electronically & hard copy)

* Get the “Protocol Submission” file.
* Record the name and the number of the submitted protocol.
* Record the receiving date and the name of the receiver.

### 5.1.9. Complete the submission process

* Check the Form.
* Check for completeness of information.
* Notify the applicants if a package is incomplete.
* State clearly the items missing in the package.
* Fill up the related parts and the missing documents.

* Stamp the receiving date on the letter and the first page of the documents. * Initial the receiver's name on the receiving documents.
* Attach an Initial Review Application form to the Research Protocol packages.
* Keep the copy of the submitted documents with original signatures in the "Submission" file.

### 5.1.10. Store the received packages

* Bind the packages together appropriately.
* Store the dated and initial original protocol packages on the IRB submission shelf for review.

## 6.0 COMMUNICATING ERC DECISIONS TO APPLICANTS

6.1 Decisions regarding submitted protocols should be officially communicated, in writing, to the applicant within10 working days of the meeting that made the decisions.

6.2 Communication of the IRB decision shall include but not limited to the following:

i. The name, title and address of the applicant
ii. The exact title of the proposal reviewed
iii. The name of the site(s) or study area
iv. The names and identification numbers (versions numbers/dates) of the reviewed documents
v. A clear statement of the decision reached by the IRB
vi. The name of IRB taking the decision: a letter head of the IRB suffices
vii. The date of the decision and signature of the Administrator or Chairperson/Vice Chairperson
viii. In case of a conditional decision, any requirements by IRB, including suggestion for revisions should be clearly explained in writing to the applicant
ix. In case of a positive decision, a statement of responsibilities of the applicant and any requirements as stipulated in the decision by the IRB
x. The validity period of the approval
xi. The final approval certificate/letter shall be countersigned by the administrator and chairperson/Vice chairperson

## 7.0 DOCUMENTATION AND ARCHIVING

7.1 All documentation and communication done by the IRB should be dated, filed, and archived

7.2 Documents should be archived according to NHREC code following the completion of a study

7.3 Documents that should be filed and archived include but are not limited to:

i. Written standard operating procedures of IRB
ii. Updated lists of IRB members
iii. CVs of members
iv. Agenda of IRB meetings
v. Minutes of IRB meetings with names of members present, date of meeting, decisions made, and any other details

vi. One copy of all materials submitted by each and every applicant
vii. Correspondence between IRB members and applicants or concerned parties regarding application, decision and follow up
viii. Copy of the decision and any advice or requirements sent to each and every applicant
ix. Progress reports received from researchers as per IRB requirements
x. Serious Adverse Events reports submitted by researchers
xi. Final reports from researchers
xii. Oversight visit reports by IRB members
xiii. Documents reviewed by IRB members should be destroyed after completion of review by the reviewers.

## 8.0 REFERENCE

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) 1996.

**ANNEX 1**

<table>
<tr><td></td><td colspan="2">Received number:</td><td colspan="2">☐☐☐/☐☐ - ☐☐</td></tr>
<tr><td>Protocol number:</td><td></td><td>Submitted Date:</td><td colspan="2"></td></tr>
<tr><td>Type of Submission</td><td colspan="2">☐ Initial Review<br>☐ Resubmission for re-review<br>☐ Protocol Amendments</td><td colspan="2">☐ Continuing Review of Approved Protocols<br>☐ Protocol Termination</td></tr>
<tr><td colspan="5">Protocol Title:</td></tr>
<tr><td>Principal Investigator:</td><td colspan="4"></td></tr>
<tr><td>Telephone number:</td><td colspan="2"></td><td>Fax:</td><td></td></tr>
<tr><td>E-mail:</td><td colspan="2"></td><td>Preferred Contact</td><td>☐ Phone ☐ Fax ☐ E-mail</td></tr>
<tr><td colspan="5">Institute:</td></tr>
<tr><td colspan="5">Delivery route: ☐ Post ☐ E-submission ☐ in person</td></tr>
<tr><td colspan="5">Documents submitted: ☐ Complete ☐ Incomplete, will submit on……..</td></tr>
<tr><td>Documents to be submitted later:</td><td colspan="2">☐ Information for subjects<br>☐ Informed consent form<br>☐ Case report forms (CRF)<br>☐ Study budget<br>☐ Investigator’s brochure<br>Others……</td><td colspan="2">☐ Check what documents are received later on.<br>☐ Information for subjects<br>☐ Informed consent form<br>☐ Case report forms (CRF)<br>☐ Study budget<br>☐ Investigator’s brochure<br>Others……</td></tr>
<tr><td colspan="5">Received by:</td></tr>
<tr><td colspan="5">Date received:</td></tr>
</table>

***Note: please bring this receipt with you when contacting the institute IRB***

NIMR - INSTITUTIONAL REVIEW BOARD

STANDARD OPERATING PROCEDURE

# INITIAL REVIEW OF APPLICATION PROTOCOL

## 1. Purpose

This standard operating procedure describes how the Institutional Review Board (IRB) manages and reviews an initially submitted protocol.

## 2. Scope

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

## 3. Responsibility

It is the responsibility of the Board 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 date due.

The IRB Secretariat is responsible for receiving, verifying and managing the contents of both the hard copies and the electronic version of the received packages. In addition, the secretariat should create a protocol specific file, distribute the packages and get them reviewed by the IRB and deliver the review results to the applicants. The IRB secretariat also set the due -date for the returns of reviewed protocols by IRB members.

## 4. Flow chart

| No. | Activity | Responsibility |
|---|---|---|
| 1. | Receive the submitted protocol package | Secretariat |
| 2. | Verify the contents of the package | IRB Members/Reviewers/Secretariat |
| 3. | Review the protocol | IRB Members/Reviewers |
| 4. | Discuss in an IRB meeting | IRB Members/Reviewers/Secretariat/Chairperson |
| 5. | Preliminary Communication of the Decision | IRB Secretariat/Chairperson |
| 6. | Final Communication of the Decision | IRB Members/Chairperson |
| 7. | Storage of the Documents | IRB Secretariat |

## 5. Detailed instructions

### 5.1 Receive the submitted protocol packages

* Check the submitted package(s.)
* Sign and date an acknowledgment form upon receiving the package(s.)
* Notify the P.I, if there are documents missing

### 5.1.1 Contents of full protocol

Protocol contents should include summary of the study, background/introduction, rationale, objectives (general and specific), clear-end points, methodology, recruitment strategy, laboratory investigations to be done, plans for analysis and publication, personnel, budget & justification and timeframe of the project, dissemination plan and community sensitization.

The informed consent form and information leaflet, in both the official and when necessary the translation into the local vernacular language. Back translation into official language may be requested by the ERC.

Data collection tools such as questionnaires, interviews/discussion guides, checklists and case record forms must also be submitted

All materials to be used (including advertisements) for the recruitment of actual research participants must be attached to the protocol

### 5.1.2a Verify the contents of the package (secretariat)

* Look for an Assessment Form.
* Set the due date for the review.

### 5.1.2b Verify the contents of the package (IRB member/reviewer)

- Receive the protocol package)
- Notify the IRB Secretariat if there are documents missing, or the specified date cannot be met.
- Check the assessment form

### 5.2 TYPES OF REVIEW

#### 5.2.1 Initial review

5.2.1.1 All new health research proposals by investigators employed by NIMR must undergo initial review by the IRB in order for the research project to be granted approval before commencement

5.2.1.2 All new health research proposals by investigators not employed by NIMR

but the proposed research is to be conducted in the host institution must undergo initial review by NIMR-IRB in order for the research project to be granted approval before commencement

5.2.1.3 Initial review of health research proposals should be done by a full IRB, unless it qualifies for expedited review and there is acceptable justification for the expedited review as per the relevant SOPs of the IRB

5.2.1.4 Full proposal as per IRB requirements should be submitted

5.2.1.5 The IRB shall assess the social need and/or value of the proposed research

5.2.1.6 The IRB shall assess the scientific merit and validity of the propose research

5.2.1.7 If human participants are to be recruited, the inclusion and exclusion criteria should be assessed for ethical and scientific appropriateness

5.2.1.8 The IRB shall assess the informed consent process to ensure that all pertinent aspects are covered

- 5.2.1.8.1 Adequate privacy and voluntariness of participants
- 5.2.1.8.2 Satisfactory procedure to preserve the confidentiality
- 5.2.1.8.3 The IRB shall determine the appropriateness of the informed consent process for the category of people to be enrolled in the study. These shall include:
  - i. provision for community consent, individual consent, proxy consent and assent;
  - ii. duration of contact with potential participants to seek consent;
  - iii. non-technicality of the consent form and its completeness;
  - iv. the language in the informed consent documents should be in lay terms
  - v. provisions for vulnerable populations;
  - vi. provision for consenting illiterate potential participants; process to eliminate undue inducement;
  - vii. provision to continue providing study information to participants throughout the study period;
  - viii. process of ensuring confidentiality;

5.2.1.9 The IRB shall also examine the information sheet and informed consent form for the following:

- i. purposes of the research,
- ii. foreseeable risks,
- iii. potential benefits,
- iv. confidentiality,
- v. voluntariness,
- vi. local contact information (PI and IRB contacts should be included)
- vii. signature options (to include a witness in the case an illiterate participant),
- viii. compensation, and
- ix. Brief questions to assess comprehension

5.2.1.10 Potential risks already stated in the proposal and any other that may have been omitted but are deemed likely to occur should be assessed in light of potential benefits

5.2.1.11 Criteria for withdrawal or discontinuation of participants should be assessed to ensure fairness and safety of participants

5.2.1.12 If a placebo is to be used, there must be scientifically and ethically acceptable evidence-based justification that must be clearly explained in the protocol

5.2.1.13 The recruitment process should be suitable for the targeted prospective participants and their communities in terms of cultural, traditional, religious or socioeconomic factors

5.2.1.14 Health research should be conducted on or with vulnerable groups such as orphaned children, pregnant women, children, prisoners and mentally ill people only if the research questions cannot be answered when non-vulnerable groups are used.

5.2.1.15 If the research project involves more than one institution and samples are to be shipped from one institution to another, a signed Material Transfer Agreement between the sample or data provider and the recipient must be submitted to the IRB.

## 5.3 Protocol amendments

5.3.1 Any intended modifications / changes or revisions from the approved protocol and/consent forms should be submitted to the IRB as protocol amendments for review before they can be implemented.

5.3.2 Investigators should submit the amended proposal with track changes and a covering letter on point by point which briefly explains and justifies the changes

5.3.3 Protocol amendment should be reviewed by the full IRB, unless it is urgent and it qualifies to undergo expedited review as per the IRB conditions and requirements specified in the relevant SOP

5.3.4 The IRB should assess if the intended protocol amendments are scientifically and ethically justifiable and if they do not compromise the safety and welfare of the participants and communities

5.3.5 Change of investigators, that is addition or removal of some PI, co-PI or other researchers originally included in the protocol is an amendment that must be reviewed and approved by the IRB. In case of addition of a new PI/co-PI or other researchers, their full CV or Bio-sketch respectively, should also be submitted

5.3.6 Implications of any proposed amendment on the timeframe and budget of the research project should also be scrutinized

## 5.4 Expedited review

5.4.1 Expedited review is when the process of review is speeded up so that an application does not wait for the normal scheduled full committee meetings

5.4.2 Expedited review should be requested and justified by the investigator through a written application to the IRB

5.4.3 For an application to qualify for expedited review, the proposed research should have minimal potential risks.

5.4.4 Minimal potential risks refers to risks which are not likely to cause serious or long lasting physical, psychological or socioeconomic harm.

5.4.5 Special attention should be given to research projects involving vulnerable populations (the issue of vulnerability to be emphasized under initial review procedures)

5.4.6 Research projects involving invasive procedures should not qualify for expedited review.

5.4.7 Research projects investigating sensitive social issues should not qualify for expedited review (Homosexuality, Commercial Sex Workers, drug abuse, child abuse, gender violence, Female Genital Mutilation, etc)

5.4.8 Research projects investigating issues that may potentially have serious negative impact at community, ethnic group or population level should not qualify for expedited review

5.4.9 Amendments from research projects with minimal potential risk to participants and community may qualify for expedited review

5.4.10 Upon receiving an application for expedited review, the IRB Administrator in consultation with the Chairperson/Vice makes the initial assessment to determine if it qualifies for expedited review

5.4.11 If it qualifies for expedited review, IRB member(s) whose area of expertise and experience is in the same field as the proposed research project and are available should be assigned to review the proposal. If the review involves a project amendment, the selected members to review the project should preferably be members who reviewed the previous version of the protocol.

5.4.12 A summary of the protocols reviewed through the expedited process should be submitted to members of the full IRB, before a full board meeting.

5.4.13 A decision arising from an expedited review will be provisional pending confirmation from the full board meeting. Such decision should be communicated to the investigator in writing. In case of a provisional approval, the investigator may proceed with the study.

5.4.14 Expedited review shall not take longer than 2 weeks to review.

5.4.15 The expedited review comments and approval or disapproval of the application should be tabled as part of the agenda for the next full IRB meeting.

5.4.16 In the event that a protocol did not attain approval from an expedited review, the protocol should be submitted for a full IRB review.

5.4.17 The full IRB meeting has the power to confirm, modify or reverse a decision emanating from the expedited review. If the decision of the full IRB committee is contrary to the decision emanating from the expedited review, detailed reasons and explanations should be recorded in minutes.

5.4.18 The applicant has to be informed about any modifications that the full IRB committee may have recommended and the ethical justification for such a decision

### 5.5 Continuing review

5.5.1 This review is for approved research projects that are due for renewal of ethical approval

5.5.2 After initial ethical approval, projects are to be reviewed annually or as required by the IRB.

5.5.3 Continuing review is based on progress reports submitted by the PI of the projects

5.5.4 Continuing review is meant to provide a mechanism of passive monitoring of the research projects so as to pick up any ethical issues that may need to be addressed to protect the welfare of participants and the integrity of the data generated

## 6.0 REVIEW THE PROTOCOL

### 6.1 Initial Review Application Form

- Check the form for completeness of the information and signatures of the principal investigator, and the Secretariat.
- Check and attach the Initial Review Application Form to the Research Protocol.

### 6.2 Reviewer's Checklist (see ANNEX 2)

- Use the reviewer's checklist to guide the review and deliberation process.

  **Note:** The completed reviewer's checklist is the official record of the decision reached by the IRB for the specific protocol.

- Consider the following criteria when performing the review:
  - minimize risks to participants;
  - risks must be reasonable in relation to anticipated benefits;
  - participants are selected equitably;
  - informed consent is adequate, easy to understand and properly documented;
  - The research plan makes adequate provision for monitoring the data collected to ensure the safety of participants, where appropriate;
  - There are adequate provisions to protect the privacy of participants and to maintain the confidentiality of data, where appropriate; and
  - Appropriate safeguards are included to protect vulnerable participants.

- Make comments where appropriate.
- Sign and date the reviewer's name.

## 7.0 IRB meeting

i. The four reviewers present brief oral summary of their comments.

ii. The Chairperson or designee entertains discussion on each

document under consideration (e.g., protocol, informed consent, investigator's and site qualifications, advertisements).

iii. 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 will be communicated to the investigator.

iv. The Chairperson or designee calls for a separate vote on each element in review.

The Board votes to either:

- Approve the study to start as presented with no modifications
- Approve the study to start with Board approved modifications to the consent. (Approved with recommendation)
- Require modifications to items noted at the convened meeting and follow-up by the Chairperson, after receipt of the requested modifications. (Approved with recommendation)
- Require modifications to the items and full Board review of the materials. (Approved with stipulation or Resubmission)
- Request further information regarding the item and full Board re-review of the material.(Approved with stipulation or Resubmission for re-review)
- Not approve the study, stating the reason for disapproval (Disapproved)

v. If the study is approved, the Board determines the frequency of Continuing Review from each investigator.

- The Secretariat sends 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 Board for frequency of continuing review, and a review of other obligations and expectations from the investigator throughout the course of the study.
- A computer generated approval and expiration date is placed on every page of each consent form approved by the IRB institute

vi. If the Board votes not to approve the study, the Secretariat immediately notifies the investigator in writing about the decision and the reason for not approving the study.

  - If the investigator wishes to appeal to the decision, he/she may do so by contacting the IRB Secretariat. The appeal process is stated in the action letter to the investigator.

vii. If the Board requires modifications to any of the documents, the Secretariat either generates the revisions to the documents, or sends 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.

## 8.0 PRELIMINARY COMMUNICATION OF THE DECISION

### 8.1 Written Communication of the Decision

- The Chairperson sends an electronic version of the completed Reviewer's checklist to the Secretariat of the institution within one working day whenever possible, but no later than 5 working days after the review has taken place.
- The Secretariat, in turn forwards the Board decision to the principal investigator (e.g., via e- mail) and files "sent" or "received" e-mail messages in the protocol file.

8.2 Decisions regarding submitted protocols should be officially communicated, in writing, to the applicant within10 working days of the meeting that made the decisions.

8.3 Communication of the IRB decision shall include but not limited to the following:

i. The name, title and address of the applicant
ii. The exact title of the proposal reviewed
iii. The name of the site(s) or study area
iv. The names and identification numbers (versions numbers/dates) of the reviewed documents
v. A clear statement of the decision reached by the ERC
vi. The name of ERC taking the decision: a letter head of the IRB suffices
vii. The date of the decision and signature of the Administrator or Chairperson/Vice Chairperson
viii. In case of a conditional decision, any requirements by IRB, including suggestion for revisions should be clearly explained in writing to the applicant
ix. In case of a positive decision, a statement of responsibilities of the applicant and any requirements as stipulated in the decision by the IRB
x. The validity period of the approval
xi. The final approval certificate/letter shall be countersigned by the administrator and chairperson/Vice chairperson

## 9.0 FINAL COMMUNICATION OF THE DECISION

### 9.1 Signature of Approval

- Obtain and complete the appropriate forms, after a decision has been reached by the IRB.
- Get signature from the Chairperson.
- Date the form.

**9.2 The Reviewer's Checklist**

- Complete the reviewer's Checklist
- Get signature of the Chairperson.
- Maintain the completed reviewer's Checklist and the minutes of the meeting relevant to the protocol review.
- Process the above tasks within 5 working days after the meeting.

**9.3 The Application Review Form (see Annex 3)**

- Get the Chairperson to sign and date the original version of this form within 5 working days and return this to the Secretariat.

**10.0 THE APPROVAL LETTER**

10.1 Prepare an Approval Letter to inform the investigator or the project manager about the Board's decision (Annex 4) State clearly the actions that need to be taken by the investigator.

10.2 For the decision disapproval, a notifying letter to the investigator or the project manager should state the followings:

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

-Verify the correctness of the wordings and spelling.

-Send the action letter to the applicant within 7 working days.

**11.0 STORAGE OF THE DOCUMENTS**

i. Keep a copy of the Approval Letter in the Correspondence file.

ii. Place the original documents of the Application Review and the Research checklist in sequence of approval number in the

iii. Approved file. Store the file on an appropriate shelf in the designated cabinet.

## 12.0 GLOSSARY

**Initial Review:** The first time review of that protocol made by three or four individual reviewers (IRB members or non-members) in advance of the full Board meeting, and comments of the reviewers will be reported to the full Board meeting.

**Stipulation** Specify as terms of or condition for an agreement, contract, and etc. state, put forward for a necessary condition.

## 13.0 REFERENCES

13.1 World Health Organization, Operational Guidelines for Ethics Committees that Review Biomedical Research, 2000.
13.2 International Conference on Harmonization, Guidance on Good Clinical Practice (ICH GCP) 1996.

## ANNEX 1

## APPLICATION FORM FOR INITIAL REVIEW

Protocol Title:
Protocol Number:
Total Participants to be included:
STUDY TYPE: (Mark " " whichever apply to the study)

| | | | |
|---|---|---|---|
| ☐ Survey | ☐ Observational | ☐ Phase II | ☐ Phase III |
| ☐ Individual based | ☐ Phase 1 | ☐ Prospective | \|Phase IV |
| ☐ Screening | ☐ Retrospective | ☐ Patient | Others..... |
| ☐ Clinical Trial: | ☐ Healthy | ☐ Community based | ☐ Vulnerable groups |
| ☐ Genetic Study | ☐ Medical | ☐ Intervention | |
| ☐ Social | ☐ Epidemiology | ☐ study | |

STUDY POPULATION:
**CHARACTERISTICS OFPARTICIPANTS PARTICIPATED:**

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Age Range: | ☐ | 0 - 17yrs | ☐ | 18=44yrs | ☐ | 45 - 65 yrs | ☐ | > 66 yrs | ☐ |
| Pediatric | ☐ | None | ☐ | < 1yr | ☐ | 1-3 yrs | ☐ | 4 -14 yrs | ☐ |
| Impaired | ☐ | None | ☐ | Physically | ☐ | Cognitively | ☐ | Mentally | ☐ |

**REQUESTED EXCLUSION OF PARTICIPANTS:**
None ☐ Male ☐ Female ☐ Children ☐ Other (specify)

**SPECIAL RESOURCE REQUIREMENTS** (Check all that apply)

| | | | | | |
|---|---|---|---|---|---|
| Intensive Care | ☐ | Organ transplantation, | | Controlled substances | |
| Pediatric Intensive | ☐ | specify..... | | (Narcotics/Psychotropics) | ☐ |
| Gene therapy | ☐ | Gynecological | ☐ | Surgery | ☐ |
| Prosthetics | ☐ | Isolation unit | ☐ | CAT scan | ☐ |
| | | Transfusion | ☐ | others, specify..... | |

**IONIZING RADIATION USE (X-rays, radioisotopes, etc):**
None ☐ Medically indicated only ☐

**INVESTIGATIONAL NEW DRUG (IND) / DEVICE (IDE):**

| | | |
|---|---|---|
| ☐ None | ☐ IND | ☐ IDE |
| | FDA No..... | FDA No..... |
| | Name:..... | Name:..... |
| | Sponsor..... | Sponsor..... |
| | Holder..... | Holder..... |

| | | |
|---|---|---|
| **PROCEDURE USE:** | **FINANCIAL DISCLOSURE:** | ☐ **Non-invasive** |
| **MULTI-SITE COLLABORATION:** | ☐ **Invasive** | ☐ **NO** |
| | ☐ **YES** | ☐ **NO** |
| | ☐ **Yes** | |

**INSTITUTE RESEARCH CONTACT**
Name:.....
Address:..... Telephone:.....
Fax:..... E-mail:.....

## ANNEX 2

**REVIEWER'S FEEDBACK CHECKLIST** (Could be sent electronically)

Protocol Rating:
1. Manuscript's HREC number:
2. Title:
3. Evaluator's name (Use known initials):
Please type Y for "yes", N for "no" and NA for "Not applicable".

| | Evaluation criteria | Rating | | | Reviewer's comments on rating |
|---|---|---|---|---|---|
| | | **Yes** | **No** | **NA** | |
| | **1. Title** | | | | |
| 1.1 | Appropriate to study core elements | | | | |
| 1.2 | Contribution to science (new facts/idea) | | | | |
| 1.3 | The title is meaningful | | | | |
| | **2. Description of the research problem** | | | | |
| 2.1 | Clear problem statement | | | | |
| 2.2 | Clear objectives addressing study aim | | | | |
| 2.3 | Good study rationale | | | | |
| | **3. Research design** | | | | |
| 3.1 | Appropriate research design | | | | |
| | **4. Data collection** | | | | |
| 4.1 | Data collection tool relevant to aim | | | | |
| 4.2 | Data collection method reliable | | | | |
| 4.3 | Appropriate research site/ participants | | | | |
| 4.4 | Appropriate sampling procedures | | | | |
| | **5. Data analysis** | | | | |
| 5.1 | Appropriate data analysis employed | | | | |
| 5.2 | Tools and methods explained | | | | |
| | **6. Scientific writing** | | | | |
| 6.1 | Scientific writing (formal tone, logical thought ess) | | | | |
| 6.2 | Lucid precise language | | | | |
| 6.3 | References correct & comprehensive | | | | |
| | **7. Overall structure of the protocol** | | | | |
| 7.1 | Core elements included | | | | |
| 7.2 | Good organisation of information | | | | |
| | **8. Researcher/ research team** | | | | |
| 8.1 | Time and material resources are adequate | | | | |
| 8.2 | Credentials of the researcher/team attached | | | | |
| | **9. Ethics** | | | | |
| 9.1 | Is there any and adequate informed consent emphasizing voluntary participation and withdrawal of participants | | | | |
| 9.2 | Any statements of post-trial benefits where applicable | | | | |

| | | | | | |
|---|---|---|---|---|---|
| 9.3 | Any provision for the current Standard of Care (SOC) | | | | |
| 9.4 | Any consideration of privacy and confidentiality of participants | | | | |
| 9.5 | Are the plans for data and statistical analysis defined and justified, including the use of stopping rules and endpoints? | | | | |
| 9.6 | Are there adequate provisions for monitoring data (DSMB)? | | | | |
| 9.7 | Is the rationale for the proposed number of subjects and research location reasonable? | | | | |
| 9.8 | Is there a clear differentiation between research procedures and standard care? | | | | |
| 9.9 | Any good justifications for the Inclusion/Exclusion Criteria for the subjects | | | | |
| 10.0 | Any description of the potential risks, discomforts, compensation and benefits/burdens for Subjects | | | | |
| 10.1 | Is there any plan to report all adverse events or side-effects in each clinical trial intervention group? | | | | |
| 10.2 | Is the time and length of the questionnaire moderate? | | | | |
| 10.3 | Any clear indication of source of funding, Is the budget proposed appropriate? | | | | |

**General Comments:**

**Reviewer's Final Comments:**

- ❑ ***Cannot be approved, does not meet ethical approval requirement.***
- ❑ ***Cannot be approved as it is no sufficient information to determine.***
- ❑ ***Can be approved after duly corrected as stated above.***
- ❑ ***Can be approved as it is, all requirements addressed at a detailed level.***

**Date:**

**Name and signature (optional):**

## ANNEX 3

NIMR-IRB

Protocol Number: NIMR-IRB .....

**APPLICATION REVIEW FORM**

Title of Protocol:

Name of Investigator:

Status:

**Statement:**
This is the..... Protocol submitted for review by NIMR-IRB and it is the.....

Protocol approved /disapproved by the IRB in year.....

Signature of Chairman/person of IRB & Date.

# ANNEX 4

## APPROVAL LETTER

The above named proposals have been adequately reviewed; the protocol and safety guidelines satisfy the conditions of NIMR IRB policies regarding experiments that use human subjects.
Therefore the studies under their reviewed states are hereby approved by Institutional Review Board, NIMR.

Name of vice IRB chairman Signature & Date of IRB vice Chairman

Name of IRB Member Signature & Date of IRB Member

**This approval is given with the investigator's Declaration as stated below;**

By signing below I agree/certify that:

1. I have reviewed this protocol submission in its entirety and that I am fully cognizant of, and in agreement with, all submitted statements.
2. I will conduct this research study in strict accordance with all submitted statements except where a change may be necessary to eliminate an apparent immediate hazard to a given research subject.
   - I will notify the IRB promptly of any change in the research procedures necessitated in the interest of the safety of a given research subject.
   - I will request and obtain IRB approval of any proposed modification to the research protocol or informed consent document(s) prior to implementing such modifications.
3. I will ensure that all co-investigators and other personnel assisting in the conduct of this research study have been provided a copy of the entire current version of the research protocol and are fully informed of the current (a) study procedures (including procedure modifications); (b) informed consent requirements and process; (c) potential risks associated with the study participation and the steps to be taken to prevent or minimize these potential risks; (d) adverse event reporting requirements; (e) data and record-keeping; and (f) the current IRB approval status of the research study.
4. I will respond promptly to all requests for information or materials solicited by the IRB or IRB Office.
5. I will submit the research study in a timely manner for IRB renewal approval.
6. I will not enroll any individual into this research study until such time that I obtain his/her written informed consent, or, if applicable, the written informed consent of his /her authorized representative (i.e., unless the IRB has granted a waiver of the requirement to obtain written informed consent).
7. I will employ and oversee an informed consent process that ensures that potential research subjects understand fully the purpose of the research study, the nature of the research procedures they are being asked to undergo, the potential risks of these research procedures, and their rights as a research study volunteer.
8. I will ensure that research subjects are kept fully informed of any new information that may affect their willingness to continue to participate in the research study.
9. I will maintain adequate, current, and accurate records of research data, outcomes, and adverse events to permit an ongoing assessment of the risks/benefit ratio of research study participation.
10. I am cognizant of, and will comply with, current federal regulations and IRB requirements governing human subject research including adverse event reporting requirements.
11. I will make a reasonable effort to ensure that subjects who have suffered an adverse event associated with research participation receive adequate care to correct or alleviate the consequences of the adverse event to the extent possible.
12. I will ensure that the conduct of this research study adheres to Good Clinical Practice guidelines.

_____ _____

Principal Investigator Name Principal Investigator's Signature & Date

NIMR - INSTITUTIONAL REVIEW BOARD
STANDARD OPERATING PROCEDURE

# INDEMNITY FOR RESEARCH

**Purpose:**
This SOP outlines the procedures regarding Clinical Trial Indemnity Cover for all research conducted within the purview of Nigerian Institute of Medical Research-Institutional Review Board(NIMR –IRB).

**Background**

The Medicines for Human Use (Clinical Trials) Regulations 2004 requires that there should be a sponsor for every clinical trial. The Sponsor is responsible for ensuring that the proposed research respects the dignity, rights, safety and well being of participants. According to ICH GCP the Sponsor is responsible for the ethical and legal aspects of the study and must ensure that there are sufficient funds in place to cover all claims that might be made against it arising from the trial.

Based on this, all research to be approved by NIMR –IRB must have a nominated Sponsor, as defined above. The Sponsor will usually be a pharmaceutical company or recognized Clinical trial organization (CRO), although it might be university, charity collaborative research group or an individual. The Sponsor is responsible for any claim for damages arising out of the conduct of the trial, e.g. based on poor science in the design of the protocol or a failure of any intervention.

The sponsor is responsible for the activities of staff and therefore must know, and has assessed, the risks associated with any research project. During the processing of the ethics approval, the Board must ensure that proper indemnity is in place before giving authorization. Any research that is carried out within this scope must demonstrate that it has the appropriate indemnity arrangements approved by the Research Department in place before any research activity commence.

The Principal Investigator (PI) is responsible for ensuring the necessary arrangements are in place and the appropriate signatures are signed by the appropriate individuals before any subject is exposed to a possible risk associated with the research.

**Definition**

The purpose of an indemnity arrangement is to provide legal protection in the event of an unforeseen adverse circumstance arising during the course of a research project. Indemnity is a form of contract to compensate an individual for loss or

damage. To cover the costs that may be incurred as a result of providing indemnification the party providing the form of indemnity should have adequate arrangements in place

## Procedure

1. The PI identifies who will indemnify the research using the Guidance on Indemnity requirements attached in Appendix 1. Assistance is available from the designated secretariat of NIMR- Institutional Review Board.
2. If the research is a clinical trial defined as an investigation or series of investigations -- conducted on any person for a medicinal purpose i.e. involves - treating or preventing a disease or diagnosing a disease - ascertaining the existence, degree or extent of a physiological condition - assisting with or altering in any way the process of conception - investigation or participating in methods of conception - inducing anesthesia - otherwise preventing or interfering with the normal operation of physiological function
   - The PI contacts the Insurance Officer with details of their proposal
   - The Insurance officer contacts the insurers who confirm acceptance of the clinical trial.
   - The PI completes the relevant form and sends it to the Insurance Officer
   - The Insurance Officer issues the relevant certificates to the PI
   - The PI sends a copy of the Clinical Trials certificate to the IRB and files a copy in the Investigator site file.

3. If the research is designed, led and sponsored by a commercial pharmaceutical or medical device company.
   - The commercial company provides an indemnity document in the standard Association of British Pharmaceutical Industry (ABPI) format. This may be an appendix to the contract/clinical trial agreement (CTA).
   - For commercial IMP (Investigational Medicinal Product)/device studies, the Sponsor will take out appropriate insurance cover in respect of its potential liability. The Sponsor must provide a copy of the relevant clinical trials insurance certificate to the IRB as evidence of cover. Such cover should be for a minimum of =N=25 million in respect of any one occurrence or series of occurrences arising from one event. Where this level of cover cannot be provided by a company, the investigator must provide the IRB with a risk analysis of the study for review and approval.
   - Where standard ABPI indemnity cannot be provided, the IRB reviews the protocol specific risks (and where appropriate, liaises with the

NHREC and NAFDAC) to assess the exposure of the Board and the investigators to litigation.

- In cases of contractual or indemnification complexity the opinion of the Board's lawyers is sought.
- The Sponsoring Company signs copies of the indemnity form and sends to the IRB
- The IRB sends a copy of the signed indemnity form to the PI, who files it in the Site Investigator File.
- If the proposal is for an intervention study:

  For clinical trials Insurance certificate covering damages on participants and errors in the protocol implementation should be submitted.

  A letter showing commitment to make the products readily available to the study community should be submitted to the IRB

3.2 During the trial the PI informs each participant in writing in the Patient Information Sheet as to what compensation will be available in the event of an injury before they consent to participate in the trial. In the event of research with no special indemnity arrangements in place for non-negligent harm the participant must be aware of this before entering the trial.

3.3 In the event of an injury or claim of injury

- The PI informs the patient that compensation can be sought and he provides written details on how to claim this by providing the participants leaflet "How to make a Complaint" available from the Patient Information Manager.
- At the earliest opportunity, the PI informs the Sponsor, employer and any other relevant party especially the IRB.

## Appendix 1: Guidance on Indemnity Requirements

Table 1: Type of Indemnity NHIS indemnity

| | |
|---|---|
| 1 | The research is carried out by a professional employed by the NHIS body. The study may be designed by a local investigator or a third party e.g. commercial company or an investigator based at the university or other NHIS body. The indemnity covers those working on the study under their direct supervision. |
| 2 | The PI/sponsor owes a duty of care to the person harmed during a clinical trial. This may be a patient, a healthy volunteer or staff. |
| 3 | Proof of indemnity is required by the Research Ethics Committee for negligent harm. |
| 4 | Proof of indemnity is required by Research Ethics Committee for no-fault harm |
| 5 | University insurance: The research is carried out by a professional employed by the University. The study may be designed by a local investigator or a third party e.g. commercial company or an investigator based at the university or other NHIS body. |
| 6 | Non NHIS work carried out on behalf of the University. This may include experimentation, research, trials and consultancy involving human subjects or volunteers not recruited by virtue of their status as NHIS patients. |
| 7 | Proof of indemnity is required by the Research Ethics Committee for negligent harm. |
| 8 | Proof of indemnity is required by the Research Ethics Committee for non-negligent harm. |
| 9 | Commercial insurance and indemnity: A commercial sponsor contract outs the research which is to be carried out by a professional employed by an NHIS body or University. The protocol is designed by the commercial sponsor and not the investigator. |
| 11 | Product trials and loans of equipment or goods Indemnity: The research will use equipment supplied by a third party i.e. commercial company |
| 12 | Indemnity is required to cover use of the equipment and is not related to clinical negligence of the PI or research team. |
| 14 | Professional Indemnity: Indemnity cover is required for private practice or other work undertaken outside the NHIS contract. |

NIMR - INSTITUTIONAL REVIEW BOARD

STANDARD OPERATING PROCEDURE

# ADVERSE EVENT REPORTING PROCEDURES

## 1.0 PURPOSE:

To identify and standardise the process for reporting Adverse Events (AEs), Serious Adverse Events (SAEs), Serious Adverse Reactions (SARs) and Suspected Unexpected Serious Adverse Reactions (SUSARs).

## 2.0. SCOPE

This SOP describes the methods to be used for the receipt, investigation, and reporting of adverse events that occur during clinical studies.

## 3.0. RESPONSIBILITY

**3.1**. The PI is responsible for accurate and timely reporting of Adverse Event (AE) in the Case Report Form (CRF), to the IRB, and the Sponsor.

**3.2**. The PI and/or study coordinators are responsible for recording all new clinical experiences, exacerbation, and/or deterioration of any existing clinical condition occurring after a study participant has entered the study on the appropriate form in the CRF. They will also provide follow-up information on all AE, until resolution or an appropriate end point is reached.

**3.3**. The PI is also responsible for reporting all serious or unexpected adverse events immediately (within 24 hours after learning of the event) to the Sponsor. The PI will also report all serious and unexpected adverse events to the IRB in a timely manner, which in no case shall exceed ten (10) working days after learning of the event.

**3.4**. The Sponsor is responsible for a complete and accurate investigation, reporting, and timely filing of AE reports to the regulatory body concerned.

**3.5**. The Sponsor is responsible for advising the PI that all Serious Adverse Events (SAE) and Investigational New Drug (IND) safety reports must be reported immediately.

**3.6**. It is the Sponsor's responsibility to follow the progression of all SAE until resolution or appropriate end points are reached and determine whether a SAE is unexpected and associated with the drug/device.

**3.7.** The PI and/or study coordinator are responsible for reviewing with the participant all AE information during study visits. The PI and/or study coordinator is also responsible for the following:

i. Document the AE in the CRF and the source documents.

ii. The study coordinator must notify the PI immediately when any AE is reported. The PI evaluates the medical condition, reports the information in the source documents and CRF, and manages it appropriately.

iii. After review and approval, the PI and/or study coordinator must report the AE to the Sponsor immediately for accurate and timely recording and reporting. The event is also recorded on the CRF, managed medically as appropriate, and the event is followed until resolution. A (SAE) Form and a description of the (SAE) and treatment if any must be filled and submitted to the IRB within ten (10) working days after learning of the event.

iv. The PI is encouraged to consult with the Sponsor and report any unusual and unexpected reactions to both the Sponsor and the IRB "Because no definition of alarming reaction is provided, investigators are left to their discretion (Good Clinical Practice)."

v. The PI is responsible for communicating reports of any SAE to the IRB and any appropriate regulating body.

**4.0. DEFINITIONS**

4.1 In order to ensure proper understanding of this SOP, the following definitions are provided:

4.1.1. Adverse Event- A medical event occurring during a clinical study that can represent a new symptom experienced by a study subject or an exacerbation or worsening of an existing condition.

4.1.2. Serious Adverse Event- Any adverse drug experience occurring at any dose that results in any of the following outcomes:

i. Death.
ii. A life threatening event.
iii. Requires or prolongs inpatient hospitalization.
iv. Persistent or significant disability/incapacity.
v. A congenital anomaly or birth defect.

Important medical events that may not result in death, be life-threatening or require hospitalization may be considered a serious adverse drug experience when, based upon appropriate medical judgment, they may jeopardize the subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition.

4.1.3 Unexpected Adverse Event

i. Studies Conducted Under an Investigational New Drug (IND)- Any AE; the specificity or severity of which is not consistent with the current Investigator Brochure or product labeling.

ii. Studies Conducted Under The New Drug Approval (NDA)- Any AE not listed in the current labeling or is different from current labeling because of greater severity or specificity. This includes an event that may be symptomatically and pathophysiologically related to an event listed, but differs from the event because of greater severity or specificity. An AE that results in death is unexpected unless the labeling indicates a possible fatal outcome.

4.1.4. Associated with The Use of the Drug- A reasonable possibility exists that the event may have been caused by the drug.

4.1.5 Increased Frequency- An increase in the rate of occurrence of a particular (AE), e.g., an increased number of reports of a particular AE after adjustment for drug/device exposure.

4.1.6 Unanticipated Adverse Device Effect- Any (SAE) on health or safety or any life-threatening problem or death caused by or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

4.1.7 Disability- A substantial disruption of a person(s) ability to conduct normal life functions.

4.1.8 Life-Threatening Adverse Drug Experience- Any adverse drug experience that places the patient or subject at immediate risk of death from the reaction as it occurred, i.e., it does not include a reaction that, had it occurred in a more severe form, might have caused death.

## 5.0. REPORTING PROCEDURES

5.1. Any clinical study event that is judged to be an (AE) should be recorded on the (CRF) and on the (AE) form during the course of the study. The PI and/or study coordinator ensures this information is captured during every study subject visit. This form and the information remain a part of the (CRF) and are filed appropriately. All supportive information is filed in the source document.

5.2. Whenever a study subject has reported ANY AE, the study coordinator discusses the event IMMEDIATELY with the PI (if possible while the study subject is there) who must evaluate the event.

5.3. If the AE is not serious, the information is recorded on the CRF, managed medically as appropriate, and the event is followed until resolution.

5.4. If the AE is "serious", all SAE are reported to the PI who reports them to the Sponsor immediately for accurate and timely recording and reporting. The SAE is also recorded on the CRF, managed medically as appropriate, and the event is followed until resolution.

5.5. If the event is an "unanticipated" adverse device effect, the PI is required to report to the Sponsor, IRB, as soon as possible but not later than ten (10) working days after the PI first learns of the event.

5.6. In addition, the PI reviews all completed AE forms for determination of SAE that require reports to the Sponsor.

5.7. The PI informs the Sponsor immediately of knowledge of a SAE. All information available on the event (hospital records, lab tests, discharge summaries, etc.) is forwarded to the Sponsor so they can determine whether the SAE is unexpected or associated and the reporting outcome of the SAE. As additional information becomes available on the SAE, it should be forwarded to the Sponsor.

5.8. All SAE reports shall be sent to the IRB within ten (10) days of learning of event occurrence.

## 6.0. RECEIPT AND RECORD OF ANY POSSIBLE ADVERSE EVENTS FROM SPONSOR (IN CASES IND SAFETY REPORTS)

6.1. All IND safety reports (AE) received from the Sponsor by the IRB will be forwarded to the PI. The PI will send copies to all staff involved in the study as well as the research pharmacist if investigational drugs are involved in the study.

6.2. The PI and/or study coordinator will file copies of these SAE and AE in the regulatory binder for that study, also known as the study file notebook.

6.3. Records of all adverse drug/device events and source documents should be kept for the same period as other study documents.

## LIST OF ABBREVIATIONS

1. (CRF) Case Report Form
2. (AE) Adverse Event
3. (SAE) Serious Adverse Event
4. (IND) Investigational New Drug
5. (NDA) New Drug Approval

NIMR - INSTITUTIONAL REVIEW BOARD

STANDARD OPERATING PROCEDURE

# CLINICAL TRIAL

**PURPOSE:**
To safeguard the rights safety, and well - being of all trial participants, especially in trials that may include vulnerable subjects.

**SCOPE:**
The sop applies to all clinical trials protocol involving human participants.

**RESPONSIBILITY:**
To safeguard the rights, safety, and well being of the all trial participants, especially trials that may include vulnerable participants. The IRB should obtain the following documents:
Trial protocol (s) / amendment(s), written informed consent form(s) and consent form updates that the investigator proposes for use in the trial, subjects recruitment procedures(e.g. advertisements), written information to be provided to participants, investigator's brochure(IB), available safety information, information about payments and compensation available to participants, the investigators current curriculum vitae and / or other documentation evidencing qualifications and any other documents that the IRB may need to fulfill its responsibilities.

1. The IRB should review a proposed clinical trial within a reasonable time and document its views in writing, clearly identifying the trial, the documents reviewed and the dates for the following:
    > Approval/ favorable opinion;
    > Modifications required prior to its approval/ favorable opinion;
    > Disapproval/ negative opinion; and
    > Termination/ suspension of any prior approval/ favorable opinion.

2. The IRB should consider the qualifications of the investigator for the proposed trial, as documented by current curriculum vitae and/ or by any other relevant documentation the IRB requests.

3. The IRB should conduct continuing review of each ongoing trial at intervals appropriate to the degree of risk to human subjects, but at least once per year.

4. The IRB may request more information than is outlined in informed consent be given to participant when, in the judgment of the IRB the additional information would add meaningfully to the protection of the rights, safety and/or well being of the participant.

5. When a non-therapeutic trial is to be carried out with the consent of the participant legally acceptable representative the IRB should determine that the proposed protocol and/or other document(s) adequately address relevant ethical concerns and meets applicable regulatory requirements for such trials.

6. Where the protocol indicates that prior consent of the trial participant or the participant's legally acceptable representative is not possible the IRB should determine that the proposed protocol and/or other document(s) adequately address relevant ethical concerns and meets applicable regulatory requirements for such trials (i.e. in emergency situations.

7. The IRB should review both the amount and method of payment to participant to ensure that neither present problem of coercion or undue influence on the trial participant. Payment to a participant should be prorated and wholly contingent on completion of the trial by the participant.

8. The IRB should ensure that information regarding payment to participant including the methods, amounts, and schedule of payment to trial participants is set forth in the written informed consent form and any other written information to be provided to participants. The way payment will be prorated should be specified.

## 4. FLOW CHART

| | ACTIVITY | RESPONSIBILITY |
|---|---|---|
| 1. | Documentation and Submission of Protocol | IRB secretariat |
| 2. | Review of clinical trial protocol | Full board Meeting |
| 3. | Communication with IRB | Investigator |
| 4. | Compliance with protocol | IRB Monitoring Team |
| 5. | Records and Reports | Investigator |

## 5. DETAILED INSTRUCTIONS

### 5.1. Documentation and Submission of protocol -

**ACTIVITY 1**

5.1.1 The Investigator(s) should be qualified by education, training, and experience to assume responsibility for the proper conduct of the trials, should meet all the qualifications specified by the applicable regulatory requirements), and should provide evidence of such qualifications through up- to-date curriculum vitae and/ or other relevant documentation requested by the sponsor, the IRB and/ or the regulatory authority (ies).

5.1.2. The investigator should be thoroughly familiar with the appropriate use of the investigational products(s), as described in the protocol, in the current investigators brochure, in the product information and in other information sources provided by the sponsor.

5.1.3. The investigator should be aware of and should comply with, GCP and the applicable regulatory requirements.

5.1.4. The investigator/ institution should permit monitoring and auditing by the sponsor, and inspection by the appropriate regulatory requirements.

5.1.5. The protocol should contain a list of appropriately qualified persons to whom the investigator has delegated significant trial-related duties.

## 5.2. REVIEW OF CLINICAL TRIAL PROTOCOL -ACTIVITY 2

5.2.1. The investigator should be able to demonstrate (e.g., based on retrospective data) a potential for recruiting the required number of suitable participant within the agreed recruitment period.

5.2.2. The investigator should have sufficient time to properly conduct and complete the trial within the agreed trial period.

5.2.3. The investigator should have available an adequate number of qualified staff and adequate facilities for the foreseen duration of the trial to conduct the trial properly and safely.

5.2.4. The investigator should ensure that all persons assisting with the trial are adequately informed about the protocol, the investigational product(s) and their trial-related duties and functions.

5.2.5. A qualified physician (or dentist, when appropriate), who is an investigator or a sub-investigator for the trial, should be responsible for all trial-related medical (or dental) decisions.

5.2.6. During and following a participant's participation in a trial, the investigator/ institution should ensure that adequate medical care is provided to a participant for any adverse events, including clinically significant laboratory values, related to the trial, the investigator/ institution should inform a participant when medical care is needed for interrcurrent illness(es) of which the investigator becomes aware.

5.2.7. It is recommended that the investigator inform the participants' primary physician about the participant participation in the trial if the participant has primary physician and if the participant agrees to the primary physician being informed.

5.2.8. Although a participant is not obliged to give his/ her reason(s) for withdrawing prematurely from a trial, the investigator should make a reasonable effort to ascertain the reason(s), while fully respecting the subject's rights.

**REVIEW ACTIVITY 2**

5.2.9. The investigational product(s) should be stored as specified by the sponsor and in accordance with applicable regulatory requirements in Nigeria.

5.2.10. The investigator should ensure that the investigational product(s) are used only in accordance with the approved protocol.

5.2.11. The investigator, or a person designated by the investigator/institution, should explain the correct use of the investigational product(s) to each participant and should check, at intervals appropriate for the trial, that each participant is following the instructions properly.

**REVIEW ACTIVITY 3**

5.2.12. The investigator should follow the trial's randomization procedures, if any, and should ensure that the code is broken only in accordance with the protocol. If the trial is blinded, the investigator should promptly document and explain to the sponsor any premature unblinding (e.g., accidental unblinding, unblinding due to a serious adverse event) of the investigational product(s).

5.2.13. In obtaining and documenting informed consent, the investigator should comply with the applicable regulatory requirements), and should adhere to GCP and to the ethical principles that have their origin in the Declaration of Helsinki. Prior to the beginning of the trial, the investigator should have the IRB written approval/favorable opinion of the written informed consent form and any other written information to be provided to participant.

5.2.14. The investigator should indicate willingness to inform the participants of any new developments after obtaining the IRB Approval, this new development on the investigational product should be indicated in the informed consent document.

5.2.15. Neither the investigator, nor the trial staff, should coerce or unduly influence a participant to participate or to continue to participate in a trial.

5.2.16. None of the oral and written information concerning the trial, including the written informed consent form, should contain any language that causes the participant legally acceptable representative to waive or to appear to waive any legal rights, or that releases or appears to release the investigator, the institution, the sponsor, or their agents from liability for negligence.

5.2.17. The investigator, or a person designated by the investigator, should fully inform the Participant or, if the participant is unable to provide informed consent, the participant's legally acceptable representative, of all pertinent aspects of the trial including the written information and the approval/ unfavorable opinion by the IRB.

5.2.18 The language used in the oral and written information about the trial, including the written informed consent form, should be as non-technical as practical and should be understandable to the participant or the participant's legally acceptable representative and the impartial witness, where applicable.

5.2.19 Before informed consent may be obtained, the investigator, or a person designated by the investigator, should provide the participant or the participant's legally acceptable representative ample time and opportunity to inquire about details of the trial and to decide whether or not to participate in the trial. All questions about the trial should be answered to the satisfaction of the participant or the participant's legally acceptable representative.

5.2.20 Prior to a participant's participation in the trial, the written informed consent form should be signed and personally dated by the participant or by the participant's legally acceptable representative, and by the person who conducted the informed consent discussion.

5.2.21 If a participant is unable to read or if a legally acceptable representative is unable to read an impartial witness should be present during the entire informed consent discussion After the written informed consent form and any other written information to be provided to subjects is read and explained to the participant or the participant's legally acceptable representative, and after the participant or the participants legally acceptable representative has orally consented to the participant participation in the trial and, if capable of doing so, has signed and personally dated the informed consent form, the witness should sign and personally date the consent form. By signing the consent form, the witness attests that the information in the consent form and any other written information was accurately explained to and apparently understood by, the participant or the participants legally acceptable representative, and that informed consent was freely given by the participant legally acceptable representative.

5.2.22 Both the informed consent discussion and the written informed consent form and any other written information to be provided to participant should include explanations of the following:

a) That the trial involves research.
b) The purpose of the trial.
c) The trial treatment and the probability for random assignment to each treatment.
d) The trial procedures to be followed, including all invasive procedures.
e) The participant's responsibilities.
f) Those aspects of the trial that are experimental.

g) The reasonably foreseeable risks or inconveniences to the participant and, when applicable, to an embryo, fetus, or nursing infant.
h) The reasonably expected benefits. When there is no intended clinical benefit to the participant, the participant should be made aware of this.
i) The alternative procedure(s) or course(s) of treatment that may be available to the participant, and their important potential benefits and risks.
j) The compensation and/or treatment available to the participant in the event of trial related injury.
k) The anticipated prorated payment, if any, to the participant for participating in the trial.
l) The anticipated expenses, if any, to the participant for participating in the trial.
m) That the participant's participation in the trial is voluntary and that the participant may refuse to participate or withdraw from the trial, at any time, without penalty or loss of benefits to which the participant is otherwise entitled.
n) That the monitor(s), the auditor(s), the IRB, and the regulatory authority (ies) will be granted direct access to the participant's original medical records for verification of clinical trial procedures and/or data, without violating the confidentiality of the participant to the extent permitted by the applicable laws and regulations and that, by signing a written informed consent form. the participant or the participant's legally acceptable representative is authorizing such access.
o) That records identifying the participant will be kept confidential and, to the extent permitted by the applicable laws and/or regulations, will not be made publicly available. If the results of the trial are published, the participant identity will remain Confidential.
p) That the participant or the participant's legally acceptable representative will be informed in a timely manner if information becomes available that may be relevant to the participants willingness to continue participation in the trial.
q) The person(s) to contact for further information regarding the trial and the rights of trial participants, and whom to contact in the event of trial-related injury.
r) The foreseeable circumstances and/or reasons under which the participants participation in the trial may be terminated.
s) The expected duration of the participant's participation in the trial.
t) The approximate number of participants involved in the trial.

5.2.23 Prior to participation in the trial, the participant or the participant's legally acceptable representative should receive a copy of the signed and dated written informed consent form and any other written information provided to the participants. During a participants Participation in the trial, the participant or the participants' legally acceptable representative should receive a copy of the signed and dated consent

form updates and a copy of any amendments to the written information provided to participants.

5.2.24 When a clinical trial (therapeutic or non-therapeutic) includes participants who can only be enrolled in the trial with the consent of the participants legally acceptable representative (e.g., minors, or patients with severe dementia), the participant should be informed about the trial to the extent compatible with the participants understanding and, if capable, the participant should sign and personally date the written informed consent.

5.2.25. A non-therapeutic trial (i.e. a trial in which there is no anticipated direct clinical benefit to the participant), should be conducted in subjects who personally give consent and who sign and date the written informed consent form.

5.2.26. Non-therapeutic trials may be conducted in participants with consent of a legally acceptable representative provided the following conditions are fulfilled:

a) The objectives of the trial can not be met by means of a trial in participants who can give informed consent personally.
b) The foreseeable risks to the participants are low.
c) The negative impact on the participant well-being is minimized and low.
d) The trial is not prohibited by law.
e) The approval/favorable opinion of the IRB is expressly sought on the inclusion of such participants, and the written approval/ favorable opinion covers this aspect.

5.2.27. Such trials, unless an exception is justified, should be conducted in patients having a disease or condition for which the investigational product is intended. Participants in these trials should be particularly closely monitored and should be withdrawn if they appear to be unduly distressed.

5.2.28. In emergency situations, when prior consent of the participant is not possible, the consent of the participant's legally acceptable representative, if present, should be requested. When prior consent of the participant is not possible, and the participant legally acceptable representative is not available, enrolment of the participant should require measures described in the protocol and/or elsewhere, with documented approval/favorable opinion by the IRB to protect the rights, safety and well-being of the participant and to ensure compliance with applicable regulatory requirements. The subject or the participant's legally acceptable representative should be informed about the trial as soon as possible and consent to continue and other consent as appropriate should be requested.

5.2.29. The investigator’s brochure which provides adequate summary of all safety, pharmacological, pharmaceutical and toxicological data available on the study product, together with a summary of clinical experience of the study product to date (e.g. recent investigator’s brochure, published data, summary of the product’s characteristics etc), must be submitted

5.2.30 Relevant mechanism(s) of monitoring and auditing the conduct of the research must be clearly spelt out in the protocol

5.2.31 In the case of clinical trials, Data Safety and Monitoring Board (DSMB) should be set up and should provide names and contacts of members, one of whom should be a national of at least one of the host countries (to be discussed by the entire group, local DSMB members) to the IRB.

5.2.32 In the case of clinical trials, there should be documentary evidence of insurance policy to cover trial participants

5.2.33 If the research project involves more than one institution and samples are to be shipped from one institution to another, a signed Material Transfer Agreement between the sample or data provider and the recipient must be submitted to the IRB

## 3.1. COMMUNICATION WITH IRB ACTIVITY SUBJECT TO PARTICIPANTS

3.1.1. Before initiating a trial, the investigator/institution should have written and dated approval/favorable opinion from the IRB for the trial protocol, written informed consent form, consent form updates, subject recruitment procedures (e.g., advertisements), and any other written information to be provided to participant.

3.1.2. As part of the investigator's/institutions written application to the IRB, the Investigator/institution should provide the IRB with a current copy of the investigator Brochure. If the Investigator's Brochure is updated during the trial, the Investigator/institution should supply a copy of the updated Investigator Brochure to the IRB.

3.1.3. During the trial the investigator/institution should provide to the IRB all documents subject to review.

## 4.1. COMPLIANCE WITH PROTOCOL- ACTIVITY 4

4.1.1. The investigator/institution should conduct the trial in compliance with the protocol agreed to by the sponsor and, if required, by the regulatory authority(ies) and which was given approval/favorable opinion by the IRB. The investigator/institution and the sponsor should sign the protocol, or an alternative contract, to confirm agreement.

4.1.2. The investigator should not implement any deviation from, or changes of the protocol without agreement by the sponsor and prior review and documented approval/favorable opinion from the IRB of an amendment, except where necessary to eliminate an immediate hazard(s) to trial subjects, or when the change(s) involves only logistical or administrative aspects of the trial (e.g., change in

monitor(s), change of telephone number(s).

4.1.3. The investigator, or person designated by the investigator, should document and explain any deviation from the approved protocol.

4.1.4. The investigator may implement a deviation from, or a change of, the protocol to eliminate an immediate hazard(s) to trial subjects without prior IRB approval/favorable opinion. As soon as possible, the implemented deviation or change, the reasons for it, and, if appropriate, the proposed protocol amendment(s) should be submitted:

a) To the 1RB/ERC for review and approval/favorable opinion,
b) To the sponsor for agreement and, if required,
c) To the regulatory authority (ies).

## 5.5. RECORDS AND REPORTS- ACTIVITY 5.

5.5.1 Essential documents should be retained until at least 2 years after the last approval of a marketing application in an ICH region and until there are no pending or contemplated marketing applications in an ICH region or at least 5 years have elapsed since the formal discontinuation of clinical development of the investigational product. These documents should be retained for a longer period however if required by the applicable regulatory requirements or by an agreement with the sponsor. It is the responsibility of the sponsor to inform the investigator/institution as to when these documents no longer need to be retained.

5.5.2. The financial aspects of the trial should be documented in an agreement between the sponsor and the investigator/institution.

5.5.3. Upon request of the monitor, auditor, IRB or regulatory authority, the investigator/institution should make available for direct access all requested trial related records.

# REVIEW OF MEDICAL DEVICE STUDY

**1. PURPOSE:**
The purpose of this procedure is to provide instructions for review and approval of medical device studies submitted to the NIMR-IRB.

**2. SCOPE:**
This SOP applies to the submission and the review processes of protocols involving the study of new medical devices in human subjects.

**3. RESPONSIBILITY:**
The IRB must determine if the proposed investigation has Significant Risk (SR) or Non-Significant Risk (NSR), and the IRB should decide if the investigation is approved or not. In determining SR or NSR, the IRB must review all information submitted by the sponsor.

The IRB should consider the nature of the harm that may result from the use of the device. If device being investigated might cause significant harm to anyone of the participants, the study will be considered SR. In deciding if a device presents significant or non-significant risks, the IRB should consider the devices 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 should consider the risks of the procedure in conjunction with the risks of the device. The IRB may also consult with the regulatory agency such as NAFDAC 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 must 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 Board meeting | IRB Secretariat/members/Reviewers |
| 3. | Activities during a Board 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

-Receive a new medical device study.
-Check the submitted package for completeness.
-Document the checking procedure
-At a minimum, the IRB must receive the following documents prior to review/approval of a medical device study:

- Proposed investigational plan
- Informed consent form
- Description of the device
- Description of participant selection criteria
- Monitoring procedures
- Reports of prior investigations conducted with the device
- Investigator's Curriculum Vitae
- Investigator's professional license(s)
- Risk assessment data/information
- Statistics used in making the risk determination.
- Application for review
- Documents Received Form
- Copies of all labeling for investigational use only

– The sponsor should inform the IRB whether other IRBs have reviewed the proposed study and what determination was made.

– The sponsor should inform the Agency's assessment of the devices risk if such an assessment has been made.

– If the sponsor believes the study is NSR, supporting information must be submitted.

– Contact the applicant to submit additional information or documents, if the application is incomplete.

### 5.2 Before the Board meeting

❖ Assign reviewers to review the study, according to the reviewer's checklist(see SOP)
❖ Prepare the documents for distribution to each member.
❖ Send the documents to each IRB member.
❖ Place the new medical device study on the meeting agenda.

### 5.3 During the Board meeting

- ❖ Reviewers present a brief oral or written summary of the study design.
- ❖ The Chairperson opens discussion about whether the study is SR or NSR
- ❖ The Chairperson leads discussion about each document under consideration (e.g. protocol, informed consent, investigation and site qualifications, advertisements).
- ❖ Decide the degree of risk.
- ❖ The Chairperson calls for a separate vote on each element in review. The IRB votes to either;
  - Approve the study to start as presented with no modifications
  - Approve the study to start with minor modifications of item(s) noted at the convened meeting and to be followed up by the Secretariat and Chairperson after receiving the requested modifications.
  - Require major modifications and /or request further information to be resubmitted and be subjected to review in the next full Board meeting
  - Disapprove the study and state the reason.
  - Note the recommendation for changes to the protocol and/or informed consent recommended by IRB member. And communicate such to the investigator.

Determine the frequency of continuing Review for the approved study.

### 5.4 After the meeting

#### 5.4.1 Prepare meeting minutes

#### 5.4.2 Notify the investigators

- The Secretariat sends 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.
- If the Board votes not to approve the study, the Chairperson or Secretariat immediately notifies 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 NIMR-IRB. This process is stated in the action letter provided to the investigator.
- If the IRB votes to require modification to any of the documents, the secretariat either generates the revisions to the documents, or sends 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 NIMR IRB.

#### 5.4.3 Storage of the documents

- Prepare an appropriate label.
- 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, clutches, electrodes, prescribed beds, pacemakers, arterial grafts, intra-ocular lenses, and orthopedic 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 (IDF):** 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 (AMA) application or a pre-market Notification submission to the regulatory agency. 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 evaluation of investigations of investigational devices, unless exempt, must have an approved IDE before the study is initiated.
An IDE is approved by an institutional review board (IRB).If the study involves a significant risk device, the IDE must also be approved by the regulatory agency, such as NAFDAC. 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 list 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 NIMR IRB for approval for the first time. This includes re-application for those studies denied approval by NIMR IRB. The probability of harm or discomfort to study participants. Acceptable risk differs depending on the conditions for Significant Risk Device (SR) which the product is being tested. A product for sore throat, for example, will be expected to have a low incidence of side effects. However, unpleasant side effects may be acceptable risk when testing a promising treatment for a life –threating illness. Significant An investigational device that : Risk (SR) (1) is intended as an implant and presents a potential for serious risk to the health, safety, or

welfare of the participants ,(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 participants. A list of examples is found in annex 2.

**7. References** 8.1 code of Federal Regulation (CFR) 21, Volume 8, part 812, April 2003,food and drug administration, U.S. Government printing office via GPO Access

**ANNEX 1**

**NON-SIGNIFICANT RISK DEVICES STUDIES EXAMPLES:**

- Bio-stimulation lasers for treatment of pain
- Caries Removal Solution
- Daily Wear Contact Lenses and Associated Cleaners and Solution
- 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) Device 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**

**SIGNIFICANT RISK DEVICE STUDIES**

**General Medical Use**

**Catheters:**

- Cardiology-diagnostic, treatment, transluminal cornaryangioplasty, intra-aortic balloon with control system
- Gastroenterology and Urology-biliary and urologic
- General Hospital-long-term percutaneous, implanted, subcutaneous and intravascular
- Neurology-cerebro vascular, 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 Value
- 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
- Extracorporeal Photophersis System
- Extracorporeal Shock-Wave Lithotriptor
- Kidney Perfusion System
- Mechanical/Hydraulic Impotence and Incontinence Device
- Implantable Pencil 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 Device

**Neurology**

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

**Obstetrics and Gynecology**

- Cervical Dilator
- Chorionic Villus Sampling Catheter, phase 11(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 Value Implant
- Retinal Reattachment System : sulfur hexafluoride, silicon 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


NIMR - INSTITUTIONAL REVIEW BOARD

STANDARD OPERATING PROCEDURE


# PROTOCOL FOR MONITORING VISITS

## 1. PURPOSE

Purpose of this document is to provide guideline for the monitoring of approved protocols by NIMR –IRB.

## 2. SCOPE

This SOP applies to protocol review and site monitoring.
It also applies to supervisory monitoring visit by member(s) of project monitoring of NIMR-IRB to approved project study site(s).

## 3. RESPONSIBILITIES EXPECTED OF THE MONITORING TEAM

a. The monitoring team must ensure that the P.I and the team have clearly stated objectives and indicators to measure adherence to submitted protocol

b. They must ensure that the team fulfilled all the stated P.I. responsibilities as contained in approval letter for the project being monitored.

c. The IRB monitoring team must be independent and spuriously objective in their opinions.

d. Conflict of interest among the monitoring team members must be clearly declared, if there is any.

e. All protocol violations must be reported without prejudice.

f. The monitoring team must ensure adequate provision for safety and confidentiality of data monitored during the study visit.

## 4. Flow chart

| No. | Activity | Responsibility |
|---|---|---|
| 1. | List of approved protocols by NIMR-IRB | IRB Secretariat (at NIMR-IRB general meeting). |
| 2. | Selection of study site to visit | NIMR-IRB (at general meeting) |
| 3. | Selection of the monitoring | NIMR - IRB (at general meeting) |
| 4. | Report of monitoring Visit | IRB Monitoring team |
| 5. | Notification of the P.I on the result of the visitation | IRB Secretariat |

Adverse Events should be recorded by the investigators and reported to the IRB as and when progress reports are due.

**Progress reports:** PIs should submit progress reports at intervals stipulated by the IRB as a condition for renewal of approval. Such progress reports enable the IRB to assess if the research project is progressing as per the approved protocol and if there are no issues that may need to be addressed

**Material Transfer Agreement** which states quantities, types and specific purpose of any samples to be moved from the institution where they are collected to another recipient institution within the same country or in another country should be signed by the provider and the recipient.

**Reports from other relevant stakeholders** such as Regulatory Authorities and Data Safety and Monitoring Boards (DSMB) that may be shared with the IRB help to assess the way approved research projects are conducted.

Information in the public domain such as publications in journals or reports in newspapers could draw attention to some research activities that were not ethical in one way or another. For instance, a publication may reveal that researchers used samples for other purposes that were not covered by the ethical approval granted in the first place. In this regards, Investigators should be obliged to submit copies of publications emanating from the approved protocol to the IRB.

Final reports which are supposed to be submitted when a research project has been completed help the IRB to determine if the whole project was conducted as per the approved protocol.

**Active monitoring:** The IRB members should physically visit the research projects in the field in order to assess if the projects are being conducted as per the approved protocols.

i. The ideal is that each and every approved study should be actively monitored to ensure adherence of health research ethics
ii. In the event that there is a study being implemented without ethical approval, urgent site visit should be carried out and appropriate action taken.
iii. IRB members should use the NIMR-IRB Oversight tool in order to ensure that appropriate issues are assessed during the visit.
iv. The number of IRB members to undertake the oversight visit should depend on the workload of the inspection activities that will be done. In order to maximize objectivity in the oversight exercise, at least 2 members of the IRB with relevant diverse expertise and another IRB member should make up the oversight team.
v. An oversight team may preferably include a community representative from the IRB where possible

**Types of Oversight visits**

i. IRB –initiated announced oversight visits: the IRB informs the PI of the project to be visited in advance of the date of the visit
ii. IRB -initiated unannounced oversight visits: the IRB does not inform the PI of the project in advance of the date of the visit

**Reasons for additional oversight visits**

i. IRB oversight visits in response to reports made directly to the IRB or circulating in the community
ii. Increased frequency of serious adverse events reports
iii. Failure to submit progress reports or final report
iv. Reports of suspected research misconduct
v. Researchers who extend their research beyond the approved time frame without formal notification and approval by the IRB
vi. Researchers that are suspected to have changed their objectives and design of the study without prior approval
vii. Any other reason that the committee feels warrants further follow up.

## 5. DETAILED INSTRUCTIONS

### 5.1. List of approved protocols

5.1.1. The secretary of the IRB compiles the list of approved protocol every quarter and submits them for ratification by the board.

5.1.2. This list must be compiled on the basis of the leaning of the approved protocols.

5 1 3. The secretary must inform the IRB appropriately on the status (commencement or non commencement) of the listed or approved protocol. In order words the secretary must have indicated the status of the approved protocol before the board starts discussing the monitoring.

5.1.4. Material Transfer Agreement (MTA) if applicable

### 5.2. Selection of study site to visit

5.2.1 The members of the Board at the general meeting will select study site to visit based on information from the secretariat. A minimum of three study sites shall be monitored per annum.

### 5.3. Selection of monitoring team

Members of the IRB will be asked to declare conflict of interest on any of the site chosen. Selection of such team must be gender sensitive, and professional inclination balanced. A minimum of two members shall be required to go on a monitoring visit per site. At least a lay person must be represented on the monitoring visit. The selection shall be guided as follows:

The team shall be comprised of the following:

1. A specialist on the discipline to be monitored
2. A lay person
3. The secretary or the assistant secretary of the board
4. Any other two members.
5. This will make up five membership of the monitoring team.

**CONTENT OF MONITORING**

| | |
|---|---|
| Protocol: | |
| Study ID №: | |
| Sponsor: | |
| Test Product: | |
| Monitor: | |
| Principal Investigator: | |
| Institution: | Centre №: |
| Visit Date | Previous Visit |
| Study staff present at the meeting: | |

N/B:- Please indicate where any information is not applicable as 'NA'.

**SECTION A**

## 1. GENERAL DISCUSSION

Has the following been discussed with Investigator and his/her staff?

1. Up-to-date information on the test product
2. In case of a multi centre clinical trial, global progress of the trial, numbers of participants, safety profile
3. Changes to the risk/benefit ratio as communicated by /Sponsor
4. Notification to IRB of changes to the risk/benefit ratio
5. Protocol amendment and/or modification, if any:
   > All amendments were discussed and approved by and Sponsor and documented before submission/notification to the IRB
   > Protocol modification if any, notified to IRB
   > Protocol modification if any notified to local authorities
6. Discuss with the investigator/laboratory responsible person of any changes in the Laboratory Normal Ranges
7. Copy of the revised normal range(s), including date of implementation, obtained (forwarded to Data Management)
8. Is there any relevant changes in Study staff since the last visit?

   A. Is the Study Staff and Authorized Staff for Study Document Completion Form updated?

   B. Curriculum Vitae retrieved if appropriate

   C. Notification to the IRB if appropriate
9. Did the investigators encounter any problems since your last visit
10. Review any recruitment issues and discuss possible strategies for improvement, if appropriate

    a. Recruitment rate calculation tool updated?
11. Participant's follow up, premature discontinuation by the investigator, withdrawal and lost to follow up
12. Global safety of the product, AE(s) occurred since your last visit

**Comments and Action:**

**INFORMED CONSENT**

1. Informed consent procedure reviewed, participants informed properly (yes/No)
2. Consent forms verified this visit:
    a. If yes, enrolled participants consents verified: (yes/No)
    b. If yes, screened but not enrolled participants consents verified (yes/No)
3. Consent forms compliance: (yes/No)

**Comments and Actions:**

**CRFs -SAFE FORMS VERIFICATION AGAINST SOURCE DOCUMENTS**

1. Were source documents available and did you have direct access?
2. CRFs check against source documents. If yes specify:
    For participants Number
    From page Number
    To page Number
3. Were CRFs- SAE Forms legible, accurate and complete?
4. Were Trial related logs legible, accurate and complete?
    a. Identification of screened and enrolled participants
    b. Assignment Sheet
    c. Specimen
5. Were Protocol deviations/violations documented on CRFs (Y/N)
6. Were CRF/SAE Forms/trial related documents corrected during the visit (Y/N)
7. Are there any corrections pending. If yes, specify
    a. Correction on CRF and trial related documents (Y/N)
    b. CRF Data Resolution Queries generated by Data Management

**Comments and Actions:**

## 4. PROTOCOL VIOLATIONS

1. Have protocol violations been detected? Yes/ No, specify: Observation
   Participant N /ID Type of violation, when and how, what actions have been/will be taken
2. Has the investigator documented protocol violations?

**Comments and Actions:**

## 5. RANDOMIZATION, REPLACEMENT AND UNBLINDING PROCEDURE

1. Randomization list/envelop check

2. Are the randomization codes securely stored?

3. Have any participants been replaced

   a. Replaced participant CRF/appropriate trial log

   b. Replacing participant CRF/ appropriate trial log

4. Has any randomization code been broken? (Yes/no)

a. Reason for broken code reported on the appropriate documents?

b. In case of accidental unblinding, procedure reviewed

List of replaced/unblinded participants

| Participant No/ID | Replaced/ unblinded Reason |
|---|---|

**Comment and Action**

## 6. ADVERSE EVENT PROCEDURES

1. Has any AE occurred? (Yes/no)

a. If yes, was it correctly reported in the AE section of the CRF and source document? (Yes/no)

2. Has any SAE occurred? (Yes/no)

a. If yes, was it correctly reported in the AE section of the CRF and source document? (Yes/no)

b. Notification of SAE by Principal Investigator to Sponsors (yes/no)

3. Notification of Serious Adverse Reaction by Sponsors and/or Principal Investigator to IRB and regulatory authorities (yes/no)

List of Adverse Events that required attention

Participant N$_o$/ID Description of the Adverse Event (if relevant, include also causality, dates and outcome)

**Comment and Actions**

**SECTION B**

**MANAGEMENT PROCEDURE: NA/A**

1. Are there relevant changes in product storage, handling and transportation condition (if appropriate) Yes/No

2. Has the product been properly dispensed and documented by authorized personnel (Yes/No)

3. Is the expiry date in accordance with product administration calendar for the centre (Yes/No)

4. Product accountability checked today? (Yes/No)

5. Product accountability log up-to-date?

6. Product accountability /Product inventory correct

7. Sufficient doses for the continuation of the trial

   a. Have new product supplies been received by the Centre Damaged doses?

   b. Copy of the acknowledgment retrieved

8. Are product supplies stored in a safe and secure manner? (Yes/No)

9. Product Retrieval, if yes specify

   a. Product Management Form completed and signed by the investigator?

   b. Return of Unused Products Form Completed (or prepared)?

   c. Product Retrieval, today? If no specify

   d. Date of retrieval Time for retrieval between _h and _h By Whom

11. Product to be destroyed on site. If yes specify

   a. Sponsor authorization for Product Destruction

   b. Product Destruction certificate completed & signed by PI

   c. Product Management Form completed and signed by the PI?

**Product Inventory** (date)

Name Presentation Batch Expiration date Comment

**Comments and Actions:**

## SECTION C

## LABORATORY SPECIMEN MANAGEMENT PROCEDURE

1. Are there relevant changes in the process for their collection, identification, handling and timely delivery to the designated laboratory (yes/no)
2. The process for their collection, identification, handling and timely delivery to the designated laboratory facility is working satisfactorily (yes/no)
3. The process for their analysis, timely result delivery and result reporting to the investigator is working satisfactorily (yes/no)
4. Trial log documented properly (yes/no)
5. Samples to be sent?
    a. a. Verification of sample (observation)
    b. Protocol violation: (identification, volume, Haemolyse, no of aliquots.).
       If yes, specify (observation)
       O Participant N /ID
       Type of violation, when and how, what actions have been/will be taken
    c. Stored in a safe and secure manner?
    d. Temperature recording sheet checked and copy filed
    e. Shipment lists complete and up-to-date
    f. Are there any specific regulatory approvals to be obtained?
    g. Shipment procedure revised
    h. Date or period plan for shipment: (observation)

6. Is anything needed for the laboratory? If yes specify :( observation)
    a. Reagents:
    b. Tubes:
    c. Labels:
    d. Shipment Material:
    e. Others:

**Comments and Actions:**

**2. TRIAL MATERIAL/EQUIPMENT MANAGEMENT PROCEDURE**

1. Are there relevant changes in the process for data collection, reporting and handling (Yes/No)

2. The process respects participants' confidentiality (Yes/No)

3. The process respects protocol confidentiality (Yes/No)

4. Documents stored in a safe and secure manner?

5. Are there relevant changes in the site facilities / equipment?

6. Is the trial material properly used?

7. Is anything needed for the continuation of the study? If yes, specify (observation)

a. CRFs needed:

b. Trial Log needed:

c. Other, specify:

8. Unused trial documents Retrieval (blank CRFs, etc.) If yes, specify:

a. Unused trial documents Retrieval Certificate completed/prepared and signed by the Investigator. (YES/NO)

b. Unused trial documents Retrieval, today? If no, specify

c. Date of retrieval , by Whom

9. Trial Material/Equipment Retrieval? If yes, specify

a. Material/Equipment Retrieval Certificate completed/prepared and signed by the investigator

b. Material/Equipment Retrieval, today? If no, specify

c. Date of retrieval , by whom

d. Specific Conditions (e.g. delicate transportation). If yes, specify:

**Comments and Actions:**

**SITE STATUS**

| Planned Enrolment | Screened | Enrolled | Ongoing | Complete | Withdrawn | Discontinued |
|---|---|---|---|---|---|---|
| | | | | | | |

**CRF STATUS**

| Patient Number(s) | CRFs Reviewed this visit | CRFs Collected this visit | Pending in the Centre and Planned for Shipment |
|---|---|---|---|
| | | | |

**GENERAL COMMENTS**

**Attached Forms and Study Documents:**

- Monitoring Follow-up Activities form
- Updated Investigator's file form
- Recruitment Rate Calculation Tool
- Study documents:

**Reported by:**

(IRB/Monitor)

**Signature:**

**Date:** {dd/mm/yy)

## 7.0. CONTENT OF THE REPORT: THE MONITORING REPORT SHALL BE GUIDED WITH THE FOLLOWING INFORMATION

1. Did the investigator state how the participants will be allocated to the intervention (e.g. random allocation", "randomized", or randomly assigned").
2. Is there a justification for the settings and locations where the trial is conducted?
3. Is there any precise details of the interventions intended for each group and how and when they will be administered. Any appropriate informed consent in place
4. Clearly defined format of how the outcome will be handled and, when applicable, any methods that will be used to enhance the quality of measurements (e.g. Multiple observations, training of assessors,).
5. Clearly sample size determination and, when applicable, explanation of any interim analyses and Stopping. Any issue bothering on the human rights of the research participants
6. Method that will be used to generate the random allocation sequence including details of any restriction (e.g. blocking, stratification). (If applicable)
7. Method(s) that will be used to implement the random allocation sequence (e.g. numbered containers or central telephone), clarifying whether the sequence, will be concealed until the assignment of the interventions (applicable)
8. Clarity on who is going to generate the allocation sequence, who will enroll participants, and who will assign the participants to their groups? (If applicable)
9. Clear statements on how the participants, those administering the interventions, and those assessing the outcomes will not be aware of the group assignment. In other words how will the masking be done? (If applicable)
10. Is there any" intention to treat? During the course of the investigation or trial?
11. What type of statistical methods that will be used to compare groups for primary outcomes(s), methods for additional analyses, such as subgroup analyses and adjusted analysis? (If applicable)
12. Plan to report all adverse events or side-effects in each intervention group.
13. Any plan for result dissemination
14. Any issue on post-trial benefit to research participants
15. Any derivation from standard ethical practice.
16. Conclusion: The P. I. Complied with the ethical issues raised.

_____ _____

Name of Monitor Monitoring Team Leader

NIMR - INSTITUTIONAL REVIEW BOARD

STANDARD OPERATING PROCEDURE

# TRAINING AND CONTINUING EDUCATION OF ETHICS MEMBERS AND PERSONNEL

## 1. Purpose

The purpose of this section is to inform the IRB personnel and members why training is necessary and how the members should seek to occasionally attend training or workshop programs to up-date themselves on the progress of technology, information and ethics.

NIMR -IRB recognizes the importance of training and continuing professional development, therefore the Institute will allocate an annual budget for specific training and study visits for IRB personnel and members. New IRB members are required to undergo a training program prior to joining the Board, once appointed by the Director General.

## 2. Scope

The SOP applies to all personnel of the IRB.

## 3. Responsibility

It is the responsibility of the IRB members to have themselves educated and trained periodically.

## 4. Flow chart

| No. | Activity | Responsibility |
|---|---|---|
| 1. | Topics for training | IRB members/Secretariat staff |
| 2. | How to get trained | IRB members / secretariat staff |
| 3. | Keeping the training record | IRB members/secretariat staff |

## 5. Detailed instructions

### 5.1 Topics for training

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

i. Good Clinical Practice (GCP)
ii. Various international and national declaration and ethical guidelines
iii. Ethical Issues
iv. Relevant laws

v. Developments in relevant science, technical and environmental, health and safety aspects
vi. Relevant requirements of health, safety and environmental laws and regulations and related documents
vii. Audit procedures.

An interchange of ideas, information and experiences with overseas institutions and organizations related to research ethics is also a form of training. International cooperation is also necessary to discuss ways of tackling harmful information distribution and joint efforts to tackle such distribution patterns. Efforts should be made to collect information on overseas trends and to attend international specialist meetings organized for the exchange of experience and information.

## 5.2 How to get trained

5.2.1. Get information about training courses, workshops, conferences, etc. which are periodically announced on websites, bulletin boards and various media channels.
5.2.2. Select the ones you need.
5.2.3. Apply for the training through the IRB secretariat to the Director General of the institute.
5.2.4. Register to attend.
5.2.5. Retire the receipt
5.2.6. You will be reimbursed the training expense up to the total cost of the training.

## 5.3 Keeping the training records

5.3.1. Complete the training form 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

## 6.0. 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

## 7.0. ATTACHMENT

**Training Record Form.**

## Annex 1

**Training Record Form**

| | |
|---|---|
| First name: | Last name: |
| Staff/Membership since: | Status: |
| Education Background: | |
| Work Experience: | |

**Training Experience:**

| S/N | Courses/Workshops/ Conferences/Meetings Attended | Organized by: | Where? | Duration | Source of Funding |
|---|---|---|---|---|---|
| 1 | | | | | |
| 2 | | | | | |
| 3 | | | | | |
| 4 | | | | | |
| 5 | | | | | |
| 6 | | | | | |
| 7 | | | | | |
| 8 | | | | | |
| 9 | | | | | |

## 8.0. 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) 1996.