GUIDELINES FOR THE RECOGNITION OF ETHICS REVIEW COMMITEES

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NATIONAL MEDICINE REGULATORY AUTHORITY
Norris Canal Rd, Colombo 01000, Sri Lanka

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1. PURPOSE

Clinical trials that require regulatory approval of the NMRA as stipulated in Clinical Trials Regulations No. 2145/2 of 14.10.2019 need to undergo ethics review by one of the recognized ethics review committees and have ethics clearance prior to getting the letter of authorization for the conduct of such trial. For this purpose, the NMRA recognizes ERCs based on defined criteria. Such recognized ERCs are listed in the 'Guidelines for the Conduct of Clinical Trials in Sri Lanka' published by NMRA. An individual ERC can make voluntary request to the NMRA to list it as a recognized ERC of the NMRA.

2. SCOPE

These guidelines stipulate the minimum requirements an ethics review committee should fulfil in order to be recognized for granting ethics approval for trials which NMRA authorization is mandatory. These requirements are based on the Ethics Review Committee Guidelines published in 2018 by the Forum for Ethics Review Committees in Sri Lanka (FERCSL).

3. APPLYING FOR RECOGNITION

1. An institutional ethics committee or an ethics committee functioning under a professional association may make a written request to NMRA, indicating its intent of being listed as a recognized ERC of NMRA
2. The request shall be addressed to CEO/NMRA and shall consist of the following:
   - Cover letter in letterhead of the ERC
   - Responses to the questionnaire given in appendix I
   - Proof of GCP certification of members of the ERC.
   - Proof of membership of FERCSL and proof of other local recognitions, if any (e.g. approval of the Ministry of Health for ERCs in hospitals and other institutions that comes under the Departments of Health)
   - Proof of international recognition, membership etc. if any (e.g. SIDCER recognition, institutional membership of FERCAP)
   - A commitment that an annual report on clinical trials approved by the ERC would be submitted to CTRD, NMRA
3. The request will be scrutinised by the Clinical Trials Evaluation Committee (CTEC) of the NMRA and further clarifications may be requested from the ERC if a need arises.
4. If required, an inspection team consist of CTEC members and officers of the CTRD may visit the premises of the ERC and may review documents maintained by the ERC.
5. NMRA will inform its decision on acceptability of the ERC (with reasons, if not accepted) within 90 working days subjected to stop clocks for furnishing clarifications.
6. No fee is charged by NMRA for the application process nor for continuity as a recognized ERC.
7. Once accepted, the recognition of an ERC will be renewed every five years.

4. REQUIREMENTS TO BE FULFILLED

In general, NMRA expects the Ethics Review Committee to adhere to the latest guidelines published by FERCSL (http://fercsl.lk/wp/wp-content/uploads/2018/12/FERCSL-Guideline-2018.pdf**)**. The following requirements shall be fulfilled by the ERC in order to be recognized for the purpose of granting ethical clearance for trials requiring regulatory approval by NMRA

6.1 The Research Ethics System

- An appointing authority as recognized by that institution should appoint the members of the ethics committee
- All Standard Operating Procedures should conform to the requirements of the WHO Standards and Operational Guidance for Ethics Review of Health Related Research with Human Participants, should be written and documented by the ERC and they should be approved by the appointing authority.
- No research with human study participants should begin until approval by the ERC has been obtained.
- The ERC should submit an annual report to the appointing authority which contains a list of protocols submitted, the decisions taken on them and a short summary of the reasons for the decisions, so that the appointing authority can monitor the effectiveness of the ethics review process.
- The ERC should have the membership in the Federation of Ethics Review Committees of Sri Lanka (FERCSL)
- An annual report on clinical trials approved by the ERC to be submitted to NMRA
- The ERC should review a minimum of 10 research proposals a year.

6.2 Institutional policy and its responsibilities

- The policy of the institution should include promoting and facilitating setting up and maintenance of an Ethics Committee and be fully supportive of its activities.
- The institution should provide access to office space, equipment, and supplies (e.g. computers, stationery, telephones, photocopying machine) to conduct administrative business, to store all committee files, and to keep documents securely.
- The institution should provide staff support for the Ethics Committee.

6.3 Policies/SOPs governing the ERC

Policies

- The ERC should ensure that its decisions about research protocols are based on a coherent and consistent application of the ethical principles articulated in international guidance documents and human rights instruments, as well as any national laws or policies consistent with those principles. These guidelines should be readily available to researchers and the public.
- The ERC should ensure that investigators and sponsors (who may attend an ERC meeting to answer questions about their research proposals and associated documents) should not be present when the ERC discusses their studies or reaches decisions about them.
- The entity creating the ERC (such as the director of an institution) or of any organization that sponsors or conducts the research reviewed by the ERC should not serve as members of the ERC
- The decisions on research protocols should be made by a full review of the protocol by the members of the ERC unless they are low-risked and qualify for expedited review.
- The deliberations should only include ERC members and staff

- The decision-making process should exclude clinicians, investigators, funding agencies, or others directly associated with the proposal in question
- Decision should be made only by those who were present during the entire discussion of a protocol
- All members should have undergone at least a one-day training workshop on ethics review
- The meetings of the ERC should be conducted in a designated place. The place should have the necessary privacy and be able to accommodate all members of the committee.
- Composition of the ERC
  - Appointments should be made according to SOPs
  - The ERC membership should have a multisectorial and multidisciplinary membership
  - Should have a minimum of 7 members
  - Should include at least 1 non-technical 1 none-medical member
  - Should have at least one member who is not affiliated to the institute
  - At least two thirds of the members should not be from the organization/s that conduct research for commercial profit

- Standards and guidance for members of the ethics committee on evaluation of research proposals should be available
  This may be done by use of a checklist. Key criteria for a checklist include, but not limited to the following:
  - Risks and potential benefits
  - Selection of study population and recruitment of research participants
  - Inducements, financial benefits, and financial costs
  - Protection of research participants' privacy and confidentiality
  - Informed consent process
  - Community considerations

- Standards and guidance for researches on the following should be available
  - Submitting an application – qualifications required, student applications, collaborative/multicentre trials etc.
  - Scientific design and conduct of the research study
  - Changes to the research protocol
  - Safety reporting
  - Ongoing reporting and follow-up reporting
  - Termination/cancellation of a study

- The SOP should include a mechanism whereby researchers, research participants, and other interested parties can lodge complaints about the ERC. Such complaints should be reviewed by an entity other than the ERC itself.

  <u>Standard Operating Procedures</u>
  Written SOPs specifying the following should be available
  1. ERC's membership
  2. The appointing authority
  3. Terms and conditions of the appointment
  4. Committee governance
  5. Duties and responsibilities
  6. Independent consultants
  7. Submissions, documents required for review

8. Review procedures
9. ERC meetings, deliberations and decision making, quorum requirements
10. Communicating a decision
11. Follow-up reviews and monitoring of proposals
12. Documentation and archiving
13. Training
14. Quality assurance

5. RENEWAL OF ERC RECOGNITION

1. NMRA will renew recognition of an ERC every five years.
2. The ERC shall furnish an updated list of members, details of any major changes done to previous SOPs and guidelines, update on memberships and international recognitions etc. to the NMRA, in order to renew its recognition.

6. ABBREVIATIONS

CEO – Chief Executive Officer
CTEC – Clinical Trials Evaluation Committee
CTRD – Clinical Trials Regulatory Division
ERC – Ethics Review Committee
FERCAPS – Forum for Ethics Review Committees in the Asian & Western Pacific Region
FERCSL – Forum for Ethics Review Committees in Sri Lanka
NMRA – National Medicines Regulatory Authority
SIDCER – Strategic Initiative for Developing Capacity in Ethical Review
WHO – World Health Organization

7. DEFINITIONS

Clinical Trial

Any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes. Interventions may include but are not restricted to substances such as drugs, cells and other biological products, vaccines, surgical procedures, radiological procedures, or any other item claimed to have therapeutic benefit. The terms “clinical trial” and “clinical study” are synonymous

Contract Research Organization (CRO)

A scientific organization (commercial, academic or other) to which a sponsor may transfer some of its tasks and obligations. Any such transfer should be defined in writing.

Ethics Review Committee (ERC)/Ethics Committee

An independent body (a review board or a committee, institutional, regional or national), constituted of medical professionals and non- medical members, whose responsibility it is to verify that the safety, integrity and human rights of the subjects participating in a particular trial are protected and to consider the general ethics of the trial, thereby providing public reassurance.

Ethics review committees should be constituted and operated so that their tasks can be executed free from bias and from any influence of those who are conducting the trial.

Good Clinical Practices (GCP) Guidelines

Means identified ethical and scientific quality requirements which are internationally recognized and which must be observed for designing, conducting, recording and reporting clinical trials that involve the participation of human subjects. Compliance with GCP provides assurance that the rights, safety, and well-being of the study participants are protected, and the results of the clinical trials are credible;

Investigator

A doctor or dentist, as the case may be, responsible for the conduct of the clinical trial and for the rights, health and welfare of the participants in the trial at a trial site. If a trial is conducted by a team of individuals at a trial site, the investigator is the responsible leader of the team and may be called the principal investigator;

Principal Investigator (PI)

A doctor or dentist, as the case may be, having specialized in the area of study and specified in an approval as the person responsible for the conduct and supervision of a clinical trial

Protocol

A document that states the background, rationale and objectives of the trial and describes its design, methodology and organization, including statistical considerations, and the conditions under which it is to be performed and managed. The protocol should be dated and signed by the investigator, the institution involved and the sponsor. It can also function as a contract.

Sponsor

An individual, a company, an institution or an organization which takes responsibility for the initiation, management and/or financing of a clinical trial. When an investigator initiates and takes full responsibility for a trial, the investigator then also assumes the role of the sponsor.

Study Participant

An individual who participates in a clinical trial, either as a recipient of the investigational product under investigation or as a control. The individual may be a healthy person who volunteers to participate in a trial, a person with a condition unrelated to the use of the investigational product, a person (usually a patient) whose condition is relevant to the use of the investigational product.

8. RELATED LEGISLATION AND DOCUMENTS

- National Medicine (Clinical Trials) Regulations 2145/2, 14th October 2019
- Operational Guidelines for Ethics Review Committees that review biomedical research, TDR/PRD/ETHICS/2000:1, WHO, 2000
- WHO Standards and Operational Guidance for Ethics Review of Health Related Research with Human Participants, WHO, 2011
- Ethics Review Committee Guideline, FERCSL, 2018

9. FEEDBACK

Staff and stakeholders may provide feedback about this document by emailing pathmaperuma.a@nmra.gov.lk

APPENDIX 1

Questionnaire for ERCs:

ERCs applying for recognition with the NMRA shall furnish the details requested in the questionnaire given below.

The Research Ethics System

- What is the legislative and regulatory framework under which your ERC functions?
- Are there specific SOPs (Standard Operating Procedures) approved by the relevant authority?
- Is it confined to approving protocols submitted by members of your institution or does it accept protocols from outside?
- Is there an appropriate and sustainable system in place to monitor the quality and effectiveness of research ethics review?
- Are there procedures to harmonise standards with other ERCs in Sri Lanka?
- Are there mechanisms to ensure that ERCs' activities are coordinated with national regulatory authorities' oversight of drugs and medical devices?
- What types of research studies are reviewed? Please give a rough %?
    - clinical trials (specify if RCT, observational study, Profit/No Profit)
    - substantial amendments
    - interviews, survey, and focus research
    - research with biological samples
    - studies involving medical records or other personal information (specify if Profit/No Profit)
    - research of health care systems
    - quality improvement research
    - compassionate use
    - number of clinical trials authorized in the last year

Establishment of the ERC

- Who is the appointing official?
- Are appointments made according to SOPs?
- If not, is it ensured that ERC composition has a multisectoral and multidisciplinary membership?
- How many members are in the ERC?
- How many non-scientific and non-medical members are in the ERC?
- Does the ERC include members who are not affiliated with your institute?
- ERC establishment date

Adequate staffing, facilities, and financial resources to allow the ERC to carry out its responsibilities

- Does the ERC have support staff adequate in number and training to carry out the ERC's responsibilities?
- Is there a scientific secretariat? If yes, is it full time/partial time
- Does the ERC have adequate resources for the staff to fulfil its assigned functions, including office space and equipment and supplies (e.g., computers, stationery, telephones, photocopying machines) to conduct administrative business, to store all committee files, and to keep documents secure?
- Does the ERC have access to appropriate space for the committee to meet and adequate means for members to communicate as needed between meetings?
- Does the ERC have adequate financial resources to permit the committee to produce high quality work?
- Income per year and expenditure per year, for the last three years.
- What are the main expenditure items?
- Are the ERC members compensated for their time and effort on the ERC?

Policies governing the ERC to ensure independence of the ERC's operations and decision-making process

- Do the ERC's policies specify that its decision-making process is free from bias or influence?
- Declaration of independence and absence of conflict of interests: how often is it presented?
- Does the ERC ensure that investigators and funders (who may attend an ERC meeting to answer questions about their research protocols and associated documents) are not present when the ERC discusses their studies or reaches decisions about them?
- Does the ERC ensure that ERC members do not participate in decisions about protocols submitted by their close colleagues?
- Do the ERC's policies specify that high-level officials of the entity creating the ERC, or of any organization that sponsors or conducts the research reviewed by the ERC (such as the director of an institution), do not serve as members of the ERC?

Training of ERC members on the ethical aspects of health-related research with human beings, and how the ERC conducts its review of research

- Are the ERC members provided with training in the following aspects when they join the committee and periodically during their committee service?
- The role and responsibilities of the ERC, and the ERC's relationship with other relevant entities, according to relevant international guidelines (e.g., GCP)
- The full range of ethical considerations relevant to research with human participants
- How such ethical considerations apply to different types of research?
- Basic aspects of research methodology and design (for members who lack such background)
- How different scientific designs and objectives may affect the ethics of a research study
- The various approaches for recognizing and resolving the tensions that can arise among different ethical considerations and modes of ethical reasoning
- Using resources prudently to maximize committee members' training opportunities.

Mechanisms to make ERC operations transparent, accountable, consistent, and of high quality

- Does the entity establishing the ERC employ reliable means to evaluate whether the staff and members routinely follow the ERC's policies, rules and SOPs with special attention to whether the ethical considerations articulated in international guidelines and national standards are being considered and applied consistently and coherently?
- Are these evaluations conducted at regular, pre-defined intervals, using a pre-defined format by knowledgeable and unbiased persons?
- Are internal assessments supplemented periodically by independent external evaluations?
- Is there a mechanism for researchers, research participants, and other interested parties to lodge complaints about the ERC? Such complaints should be reviewed by an entity other than the ERC itself, and appropriate follow-up actions should be taken.
- Is there a minimum number of meetings per year?
- Is there a website for the ERC? If yes, how often is it updated?
- Does the ERC make its decisions public?

Standards and guidance for members of the research ethics committee

- Does the ERC base its decisions about research protocols on a coherent and consistent application of the ethical principles articulated in international guidance documents and human rights instruments, as well as any national laws or policies consistent with those principles?
- Does the ERC make clear the specific ethical guidelines on which it relies in making decisions and make them readily available to researchers and the public?

Decisions on research protocols by ERC

- Are decisions on research protocols designated for full review based on a thorough and inclusive process of discussion and deliberation by all members of the ERC?
- How are decisions made? By consensus or by voting?
- Is there an expedited review procedure for emergency situations and/or low-risk protocols?

Are there written policies specifying the following?

- ERC's membership
- Committee governance
- Review procedures
- Decision-making communications
- Follow-up
- Monitoring
- Documentation and archiving
- Training
- Quality assurance

Does the ERC provide guidance for researchers?

- Submitting an application - qualifications required, student applications, collaborative/multicentre trials etc. -
- Conduct of research -
- Any changes made to research protocol -
- Safety reporting -
- Ongoing reporting and follow-up -
- Termination/cancellation of a study –

Indicate priority areas of improvement