

A Snapshot Summary and Comparative Analysis of Selected Ethics Review Committees Reviewing Clinical Trials in Sri Lanka

Thurayratnam Chenthuran

Department of Anatomy, Faculty of Medicine, University of Jaffna

*Email: chen.educ@gmail.com

Abstract – In Sri Lanka, and across the world, ethics is becoming an ever increasingly integral part of clinical practice and biomedical research. Comprehensible and transparent ethics standards are essential to public trust in scientific research studies. In the pursuit of ethical research, Ethics Review Committees play a momentous role in the review and monitoring of biomedical research, especially in the case of clinical studies. National legislation and specific legal guidelines which systematically regulate the establishment, functioning, registration, and/or accreditation of such committees in Sri Lanka are yet to be developed. The National Medicines Regulatory Authority, an independent authority within the Sri Lankan Ministry of Health, plays an important role in the regulation of clinical trials in Sri Lanka. This review, albeit briefly, highlights the history of bioethics, the current state of Ethics Review Committees in Sri Lanka, and the recent efforts taken to assess their operations to ensure they meet international standards. In addition, this manuscript critically analyzes the membership composition and quorum requirements of selected Ethics Review Committees in Sri Lanka, as well as the challenges faced by these committees today.

Keywords: Ethics review committee, membership composition, clinical trial, quorum

1. INTRODUCTION

Bioethics is an indispensable component of principled medical practice and research, especially in the case of clinical studies. One of the earliest records of medical ethics has its roots in the fifth century BCE, the exposition of the Oath of Hippocrates, which addresses the protection of the rights of patients [1]. “I will do no harm or injustice to them” (my patients) is one of the fundamental tenets of the Oath [2] and is still applicable to clinical studies today.

In the sixth century BC, the first research resembling a clinical trial was carried out by King Nebuchadnezzar, ruler of Babylon. Since then, the evolution of more scientifically advanced clinical research has been marked by innovative experiments, for example the works of; James Lind (parallel arm medical experiment); Austin Flint (comparison of an active treatment with that of dummy remedy); and the randomized trial on streptomycin for treating pulmonary tuberculosis [3]. The recent COVID – 19 pandemic resulted in the implementation of a vast number of clinical trials due to significant morbidity and mortality

associated with the disease and its long term impact on the health care system and economy. As of now 12,966 COVID-19 related clinical trials have been registered in the International Clinical Trials Registry Platform of the World Health Organization. As of the date of preparation of this manuscript, Sri Lanka is involved in 25 COVID-19 trials [4]. Although ethics is an integral part of research, incidents in human history have demonstrated that anticipated scientific outcomes have led scientists to overlook ethical principles at times, breaking the fundamental trust between researchers and the public.

2. REGULATION OF CLINICAL STUDIES IN SRI LANKA

Sri Lanka universally supports and promotes ethical research. Conducting a clinical trial in Sri Lanka requires approval beforehand from one of the Ethics Review Committees (ERCs) recognized by the Clinical Trials Evaluation Committee (CTEC) of the National Medicines Regulatory Authority (NMRA), an independent authority in the Ministry of Health, Sri Lanka. The NMRA was established by an Act of

Parliament, the National Medicines Regulatory Authority Act, No.5 of 2015 [5]. Other requirements for clinical trials include obtaining approval from the Clinical Trials Evaluation Committee (CTEC) itself, and registration of the trial in the Sri Lanka Clinical Trials Registry (SLCTR) [6]. In addition, obtaining approval (or a no-objections certificate) from the head(s) of the institution(s) of the trial site(s) is also a mandatory requirement to conduct a clinical trial.

At present, though Phase III and Phase IV clinical trials are permissible in the country, Phase I (first-in-man) trials are not allowed to be conducted. Applications to conduct Phase II clinical trials shall be accepted for consideration if they satisfy the criteria established by the NMRA. It is noteworthy that at least 43 applications for clinical trials were submitted to the NMRA during the last five years (from 2018 to 2022). It is also notable that clinical trials for certain categories of medicines are not subject to regulatory review, and approval from the CTEC is not required. However, they still require both ethical clearance and registration with the SLCTR [5].

3. ETHICS REVIEW COMMITTEES IN SRI LANKA

ERCs, also referred to as Institutional Review Boards (IRBs), play a significant role in the advancement of science by providing comprehensive, competent, autonomous and timely reviews of research protocols, and the ongoing monitoring of approved studies. Their review process must be impeccable and comply with applicable institutional (e.g. Standard Operating Procedure [SOP]) [7], national (e.g. guidelines of Forum for Ethics Review Committees of Sri Lanka [FERCSL]) [8], and international guidelines (e.g. Declaration of Helsinki) [9] to ensure ethical principles and standards are upheld. In addition, ERCs must operate in accordance with relevant Government legislation (if any) regulating their practices.

The first institutional ERC in Sri Lanka was established in the Faculty of Medicine, University of Colombo in 1981. Subsequently, the medical faculties of the University of Ruhuna and the University of Jaffna formed their own ERCs in the years 1984 and 1985 respectively [10]. A survey conducted by Mendis et al. (2005) which reviewed the ERCs in Sri Lanka documented (2004 – 2005) information on fifteen ERCs in the country [11]. Another study reported the existence of ERCs in eight faculties in the country including that of the Faculty of Arts, University of Colombo. Among these eight ERCs, six were independent committees, and two were subcommittees of research committees. In addition, the Sri Lanka Medical Association (SLMA) and Medical Research Institute (MRI) had their own ERCs [12]. In 1991, the first national ERC in Sri Lanka was established at the Natural Resources Energy and Science Authority (NARESA) [13].

Today, at least thirty-three ERCs are being established in the country [14,15]. The rapid increase in the number of ERCs suggests that there is an increased demand for ethical clearance of research proposals in the country. This increase in ERCs could be attributable to the overall promotion of research in the country; specifically, researchers seeking ethical clearance to move forward with their studies in real world applications.

Currently, there is no legally empowered local authority, specific national legislation, or legal guidelines to regulate the establishment, functioning, registration and/or accreditation of ERCs in Sri Lanka. Therefore, the actual number of ERCs functioning in the country is not known. At present, twenty-six ERCs established at universities, hospitals, professional colleges, associations, and other health institutes have been accepted by the Ministry of Health, Sri Lanka [15].

Due to the nature of their work, ERCs may come under pressure from external influences, including but not limited to: institutional, professional, political, and/or financial

stakeholders. Regardless, it is crucial that ERCs operate independently to uphold their ethical standards and maintain trust in the scientific community and the public. Members of ERCs must have sufficient knowledge, training, and interest in research ethics and should be prepared to devote a substantial amount of time towards the betterment of society.

It is crucial that newly appointed members of ERCs complete their training on research ethics, SOPs, and GCPs at the earliest available opportunity. The University of Jaffna's Faculty of Medicine, goes even further and stipulates a time frame for this training. Additionally, their ERC requires that existing members must undergo training on research ethics and GCPs every three years to retain their membership [7]. These measures place the members of ERCs in a better position to review various types of research proposals with the most up to date information. These policies are in place to ensure that members are fully aware of the societal impact of approving an improper research study, or disapproving of a valuable and ethically acceptable study.

4. FORUM FOR ETHICS REVIEW COMMITTEES OF SRI LANKA (FERCSL)

The Forum for Ethics Review Committees of Sri Lanka, FERCSL, is a local organization whose mission is "fostering improved understanding and implementation of ethics review of biomedical research in Sri Lanka" [14]. As of now, twenty-three ERCs have obtained their voluntary membership in FERCSL. The activities of FERCSL are planned and implemented by a management committee which has representation from each registered ERC. The main functions of FERCSL include, but are not limited to, improving communication between ERCs, organizing meetings / symposia / training sessions, and stipulating SOPs and guidelines for member ERCs. As part of its activities, FERCSL facilitates educational opportunities and training for members of ERCs; for example, through GCP workshops

[14]. This will ensure that the decision making of ERC members will be accurate, rational, logically consistent, and without prejudice. It serves as one of the committees of the Sri Lanka Medical Association (SLMA) [16].

In order to secure NMRA approval for a clinical trial, ethical clearance must be obtained from one of the nine ERCs that they recognize. Seven of these ERCs are established within medical faculties; The University of Colombo, The University of Kelaniya, The University of Peradeniya, The University of Ruhuna, The University of Jaffna, The University of Sri Jayewardenepura, and The Rajarata University of Sri Lanka. The remaining two ERCs are established at the Medical Research Institute and the Sri Lanka Medical Association [5].

5. ACCREDITATION AND RECOGNITION OF ERCS IN SRI LANKA

Since their inception, ERCs in Sri Lanka have been keen to assess and improve their standards by internal and / or external review. As a result, Sri Lanka's first formal institutional ERC, the ERC of the University of Colombo's Faculty of Medicine, became the first ERC in Sri Lanka to obtain an international recognition from the SIDCER (Strategic Initiative for Developing Capacity in Ethical Review) recognition programme of the Forum for Ethical Review Committees in the Asian and Western Pacific Region (FERCAP) in 2009. The experiences gained during the programme drove other ERCs in the country to perform a self-evaluation to identify strengths / capabilities and weaknesses / deficiencies (if any) and to take actions as appropriate. As a result, another eight ERCs have obtained their SIDCER recognition including that of the Postgraduate Institute of Medicine (PGIM), Colombo [17]. In addition, five of these ERCs were successful in retaining / renewing their SIDCER recognition.

At present, all except one of the ERCs that are recognized by the NMRA are also recognized by the SIDCER programme. However, an ERC recognized by the SIDCER recognition

programme is not inherently recognized by the NMRA for granting regulatory approval for clinical trials. It is noteworthy that recognition from the NMRA and the SIDCER programme are provided based on the voluntary request made by an ERC and the latter usually involves a survey through direct site visits to the institution where the ERC is located. The financial commitment involved in the SIDCER recognition programme may prevent certain ERCs, which have limited funding opportunities, from carrying out surveys and becoming recognized.

As it stands today, any proposal unapproved by one ERC can be considered and may be accepted by another ERC if there are any differences in their SOPs and/or their implementation. In order to ensure the protection of participants in research studies, membership composition, function, and the quality of the review process must become uniform throughout the country.

6. SPECIAL REVIEW OF NOTABLE ERCS IN SRI LANKA

The author of this paper conducted a web based comparative analysis of the eight ERCs recognized by both the NMRA and the SIDCER recognition programme to identify any common characteristics or patterns in membership composition. The analysis focuses on factors such as professional qualifications, community involvement, their presumed gender, and their affiliations [18, 19, 20, 21, 22, 23, 24, 25]. It should be noted that the details of certain ERC members were not readily accessible. Therefore, the results are based on available data and should be interpreted accordingly.

As per the guidelines of FERCSL, the total number of members in an ERC is suggested to be between seven to fifteen [8]. The NMRA also agrees with the minimum number of members (i.e. 7) recommended by FERCSL [5]. All except one of the ERCs have more than the proposed maximum number of members; moreover, four ERCs were found to have twenty or more members. The accommodation of more

members, particularly those with unique specialties, could expand the capabilities of ERCs. Ideally, ERCs should be multidisciplinary, multisectoral, and pluralistic in its membership composition [8].

Only one of the eight ERCs studied [18] reviewed clinical trials through a separate subcommittee. This sub-committee referred to as the "Clinical Trials Subcommittee" (CTSC) is composed of 17 members, including six members from the main ERC committee. The proportion of members who have allopathic medical qualifications (MBBS, BDS or equivalent) in the CTSC is 70.59% which is substantially higher than the main ERC committee's 60%. This observation may be explained based on the specialized nature of work carried out by the subcommittee. In contrast, the main committee deals with a broad variety of biomedical research that involves a breadth of specimens and / or data of human participants (including genomic research and clinical trials), health-related research (involving communities or healthcare systems), and animal studies related to human health [18]. Among these eight committees, allopathic medical professionals were found to compose between 50% to 81.25% of ERC membership. The remaining committee members of the ERCs consisted of (but not limited to) indigenous medical professionals, allied health professionals, and members conversant with social values. It is notable that four ERCs have a non-affiliated member conversant in indigenous medicine. The same four ERCs have at least one member who is conversant in allied health sciences. All ERCs studied have accommodated at least one member who is conversant in legal matters (attorney at law or with a degree in Law) in their (main) committee.

The guidelines of FERCSL advocate for a gender balanced membership composition [8]. Half of the studied ERCs had more females than males as members with a ratio as high as 76% female [18]. It was observed that one ERC demonstrated 50% gender balance among its

members. Currently, all ERCs belonging to universities satisfy the FERCSL and NMRA requirements by having at least one member outside the institution. University of Jaffna's ERC, has the highest proportion of non-affiliated members (68.75%) [19]. Having more non-affiliated members could be considered a desirable feature as it could avoid or minimize any direct or indirect influences from the administration of the institution on the review process.

In general, a quorum is required to constitute an ERC meeting and make decisions on agenda items including research proposals submitted for ethical review. According to the SOPs of the ERCs based in the University of Jaffna, University of Sri Jayewardenepura and University of Kelaniya, the minimum number of members who have to be present to have a valid meeting vary from 31.25% (5 out of 16) of members [19], 35% (7 out of 20) of members [20], and 54.35 % (half plus one of the existing 23) of members [21]. The SOPs of these ERCs also specify the presence of at least: one community representative [19], one non-medical member and one non-affiliated member [20], or one non-affiliated / lay member [21] as a prerequisite to meet quorum. Using precise, consistent terminology and definitions in the SOPs, for example, when referring to non-affiliated members, non-medical members, non-scientific members / lay members, would improve the quality of the review process.

ERCs, in exceptional circumstances, may have provisions to conduct meetings without quorum at the discretion of the Chair. Whereas some ERCs cannot make a decision without quorum [21], others may ratify the decisions taken by the ERC in such occasions as long as at least one lay representative and one non - affiliated member support the proposal [20].

7. FINANCIAL CONSTRAINTS

It appears that most, if not all, ERCs generate their funding through charging a fee from the applicants. Improving the quality of the review

process depends, at least partially on, the allocation of dedicated funding to the activities of ERCs, especially considering the contribution made by the committee not only to institutions but also to the country. Additional funding allocation to ERCs from their host institutions would open opportunities to organize workshops / training programmes on bioethics for researchers, more extensively monitor approved trials, and obtain certification from international recognition programmes. These measures, in turn, would improve the quality of research throughout the country and improve the standing of Sri Lankan clinical research worldwide.

In conclusion, Sri Lanka has a rapidly developing ERC domain, and having legislative guidelines for the establishment, registration, functioning, and accreditation of ERCs would help to further standardize and advance bioethics in the nation. A formal accreditation system would ensure that all the registered ERCs in the country have at least the minimum standards required to review research protocols and approve clinical studies. Legislation could potentially go even further to establish a national database of ERC proposals in order to centralize and share information (reducing inconsistencies amongst ERCs), and preventing accidental duplication of studies.

It is a shared responsibility of the investigators, sponsors, participants, ERC members and all the other stakeholders to ensure that clinical studies are appropriately designed, scientifically valid and acceptable on ethical grounds. As custodians of patient health and safety, medical practitioners have an unwavering duty to the public to conduct research with the greatest standard of care and respect.

8. REFERENCES

1. Riddick FA. The code of medical ethics of the American Medical Association. *Ochsner Journal*. 2003, 5(2):6-10.
2. National Library of Medicine, National Institutes of Health, USA. https://www.nlm.nih.gov/hmd/greek/greek_oath.html (accessed on 8th February 2023).

3. Collier R. Legumes, lemons and streptomycin: a short history of the clinical trial. 2009, 180 (1): pp. 23-24.
4. International Clinical Trials Registry Platform (ICTRP), World Health Organization (WHO). <https://trialsearch.who.int> (accessed on 16th February 2023).
5. National Medicines Regulatory Authority (NMRA). <https://nmra.gov.lk/index.php?lang=en> (accessed on 8th February 2023).
6. The Sri Lanka Clinical Trials Registry (SLCTR). <https://www.slctr.lk/> (accessed on 8th February 2023).
7. Standard Operating Procedures (Version 4.0), Ethics Review Committee, Faculty of Medicine, University of Jaffna. <https://www.med.jfn.ac.lk/wp-content/uploads/2022/07/ERC-SOP-V4-Senate-approved.pdf>. (accessed on 9th February 2023).
8. Ethics Review Committee Guidelines (2018). A FERCSL Operational Guidance for Committees that Review Biomedical Research Proposals. <http://fercsl.lk/wp/wp-content/uploads/2018/12/FERCSL-Guideline-2018.pdf> (accessed on 9th February 2023).
9. World Medical Association Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects (amended in 2013). <https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/> (accessed on 9th February 2023).
10. Dissanayake, V.H.W., Lanerolle, R.D. and Mendis, N., 2006. Research ethics and ethical review committees in Sri Lanka: a 25-year journey. *Ceylon Medical Journal*, 51(3), pp.110-113.
11. Mendis, N, Lanerolle, R and Abeysurua, K.C. Review of Ethical Review Committees in Sri Lanka. *Ethical Review Committee, Faculty of Medicine, University of Colombo* (2004 – 2005). pp. 1- 36.
12. Perera, J., Galaboda, D. and Gunawardena, D. 2005. Ethical review committees in Sri Lanka: a national framework is required. *Ceylon Journal of Medical Science*, 48, pp.61–65.
13. National Guidelines for the Establishment and Functioning of Ethical Review Committees in Health Care Institutions in Sri Lanka (2013). Education, Training and Research Unit, Ministry of Health, Sri Lanka. http://www.health.gov.lk/moh_final/english/public/elfinder/files/publications/2022/Batch221-1.pdf (accessed on 9th February 2023).
14. Forum for Ethics Review Committees of Sri Lanka. <http://fercsl.lk> (accessed on 10th February 2023).
15. National Health Research Council, Ministry of Health, Sri Lanka. <http://nhrc.lk/newweb/index.php/research-ethics> (accessed on 10th February 2023).
16. Sri Lanka Medical Association, Sri Lanka. <https://slma.lk/> (accessed on 10th February 2023).
17. The SIDCER-FERCAP Foundation. <https://www.sidcer-fercap.org/pages/recognized-ecs-irbs.html> (accessed on 11th February 2023).
18. Ethics Review Committee, Faculty of Medicine, University of Colombo. <https://med.cmb.ac.lk/erc/members/#1528093276540-fe859666-35eb> (accessed on 11th February 2023).
19. Ethics Review Committee, Faculty of Medicine, University of Jaffna. <https://www.med.jfn.ac.lk/ethics-review-committee/> (accessed on 9th February 2023).
20. Ethics Review Committee, Faculty of Medical Sciences, University of Sri Jayewardenepura. <http://medical.sjp.ac.lk/index.php/ethics-review-committee-committee-members> (accessed on 13th February 2023).
21. Ethics Review Committee, Faculty of Medicine, University of Kelaniya: <https://medicine.kln.ac.lk/prog/erc/index.php/our-people/affiliated-staff> (accessed on 13th February 2023).
22. Ethics Review Committee, Faculty of Medicine, University of Peradeniya: <https://med.pdn.ac.lk/admin/erc/committee.html> (accessed on 13th February 2023).
23. Ethics Review Committee, Faculty of Medicine, University of Ruhuna: <http://www.medi.ruh.ac.lk/ethics/> (accessed on 14th February 2023).
24. Faculty of Medicine and Allied Sciences, Rajarata University of Sri Lanka: <http://med.rjt.ac.lk/ethics-review-committee> (accessed on 14th February 2023).
25. Ethics Review Committee, Sri Lanka Medical Association (SLMA), Sri Lanka. <https://slma.lk/ercwp/members/> (accessed on 14th February 2023).