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Research ethics committees: Need for harmonization at the national level, the global and Indian perspective

Abstract

Ethics committee (EC) organization and standardization is an important aspect of clinical research. There is a healthy trend worldwide to register and/or accredit research ECs reviewing clinical research. This article tries to focus on the existing model of ECs worldwide, as against the Indian backdrop. The article reviews literature, journals, websites, and studies conducted in 10 different countries and outlines the working model of ECs in these countries. The challenges faced during the ethical review, especially in case of multicenter trials, have been identified. A solution has been suggested to overcome these challenges, and to ensure the overall smooth functioning of clinical trials. The article proposes the development of national and regional central ECs to counter the current drawbacks in the ethical review mechanisms in India.

Key words: Accreditation, central review, ethics committees, harmonization, registration

INTRODUCTION

Ethics committees (ECs) constitute an important pillar in the foundation of ethical clinical research. Over the past few years the nature, functioning, and constitution of ECs has evolved globally. The objective of this article is to focus on the model of ECs in different parts of the world and to analyze the global perspective against the current Indian backdrop. The article explores the nature of the existing centralized and regional ECs in certain countries and seeks to understand whether having a similar model in India, is the need of the hour.

Background

ECs for research first came into existence as early as the 1960s. In 1975, the first revision of Declaration of Helsinki (DOH)[1] recommended that: Any experiment involving human beings must be submitted to an independent committee for review, comment, and guidance. In 1979, the Belmont report[2] drafted in the US, once again emphasized on the need of review by ECs for all clinical trials. In 2002, Council for International Organization of Medical Sciences (CIOMS) came up with international ethical guidelines for biomedical research involving human subjects. The DOH is currently undergoing its seventh revision in 2013. Compensation to trial participant and post-trial access of beneficial medicines to participant are two important issues under discussion.[3]

In India, Indian Council of Medical Research (ICMR) released a 'Policy Statement on Ethical Considerations involved in Research on Human Subjects' in February 1980. This was the first policy statement giving official guidelines for establishment of ECs in all medical colleges and research centers in India.[4] ICMR finalized 'Ethical Guidelines for Biomedical Research on Human Subjects' in the year 2000. The guidelines were revised in 2006. New changes related to the registration of ECs in India were brought about by CDSCO in the amendment to Schedule Y, 2013.[5]

Access this article online	
Quick Response Code:	Website: www.picronline.org
	DOI: 10.4103/2229-3485.128022

METHOD AND CONTENT

To understand the functioning of ECs globally, a literature search was undertaken and ECs of 10 countries actively involved in clinical research were studied. EC's websites, wherever available, were accessed. Scientific articles and news in journals were also reviewed to collect the necessary information, in a period of 1 month from 1st July-31st July 2013.

The EC scenario in the different countries studied is as follows:

United Kingdom

The entire UK ethics system was managed and coordinated by the Central Office for Research Ethics Committee (COREC) established in 2000 by the Department of Health. Ten multicenter ECs and 300 local ECs had been established under COREC.

In 2007, COREC became the National Research Ethics Service (NRES). The NRES oversees a three stage accreditation process for research ECs (RECs). The first stage is a Self-Assessment Tool (SAT), which reviews RECs' compliance with Standard Operating Procedures (SOP) for research ECs in the UK. The second step involves on-site review by the NRES, wherein the training records, membership records, sample study files, accommodation, equipment, and office procedures are reviewed. Finally, the auditor conducts an observation of an REC meeting. An REC either receives full accreditation or provisional accreditation. Audit and accreditation are repeated every 3 years.[6]

Italy

In Italy, the ethical review of clinical trial goes through three phases: First, the clinical trial application submission to the institutional/independent EC (IEC) of both the coordinating and the participating centers; second, the issuance of the "single" opinion by the IEC of the coordinating center and, in case of positive opinion, the acceptance or refusal by the IEC of each participating center; and third, in case of acceptance, the trial contracts signature between the coordinating and each participating center.

An advantage here is that a "single document", reduces the variability of the "center-specific" documentation, and also the activation time of the participating centers for multicenter clinical trials. In 2008, the Italian Medicines Agency (AIFA) promoted a project for electronic submission of all the necessary documentation concerning a clinical trial (project e-submission). The project involved IECs, Italian National Health Institute (ISS), Sponsors, and Contract Research Organizations (CRO). One of the objectives of the project was to define a detailed list of "center-specific" documents required by the IEC. Eighty percent participants considered the proposed single document as acceptable.[7]

China

The Ministry of Health's National Biomedical Research Ethics Committee manages and oversees all biomedical research ethics in China. The interaction of the local ECs with the national committee is for professional guidance.[8] Most of the ECs existing in China are hospital ECs which have developed over a period of 10 years. IECs also exists in China. They have been established in compliance with World Health Organization (WHO), United Nations Educational, Scientific and Cultural Organization (UNESCO), and Good Clinical Practice (GCP) guidelines. For example, IEC at Shanghai Clinical Research Center is responsible for the review of clinical research conducted in Shanghai or other cities in China.[9]

USA

All institutional review boards (IRBs) have to be registered with the Department of Health and Human Services. An IRB must be registered before it can be designated under an assurance approved for federal wide use by Office of Human Research Protection (OHRP). IRB registration becomes effective when reviewed and accepted by OHRP. The registration will be effective for 3 years. Each IRB must be registered electronically through http://ohrp.cit.nih.gov/efile. If an organization lacks the ability to register an IRB electronically, it may send its IRB registration information in writing to OHRP. An institution can designate a registered IRB operated by another institution, after establishing a written agreement with that institution.[10]

Australia

The National Health and Medical Research Council (NHMRC) in Australia is implementing a national approach for single ethical review through the Harmonization of Multicenter Ethical Review (HoMER) Initiative. Researchers who are conducting multicenter trials in Australia are required to submit their research protocol to one certified human research ethics committee (HREC) for review. Tools have been constructed to support the single ethical review, including the National Certification Scheme, standardized participant information and consent forms, HREC template letters, and information on the roles and responsibilities of key stakeholders in the new review system.[11]

Not all organizations that conduct research have their own HREC. Some organizations have established an HREC to

provide the service of ethical review to researchers who do not have an HREC at their own organization. Ethics Committee Certification provides assurance that the policies, processes, and procedures of an institution and its HREC comply with an agreed set of national criteria for the conduct of an ethical review of research. Certification involves the institution carrying out a self-assessment of its ethical review processes and supporting structures against agreed national criteria. This is followed by a desktop assessment by the certifying body, and an on-site visit to verify institutional claims and practices.[11]

New Zealand

New Zealand has a centralized Human Research Council Ethics Committee, (HRCEC) which is a multiregional committee. It approves the Health and Disability Ethics Committee (HDEC) and the institutional/other ECs. The HDEC is funded by the New Zealand Department of Health. The Health Research Council accredits the local research committees. Accreditation involves a combination of self-assessment and external reviews, focusing on issues like committee membership, operating procedures, and the documentation of meetings. The local ECs can review low risk health and disability research, but all other research is referred to the HDEC. A few examples of trials which need to be referred to HDEC include any research study which involves participants who are patients/clients of any organization providing health services, disability services, or institutionalized care, and: (a) The IEC lacks the clinical or other expertise to make an appropriate ethical judgment, and is unable to obtain the appropriate expertise for reviewing that research; or (b) the study poses risk of more than minimal harm to participants; or (c) there is a real or apparent conflict of interest which would prevent the IEC from providing independent review.[12]

Japan

Japanese GCP mandates that a research EC must be established by every institution where clinical trials are conducted, unless that institution is too small to operate its own REC in which case the head of that institution can designate a REC established by another institution. Medical schools and the majority of hospitals have established their EC voluntarily without any governmental regulation. The standardization in the composition of ECs all over Japan has been brought about by (a) Liaison Society for Ethics Committees of Medical Schools set up in 1988, and (b) because of the ethical guidelines issued by the government.[13] At medical schools and the majority of general hospitals, there are actually two types of ECs: An EC that reviews and monitors drug clinical trials called a clinical trial review committee, and an EC that reviews protocols from researchers affiliated with the institution (EC). Clinical trial review committees are regulated by the Ministry of Health, Labor and Welfare and function in accordance with the Pharmaceutical Law and the Guidelines for GCP.

Canada

In Canada most academic centers have their own research EC which is known as Research Ethics Board (REB). The National Council on Ethics in Human Research assists REBs in interpreting and implementing guidelines for ethics of research in humans and to establish ongoing mechanism to assess functions of REBs. For multicentric research, alternative ethical review models are acceptable. Individual IRBs may be authorized to accept review undertaken by an external Research Ethics Board following an official agreement between the institute and the IRB. External, specialized, or multi-institutional REBs may be established regionally, provincially/territorially, or nationally; as necessary. Two or more institutions may choose to create a single joint REB, or to appoint an external REB, to which they delegate research ethics review. This delegation of review may be based on geographical proximity or other considerations such as resources, volume of reviews, or shared expertise.[14] This is beneficial in case of multicentric trials as it saves time and resources.

Korea

Korea's National Bioethics committee oversees the ethics in clinical research. Independent and IRBs exist in Korea. Both independent and academic IRBs have conflicts of interest inherent in their structure. Also review of multicenter trials by different IRBs causes delays and inconsistencies. As per a study published in the Korean Anesthesiology Journal, the central IRB model with facilitated review process has been suggested as a way to lessen the burden on local IRBs. Also a review of the scientific benefits of the trial is often beyond the scope of the local IRB. Accreditation of IRBs has been suggested as an effective approach to improving quality in human subject protection.[15]

India

The CDSCO has undertaken the process of registering ECs in India in 2013. It is now mandatory to seek approval from an EC which is registered with CDSCO, before starting any clinical study in India.[16] This is a milestone in the evolution of clinical research in the country. More than 500 ECs have been registered as of today. The IECs have received approval from CDSCO to evaluate bioavailability-bioequivalance (BA-BE) studies only. The institutional ECs have received approval to review clinical trials. The registration has been issued for a period of 3 years, after which the committees need to reapply.

Since all hospitals may not have the financial and operational capabilities to form and operate an EC,

they shall have the option of approaching a registered institutional EC from their locality for review of their research documents. But all institutional ECs may not be equipped to handle outside projects, and the individual clinician researcher may not be able to pursue research due to lack of access to IEC. Also, although ECs are responsible for ongoing review and monitoring of trial activities; due to lack of space, infrastructure, time, funds, and administrative support; most ECs restrict themselves to an initial review and approval of study protocol.[17] Ensuring uniformity and fairness in compensation payments in a trial is another challenge faced by the ECs. It would be best if the assessment of causality and the method for calculating the quantum of compensation was determined upfront and EC confirmation taken before the start of the study.[18] But there are no definitive guidelines available to aid the EC to ensure that the patient is rightly compensated.

An ideal solution would be the formation of national and regional ethics committees under the wings of CDSCO. These committees could play a supervisory role in guiding the institutional ECs and also review documents for independent researchers. This would serve to make the existing ECs uniform and resourceful and may pave way to the harmonization of the EC review process, which would benefit the research industry as a whole.

The research EC data collected from all the above countries has been summarized in Table 1.

MERITS AND DEMERITS OF INSTITUTIONAL ETHICS COMMITTEES

The advantages of institutional ECs are that the research EC members are more familiar with the research settings, monitoring of ongoing research is easier and it is possible to impose institutional sanctions for violations by investigators. However, this model has several drawbacks. Conflicts of interest are more likely because the institution hosting the research EC has an interest in the research proceeding.[19] Also, an increasing amount of research now takes place at multiple sites. There is duplication of resources and prolonged time intervals are required for multiple EC reviews. Another hurdle faced by sponsors and CROs, in case of multicentric trials is the variability in the documents required for EC submission and the varied spectrum of inconsistent responses/judgments obtained from different ECs which leads to precious loss of time and money for the sponsor. A common application form for all ECs across India was suggested as an important step to achieve uniformity in functioning of ECs.[20]

Experiments with centralizing review

The Canadian Model of Central Ethics Committee review, the Ontario Cancer Research Ethics Board, and the US National Cancer Institute's Central Institutional Review Board, have had broadly positive results with centralization of EC review. The centralization of review reduced the duplication of documents during submission and ongoing monitoring phases.[21]

A study showing an analysis of centralized and non-centralized review in five English-speaking countries suggests that centralizing at least the administrative aspects of ethics review is helpful in reducing delays and excessive work from multisite trials. Also, a key change in the US Advance Notice of Proposed Rulemaking requires there to be just one IRB of record for all domestic sites involved in a multisite study.[22]

An article in the Journal of Nursing suggests that the system of institution-based ECs is inefficient with increase in multicenter studies. Two proposals were made in the article: (1) Regional ethics organizations and (2) web-based program for cooperative IRB review. Online submission of IRB application shall save both time and resources.[23]

Another recent study published in 2013, in London, stated that investigators are experiencing numerous challenges in the research ethics review of their trials; like excessive

Table 1: Country-wise data of ethics committee model

Country name	Centralized EC/regional EC	Local EC	Registration required	Accreditation required	E-submission projects	Post-approval study monitoring mandatory
UK	√	√	√	√		√
Italy	√	√		√	√	√
China	√	√	√			√
USA		√	√			√
Australia	√	√	√	√	√	√
New Zealand	√	√		√		√
Japan		√				√
Canada	√	√				√
Korea	√	√				√
India		√	√			√

EC=Ethics committee

delays, variability in process and outcome, and imposed requirements that can have negative consequences for study conduct.[24]

CONCLUSION

After taking into account the existing challenges experienced in the ethical review process of clinical trials, the formation of national and regional ethics committees can be considered as a viable solution. This shall help to bring about harmonization in the EC review process. The national review committee may be approached for multicentric trials, while the regional ECs can review documents for the independent researchers and also serve as a guiding force for the institutional ECs. This shall allow adequate monitoring on the research sites, and ensure experienced and qualified staff as EC members. Online submission of EC review articles shall also save time and effort for the sponsors and investigators. This will encourage more sites to take part in research activity, as they shall not be faced with the administrative and financial burden of maintaining an EC. This will also speed up the EC review process, and bring about the much needed fertile landscape for the growth of clinical research in India.

REFERENCES

1. Declaration of Helsinki (1975)/CSEP: Codes Repository. Available from: http://www.ethics.iit.edu/ecodes/node/3931 [Last accessed on 2013 Jul 17].
2. The Belmont Report: Ethical principles and guidelines for the protection of human subjects of research. US Department of Health and Human Services, 1979, 45 CFR 46. Available from: http://www.hhs.gov/ohrp/humansubjects/guidance/belmont.html [Last accessed on 2013 Jul 17].
3. Moris K. Revising the Declaration of Helsinki. Lancet 2013;381:1889.
4. Sanmukhani J, Tripathi B. Ethics in clinical research: The Indian perspective. Indian J Pharm Sci 2011;73:125-30.
5. System of prescreening of applications for registration of ethics committees. Available from: http://www.cdsco.nic.in/prescreening_checklist.htm [Last accessed on 2013 Jul 11].
6. Quality Assurance. Accreditation Scheme for National Ethics Research Service. NHS. Available from: http://www.nhmrc.gov.au/_files_nhmrc/file/health_ethics/hrecs/UK_NHS_Accreditation_Process_vers_3_22_05_20082.pdf [Last accessed on 2013 July 12].
7. De Feo G, Chiabrando G, Cannovo N, Galluccio A, Tomino C. Harmonization of the practice of independent ethics committees in Italy: Project E-submission. PLoS One 2012;7:e48906.
8. Hennig W. Bioethics in China: Although national guidelines are in place their implementation is difficult. EMBO Rep 2006;7:850-4.
9. Independent Ethics Committee. Shanghai Clinical Research Center. Available from: http://www.scrcnet.org/IEC_en.asp [Last accessed on 2013 Jul 30].
10. IRBs and Assurances. HHS.gov. US Department of Health and Human Services. Available from: http://www.hhs.gov/ohrp/assurnces/index.html [Last accessed on 2013 Jul 12].
11. Human Research Ethics Portal. National Health and Medical Research Council. Australian Government. Available from: http://www.hrep.nhmrc.gov.au/national-approach [Last accessed on 2013 Jul 12].
12. Ethics and regulatory. Health Research Council of New Zealand. Available from: http://www.hrc.govt.nz/ethics-and-regulatory [Last accessed on 2013 Jul 30].
13. Akabayashi A, Slingsby B, Nagao N, Kai I, Sato H. An eight-year follow-up national study of medical school and general hospital ethics committees in Japan. BMC Med Ethics 2007;8:8.
14. TCPS 2. Tri-Council Policy Statement. 2010. Available from: http://www.pre.ethics.gc.ca/pdf/eng/tcps2/TCPS_2_FINAL_Web.pdf on July 2013 [Last accessed on 2013 July 30].
15. Kim WO. Institutional review board (IRB) and ethical issues in clinical research. Korean J Anesthesiol 2012;62:3-12.
16. Central Drug Standard Control Organization. Gazette Notification, Feb 08.02.2013 (GSR 72(E). Available from: http://www.cdsco.nic.in/ [Last accessed on 2013 Jul 11].
17. Pandiya A. Quality of independent review board/ethics committee oversight in clinical trials in India. Perspect Clin Res 2011;2:45-7.
18. Mukherjee S. Compensation conundrum. Perspect Clin Res 2012;3:4-7.
19. Wolf LE, Zandecki J. Conflicts of interest in research: How IRBs address their own conflicts. IRB 2007;29:6-12.
20. Shetty YC, Marathe PA, Billa GV, Nambiar CP. A study to assess completeness of project application forms submitted to Institutional Ethics Committees (IEC) of a tertiary care hospital. Perspect Clin Res 2012;3:133-8.
21. Kotecha JA, Manca D, Lambert-Lanning A, Keshavjee K, Drummond N, Godwin M, *et al*. Ethics and privacy issues of a practice-based surveillance system: Need for a national-level institutional research ethics board and consent standards. Can Fam Physician 2011;57:1165-73.
22. Fitzgerald MH, Philips PA. Centralized and non centralized ethics review: A five nation study. Account Res 2006;13:47-74.
23. Nowak KS. Bankert EA, Nelson RM. Reforming the oversight of multisite clinical research: A review of 2 possible solutions. Account Res 2006;13:11-24.
24. Chaudhry SH, Brehaut JC, Grimshaw JM, Weijer C, Boruch R, Donner A, *et al*. Challenges in the research ethics review of cluster randomized trials: International survey of investigators. Clin Trials 2013;10:257-68.

How to cite this article: Walanj AS. Research ethics committees: Need for harmonization at the national level, the global and Indian perspective. Perspect Clin Res 2014;5:66-70.

Source of Support: Nil. **Conflict of Interest:** None declared.