Medical Ethics

Ethics committees in India: A study to assess the implementation of registration requirements as per New Drug and Clinical Trial Rules and the scale of standardization

MURUGANANTHAN KRISHNAN, HAJA S. SHERIEF

Ethics committees (ECs) are responsible to safeguard the rights, safety and well-being of all trial subjects of reviewed and approved study/trial protocol, as per set international standards within the Good Clinical Practice (GCP) guidelines of the International Conference on Harmonization (ICH) of Technical Requirements for Registration of Pharmaceuticals for Human use[1] and Declaration of Helsinki.[2] In India, clinical trials (CTs), bioavailability/bioequivalence (BA/BE) study, biomedical and health research are governed by the New Drug and Clinical Trial Rules (NDCT),[3,4] 2019 vide notification number G.S.R.227(E) dated 19 March 2019.

- The ECs related to CTs, BA/BE are registered with the Central Drugs Standard Control Organization (CDSCO), Directorate General of Health Services, India appointed by the Ministry of Health and Family Welfare (MoHFW), Government of India. The registration of an EC for CT, BA/BE is valid for a period of 5 years from the date of its issue, unless suspended or cancelled by the central licensing authority and is to be renewed every 5 years.
- The ECs related to biomedical and health research are registered with the authority designated by the Central Government in the MoHFW, Department of Health Research (DHR) under National Ethics Committee Registry for Biomedical and Health Research (NECRBHR). The provisional registration is granted on receipt of an application which is valid for a period of 2 years. On scrutiny of documents submitted and if satisfied as per requirements, the final registration is granted by the DHR, which is valid for a period of 5 years from the date of its issue, unless suspended or cancelled by the designated authority at the DHR.

The National Ethical Guidelines for Biomedical and Health Research Involving Human Participants by ICMR (2017)[5] recommends that ECs should register with the relevant authority as per the regulatory requirements. It also mentions that the certification and accreditation by ECs are voluntary exercises and help in quality assurance and quality improvement to ensure adherence to best practices in protecting the dignity, rights, safety and well-being of study participants. Accreditation is a long-term strategy.[6,7] The National Accreditation Board for Hospitals and Healthcare Providers (NABH)[8] was set up to establish and operate EC accreditation programmes for the CDSCO registered ECs. The accreditation is valid for a period of 3 years. The EC involved in review and approval of observational studies, registry trials, non-interventional clinical trials/research, biomedical health research are excluded from accreditation.

The NDCT mandates approval from a registered EC for the conduct of CT, BA/BE, biomedical or health research. The list of EC registration and re-registration within the CDSCO (along with the registration and re-registration letter), the list of EC registration with the DHR and accreditation are available in the public domain. We evaluated the status of registered, re-registered and accredited ECs in the country during 2013–2021 to understand the implementation of new requirements on registration of EC as per NDCT 2019 and assess the scale of standardization. We also documented the progress and pattern of registrations and distribution all over India.

METHODS

The EC registered and re-registered from Indian regulatory authority websites—CDSCO,[9] DHR[10]—NAITIK portal (*naitik.gov.in*) and NABH[8] during 2013–2021 were extracted manually. The status of ECs analysed according to the states within the country, type (institution or independent) of EC, year-wise distribution on registration, re-registration and accreditation status to assess the scale of diversity. The data used for this study were obtained from publicly available websites and not linked to any identifiable individual. No explicit individual consent was required. A descriptive analysis was done for the information extracted from different sources using Microsoft Excel.

RESULTS

According to the list of medical colleges approved by the Medical Council of India, dental colleges, hospitals with Diplomate National Board (DNB) courses, hospitals accredited with the NABH, Scientific and Industrial Research Organization (SIRO) recognized by the Department of Science and Industrial Research (DSIR) and Indian Institute of Technology, there are 2414 eligible ECs for oversight of research activities involving

Novartis India Limited, INSPIRE BKC, Bandra Kurla Complex, Mumbai 400051, Maharashtra, India
MURUGANANTHAN KRISHNAN Global Drug Development

Nanda College of Pharmacy, Erode, Koorapalayam 'Pirivu' Pitchandampalayam post, Erode 638052, Tamil Nadu, India
HAJA S. SHERIEF Department of Pharmacology

Correspondence to MURUGANANTHAN KRISHNAN; *murugananthan.K@novartis.com*

[To cite: Krishnan M, Sherief HS. Ethics committees in India: A study to assess the implementation of registration requirements as per the New Drug and Clinical Trial Rules and the scale of standardization. *Natl Med J India* 2023:**36:**109–11. DOI: 10.25259/NMJI_986_21]

human participants. According to the list of ECs registered, 1122 (46%) ECs from these institutions are registered with the CDSCO and 702 (29%) ECs are with the DHR (Table I). The registered and re-registered ECs with the CDSCO, registered ECs with the DHR and accredited ECs across Indian states and Union Territories (UTs) are shown in Table II. Figure 1 shows the trend of registrations and re-registrations of ECs with the CDSCO, during 2013–2021, accreditation of ECs during 2018–2021 and registration of ECs with the DHR during 2019–2021.

Registration and re-registration of EC with CDSCO

About 87% of registered ECs are institutional; the remaining (13%) are independent ECs. Maharashtra and Gujarat lead the list of registered ECs with the CDSCO followed by Andhra Pradesh, Tamil Nadu, Delhi, Karnataka and Kerala.

TABLE I. List of ethics committees (ECs) registered with different agencies

Agency	*n* (%)
Healthcare institutions (medical colleges, dental colleges and hospitals) and medical research institutions	2414 (%)
Registered with CDSCO	1315 (54)
CDSCO—corrected*	1122 (46)
Institutional ECs	973 (87)
Independent ECs	149 (13)
Re-registered with CDSCO	1660
Re-registered with CDSCO—corrected*	1416
Institutional ECs	1286 (91)
Independent ECs	130 (9)
Registered with DHR	702 (29)
Provisional registration (2 years)	675 (97)
Institutional ECs	657 (97)
Independent ECs	18 (3)
Final registration (5 years)	27 (3)
Institutional ECs	26 (96)
Independent ECs	1 (4)
Accredited with NABH	179
Accreditation/certification valid	128
Accreditation/certification expired	14
Provisionally accredited	8
Renewal under progress	19
Suspended/voluntary withdrawal	10

*data extracted from website as of 7 December 2021 and of the EC registration and re-registration certificates uploaded in CDSCO, duplicate entries were removed. CDSCO Central Drugs Standard Control Organization DHR Department of Health Research NABH National Accreditation Board for Hospitals and Healthcare Providers

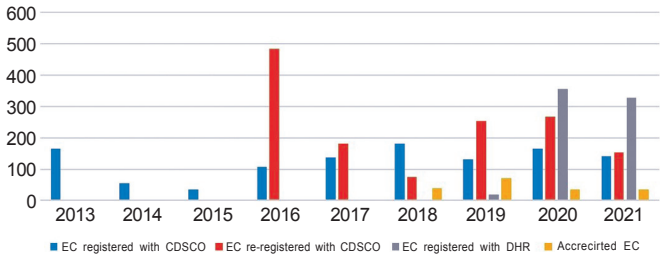

FIG 1. Year-wise ethics committees registered and re-registered with the Central Drugs Standard Control Organization (CDSCO), Department of Health Research (DHR) and accredited ethics committees (EC)

Registration of EC with DHR

About 97% of registered ECs are institutional and overseeing biomedical and health research (i.e. academic clinical trials). The registration of ECs for biomedical and health research under the DHR as per NDCT rules 2019 started with a low proportion in 2019 (18, 2.5%). The registrations peaked in 2020 (357, 51%) and 2021 (327, 46.6%), despite the impact of Covid-19 lockdowns. This depicts the commitment of ECs for regulatory compliance. Other possible reason could also be the need of initiation of biomedical and health research on Covid-19-related studies, which was the need of hour. Maharashtra (114, 16.2%) leads in registration of EC with the DHR for approving biomedical and health research, followed by Tamil Nadu (91, 12.9%), Karnataka (85, 12.1%) and Andhra Pradesh (73, 10.9%). Several states and UTs (Andaman and Nicobar Island, Chandigarh, Daman and Diu, Himachal Pradesh, Jammu and Kashmir, Jharkhand, Manipur, Meghalaya, Mizoram, Nagaland, Sikkim) had less than 5 registered ECs. There were no registered ECs from Arunachal Pradesh, Lakshadweep, Dadra and Nagar Haveli and Tripura.

Accreditation

Only 16% of registered ECs were accredited with the NABH. The accreditation of ECs with the NABH had an impact in 2020 (35, 20%) and 2021 (35, 20%) compared to 2019 (71, 40%) due to Covid-19-imposed lockdown. The slow accreditation may be due to lack of motivation as it is a voluntary self-improvement process, huge workload, lack of dedicated workforce, etc. Maharashtra (53, 29.6%) leads with the most accredited ECs in the country, followed by Karnataka (22, 12.3%) and Tamil Nadu (20, 11.2%). Half the states/UTs (19 states) did not have even a single accredited EC.

DISCUSSION

This is possibly the first effort to profile ECs registered/re-registered with the CDSCO, ECs registered with the DHR and accreditation with the NABH, as per the NDCT. There is lack of clarity on the target ECs operating as the ECs continue their new registrations annually: 142 new ECs registered in 2021, 166 in 2020, 132 in 2019. The registered institutional ECs does not reflect the total number of ECs that exist in the country. The possible reasons could be that few institutions are unaware of the registration requirements or the EC institutionalized considering the demand of research uptake. The registrations and re-registrations of ECs during 2013–18 lost their validity in 2021, considering that their registrations were valid for 3 years. As of December 2021, a total of 1115 ECs possessed valid registrations, i.e. the registered ECs (440) and re-registered ECs (675) during 2019–21 may possess valid registrations.

The data regarding number of applications under review and rejected are missing in the registration of ECs with the CDSCO while registration with the DHR provides a provisional certificate (validity for 2 years) and final registration (valid for 5 years) after scrutiny of applications. The NABH data provide details on application, accredited list and status such as renewal under progress, suspended, voluntary withdrawal and provisional accreditation. The skewed distribution of ECs among states and concentration in certain states suggests that research is under-represented geographically with limited access for patients to participate in clinical trials—particularly for orphan drugs. One of the limitations of our study is that the data and information published on websites of the concerned agencies were analysed,

TABLE II. Accredited ethics committees (ECs) across Indian states and Union Territories

State/ Union Territory	Registered with CDSCO*	Re-registered with CDSCO*	Registered with DHR (provisional+final)	Accreditation with NABH
Andaman and Nicobar Islands	1	0	1	0
Andhra Pradesh	127	121	28	4
Assam	14	13	6	2
Bihar	12	7	4	1
Chandigarh	0	2	2	0
Chhattisgarh	20	7	0	0
Daman and Diu	1	0	0	0
Delhi	94	87	53	12
Goa	9	6	1	0
Gujarat	165	176	44	14
Haryana	20	32	18	5
Himachal Pradesh	3	4	3	0
Jammu and Kashmir	4	2	3	0
Jharkhand	8	3	5	0
Karnataka	84	155	85	22
Kerala	32	89	50	8
Madhya Pradesh	16	21	13	2
Maharashtra	165	309	114	53
Manipur	0	1	2	0
Meghalaya	0	1	1	0
Mizoram	4	0	3	0
Nagaland	0	0	1	0
Odisha	16	24	8	2
Puducherry	5	12	11	1
Punjab	18	26	15	5
Rajasthan	40	51	20	6
Sikkim	1	2	1	0
Tamil Nadu	102	115	91	20
Telangana	49	15	45	6
Tripura	2	0	0	0
Uttar Pradesh	72	66	39	3
Uttarakhand	6	6	5	0
West Bengal	31	63	23	13
Total	1122	1416	702	179

*number represents as per data compilation from the CDSCO website, corrected by deleting duplicate entries of registrations no ECs registered from Arunachal Pradesh, Lakshadweep, Dadar and Nagar Haveli, and Tripura CDSCO Central Drugs Standard Control Organization DHR Department of Health Research NABH National Accreditation Board for Hospitals and Healthcare Providers

which may have incomplete or missing data due to lags in posting information on websites.

NDCT 2019 brought clarity for registration of ECs which review biomedical and health research under the DHR. The registration of ECs with the DHR are positively trending in scale, while accreditation with the NABH was stagnant during the Covid-19 years. The possible explanation for low volume of registered ECs undergoing accreditation needs to be explored with evidence for value proposition of accreditation on quality oversight. The current governance model also imposes on the governing bodies of EC registration to conduct inspections to ensure regulatory adherence and harmonized functioning. Alternatively, the NABH accreditation should be stimulated to strengthen and harmonize EC functioning and quality oversight.

Promoting digital EC functioning in the era of technology may ease the monitoring of EC functioning by regulators. The ECs are empowered for patient protection and quality oversight; hence, capability building to scale up the functioning of ECs in the technological era is the need of the hour.

REFERENCES

1 ICH. The International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use. Guideline for Good Clinical Practice, ICH Available at *https://database.ich.org/sites/default/files/E6_R2_Addendum.pdf* (accessed on 7 Dec 2021).

2 World Medical Association Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects, Available at *https://jamanetwork.com/journals/jama/fullarticle/1760318* (accessed on 7 Dec 2021).

3 Central Drugs Standard Control Organization, New Drug and Clinical Trials Rules 2019, Available at *https://cdsco.gov.in/opencms/export/sites/CDSCO_WEB/Pdf-documents/NewDrugs_CTRules_2019.pdf* (accessed on 7 Dec 2021)

4 Singh N, Madkaikar NJ, Gokhale PM, Parmar DV. New drugs and clinical trials rules 2019: Changes in responsibilities of the ethics committee. *Perspect Clin Res* 2020;**11:**37–43.

5 ICMR, National Ethical Guidelines for Biomedical and Health Research involving Human participants, Available at *https://ethics.ncdirindia.org/asset/pdf/ICMR_National_Ethical_Guidelines.pdf* (Section 4.15, page 48) (accessed on 7 Dec 2021).

6 Ghooi RB. Accreditation—A solution for problems or a fresh problem? *Perspect Clin Res* 2015;**6:**123–4.

7 Potkar C. Accreditation of research in India: One step at a time. *Perspect Clin Res* 2014;**5:**1–2.

8 National Accreditation Board for Hospitals and Healthcare Providers (NABH) Available at *www.nabh.co/ClinicalTrial.aspx* (accessed on 21 Dec 2021)

9 Central Drugs Standard Control Organization, Ethics Committee, Available at *https://cdsco.gov.in/opencms/opencms/en/Clinical-Trial/Ethics-Committee/* (accessed on 7 Dec 2021).

10 Department of Health Research Available at *https://naitik.gov.in/DHR/Homepage* (accessed on 7 Dec 2021).