Review Article

Ethics Committees in India: Past, present and future

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Abstract

Following watershed amendments in Schedule Y India's star rose rather rapidly on the clinical research (especially clinical trials) horizon. Just as dramatic was the fall of this empire. At the centre of these events has been the participant and indirectly, the Ethics Committee (EC) that is established primarily to protect this individual. This paper traces the evolution of the concept of ECs in India, examines the current state of these committees in the country and suggests the way forward.

The Past: The requirement for an EC to oversee clinical research was first made in the ICMR Policy Statement for Ethics published in 1980 and then again in the Schedule Y (1988). Later, both the Amended Schedule Y (2005) assigned regulatory responsibility on the EC and the ICMR Guidelines (2006) described the functioning of ECs. Several challenges including inadequate formal training, contribution from non-technical members, administrative support as well no SOPs and a heavy workload were identified. In the absence of regulatory oversight of ECs, the introduction of the Clinical Trial Registry - India (CTRI) and self-regulation through voluntary accreditation programs brought a measure of accountability and transparency.

The Present: A slew of regulatory reforms led to more than 1000 ECs to be registered with CDSCO although the actual impact on participants' protection and safety of these new regulations still remains to be seen.

Way Forward: A method to oversee all ECs, improved functioning of ECs including on site monitoring, central ECs for multicentric studies, the development of metrics to assess the ability of ECs to protect the participant are other ideas for the future.

Conclusions: Although ECs in India have evolved from being mere rubber stamps for approval of protocols to efficiently functioning accredited ECs, yet there is much to be done for and by Ethics Committees.

Keywords: Accreditation of Ethics Committee, Ethics Committee Registration, research participant, Schedule Y

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INTRODUCTION

With a population of over 1.3 billion and a high disease burden,[1] India must engage in clinical research relevant to its health-care needs to build evidence that drives policy. Yet, this was not so in the past. The National Health Policy of India observed that "In our country, where the aggregate annual health expenditure is of the order of Rs. 80,000 crores, the

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expenditure in 1998–99 on research, both public and private sectors, was only of the order of Rs. 1150 crores. It would be reasonable to infer that with such low research expenditure, it is virtually impossible to make any dramatic breakthrough within the country, by way of new molecules and vaccines."[2]

However, the last decade saw a marked and dramatic change in the landscape. Following watershed amendments in Schedule Y, India's star rose rather rapidly on the clinical research (especially clinical trials) horizon. The country's contribution to global clinical trials grew from 0.9% in 2008 to 5% in 2013.[3] This led to both optimistic forecasts that India could attract up to 10% of the global market of clinical trials,[4] and morose, sometimes crusty observations that India was being colonized again.[5] Reality was somewhere in between as always.

Just as dramatic as the rise was the fall of this empire. At its peak in 2010, the clinical trial industry started floundering with the global economic meltdown[3] and then more perilously in 2013 following the slew of regulatory changes brought about following Supreme Court orders and observations of the Parliamentary Standing Committee Reports.[6,7]

Against this background, it is pertinent to review the status of Ethics committees (EC) that are established primarily to protect a research participant's rights, dignity and ensure her/his well-being. This paper traces the evolution of the concept of ECs in India, examines the current state of these committees in the country, and suggests the way forward. For the purpose of this article, we have divided the decade (2005–2015) into three sections: The past which covers 2005–2013, the present running from 2013 to 2015, and the future after that.

THE PAST (2005–2013)

It was as far back as 1975 when the second revision of the Declaration of Helsinki adopted at the 29th World Medical Association General Assembly in Tokyo recommended, "The design and performance of each experimental procedure involving human subjects should be clearly formulated in an experimental protocol which should be transmitted to a specially appointed independent committee for consideration, comment, and guidance."[8] The Belmont Report issued in 1979 further emphasized the need for review of all clinical research by ECs.[9]

In India, the requirement for an EC to oversee clinical research was first made in the Indian Council of Medical Research (ICMR) Policy Statement for Ethics published in 1980[10] and then again in the original version of the Schedule Y issued in 1988.[11] Schedule Y (1988) mentioned said, "It is desirable that protocols for clinical trials be reviewed and approved by the Institution's Ethical Committee. Since such committees at present do not exist in all institutions, the approval granted to a protocol by the Ethical Committee of one institution will be applicable to the use of that protocol in other institution, which do not have an Ethical Committee. In case none of the trial centres/institutions has an Ethical Committee, the acceptance of the protocol by the investigator and its approval by the Drugs Controller (India) or any officer as authorized by him to do so will be adequate to initiate the trials."

Then, came the Indian good clinical practices (GCP)[12] in 2001, the watershed Amended Schedule Y[13] in 2005, and the ICMR's Ethical Guidelines For Biomedical Research On Human Participants in 2006.[14] Schedule Y (2005) detailed for the first time regulatory requirements of an EC. The ICMR guidelines released by the same Ministry (Health and Family Welfare) a year later described in more detail the composition, roles, and responsibilities of an EC. Some salient differences between these two documents are highlighted in Table 1.

It is interesting to note that both the Amended Schedule Y (2005) and the ICMR Guidelines (2006) referred to "independent ECs (IEC[Ind])" favorably. The Schedule Y clearly stated, "The trial site(s) may accept the approval granted to the protocol by the ethics committee of another trial site or the approval granted by an independent ethics committee (constituted as per Appendix VIII), provided that the approving ethics committee(s) is/are willing to accept their responsibilities for the study at such trial site(s) and the trial site(s) is/are willing to accept such an arrangement and that the protocol version is same at all trial sites"[13] while the

Table 1: Salient differences in Schedule Y (2005) and Indian Council of Medical Research Ethical Guidelines (2006) in the Ethics Committee constitution and functioning

Topic	Schedule Y	ICMR
Number in the committee	At least 7	8-12
Responsibility of EC	To safeguard the rights, safety, and well-being of all trial subjects and particular care to protect vulnerable participants	To review scientific and ethical soundness in addition
Training for members	Not mentioned	Need for periodic training in national and international ethical guidelines and regulations specified
Review procedures	A list of documents to be reviewed given in letter of approval draft	Described in detail

ICMR=Indian Council of Medical Research, EC=Ethics Committee

ICMR Guidelines said, "There are also independent ethics committees (IEC[Ind]) functioning outside institutions for those researchers who have no institutional attachments or work in institutions with no ethics committee."[14] At that time, therefore, there was no limitation to the "IEC(Ind) s" overseeing clinical trials. This aspect bears relevance to the current change in thought at regulatory level about what an IEC(Ind) may oversee.

Functioning of Ethics Committees

Several papers addressed conditions under which ECs functioned in the time before 2013 when the clinical research was booming in the country. Basic issues such as lack of formally trained manpower (leading to mere scientific review), a heavy workload, inadequate space allocated for EC operations, and lack of administrative support were identified as important challenges leading to concerns whether the country was ready to take on a load of research. Infrequent meetings (at times only twice a year!) led to delays in approvals and constrained ECs to initial review and approval of protocols. Continued monitoring was often not undertaken, except for cursory review of serious adverse events (SAEs) and annual reports. The lack of active participation by the nonmedical members in the discussions at the meetings and the absence of standard operating procedures (SOPs) were other issues identified.[15,16] There was no requirement for members to declare conflict of interest which could compromise the functioning of the EC.[17]

In a questionnaire-based study conducted by the ICMR[10] (in which 32 medical colleges and ICMR institutes participated out of 147 approached), it was found that no legal expert was appointed to most committees and appointment procedures were unethical and included lobbying. This survey found that committees reviewed up to sixty projects per meeting and minutes and record keeping was poor.

In 2005, an editorial by Dr. Vasantha Muthuswamy, then the Senior Deputy Director General, ICMR, said, "Many IECs lack the expertise to adequately fulfill the mission of protecting the research participants. In most instances, the ethics approval can be regarded only as a minimal ethical standard for research."[18] This editorial went on to say, "There are no SOPs for these committees which may or may not meet regularly and have varied methods of evaluation and decision-taking process. They end up doing scientific review of the research proposals and scrutinize the consent forms as the only proof of ethical requirement."[18] It was recommended that ethics review mechanisms needed drastic improvement, for India to face the challenge of becoming a "global hub" for clinical trials.

At that time, investigators and sponsors alike considered ECs as obstacles, and in turn, ECs had inadequate or no "teeth" to do what they were supposed to do, which was, protect the research participant!

This did not change even when the number of clinical trials done in India peaked. A survey of 11 ECs revealed a lack of knowledge of Schedule Y among the EC members, coupled with inadequate training in GCP, inability to enlist the essential documents for EC review, and failure to realize the important role of EC approval in clinical research.[19] A suboptimal understanding of ethical issues among members and a need of formal training in ethics along with the need of networking among various ECs were reiterated in a study from Pune.[20]

The observations of the Parliamentary Standing Committee in their report on the human papillomavirus (HPV) vaccine[7] noted that the ECs that oversaw the HPV trials did not meet periodically to assess the progress of the project and review SAE reports. They appeared to exist only as a formality said the report. The Committee strongly recommended that there should be a mechanism in place to take appropriate action against such dereliction of duty on the part of the ECs and that the functioning of ECs should be regularly monitored.

The nontechnical members of an EC are central to its functioning and their contribution is of immense value. A survey among laypersons serving on ECs revealed several of them did not review informed consent documents (ICDs), those who said they did not understand technical terms in the ICDs, and one-third were unaware that their presence was vital for quorum to be met.[21] Other papers have also identified the lack of active participation of nonmedical members in the Committee's deliberations, as well as the fact that they lack training and are diffident.[22,23]

A review[24] identified 31 articles published between 2004 and 2012 related to the topic of the challenges faced while establishing Institutional ECs (IECs) and their functioning. The most common challenge mentioned in these articles was inappropriate functioning of IECs ($n = 17$), followed by inappropriate structure ($n = 14$). Other challenges included lack of oversight by regulatory bodies ($n = 14$) and inadequate training of EC members and investigators ($n = 13$). The need for administrative and financial support to ECs has been a common cry[25-27] as has been the creation of a central registration system.[18]

An important function of an EC is continuing monitoring, which is often passive monitoring, for example, reviewing SAE reports, periodic status reports, and protocol deviations. Active site monitoring was not practiced in the past, and IEC members were not trained to conduct monitoring. The EC of KEM Hospital (Mumbai) conducted seven site visits

during 2008–2009 using a standardized format[28] to monitor adherence to protocol and the informed consent process. The monitoring identified issues related to informed consent (6/7), protocol deviation (5/7), reporting of study progress to the IEC (3/7), recruiting additional participants without IEC approval (2/7), reporting of SAEs (1/7), investigator's lack of awareness of protocol and the ICD.[29]

Oversight of Ethics Committees

In the time before 2013, although the regulator issued inspection plans for sites and sponsors, nothing was forthcoming for ECs. There was no oversight of ECs. A study reported a high degree of noncompliance of study approval letters issued by ECs to the Schedule Y/ICMR guidelines. For example, the quorum was not met (no legal experts and social scientists) in the EC meetings, and the ECs did not review essential documents such as the clinical trial agreement and the insurance policy.[30]

During this time, one important development that brought some transparency to EC oversight was the introduction of the Clinical Trial Registry-India (CTRI).[31] The CTRI was set up in 2007 at the National Institute of Medical Statistics, ICMR, New Delhi, as a free and online system for registration of all clinical trials being conducted in India (http://ctri.nic.in/Clinicaltrials/login.phpd). Since June 15, 2009, the Drugs Controller General of India made registration in the CTRI mandatory for regulatory trials. Although this portal brought in some transparency, information on ECs was often incomplete and did not really achieve any real oversight of ECs.

In the absence of regulatory oversight, self-regulation through voluntary accreditation programs was undertaken by some ECs. Five ECs were recognized by the Forum for Ethics Review Committees in Asia-Pacific (FERCAP) under the Strategic Intiative for Developing Capacity in Ethical Review (SIDCER) Recognition Program in this period.[32] The SIDCER is an initiative by WHO to build capacity in ethics review globally. These included Seth Gordhandas Sunderdas Medical College and King Edward Memorial Hospital's Institutional Review Board (IRB) (Mumbai, 2009, 2012), The IRB, Tata Memorial Centre (Mumbai, 2009, 2012), IEC of Sanjay Gandhi Postgraduate Institute of Medical Sciences (Lucknow, 2011), Institutional Human EC of PSG Institute of Medical Sciences and Research (Coimbatore City, 2012), and IEC, National Institute for Research in Tuberculosis (NIRT), ICMR (Chennai, 2013) and a couple of these were re-recognized 3 years later. The Forum for Ethics Review Committees in India (FERCI) assisted in this effort.

Similarly, three organizations were accredited by the Association for the Accreditation of Human Research Protection Programs (AAHRPP). These included Jehangir Clinical Development Centre Pvt. Ltd., Pune (2012), Kasturba Hospital, Manipal, Karnataka, India (2011), and Manipal Hospitals, Bengaluru, Karnataka, India (2011).[33]

Training efforts

Several organizations have, over the last few years, conducted formal training for members of EC in India. The Indian Society for Clinical Research has established a Training Council which aims to help in capacity building of clinical research professionals (including EC members) on various topics related to clinical research since 2005.[34] Similarly, the Clinical Development Services Agency (CDSA) under the Department of Biotechnology, Government of India, has trained over 4500 EC members since 2009 in about 50 workshops.[35] FERCI[36] is a registered society set up as the national chapter of FERCAP, the latter being an initiative undertaken by WHO TDR (Tropical Diseases Division). FERCI has established a network of ECs in India and has been contributing to training and awareness regarding research ethics through various ventures- freely downloadable detailed model SOPs incorporating current regulations, and holding conferences every alternate year. Recently FERCI in collaboration with PATH (CREaTe – FERCI initiative) has created 5 softwares to facilitate the functions of ECs and trained 23 ECs, which are now named "Smart ECs".[37]

What recommendations were made?

In this period, several articles were written passionately asking for reforms and several solutions[24] were suggested that would improve EC functioning and their oversight. Issues related to constitution of the EC were on the top of the list of challenges that ECs faced, and authors strongly urged institutions to lend the ECs administrative and financial support to enable them to make improvements in their structure.[25-27]

To improve functioning of ECs, the need to have and follow SOPs was stressed.[38] Other suggestions included the need to set up separate scientific review boards,[39] use of checklists for review of protocols,[38] mandatory CTRI registration, and regular monitoring of the study.[22,31] Establishment of EC consortia[40] or a state-level EC to address multicenter studies and minimize "EC shopping" were other suggestions.[15]

A large number of papers addressed the need for training investigators in ethics and research methods.[24] The need to give the ICMR guidelines greater legal authority has been stressed.[38] An interesting recommendation was to make the need for having an established IEC as a prerequisite for Medical Council of India recognition for medical colleges.[25]

THE PRESENT (2013–2015)

The years after 2013 brought much transparency and some control over the constitution and functioning of ECs which were also entrusted with increasing responsibility in regulatory trials. The major drivers for this are the regulatory reforms listed in Table 2.

The major milestone in the history of ECs in India was the requirement of registration with Central Drugs Standard Control Organization (CDSCO).[42] As on August 1, 2016, there were 1083 registered ECs, of which 841 (77.7%) were institutional and 242 (22.3%) were independent.[52] The IECs(Ind) were not allowed to oversee clinical trials - only BA/BE studies were allowed. However, it is not clear whether IECs(Ind) can oversee nonregulatory clinical trials and other observational studies. Incidentally, the time to approval of an EC after application to the CDSCO had a median (range) of 77.5 (24–919) days with a significant difference ($P = 0.002$) between the Institutional 58 (5–919) and IECs(Ind) 165.5 (24–822) days.[53]

Maharashtra has the highest number of ECs registered (259/1083, 23.9%), followed by Gujarat (125/1083, 11.5%) and Karnataka and Tamil Nadu (112/841, 10.3%). The least number of registered ECs is in Himachal Pradesh ($n = 2$) and Jharkhand, Sikkim, and Jammu and Kashmir ($n = 1$ each). Some states and Union Territories, namely, Arunachal Pradesh, Manipur, Meghalaya, Tripura, Andaman and Nicobar, Dadra and Nagar Haveli, Daman, and Lakshadweep, do not have a single EC. A large number of ECs in a single state and lack of even a single one in several others reflect a skewed distribution of research in the country and needs to be addressed by policy makers and organizations such as the ICMR.[54] Another issue of concern is that of the medical colleges approved by the Medical Council of India to conduct postgraduate courses, several do not have registered ECs. Today with academic nonregulatory type of studies needing approval by registered ECs, this will need to change.

Table 2: List of regulations that impacted Ethics Committees

GSR/ notification number	Date	Concerning
GSR 53 E[41]	January 30, 2013	SAE reporting and compensation
GSR 72 E[42]	February 8, 2013	Registration of ECs
Formula[43]	Late 2013	Formula to determine the quantum of compensation in the cases of clinical trial-related SAEs of deaths occurring during clinical trials
Office order[44]	November 19, 2013	AV recording of informed consent
GSR 889E[45]	December 12, 2014	Modification of SAE reporting timelines and care of the participant injured during research
Formula[46]	December 15, 2014	Formula to determine the quantum of compensation in the cases of clinical trial-related SAEs other than deaths occurring during clinical trials
GSR 611 E[47]	July 31, 2015	AV consent in cases of vulnerable population and research on NCEs
GSR 313 A[48]	March 16, 2016	Academic studies on "new drugs" already in the market need IEC approval and notification to DCGI
Addition of new site[49]	August 3, 2016	Only IEC permission required, no DCGI approval needed
Cap of 3 trials per PI removed[50]	August 2, 2016	IEC to determine
Re-registration of ECs[51]	2016	Requirements for reregistration

SAEs=Serious adverse events, AV=Audiovisual, NCEs=New chemical entities, IEC=Independent Ethics Committee, DCGI=Drugs Controller General of India, GSR=General statutory rules, ECs=Ethics Committees, PI=Principal investigator

As has been said above, in the absence of all ECs registering with the CDSCO, the CTRI remains a very powerful source of information and gives a degree of transparency and some accountability to EC functioning. However, a cursory study of the CTRI website for EC information reveals several issues that need to be addressed by the organization. We examined 722 studies registered in the CTRI in 2016 (till August 10, 2016) and found as many as 67.6% (488/722) studies registered retrospectively. Around 488 ECs, 94% (454/488) of which were institutional were overseeing these studies. As many as 211/488 (43.2%) were not registered with the CDSCO. Interestingly, 153 (21%) studies were from the AYUSH sector (whose ECs are not registered with CDSCO). An important finding was that the name of the EC that investigators from the same institution registered in the CTRI varied for different studies. Thus, one institution would have as many as ten "names" for their Institutional Committee making it difficult to draw any conclusion.

On another note, we found that only about 82.4% EC registration approval letters could be downloaded from the CDSCO website.[53] This situation is likely to improve now as the re-registration of IECs is expected to be primarily online.[55] We assessed the effect of these regulations on our IEC and found that although the number of regulatory studies reviewed by our IEC remained the same, the number of studies actually approved decreased with an increase in the turnover time. The administrative workload rose with increased documentation and expenses.[54] We also found a significant effect on SAE reporting![56]

The new checklist for re-registration is stricter in requirements, and it is encouraging to note that training certifications of each member have to be submitted and monitoring has been made a requirement and data of monitoring has to be shown.[51]

The recent registration process of EC by the CDSCO required submission of SOPs (including the need for a separate SOP for handling projects that studied vulnerable populations). We studied SOPs of IECs of ten medical colleges/hospitals that were freely available (on the internet). We do not mention the names of the institutions as this is not an individual critique, but rather an exercise to assess the strengths and areas for improvement that ECs may address when making SOPs. We found that in general all SOPs mentioned a structure and composition that was in general as per the regulations and guidelines; however, only 1/10 stated that the composition would be multidisciplinary and multisectoral, a very important issue that must be adhered to. All mentioned how the EC would be constituted (always appointed by the Director/Principal, and none had these individuals as Chair), but none described the desirable qualities of each member in terms of their functions. Surprisingly, not one had a SOP for writing an SOP! And even more surprisingly, only some actually specified the effective dates (especially validity date). All the SOPs we downloaded were a single document describing the various activities. Only two had "appendices" which were templates for applications or approval letters. Interestingly, only 3/10 mentioned the need for confidentiality and conflict of interest declaration and none had a separate SOP for studies on vulnerable populations in spite of the regulatory requirement.[42] No SOP addressed the way complaints from patients/participants would be handled. In spite of regulatory requirement, only 4/10 mentioned the correct quorum (most said the number but not the expertise that was needed). The way the meeting was to be conducted, and minutes recorded were also poorly addressed. None had any timeline for EC procedures specified. This analysis indicates that although registration has achieved some transparency, there is a long way to go.

The actual impact on participants' protection and safety of these new regulations still remains to be seen although the impact of the regulations on the functioning of ECs is evident with a hugely increased responsibility and workload [Table 3].

Recognition/accreditation systems

While in the earlier years, some ECs did undergo accreditation processes, the numbers increased in the subsequent years. In 2014, the ECs of two ICMR Institutes (Institutional Human EC, National Institute of Epidemiology, Chennai, and the National Institute for Research in Reproductive Health EC for Clinical Studies, Mumbai), as well as IRB, Y.R. Gaitonde Centre for AIDS Research and Education, Chennai, were recognized by SIDCER. Further in 2015, the IEC Fortis Escorts Heart Institute, New Delhi, receieved SIDCER recognition.[32] In 2014, The Sahyadri Hospital Ltd., Pune; St. John's National Academy of Health Sciences, Bengaluru; and the Tata Memorial Centre, Mumbai, also obtained AAHRPP accreditation.[33] Some institutes such as the KEM Hospital, Mumbai, and Tata Hospital have been re-recognized twice more and the NIRT, Chennai, once more. These are encouraging observations that confirm the functioning of these committees along the international standards. The recognition processes have been described to have impacted the functioning of ECs favorably.[57] Each time, an EC gets re-recognized, the bar is set higher, and the quality of human research participant protection improves (personal communication).

WAY FORWARD

What then is the way forward for ECs in India? With increasing responsibility, there is a growing need for improved functioning so that research participants are protected and ethical clinical research, which is the need of the hour in our country, is promoted.

By far, the most important aspect that needs to be addressed is to have in place a method to oversee all ECs - either by voluntary accreditation (as described earlier) processes or by regulatory inspections. The National Accreditation Board for Hospitals and Healthcare Providers, Quality Council of India,[58] in consultation with various stakeholders, has formulated draft accreditation standards for clinical trial sites, ECs, and investigators, and inspectors have been trained. However, the process of mandatory accreditation has not yet started. Accreditation, which is a process meant to continuously improve working of the EC, is best left to be taken up voluntarily and concerns have been described the mandatory accreditation process.[59] The need of the hour is to initiate routine regulatory inspections of ECs. In the meantime, the re-registration process of ECs has begun and this time around the CDSCO is asking for evidence for statements (e.g., training of EC members, monitoring of studies, SAE review details)[51] made in the application form. This itself will impose certain discipline in ECs.

Although, in general, the composition and quorum are maintained in all registered ECs due to the regulatory requirements, the way projects reviewed, approved, and continuously monitored still need attention. The use of checklists is desirable with a better assessment of benefits and risks. This is especially true at continuing review where benefits and risks may change as new data emerges.[38,39]

Continuous monitoring is an activity that ECs do not undertake always. Apart from the review of continuing reports, protocol deviations,[60] and SAEs,[56] ECs must make efforts to conduct on-site monitoring.[29]

High-quality clinical research must be encouraged at postgraduate teaching institutes, and for this, an optimally

Table 3: Evolution of Ethics Committees in India in response to changes in regulatory guidelines (2005-2016)

Function of EC	Amended Schedule Y January 2005	Registration notification by CDSCO (GSR 72 [E]) February 8, 2013[42]	New notifications 2013-2016 (till date)	Re-registration notification by CDSCO February 2016 onward[51]
Training of EC members	Not specified	Made mandatory Policy to be made by EC	-	Proof of GCP training to be submitted
Qualifications of EC members	Not specified	Postgraduate qualification mandatory for medical members	-	No change
Quorum requirements	Stated	Stated	-	No change
SOPs	Need stated Format of approval letter of EC	Soft and hard copies needed Separate SOPs on review of vulnerable populations studies, training and conflict of interest		No change
Informed consent document	Elements needed stated	-	Amended to add patient income and nominee details vulnerable groups[41] Audio-visual recording made compulsory for new drug trials involving vulnerable groups[47]	
Continued EC oversight during conduct of studies	Review through progress report and/or site monitoring	Review through progress report and/or site monitoring	-	Methods used by EC for monitoring clinical trials have to be described, with a brief description
Documentation and record keeping	Need mentioned	5 years archival of EC documents		
SAE reporting	Format of submission form and timelines for investigators and sponsor	-	Procedure for submission by EC added with revised timelines for report submission by stakeholders[41,45] ECs opinion on causality and compensation considered by DCGI[41,45]	SAE review details to be submitted
Study related injury	Requirement for treatment and compensation provision specified	-	Criteria defined for study related injury for eligibility to decide compensation[41] Formulae for calculating compensation amount for the study-related injury for ECs and investigators[43,46]	SAE review and actions - details of medical management and compensation to be submitted
New responsibilities on ECs entrusted by DCGI	-	-	Academic nonregulatory studies for testing off-label indications to be approved by ECs only[48] To decide suitability of investigator, number of trials to be done simultaneously by an investigator[50] To decide suitability of site[49]	

CDSCO=Central Drugs Standard Control Organization, SOPs=Standard operating procedures, GCP=Good clinical practice, DCGI=Drugs Controller General of India, ECs=Ethics Committees, SAE=Serious adverse event, GSR=General statutory rules

functioning EC is needed. Institutes must encourage the setup of such ECs which have infrastructural and financial support from the Institute while having an internal audit mechanism in place for the EC.[54]

The concept of having a central EC for multicenter studies was suggested some years ago with cogent arguments in favor, to improve ethical oversight and minimize the variability that arises out of multiple ECs overseeing the same protocol.[61,62] This idea is supported by the US Food and Drug Administration and Office for Human Research Protections.[63,64] This is something India needs to consider. However, local sociocultural issues including review of consent forms in regional languages will have to be deliberated by local ECs at the site.[65] And finally, what is paramount is to see whether ECs function to achieve their primary objective - that of protecting the research participant. It has been said before that while we have tools to assess whether ECs adhere to policies and SOPs, there are not adequate tools to assess whether ECs actually protect participants.[66] The IRB Researcher's Assessment Tool (RAT) is one such tool,[67] which has been used in Gujarat to assess the functioning of the IECs at two medical colleges.[68]

CONCLUSIONS

We have seen in this paper that ECs in India have evolved from being mere rubber stamps for approval of protocols

to efficiently functioning accredited ECs. Yet, considering the vastness of the country and the teeming population demanding quality research to generate evidence that will assist policy decisions, the need for unbiased, peer supervision of this research by efficient and regulated ECs is undoubted. Clearly, there is much to be done for and by Ethics committees.

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