Addressing challenges faced by trial sites and investigators

Clinical research, including clinical trials, done appropriately, helps advance science and improves treatments. It is also important that during such research, the safety, well-being, and confidentiality of participants are protected and that the data integrity is maintained. Besides the research participants, investigators, regulators, and the government, the society at large is also an important stakeholder in clinical research. Thus, the society and the public at large require an assurance that the research being carried out is of the highest quality and that while pursuing research, adequate guarantees are provided for the protection of research participants’ rights, health, and well-being.

The committee under the chairmanship of Dr. Ranjit Roy Chaudhury was established to formulate policy guidelines for approval of new drugs, clinical trials, and banning of drugs. It recommended, among other things, that the Quality Council of India (QCI) proposes a system for accreditation of investigators, research sites, and ethics committees. Such a system is expected to establish norms or standards for conducting various research-related activities and oversee the functioning of investigators, research sites, and ethics committees through periodic assessments. The National Board for Hospitals and Healthcare Providers (NABH) published Accreditation Standards for Ethics Committee, Investigator, and Clinical Trial Sites. This document described standards for six areas: infrastructure and facilities; qualification, experience, and training of investigators; site standard operating procedures (SOPs); protection of participants’ rights, safety, and well-being; clinical trial materials, documentation, and IT systems; and clinical trial oversight.

This issue of the journal carries an interesting article regarding the challenges faced by investigators and the compliance of clinical trial sites with the draft QCI guidelines. As conceded by the authors, the study findings do not represent the situation in the whole country, as the study enrolled only thirty investigators from a single city in the country. It could, however, be argued that the study findings probably projected the best possible situation in the country at the time the study was conducted (2016–2017), as it enrolled only qualified investigators experienced in conducting several regulatory studies. Furthermore, no site verifications or inspections were conducted to determine the actual situation at trial sites. The study findings do not paint an encouraging picture, to say the least.

The authors have presented the data regarding key challenges faced by investigators in terms of frequency of occurrence. For example, under the “infrastructure space” theme, six issues were listed and a total of 39 responses were obtained from 29 investigators. “Archival” was marked by 10 investigators, and the authors have rightly chosen to state that “archival” accounted for 25% (10/39) of the total frequency under the theme. However, another way of looking at the same data could be that 10 out of 29 investigators, that is, 34.5% of investigators, reported “archival” as a challenge. Whichever way one looks at the data, it shows that investigators are facing great difficulties while conducting research. The main issues flagged by investigators included (with percentage of investigators reporting the issue mentioned in parentheses):

- Space constraints: For archival (34.5%), obtaining consent (31%), follow-up (24.1%), medical care (17.2%), and document storage (24.1%)
- Equipment: Lack of validation of laboratory procedures (20.1%) and no system for regular maintenance and calibration (16.7%)
- Staff: Staff shortage (48%), less experienced staff (52%), and high attrition and turnover (56%)
- SOPs: Training of staff only during violations (32%)
- Safety management: No intensivist in the team and serious adverse events (SAEs) reported late (18.2% each)
- Informed consent process and its documentation: Inability of participants to understand technical language (64%), no documentation of a copy of Informed Consent Document (ICD) being given to the participant (39.1%), and wrong version of the consent form used (21.7%)
- Clinical trial documentation: Incompletely filled documents (20%), no internal monitoring (23.3%), and no provision for data retrieval (23.3%).

Some of the observations in the study are perplexing. Every investigator (who responded to the theme of infrastructure space) flagged space constraint for one or the other research-related activity. This is to be expected, as all the investigators were working in Mumbai, where space is available, only at a premium. However, while answering...
the “checklist,” 83% of investigators stated that they have adequate space for the conduct of clinical trial! It is noteworthy that 21% of investigators reported no issues pertaining to equipment. Similarly, a proportion of investigators reported no issues pertaining to staff (20%), SOPs (36%), safety management (59.1%), informed consent process (12%), and documentation (43.5%).

The authors have rightly surmised that many of these issues can be addressed if institutions provide greater support to their research investigators. Many managers see patient care as the main, if not the sole focus, of the institutions they manage and relegate research to a subsidiary status. This mindset has to change and institutions should provide for basic infrastructure, adequate support staff, and appropriate training for those assisting in and conducting clinical research. However, investigators also need to fasten their seat belt. Late reporting of SAEs, incomplete documentation, use of inappropriate version of the informed consent document, among others indicate deficient supervision over and/or inadequate training of junior colleagues. They should also take the initiative for formulating and updating SOPs and for training their staff in the implementation of the SOPs. The investigators can ease some of the constraints by collaborating with other investigators in the institution by sharing resources such as space and staff. Some investigators cited “research participants not being able to understand the technical language in the ICD” as a key challenge. This is surprising as the investigators should be involved in the drafting of ICDs, as it is the investigators who know the educational and social characteristics of the population from which study participants are enrolled. Hence, they should take the initiative to amend the ICD template provided by the sponsors and decide the appropriate content of the ICD for their site. It is also astonishing that none of the investigators mentioned “time constraints” (maybe it was not even listed), as one of the challenges. I suspect that at least some of the issues are related to time constraints and this is because the senior consultants and faculty have to participate actively in patient care, educational and administrative activities, as well. In any case, investigators should ensure that, despite various constraints, they conduct research that does not compromise the science, data integrity, and most importantly, the safety and well-being of the participants.

Many observations in this study, in fact, raise concerns pertaining to participant safety and well-being (36.7% of investigators reporting lack of equipment for routine medical assessment and devices for emergency treatment and management), respect for participant autonomy (reporting of participants not understanding the technical language in the participant information sheet, use of incorrect version of the informed consent document, and lack of documentation of a copy of ICD being given to research participants), participant privacy (space constraints for obtaining consent), quality of laboratory data generated (issues related to laboratory procedures not being validated and no regular calibration of equipment) and data integrity (incompletely filled study documents, no internal monitoring, and no provision for data retrieval). From the data, we do not get any idea, as to whether these issues occurred occasionally or frequently. Furthermore, these observations were made more than 4 years ago, and it is hoped that the situation has improved due to various initiatives (formulation of the National Ethical Guidelines for Biomedical Research And Health Research involving Human Participants, implementation of the New Drugs and Clinical Trials Act, mandatory registration of ethics committees and prescription of mandatory training requirements for researchers, etc.) taken by the institutional ethics committees, regulatory bodies, the Indian Council of Medical Research, and the Government of India.

A survey of the functioning of at least a representative sample of research sites in the country needs to be carried out. The survey findings will be useful not only for the concerned sites but also for the institutions to focus on areas of deficiency and plan and implement corrective measures. The NABH has undertaken accreditation of ethics committees on a voluntary basis.[8] The time has come to take the process forward by initiating a similar process for research sites and investigators. In fact, the accreditation process may be supplemented with a grading system. Accreditation process that involves interviews, inspection, and review of documentary evidence helps the participants in identifying the areas requiring correction, and it also provides a public assurance about the quality of the processes implemented.[8] A grading system can stimulate the participants (whether ethics committees, investigators, or sites) in seeking higher grades through improvement in their functioning. It is true that accreditation will not address all issues and lacunae. However, when combined with other actions such as greater institutional commitment to quality research, improving oversight, and periodic training, one can expect considerable improvements in the way research is conducted in the country.
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