Need for revision: EC process, members’ training, and compensation formula in the New Drugs and Clinical Trials Rules 2019

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Abstract

The New Drugs and Clinical Trial Rules (NDCTR) came in force in 2019, these brought in some changes, but certain earlier parts, such as Rule 122 DAB, were incorporated unchanged. A few sections of the NDCTR are problematic and need revision for the smooth conduct of clinical trials in India. Training of Ethics Committee (EC) members and other stakeholders is a very important driver for clinical research but has not been defined clearly. In addition, some processes of EC review need a relook. Compensation formulae were finalized in 2013; now, the altered economic situation has eroded the value of money. Hence, for the protection of research participants, an urgent review of the compensation formula is suggested.

Keywords: Approvals, compensation, ethics committee members, inflation, training

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Quick Response Code: www.picronline.org

How to cite this article: Ghooi RB. Need for revision: EC process, members’ training, and compensation formula in the New Drugs and Clinical Trials Rules 2019. Perspect Clin Res 2022;13:129-31.
This rule, finds support from all quarters, since the training of members of the EC is essential to make the EC competent to fulfil its mandate. However, in the past 2 years, the Central Licensing Authority (CLA) has made no recommendations about the contents, nature, or frequency of training nor has it identified any organization, institute, or body who is authorized to impart the training. This leaves ECs in a dilemma as to how to get their members trained. Sporadically, the Indian Council of Medical Research (ICMR), Clinical Development Services Agency (CDSA), and Central Drugs Standards and Control Organization (CDSCO) do conduct some training, but since the CLA has not recognized any of these as training organizations, on paper at least members of ECs are untrained.

CDSA that is an extramural unit of the Translational Health Science and Technology Institute has prepared a scheme for training all stakeholders of research. The scheme known as GCPs Professional Certification Scheme has laid down the minimum competencies for stakeholders, their training, and certification. It proposes recognition of organizations/institutes with adequate infrastructure, personnel, and processes as Training Institutes and Personnel Certification Bodies. On initial examination, the scheme seems a good one and could be implemented, with minor changes. However, there has to be support from the CLA in terms of approval and recognition of the scheme.

The entire scheme is going to require significant inputs in the form of time, effort, and finance to become successful, and it is expected that the implementation of the scheme will enhance the competence of all stakeholders. The scheme will have a snowball effect on the quality of clinical research, which would help this sector to grow parallel to other sectors. The progress of the country is there for all to see, and clinical research sector can ill afford to lag behind. However, it becomes very difficult to convince organizations to adopt a scheme that does not have CLA’s stamp of approval. In the absence of any proactive support from the CLA, training of EC members and growth of clinical research will remain a nonstarter.

In the past 5 years, ECs, NABH, and the assessors have spent a large amount of time and effort to complete accreditation of 10.8% of reregistered ECs. However, there is not a word from the CLA whether accreditation is mandatory, necessary, or even desired. In this situation, it is surprising that even 10.8% of the country’s ECs opted for accreditation; had the CLA made this mandatory, ECs across the country would have been in a higher plane of activity.

The part of the NDCTR that needs a relook is Rule 25 (iii). The sub rule is a puzzle; it states as follows:

_in case an EC of a clinical trial site rejects the approval of the protocol, the details of the same shall be submitted to the Central Licensing Authority prior to seeking approval of another EC for the protocol for conduct of the clinical trial at the same site;

The EC has the responsibility of protecting research participants, which it does by reviewing all documents of the study and gauging the suitability of the site and the investigator to conduct the study. Our own experience is that for most ECs, approval of proposals is the norm. Proposals are rarely rejected, and when they are, it is for a very good reason. Rule 25 (iii) allows an unrelated (external) EC to override the decision of the original EC. This should be conditional, depending on the reason for rejection, and No Objection Certificate from the original EC should be required. If the institutional EC has found the proposal unsuitable on merits, then another EC cannot decide otherwise. Such action will run contrary to the principle that the EC must protect the rights and well-being of participants. It is suggested that this subrule be modified urgently.

The third issue we would like to point out regards compensation for trial-related injuries and death. Compensation is a very controversial issue, and there is little consensus on whether it should be paid or how it should be calculated.[6,7] There have been fears that compensation rules will hit clinical research hard and will make India a less attractive destination for research.[7] Many ECs are unclear about causality assessment and the assessment at best is subjective.[7] The most important formula is the one that is used for compensation for trial-related death, compensation for nonfatal injuries is derived from the formula for death. The formula for calculating compensation has three factors in the nominator and one factor in the denominator. The base amount (Rs. 8.0 lakhs), along with an age-dependent factor (F) and a risk-related factor (R) form the nominator while the denominator is 99.37.
The base amount chosen was fixed at Rs. 8.0 lakhs, considering that if the compensation so calculated were to be invested in a fixed deposit, it would yield an annual interest that would be adequate for survival. This formula was developed in 2013, but unfortunately, it has no mechanism to compensate for inflation. The value of money, we all know, changes with time because of this culprit. The value of the base amount of Rs. 8 lakhs has gone down significantly and now it is equal to only Rs. 5.3 lakhs. This means that because of inflation, compensation for the loss of a human life is now 66% of what it was in 2013. Although the maximum and minimum amount of compensation that is paid for a trial-related death of a participant remains at 73.59 and 4.0 lakhs, respectively, the value of the money is less today.

The reigning interest rate in 2013, when the formula was proposed and implemented was 9% (maximum rate offered by State Bank of India for a fixed deposit of 10 years to a senior citizen). However, the maximum interest rate payable by the same bank under identical conditions is now 6.3%. The compensation amount when kept in fixed deposit, thus yields 30% less interest. The compensation for life thus suffers a double whammy due to fall in the value of money and interest rate. If the interests of research participants are to be protected, there is an urgent need to update the compensation formula.

Biomedical and health-care research is guided by the National Ethical Guidelines for Biomedical and Health Research ICMR (2017), and not the NDCTR. The compensation guidelines for research-related injury are similar, although no details are provided for the calculation of the same. Admitted that the risk of research-related harm is much lesser in biomedical and health research than in drug trials, yet how the investigators are going to make the resources available for reimbursement of medical expenses or compensation is not clear. Finally, since biomedical and health research studies do not come under the CDSCO, one wonders whether the EC’s orders for the payment of compensation will be obeyed and what can be done if the sponsors/investigators flout the EC orders.

The last issue that needs attention is the need for insurance in clinical trials. Insurance protects the sponsor and also helps the participant get reimbursement or compensation in a time-bound manner. The absence of insurance could be used by sponsors as an excuse to delay payments; hence, ECs insist on insurance details while reviewing proposals. In some trials (dermatological and nutritional), the risk of injuries is extremely low. Here, the insurance premia far exceed the total reimbursement or compensation ever required to be paid. In these situations, trial insurance becomes an unavoidable burden for the sponsor. However, NDCTR is quiet about insurance, is it compulsory or not? The word “insurance” appears only once in the NDCTR, and that too in the format for EC’s letter to the investigator.

The authorities may argue that since it is not specified that insurance is compulsory, no further clarification is necessary. However, since there is confusion in the minds of EC members, a clarification will inspire confidence among them. After all, the purpose of the rules is to improve the clinical research process; anything that helps toward this goal should be done by the regulators, who are important stakeholders.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

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