Clinical trial agreements and insurance policies – role of the EC

The World Medical Assembly, at its 29th meeting in Tokyo, suggested that "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"; thus, paving the way for the establishment of the Institutional Ethics Committee (IEC), whose principal responsibility is to protect the rights and well-being of the research participants.[1]

Over the last 45 years, the IEC has evolved into an important body that is essential for clinical research. The scope and powers of the IEC have grown substantially, and more documents have been added to those initially envisaged for review, including clinical trial agreements and insurance policies. No doubt, the increase in documents has increased the workload of the ethics committee, but as it has led to increase in the protection of participants, it is justified. This issue of the journal publishes a paper from Dr. Kalikar and her colleagues of the All India Institute of Medical Sciences, Nagpur, on the review of Clinical Trial Agreements and Insurance policies of trials by their Ethics Committee.[2]

Clinical Trial Agreements are documents, drafted by lawyers, and usually signed by three parties, the sponsor, investigator, and the site. These agreements spell out the responsibilities of each of the parties, detailing all financial arrangements. Most EC members find these agreements intimidating since they contain legal language, however, the legal expert of the EC can decipher them easily. The main concern of the EC is whether the Clinical Trial Agreements (CTAs) have requisite clauses defining the sponsors' responsibility toward participants. As per Chapter VI of the New Drugs and Clinical Trial Rules 2019 (NDCTR), the sponsor is responsible for reimbursement of medical expenses or compensation for trial-related injuries.[3]

Legal experts assure that the provisions of the NDCTR are binding on the sponsor, whether or not these are clearly spelt out in the CTA. Irrespective of what may be stated in the CTA, the law of the land supersedes all agreements. Yet, the ECs' concern on behalf of participants is real since faulty CTAs could delay the payment to participants. It is heartening that no sponsor can take shelter of a faulty CTA to deny these payments, as protections granted by law cannot be diluted by agreements. The CTA also spells out the responsibilities of the sponsor toward the investigator and the site, which need a thorough review since the NDCTR does not provide any protection in case of faulty CTAs.

Clinical trials are expensive to conduct, and expenses such as reimbursements and compensation for trial-related injuries are difficult to budget for. These are therefore billed on a "pass-through" basis. To offset these unforeseen costs, the sponsors insure the trial (and participants) depending upon risk perceptions. The International Council on Harmonization Guideline (E6R2) recommends insurance to protect investigators and sites against claims from participants.[4] The NDCTR no longer specifies that clinical trial insurance is compulsory, something that Schedule Y once did. In the past, Schedule Y made a special mention of trial insurance, but this appears to have been dropped in the current regulations.

The need for insurance of clinical trials (or participants) seems very logical, but is it legally essential? Different stakeholders have different views. Insurance companies and brokers suggest that insurance provides a cover against legal liabilities[5] and have made model trial policies available.[6] They, however, refrain from commenting on the requirement of clinical trial insurance by law. European rules require insurance for clinical trials,[7] but rules differ in different states of the US,[8] leading to confusion rather than guidance.[9]

Clinical trials in India are conducted under the NDCTR that puts the onus of payment of reimbursement or compensation squarely on the sponsor stating "….trial subject shall be provided financial compensation by the sponsor or its representative…." The sponsor has the choice to pay from his own resources for these or may recover these costs from the insurer if an insurance policy exists. The regulator does not seem to be concerned how the sponsor protects himself against these expenses. This is good for trials in which very few SAEs are expected,

where the insurance premia often exceed the total costs on account of reimbursements and compensation for trial-related injuries. High insurance costs have been blamed for the fall of trials in Europe too.[10]

The ICMR guidelines do make many references to insurance, but the overall impression is that the investigator/researcher should have the resources to pay for research-related harm. Section 2.6.4 of the Guidelines state "It is the responsibility of the host institution to provide compensation and/or cover for insurance for research-related injury or harm to be paid as decided by the EC."[11] Thus, in biomedical and health research too, there is no clear-cut requirement to have trial insurance, so long as the investigator meets the expenses of reimbursement or compensation.

A detailed understanding about the CTA and insurance is very essential for EC members and investigators. At present, the trial rules are very clear and protection of the participants is ensured by the rules under which clinical trials are conducted. Investigators and sites need to be very cautious about the clauses in the CTA since their interests are at stake. EC members need not be unduly disturbed about insurance since sponsor's responsibilities are defined by NDCTR, and the presence of absence of insurance policies has little impact on participants.

In the current paper,[2] the authors have found that the responsibilities of the parties were specified in most (97%) CTAs, though scope of agreement features only in 21% of cases. Insurance policies were more complete and 88.5% provided details of the type of injuries covered, while 91% had details of the period of cover. The results of the study suggest that insurance companies are more careful in preparing policies while CTAs could be improved. The observation of the authors should give a lot of confidence to investigators and EC members but remind them to read the documents carefully before approving them.

Ravindra Bhaskar Ghooi

Scientia Clinical Services, Pune, Maharashtra, India

Address for correspondence: Dr. Ravindra Bhaskar Ghooi, Scientia Clinical Services, E 516, The Island, Wakad, Pune - 411 057, Maharashtra, India.
E-mail: ravindra.ghooi@gmail.com

REFERENCES

1. World Medical Association, the Declaration of Helsinki; 1975. Available from: https://www.wma.net/what-we-do/medical-ethics/declaration-of-helsinki/doh-oct1975/. [Last accessed on 2022 Feb 03].
2. Kalikar MV, Dakhale GN, Sinha VV, Giradkar AB. Analysis of clinical trial agreement and insurance policy submitted to the ethics committee of a tertiary care teaching institute in central India. Perspect Clin Res 2022;13:151-4.
3. CDSCO, New Drugs and Clinical Trail Rules; 2019. Available from: https://cdsco.gov.in/opencms/export/sites/CDSCO_WEB/Pdf-documents/NewDrugs_CTRules_2019.pdf. [Last accessed on 2022 Feb 03].
4. European Medicines Agency, ICH E6 R2 Good Clinical Practice. Available from: https://www.ema.europa.eu/en/ich-e6-r2-good-clinical-practice. [Last accessed on 2022 Feb 03].
5. Howden Insurance Brokers India Pvt. Ltd., Clinical Trial Liability. Available from: https://www.howdenindia.in/Products-Services/Liability/Clinical-Trial. [Last accessed on 2022 Feb 03].
6. Raheja QB. Clinical Trials Insurance Policy. Available from: https://www.irdai.gov.in/admincms/cms/Uploadedfiles/NLP1516/68.pdf. [Last accessed on 2022 Feb 03].
7. Minacori R, Sacchini D, Cicerone M, Spagnolo AG. Insurance and clinical trials. Contemp Clin Trials 2012;33:573.
8. Baquet CR, Mishra SI, Weinberg AD. A descriptive analysis of state legislation and policy addressing clinical trials participation. J Health Care Poor Underserved 2009;20:24-39.
9. Obeng-Gyasi S, Kircher SM, Lipking KP, Keele BJ, Benson AB, Wagner LI, *et al.* Oncology clinical trials and insurance coverage: An update in a tenuous insurance landscape. Cancer 2019;125:3488-93.
10. Avilds MR. Compensation of research-related injuries in the European Union. Eur J Health Law 2014;21:473-87.
11. Indian Council of Medical Research, National Ethical Guidelines for Biomedical and Health Research Involving Human Participants. ICMR; 2017. Available from: https://main.icmr.nic.in/sites/default/files/guidelines/ICMR_Ethical_Guidelines_2017.pdf. [Last accessed on 2022 Feb 03].

Access this article online

Quick Response Code:

Website: www.picronline.org

DOI: 10.4103/picr.picr_271_21

How to cite this article: Ghooi RB. Clinical trial agreements and insurance policies – role of the EC. Perspect Clin Res 2022;13:121-2.

Received: 31-12-21, **Accepted:** 20-01-22, **Published:** 30-06-22.