

A REVIEW ON CURRENT STRATEGIES OPTED BY REGULATORY BODIES FOR INDIAN CLINICAL TRIALS

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ABSTRACT

Currently India is the major hub of Asian country which conducts various multicentre clinical trials. The conduct of these clinical trials is being critically reviewed at both national and international platforms. The Regulatory Bodies of India is upgrading the quality of the Clinical trials to meet up the international standards. It is essential that now all clinical trials conducted in India should as per the International conference of Harmonization-Good Clinical Practices Guidelines (ICH-GCP) for clinical trials and follow the recently amended Schedule Y of the Drugs and Cosmetics Act. The regulatory guidelines in terms of serious adverse events (SAEs) reporting, audio-visual (AV) consulting, informed consent, compensation in case of injury or death in clinical trials have been currently modified. This article provides an

insight into the recent changes with respect to the regulations of clinical trials and its impact on the clinical research industry in India.

KEYWORDS: Regulatory bodies, Clinical Trial, DCGI and CDSCO.

INTRODUCTION

❖ Regulatory bodies involved with clinical trials in India

The key responsibility of Regulatory bodies in clinical trials is to ensure quality drug supply and maintaining health and well-being of trial participants. In India, the central government's Central Drugs Standard Control Organisation under the Ministry of Health and Family Welfare(headed by the Drug Controller General of India) develops standards and regulatory

measures for drugs, diagnostics and devices; lays down regulatory measures; and regulates the market authorisation of new drugs as per the Drugs and Cosmetics Act.^[1]

The CDSCO office regulates the clinical trials via its central office at New Delhi and four zonal offices situated at Mumbai, Chennai, Kolkata and Ghaziabad.^[2] These zonal offices work in close collaboration with the state offices to bring about uniform enforcement of the regulations imposed by the central government. Some of the important rules that regulate clinical trials in India include.

a) Schedule Y of Drugs and Cosmetic Act and Rules (Amended in 2005): These are the requirements and guidelines for permissions to import and manufacture new drugs for sale or to undertake clinical trials.^[3]

b) GCP guidelines issued by CDSCO in 2001: These guidelines specify - the design, conduct, termination, audit, analysis, reporting and documentation of the studies involving human subjects. They ensure safety and well-being of subjects and verify the authenticity of the data being generated. They must be followed at all stages of drug development.^[4]

c) Ethical guidelines for Biomedical Research on Human Subjects by ICMR (amended in 2006): They lay down the principles of essentiality, voluntariness, non-exploitation, privacy and confidentiality of subjects.^[5]

Despite having many principles and bodies to regulate clinical trials, nothing much is seen in practice. The 59th report of Parliamentary Standing Committee on Health and Family Welfare stated gross lack of qualified staff, lack of co-ordination between various agencies, improperly conducted trials for 39 drugs and 33 new drugs approved without conducting clinical trials on Indian patients in the period of January, 2008 to October, 2010.^[6]

This report opened the eyes of the regulatory bodies and various amendments are applied to make conduct of clinical trials more stringent, reliable and transparent in India. This might have not have helped with the number of clinical trials but protecting the rights of the subject has gained supremacy.^[7]

❖ Need for Amendments in Guidelines

The conduct of clinical trials in India has been critically reviewed at national and international platforms. The media outcry over trials being conducted unethically, gross

negligence of the sponsor and its representatives to provide the free medical treatment and adequate compensation to subjects for trial related death(s) and injuries have negatively impacted on the industry. Much of what has happened is unfortunately the aftermath of unsatisfactory performance of all stakeholders of clinical trials, i.e., the sponsor, investigator, Ethics Committee and the regulatory authority.

Accordingly, Central Drugs Standard Control Organization (CDSCO) introduced several amendments in the Schedule Y of drugs and cosmetic rules with a view to regulate the quality of trials conducted in India. All stakeholders of clinical trials should welcome these recent amendments as this is a sincere attempt to improve the quality of clinical trials and to ensure that the rights, well-being and safety of trial subjects are upheld.^[8] The salient recent amendments in Gazette Notifications pertaining to clinical trials include.

- 1) AV Consenting Rule - GSR 611 (E) Released.
- 2) Drugs and Cosmetics (5 Amendment) Rules 2015.
- 3) Amended compensation rule – GSR 889 (E) Released.
- 4) Draft Drugs and Cosmetic (AMENDMENT) BILL, 2015.
- 5) Drugs and Cosmetics (Third Amendment) Rules 2015.
- 6) Drafts Standards and Application format for accreditation of Ethics Committee, Investigator and clinical trial site.
- 7) Presubmission meeting proposed to be initiated by Central Drugs Standard Control Organisation (CDSCO).

1) AV Consenting Rule - GSR 611 (E) Released

- Central Drugs Standard Control Organisation (CDSCO) has issued amended AV consenting rules and addition of essential elements in Inform consent documents.
- As per GSR 611 (E): AV recording will be applicable in case of New chemical entity or New Molecular entity including procedure of providing information to subject and his understanding on such consent, shall be maintained by the investigator for record.
- Notification also provides better clarity for Anti HIV and Anti Leprosy drug i.e. only Audio recording will be applicable.^[9]

2) Drugs and Cosmetics (5 Amendment) Rules 2015

- Draft amendment of D and C rules as per GSR 611 (E) has been released by CDSCO

- The amendment substitute “Essential Elements” of Inform consent documents regarding Failure of treatment and Placebo control trial.^[9]

3) Amended compensation rule – GSR 889 (E) Released

- Central Drugs Standard Control Organisation (CDSCO) has issued amended compensation rules providing more clarity on the definition of the term “related to clinical trials (CT)”
- Clarifications provided for serious adverse event (SAE) reporting timelines to specify that in case of SAE not reported within 24h of occurrence, the investigator needs to provide reasons for the same
- Notification also provides better clarity on various other aspects of the compensation rules, the gazette notification can be accessed at following.^[10]

4) Draft Drugs And Cosmetic (AMENDMENT) BILL, 2015

- Draft Drugs and Cosmetics (Amendment) bill 2015 has been released for public comments
- The bill makes the provision for CT under Drugs and Cosmetics Act.
- Provisions also made for import, manufacture and CT with devices.
- The bill also makes the provisions for CT with cosmetics.
- Penalties have been proposed for various offences like conduct of CT without permission from licensing authority and Expert Committee (EC), violation of conditions of clinical trial permission, not providing compensation, etc.
- Bill makes the provisions for appeal mechanisms for parties aggrieved by the orders under the amended act as well complete draft of the bill can be accessed at the following.^[11]

5) Drugs and Cosmetics (Third Amendment) Rules 2015

- Draft amendment of D and C rules as per GSR 69(E) has been released by CDSCO.
- The amendment omits Rule 122DAA which defines a clinical trial and the definition of clinical trial has been provided as part of the explanation to Rule 122DA.
- The amendment also defines certain terms such as global clinical trial (GCT), IND and new chemical entity (NCE) as part of the explanation to Rule 122DA along with definition of CT.

- Amendment makes the provision for providing information regarding “assessment of risk versus benefit to patients,” “innovation vis-à-vis existing therapeutic option,” and “unmet medical need in the country” mandatory as part of form 44 and Appendix I of Schedule Y.
- Draft notification can be accessed at following.^[11]

6) Drafts Standards and Application format for accreditation of Ethics Committee, Investigator and clinical trial site

- CDSCO has issued draft standards for accreditation of EC and sites as per recommendations of an EC under the Chairmanship of Prof. Ranjit Roy Chaudhury.
- The Ministry of Health and Family Welfare decided to assign the job of accreditation to Quality Council of India.
- The Accreditation Standards and format for application for Accreditation prepared by Quality Council of India are uploaded on CDSCO website for comments/suggestions of stakeholders.
- Accreditation standards and formats can be accessed at following.^[13]

7) Presubmission meeting proposed to be initiated by Central Drugs Standard Control Organisation (CDSCO)

- CDSCO has decided to introduce a system of formal Pre submission Meetings of applicants with CDSCO officers and subject experts to discuss regulatory pathway in respect of specific application for approval of clinical trial, new drug, medical device etc.
- The system will facilitate to understand the regulatory pathways required to be followed by the applicants for approvals resulting in bringing transparency, accountability, predictability, and speedy disposal of cases.
- Notice inviting comments for the proposal was issued by CDSCO, the same can be accessed at following.^[14]

❖ CONCLUSION

The recent regulatory amendments call for a fresh breath of air in the clinical research industry gripped by ethical issues and non-transparency. The clinical investigators, sponsors and regulatory bodies play a critical role in ensuring high quality studies. The road has been bumpy and there are lots of hurdles to maintain the patient safety with high quality standards.

All that can be expected in the coming few years are more refinements to cover the loopholes in the regulations to make India a trial and patient friendly global destination.

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