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Regulatory Insight

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New Drugs and Clinical trials Rules, 2018

GEOGRAPHY
India

SECTOR
Medicine (Drugs)

SUB SECTOR
Pharmaceuticals

CATEGORY
New drugs, Clinical trials, Bioavailability, Bioequivalence, Ethics committee

REGULATOR
Central Drugs Standard Control Organisation (CDSCO)

STATUS : NOTIFICATION
Open for comments –Within 45 days from the date of publication in the official gazette.

BACKGROUND

Indian regulations are changing at a fast pace, to say the least ! This rapid and systematic change is a result of initiatives which were taken some time back but are finally seeing the light of the day. These changes are being implemented in almost all spheres of the Indian constitution to help the country move forward in the right direction. Where this leads us, as a nation, is yet to be seen.

From the Indian drug regulatory perspective, changes are being implemented at a fast pace and the improved regulations for New Drugs and Clinical trials, though in the "Notification" stage is forward looking and required at this juncture to put a direction for growth to the drug development industry, which is still at a very nascent stage in India. Recent regulatory turmoil affecting clinical trials in India, disrupted India from being one of the favored destinations for global clinical trials. This has indeed instigated this draft regulation with an objective to bring in more clarity, transparency, accountability and direction to clinical studies in India.

PROPOSED REGULATION

The regulation(Notification) titled "New Drugs and Clinical trials Rules, 2018" was published as a Gazette Notification G.S.R. 104 (E)XX on 1st of February 2018 and made available to the public on 1st of February 2018. Objections and suggestions to be considered by the Central Government are being invited, within a period of 45 days from the date of availability to the public.

IMPACT SUMMARY :

Sl.	Categories	Activities
1.	New drugs	Application and Approval process towards : • Import – for testing (clinical trials, bioavailability, bioequivalence) and for sale & distribution • Manufacture – for testing (clinical trials, bioavailability, bioequivalence) and for sale & distribution
2.	Investigational new drug	Application and Approval process towards : • Import – for testing (clinical trials, bioavailability, bioequivalence) and for sale & distribution • Manufacture – for testing (clinical trials, bioavailability, bioequivalence) and for sale & distribution
3.	Clinical trials	Application process, Approval process, Conduct
4.	Bioavailability	Application process, Approval process, Conduct
5.	Bioequivalence	Application process, Approval process, Conduct
6.	Ethics committee	Constitution, Responsibility, Location, Application process, Approval process.

INTRODUCTION

These rules called the New Drugs and Clinical trials Rules, 2018 shall come into force after their final publication in the Official Gazette as a final version. It applies to all new drugs, investigational new drugs for human use, clinical trials, bioequivalence studies, bioavailability studies and Ethics Committees.

It has been structured as a supersession of Part XA and Schedule Y of the Drugs and Cosmetics Rules, 1945, and contains Twelve (12) Chapters and One Hundred & Five (105) Rules. Along with Eight (8) Schedules and around Twenty seven (27) Forms, its quite comprehensive and all inclusive.

OVERVIEW OF PROPOSED CHANGES

The proposed changes through this regulation encompasses all areas of New drug, Clinical studies and Ethics committees. Although most of the procedures have been retained, there are very critical and important changes being proposed which bring in the required clarity, transparency and accountability in these areas. Proposed critical changes, are presented below, in brief, to help the reader have an overview of the changes and help them understand how these changes can affect their areas of interest.

- **Definitions (Chapter I)** :
  - A few definitions such as Biomedical and health research, New drug (inclusion of phytopharmaceutical drug), Phytopharmaceutical drug, Orphan drug etc., have been defined or modified to enhance its scope of applicability. Differentiation between efficacy and effectiveness gives the reader a better insight into how they are defined and applied.

- **Ethics committee (Chapters III & IV) :**
  - Responsibility of EC has been increased to not only review and accord approval to a clinical trial protocol and other clinical trial related documents, but also oversee before initiation and throughout the duration of the conduct of clinical trial at every clinical trial.
  - The ethics committee have been classified into two different types – ones that approve and oversee clinical studies (clinical trials, bioavailability & bioequivalence studies) and those that approve Biomedical and health research. Constitution of these ethics committees are slightly different and applicable guidelines are also different.
  - A major change is the formal notification of timelines and the option to reject an application if it does not comply to application requirements. Application for EC registration should be decided within a period of forty five(45) days by the designated authority. If the application is rejected, it should be notified to the applicant with reasons for this rejection. If the applicant is not satisfied with the rejection then there is an option to appeal to the Ministry of health and family welfare within Sixty (60) days from the date of receipt of the rejection order.
  - In case of an EC that approves a clinical trial at a clinical site or a bioavailability study or a bioequivalence study, the EC should be located within the same city or within a radius of 50 km of the clinical trial site.

- **Clinical studies (Chapter V & VI) :**
  - These chapters are applicable to Clinical trials, Bioavailability and Bioequivalence studies of New drugs and Investigational new drugs. One of the important changes proposed is the option for the designated authority to either approve, ask for resubmission after rectifying observed deficiency or reject the application in its entirety, after providing appropriate reasons.
  - If the applicant is provided an option to resubmit the application after rectification, within a specified time as decided by the designated authority, the application is expected to be complete in all respects along with rectification of deficiencies pointed out the authority. If deficiencies are noticed again the application will be rejected.
  - In case of a rejection, the applicant can request the central licensing authority to reconsider the application within a period of Sixty (60) days from the date of rejection. One more option available to the applicant who is aggrieved by the decision of the Central Licensing Authority is to appeal to the

Central Government within Forty five (45) days from the date of such a decision.

- Another important change is the timeline of Forty five (45) days for the designated authority to either approve, ask for rectification or reject the application. If the applicant does not receive any communication from the central licensing authority within 45 days then permission to conduct the clinical trial is deemed to have been granted by the Central Licensing Authority.
- Post trial access of investigational new drug or a new drug should be provided free of cost in specific cases, by the sponsor in case its recommended by the investigator and approved by the EC.
- No permission from the Central Licensing Authority is required for conducting an academic clinical trial, provide the trial conforms to the definition of an Academic trial according to the condition specified under these rules.
- In case of bioavailability study or bioequivalence study of a new drug or an investigational new drug, the application to the Central Licensing Authority can be either approved, rejected or notified for rectification within a period of Ninety (90) days from the date of receipt of the application.
- If the applicant is provided an option to resubmit the application after rectification, within a specified time as decided by the designated authority, the application is expected to be complete in all respects along with rectification of deficiencies pointed out the authority. If deficiencies are noticed again the application will be rejected – within a period of 90 days.
- In case of a rejection, the applicant can request the central licensing authority to reconsider the application within a period of Sixty (60) days from the date of rejection. One more option available to the applicant who is aggrieved by the decision of the Central Licensing Authority is to appeal to the Central Government within Forty five (45) days from the date of such a decision.

- **New drugs or Investigational new drugs :**
  - Manufacture – for testing (Chapter VIII) :
    - New drugs(active pharmaceutical ingredient or pharmaceutical formulation) and Unapproved New drugs (active pharmaceutical ingredient or pharmaceutical formulation) for the purpose of clinical trials or bioavailability and or bioequivalence studies are to be manufactured in accordance with the principles of Good Manufacturing Practices (GMP).
    - Decision(approval, rejection, opportunity for rectification) on a submitted application to be communicated to the applicant by the Central Licensing Authority within a period of Ninety (90) days from the date or receipt of the application.
    - The permission holder is required to keep track of the drug supply including the quantity expired and action taken against the expired product.
    - Manner of labelling for a new drug (approved and unapproved)has also been clearly specified.

  - Manufacture – *for sale & distribution (Chapter X) :*
    - Requirement of animal studies and results of local clinical trials in the application and conditions under which these requirements can be exempted, modified or relaxed in case of new drugs are specified.
    - Decision(approval, rejection, opportunity for rectification) on a submitted application to be communicated to the applicant by the Central Licensing Authority within a period of Ninety (90) days from the date or receipt of the application.
    - The permission holder is required to keep track of the drug supply including the quantity expired and action taken against the expired product.
    - Manner of labelling for a new drug (approved and unapproved)has also been clearly specified. Responsibility and or liability towards off label use of the product is also outlined.
    - The applicant is also required to submit Periodic Safety Update Reports (PSUR's) as part of post marketing surveillance.

  - Import – *for testing (Chapter IX) :*
    - New drugs(active pharmaceutical ingredient or pharmaceutical formulation) to be imported for the purpose of clinical trials or bioavailability and or bioequivalence studies have to be manufactured in accordance with the principles of Good Manufacturing Practices (GMP). The

responsibility to ensure the product is manufactured as per GMP rests on the licensee.
- Decision(approval, rejection, opportunity for rectification) on a submitted application to be communicated to the applicant by the Central Licensing Authority within a period of Ninety (90) days from the date or receipt of the application.
- Manner of labelling for a new drug (approved and unapproved)has also been clearly specified.
- The permission holder is required to keep track of the drug supply including the quantity expired and action taken against the expired product.

- *Import* – for *sale & distribution (Chapter X) :*
  - Requirement of results of local clinical trials in the application and conditions under which this requirement can be exempted are specified. Also, requirements of animal studies and conditions under which this requirement can be modified or relaxed in case of new drugs are specified.
  - Decision(approval, rejection, opportunity for rectification) on a submitted application to be communicated to the applicant by the Central Licensing Authority within a period of Ninety (90) days from the date or receipt of the application.
  - The applicant is also required to submit Periodic Safety Update Reports (PSUR's) as part of post marketing surveillance.
  - Manner of labelling has also been clearly specified.

- **OTHERS**
  - Much awaited formal process or procedures for Pre-submission meetings, Post-submission meetings, Debarment of applicant, Order of Suspension or Revocation in public domain have also been clearly outlined.
  - Process to manufacture and import unapproved new drug for treatment of patients in government hospital and government medical institutions has been clearly outlined.
  - Substantial increase in fees across all categories of licenses, permissions and registration certificates.

- **REFERENCE :**
  - G.S.R.104(E).— NOTIFICATION – New Drugs and Clinical trials Rules, 2018; Ministry of Health and Family Welfare (Department of Health and Family Welfare); New Delhi, the 1st February, 2018. http://www.cdsco.nic.in/writereaddata/GSR%20104(E)%20dated%2001_02_2018_New%20Drugs%20&%20CLinical%20Trial%20Rules,%202018.pdf – *accessed on 18 February 2018 at 11.45 am.*

CONTACT US
Dr C Omprakash
Technical Director & Partner
e-mail : om(at)vyomusconsulting.com
Mob : +91 733 813 0164
Ph : +91 80 26636149