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A REVIEW ON NEW DRUG APPROVAL PROCESS IN INDIA

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ABSTRACT

A regulatory process, by which a person/organization/sponsor/innovator gets authorization to launch a drug in the market, is known as drug approval process. In general, a drug approval process comprises of various stages: application to conduct clinical trials, conducting clinical trials, application to marketing authorization of drug and post-marketing studies. Every country has its own regulatory authority, which is responsible to enforce the rules and regulations and issue the guidelines to regulate the marketing of the drugs. This work focuses on the drug approval process in India. The new drug approval process in India is standardized and well controlled, involving multiple steps and organizations. At the central level, DCGI, under the Ministry of Health and Family Welfare, approves the drug or medical device for marketing. Manufacturing licenses are approved at the state level by state drug control authorities. Monitoring is also performed by state agencies in coordination with the CDSCO.

KEYWORDS: Drug approval process, Clinical trials, Marketing.

INTRODUCTION

NDA is an application submitted to the FDA for permission to market a new drug. To obtain this permission a sponsor submits preclinical and clinical test data to NDA for analyzing the drug information, description of manufacturing procedures.

After NDA received by the agency, it undergoes a technical screening. This evaluation ensures that sufficient data and information have been submitted in each area to justify "filing" the application that is FDA formal review. At the conclusion of FDA review of an NDA, there are three possible actions that can send to sponsor:

Not approvable - This letter consists of list of deficiencies.

Approvable - It means that the drug can be approved but minor deficiencies that can be corrected like-labeling changes and possible request commitment to do post-approval studies.

Approval - It state that the drug is approved.

If the action taken is either an approvable or a not approvable, then FDA provides applicant with an opportunity to meet with agency and discuss the deficiencies.[1]

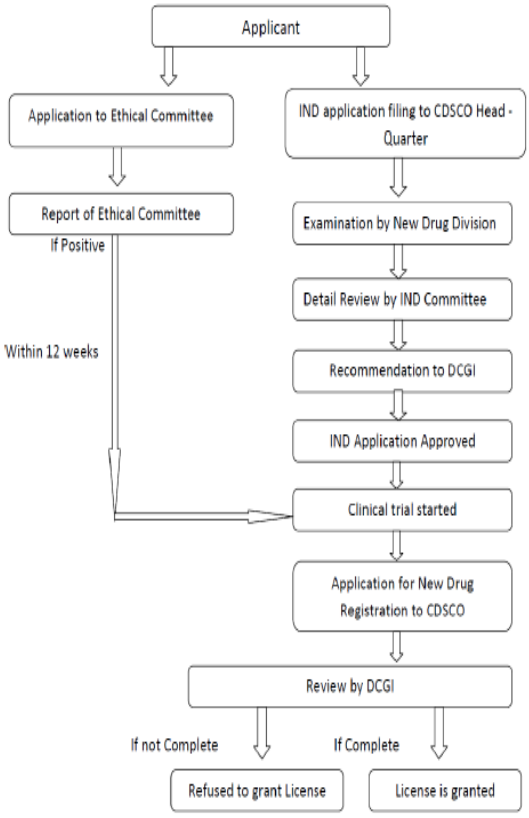

Figure 1: Drug Approval Process In India.

Agencies Involved in Drug Regulation

The CDSCO is the central authority overseeing the drug industry, as mandated under the Drugs and Cosmetics Act. The organization has six zonal offices, four sub-zonal offices, 13 port offices, and seven laboratories under its control. Its major functions are controlling drug imports, approving drug development and clinical trials, and overseeing Drugs Consultative Committee and Drugs Technical Advisory Board meetings. DCGI is the main licensing authority, which directly issues permission for new drugs and devices. It oversees clinical trials as well.[2]

- When a company in India wants to manufacture/ import a new drug it has to apply to seek permission from the licensing authority (DCGI) by filing in Form 44 also submitting the data as given in Schedule Y of Drugs and Cosmetics Act 1940 and Rules 1945.
- In order to prove its efficacy and safety in Indian population it has to conduct clinical trials in accordance with the guidelines specified in Schedule Y and submit the report of such clinical trials in specified format.
- But a provision is there in Rule- 122A of Drugs and Cosmetics Act 1940 and Rules 1945 that the licensing authority may waive certain trails if he considers that in the interest of public health he may grant permission for import of new drugs basing on the data of the trials done in other countries.
- Similarly, there is another provision in Rule- 122A which says that the clinical trials may be waived in the case of new drugs, which are approved, and being used for several years in other countries.
- Section 2.4 (a) of Schedule Y of Drugs and Cosmetics Act 1940 and Rules 1945 says for those drug substances which are discovered in India all phases of clinical trials are required.
- Section 2.4 (b) of Schedule Y of Drugs and Cosmetics Act 1940 and Rules 1945 says that for those drug substances which are discovered in countries other than India; the applicant should submit the data available from other countries and the licensing authority may require him to repeat all the studies or permit him to proceed from Phase III clinical trials.
- Section 2.8 of Schedule Y of Drugs and Cosmetics Act 1940 and Rules 1945 says that the licensing authority may require pharmacokinetic studies (Bioequivalence studies) first to show that the data generated in Indian population is equal to data generated abroad and then require him to proceed with Phase III trials.
- In summary, the exact requirements of Clinical trials may change from case to case and depend on the extent to which licensing authority is satisfied about its safety and efficacy.
- The process of approval of new drug in India is a very complicated process, which should meet necessary requirements along with NDA to FDA. The need of the present work is to study and document the requirements for the process of approval of new drug in India.[3]

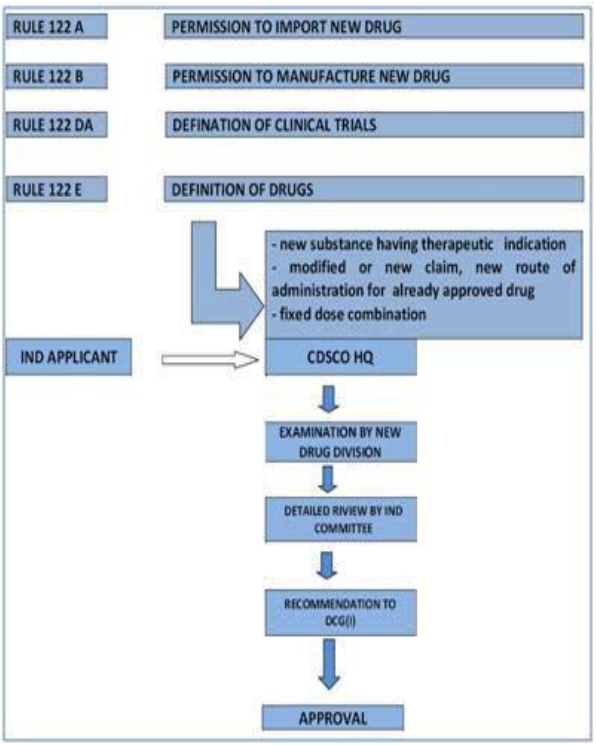

Figure 2: Pictorial Representation of Drug Approval Process in india.

Stages of Approval[4,5,6]

1. Submission of Clinical Trial application for evaluating safety and efficacy.
2. Requirements for permission of new drugs approval.
3. Post approval changes in biological products: quality, safety and efficacy documents.
4. Preparation of the quality information for drug submission for new drug approval.

1. Submission of Clinical Trial Application for Evaluating Safety and Efficacy

All the data listed below has to be produced.

(a) Phase-I & phase- II clinical trial

➢ General information

- Introduction about company: Brief description about company
- Administrative headquarters: Provide address of company headquarters
- Manufacturing Facilities: Provide address of company headquarters
- Regulatory and intellectual property status in other countries
- Patent information status in India & other countries

➢ Chemistry manufacturing control

- Product Description: A brief description of the drug and the therapeutic class to which it belongs.
- Product Development.

- Strain details.
- Information on drug substance.
- Information on drug Product.

- Non-clinical data: References: schedule – Y, amendment version 2005, Drugs and Cosmetics Rules, 1945.

- Proposed phase-I / II studies: protocol for phase-I / II studies.

(b) Phase-III clinical trial

All the information is as same as phase-I & phase- II clinical trial

- General information
- Chemistry manufacturing control
- Non-clinical data
- Proposed phase-III studies

2. Requirements for permission of New Drugs Approval

- The manufacturer / sponsor have to submit application on Form 44 for permission of New Drugs Approval under the provisions of Drugs and Cosmetic Act 1940 and Rules 1945.
- The document design is as per the International submission requirements of Common Technical Document (CTD) and has five Modules.

Module I: Administrative/Legal Information

This module should contain documents specific to each region; for example, application forms or the proposed label for use in the region. The content and format of this module can be specified by the relevant regulatory authorities.

Module II: Summaries

Module 2 should begin with a general introduction to the pharmaceutical, including its pharmacologic class, mode of action and proposed clinical use. In general, the introduction should not exceed one page. The introduction should include proprietary name, nonproprietary name or common name of the drug route of administration, and proposed indication(s). It contains the CTD summaries for quality, safety, efficacy information. This module is very important, as it provides detailed summaries of the various sections of the CTD. These include: A very short introduction. Quality overall summary, Non clinical overview, Clinical over view, Non clinical written and tabulated summaries for pharmacology, pharmacokinetics, and toxicology.

Module III: Quality information (Chemical, pharmaceutical and biological)

Information on quality should be presented in the structured format described in the guidance M4Q. This document is intended to provide guidance on the format of a registration application for drug substances and their corresponding drug products. It contains of all of the quality documents for the chemistry, manufacture, and controls of the drug substance and the drug product.

Module IV: Non-clinical information

Information on safety should be presented in the structured format described in the guidance M4S. The purpose of this section is to present a critical analysis of the non-clinical data pertinent to the safety of the medicinal product in the intended population. The analysis should consider all relevant data, whether positive or negative, and should explain why and how the data support the proposed indication and prescribing information. It gives final copy of all of the final nonclinical study reports.

Module V: Clinical information

Information on efficacy should be presented in the structured format described in the guidance M4E. It gives clinical summary including biopharmaceutics, pharmacokinetics and pharmacodynamics, clinical pharmacology studies, clinical efficacy, clinical safety, synopses of the individual studies and final copy of detailed clinical study reports.

3. Post approval changes in biological products

The post approval changes are the changes made to biological products that have received an approval and to provide the data to support a change, which would be considered sufficient to allow a determination of the impact of the change on the quality of the approved products as it relates to safety, efficacy and/or effective use of the products. After the approval of NDA or ANDA, the applicant may make post approval changes, provided the changes are reported to the FDA under the appropriate categories. Section 506 A of the Federal Food, Drugs and Cosmetics act and 21 CFR 314.70 provide for three reporting categories of the post approval changes namely: major change, moderate change and minor change. There are many reasons for making changes to pharmaceutical products after the original regulatory approval is obtained. Company change control procedures should detail how changes are evaluated and implemented as well as how the change impacts stability and what data will be needed to support the change.

4. Preparation of the quality information for drug submission for new drug approval

a) Drug substance (name, manufacturer).
b) Characterization (name, manufacturer).

- Physicochemical characterization.
- Biological characterization.

c) Drug product (name, dosage form).
d) 4) Control of drug product (name, dosage form).
e) Appendices.

- Facilities and equipment (name, manufacturer).
- Safety evaluation adventitious agents (name, dosage form, manufacturer).

RESULTS AND DISCUSSION

Table 1: Principle Requirements for approval.

Requirements	India
Agency	One agency DCGI
Registration Process	One registration process
TSE/BSE study data	TSE/BSE study data required
Post Approval changes	Post approval changes: Major quality changes Moderate quality changes and Minor changes.

Table 2: Administrative Requirements.

Requirements	India
Application	MAA
Number of copies	1
Approval timeline	12-18 Months
Fees	50,000 INR
Presentation	Paper

Table 3: Finished Product Control Requirements.

Requirements	India
Justification	ICH Q6A
Assay	90 - 110 %
Disintegration	Required
Colour Identification	Required
Water Content	Required

Table 4: Manufacturing & Control.

Requirements	India
Number of batches	1
Process Validation	Required
Batch Size	Pilot scale batch

Table 5: Stability Requirements.

Requirements	India
Number of batches	2 Pilot Scale/Production scale(If API Stable) 3 Primary Batches (If API unstable)
Condition: Long term stability, Accelerated stability,	Long term: 30°C/70%RH Accelerated:40°C/75%RH (0,3,6 months)
Minimum time period at Submission	6 Months Accelerate & 6 Months long term
Container orientation	upright and inverted
Clause	ICH Q1F
QP Certification	Required

Table 6: Bioequivalence Requirements.

Requirements	India
CRO (Audits)	CDSCO
Fasted / Fed	As CDSCO recommendation
Retention of samples	3 years from date of filing the application
BE study for generic drugs	Against US/EU/Australia RLD in any country except Thailand, where BE to be done locally against local reference product.

CONCLUSION

The drug approval process in India has seen fast progress in order to keep up with industry and public health expectations. Timelines for processes are becoming shorter and more defined. Indian authorities are cognizant of their responsibility to ramp up regulations and to enforce them in order to meet the continuously evolving global standards**.** The primary purpose of the rules governing medicinal products in US, Europe & India is to safeguard public health. It is the role of public regulatory authorities to ensure that pharmaceutical companies comply with regulations. There are legislations that require drugs to be developed, tested, trailed, and manufactured in accordance to the guidelines so that they are safe and patient's well - being is protected.

REFERENCES

1. Process of approval of New Drug in India with emphasis on clinical trials by N. Vishal Gupta et.al., March-April 2012; 13(2): Article-004, International journal of Pharmaceutical Sciences Review and Research.
2. Clinical Trial & Global Clinical Trial [Internet]. [Cited 2014 January]. Available from: http://cdsco.nic.in/clinical_trial.htm.
3. The New Drug Approval Process [Internet]. [Cited 2014 January]. Available from: http://www.fda.gov/cder/handbook.
4. CDER Guidance: IND application process (interactive session) [Internet]. [Cited 2014 January]. Available from: www.fda.gov/cder/regulatory/applications/ind_page_1.htm.
5. Guidance for industry on preparation of common technical document for import/ manufacture and marketing approval of new drugs for human use. (NEW DRUG APPLICATION–NDA) [Internet]. [Cited 2014 January]. Available from: http://cdsco.nic.in/CTD_Guidance%20-Final.pdf.
6. The Drug Approval Process in India May 26, 2016. By Dinesh Pendharkar, MD, PhD, and Nagalakshmi Ananda Padmanabhan.