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REGULATORY REQURIMENTS FOR THE REGISTRATION OF GENERIC DRUGS IN INDIA

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ABSTRACT

The present study describes the process of regulatory submission and generic drug registration in Europe. The information and data for the compilation of the present review has been obtained from the relevant journals and from the official websites of respective drug regulatory authorities of Europe. The generic drug approval process differs from one country to another. Europe follows multiple registration processes and the applicant decides the pathway based on the product category while the other three countries stick to a single registration process. All four countries follow the electronic CTD format for submitting the regulatory documents which allows the evaluation process more convenient and easier. The British Pharmacopoeia is a single reference guide for the quality control of medicines in all four countries under this study. From this study, it was concluded that in Europe it takes about 12 months for dossier review for the approval of the generic drug.

KEYWORDS: Generic Drug, Abbreviated New Drug Application (ANDA), European Medicines Agency (EMA) guidelines.

1. INTRODUCTION[1-4]

A generic drug is a medication created to be the same as an existing approved brand name drug in dosage form, safety, strength, route of administration, quality, and performance characteristics.

Beginning of Generics

On September 24, 1984, in the 98th United States Congress, the act named The Drug Price Competition and Patent Term Restoration Act was passed, informally known as the Hatch-Waxman Act, encouraging the manufacture of generic drugs by the pharmaceutical industry and established the modern system of government generic drug regulation in the United States.

The requirement was an abbreviated new drug application (ANDA) to be submitted by the pharmaceutical companies to the regulatory authorities for getting the approval to market a generic drug. ANDA process does not require the manufacturer to carry out repeat testing of generics in animals which is often time consuming, as their branded versions have already been tested and approved for the safety and effectiveness. They are formulated when patent and other exclusivity rights of the innovator have expired.

Implementing Authorities

- **Central Government**

Central Drugs Standard Control Organization (CDSCO)

- **State Government**

State Drug Licensing Authorities

Responsibilities

Central Responsibilities

New Drug Approvals/Medical Devices

- Import of Drugs/Medical Devices
- Clinical Trails
- Standards for Drugs
- Amendments to Act and Rules
- Pharmacovigilance

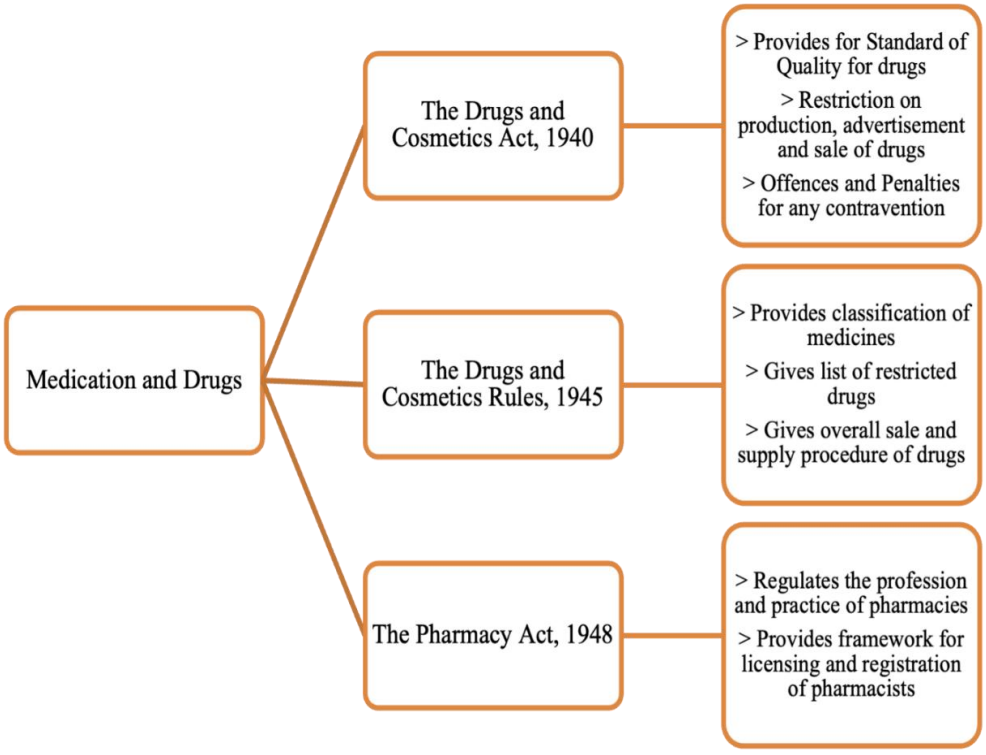
State Responsibilities

- License for Manufacture, Sale and Distribution
- Monitoring quality of Drugs and Cosmetics
- Investigations and Prosecutions

Central Drugs Standard Control Organization

- National Regulatory Authority of India
- Headed by Drugs Controller General (India)
- Headquarters at New Delhi

In India import, manufacturing, sale and distribution of drug is regulated under Drugs and Cosmetics Act 1940 and Drugs and Cosmetic Rules 1945 (hereinafter refer as Act) made there under. At present, bulk drug (Active Pharmaceutical Ingredients) and finished formulations are regulated under the said Act. Any substance falling within the definition of drug (Section 3b of the Act) required to be registered before import into the country. Not only drug but the manufacturing site needs to be registered for import. If the drugs, fall within the definition of New Drug (Rule 122 E of the Act), the new drug approval is the pre-requisite for submission of application for Registration and or import of drug. The application for Registration and import can be made to the Licensing Authority under the Act i.e. to the Drugs Controller General (I) at CDSCO, FDA Bhawan, Kotla Road, Near Bal Bhawan, New Delhi by the Local Authorized Agent of the foreign manufacturer having either manufacturing or sale License or by the foreign manufacturer having a whole sale License in the country.



2. Drug Approval Process in India[5-8]

The Drug and Cosmetic Act 1940 and Rules 1945 were proclaimed by the India's parliament to regulate the import, manufacture, distribution and sale of drugs and cosmetics. The Central Drugs Standard Control Organization (CDSCO) and the office of its leader, the Drugs Controller General (DCGI) was established. In 1988, the Indian government added Schedule Y to the Drug and Cosmetics Rules 1945. Schedule Y provides the guidelines and requirements for clinical trials, which was further revised in 2005 to bring it at par with internationally accepted procedure. 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.[4] 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.

Rules

- Rule 122 - A: Application for permission to import new drug
- Rule 122- B: application for approval to manufacture new drug other than the drugs specified under Schedule C and C (1).
- Rule 122 - D: Permission to import or manufacture fixed dose combination.
- Rule 122 - DA: Application for permission to conduct clinical trials for New Drug/Investigational New Drug.
- Rule 122 - DAB: Compensation in the case of injury or death during the clinical trials.

Stages of approval

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

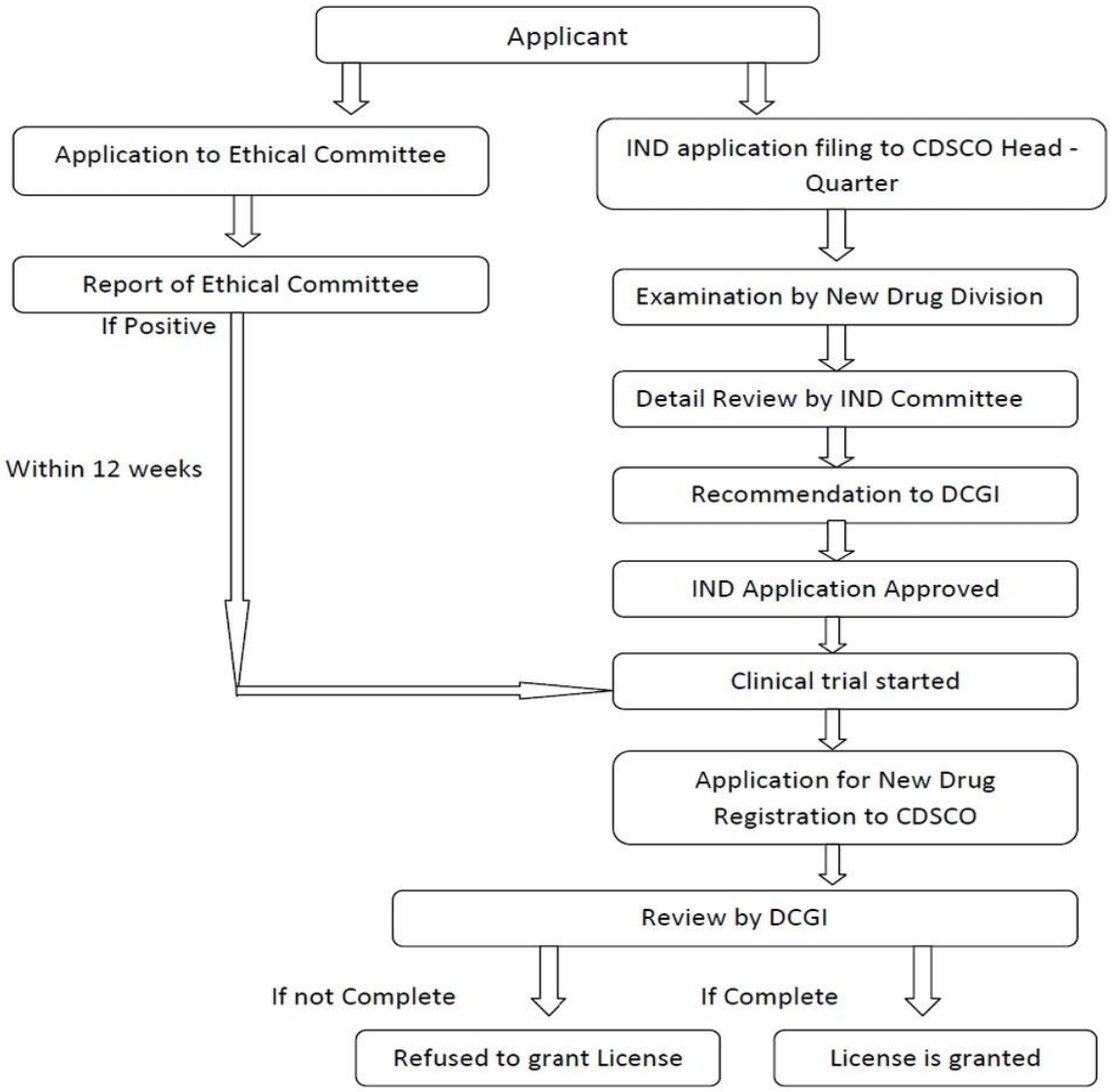


Fig. 1: Flow Chart of Drug Approval Process in India.

Indian Generic Pharmaceuticals Market India is primarily a branded generics (molecular copy of an off patent drug with a trade name) market. However, it is important to note that generic versions of molecules which still had patent protection in the rest of the world were produced (by reverse engineering) and marketed in India by domestic market participants until 2005, since India did not follow any patent protection laws up to 2005. Hence, the Indian generic market size includes the sales value of generic drugs sold by both big pharma companies (generic copies of the innovator's molecule sold under a different trade name) as well as Indian generic companies. The Indian pharmaceutical industry, which is the third largest globally in terms of volume, had a total production output of $23.24 billion in 2010, and was the thirteenth largest, in terms of value. The domestic Indian pharmaceutical market was worth $12.24 billion in 2010, and grew at a significant rate of 17.0 percent per year.

3. Regulation of drug approval process[9-12]

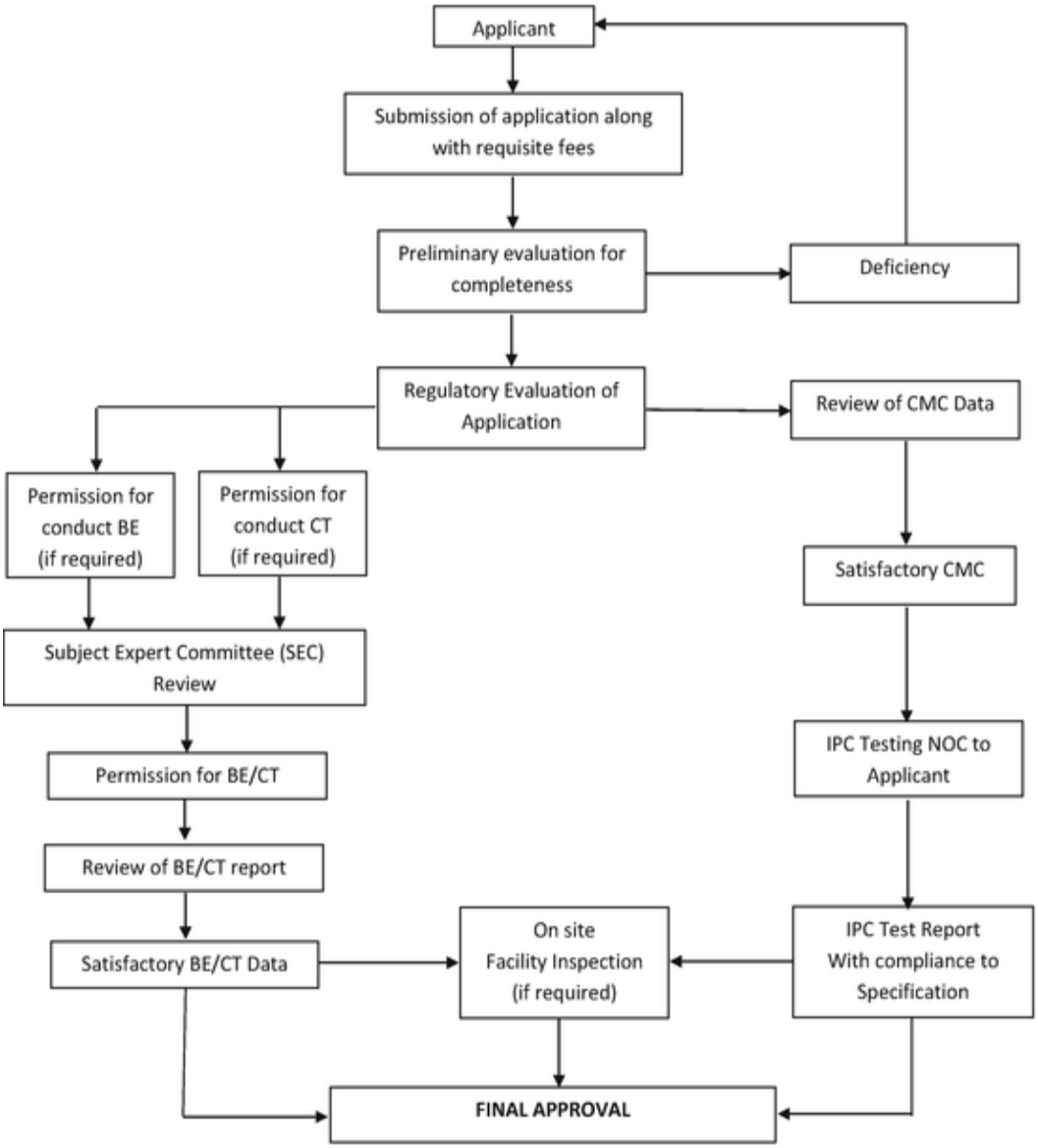


Fig. 2: Regulation of drug approval process in India.

4. CONCLUSION

Globalization of the pharmaceutical industry has created the need to harmonize the recommendations for the development of new pharmaceuticals, as well as the regulatory requirements of various countries. Substantial documentation and data are required in these types of submissions, resulting in large, complex applications. Thus, a common format of

submission will help in overcoming these hurdles. In India, CDSCO adopted CTD format for technical requirements for registration of pharmaceutical products in 2009-2010. Still of the CDSCO approval, there are certain companies that do not have knowledge about the primary requirements for preparation of dossier according to the CTD format. Finally, there needs to be a reaffirmation and fine balance between the tenacities of gaining market access of pharmaceuticals is to protect the public health and facilitate healthy growth of pharmaceutical manufacturers. Pharmaceutical product approval process should be seen as a critical step in ensuring access to safe and effective drugs.

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