

Regulatory Requirements and Drug Approval Process in India, Europe and US

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Abstract

Current constrain of Regulatory Affairs reveals diverse countries need to follow different regulatory requirements for Marketing Authorization Application (MAA) approval of new drugs. 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. Once a lead drug molecule has been discovered, nonclinical studies of a drug should be conducted to ensure efficacy and safety. Then, clinical trials can be performed, after an application is submitted to competent authority of the concerned country. The three phases of clinical trials are conducted as per the protocol. The competent authority reviews an application submitted to get approval for marketing the drug and approves it if satisfied that the drug supports quality, safety and efficacy concerns. Even after the approval of new drug, government should monitor its safety by post marketing surveillance which is considered as Phase IV. Though certain aspects of drug approval process are similar among different countries, some differences do occur. In this present exertion study expresses the drug approval process and regulatory requirements according to US Food and Drug Administration (UDFDA), European Medical Agency (EMA) and Central Drug Standard Control Organization (CDSCO). This review outlines advances in therapy and the main spotlight for the improvement and advance of cell therapies that are being confronted today.

Keywords: Drug approval; Regulatory requirements; USFDA; CDSCO

Introduction

Currently different countries have to follow different regulatory requirements for approval of new drug. For Marketing Authorization Application (MAA) a single regulatory approach is applicable to various countries is almost a difficult task. Therefore, it is necessary to have knowledge about regulatory requirement for MAA of each country. Each country has its own regulatory requirements which have to be satisfied to approve a new drug in that particular country. It is difficult to go for a single regulatory approach for approval of a new drug in different countries. Hence there is a need for gaining awareness on regulatory issues of various countries [1,2]. It is well known that the United States of America (USA) and the European Union (EU) are the most potential markets for drug products in the world; so many companies focus on their pharmaceutical legislations. Hence, this article highlights the regulatory strategies of US, EU and India. Firstly, when a lead molecule is identified for a target disease, it should be optimized. After the discovery of a drug, pre-clinical trials are conducted on animals to ensure safety and efficacy. An application should be submitted to competent authority of a concerned country to get permission for conducting clinical studies. Clinical trials are performed in four phases to assure safety, efficacy and then the drug dose is optimized in humans. A Marketing Authorization Application (MAA) is then submitted, which is approved by the competent authority, if the drug satisfies the requirements of safety and efficacy and proves that its benefits outweigh its risks (Figure 1).

New Drug Application (NDA) is an application submitted to the individual regulatory authority for authorization to market a new drug i.e. innovative product. To gain this permission a sponsor submits preclinical and clinical test data for analyzing the drug information, description of manufacturing trials.

Different phases of clinical trials

- ◇ Pre-clinical study
- ◇ Phase I - Clinical trial
- ◇ Phase II - Exploratory trial
- ◇ Phase III- Confirmatory trial

- ◇ Phase IV- Post Marketing trial.

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. At the conclusion of the review of an NDA, there are 3 possible actions that can send to sponsor:

- ◇ Not approvable- in this letter list of deficiencies and explain the reason.

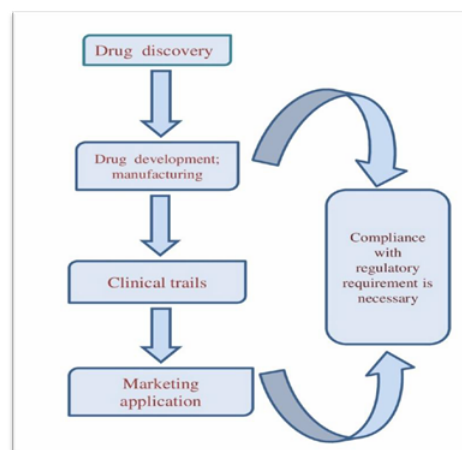


Figure 1: Regulation of Drug Approval Process.

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- ◇ Approvable - 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 the regulatory body provides applicant with an opportunity to meet with agency and discuss the deficiencies [3].

Drug Approval Process in India

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 [5].

Rule

122A of the Drug and Cosmetics Act 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. Demonstration of safety and efficacy of the drug product for use in humans is essential before the drug product can be approved for import or manufacturing of new drug by the applicant by Central Drugs Standard Control Organization (CDSCO). The regulations under Drugs and Cosmetics Act 1940 and its rules 1945, 122A, 122B and 122D describe the information required for approval of an application to import or manufacture of new drug for marketing [3]. For an investigational new drug, the sponsor needs to provide detailed information to the DCGI about:

1. Generic name
2. Patent status
3. Brief description of physico-chemical/biological
4. Technical information
 - α) Stability
 - β) Specifications
 - χ) Manufacturing process
 - δ) Worldwide regulatory status
 - ε) Animal pharmacology and toxicity studies

5. Published clinical trial reports
6. Proposed protocol and pro forma
7. Trial duration
8. During master file
9. Undertaking to Report Serious or Life-threatening Adverse Drug Reactions.

The need for local clinical trials in India depends on the status of drug in other countries. If the drug is already approved in other countries, generally Phase III trials are required. Phase I trials are not allowed in India unless the data is available from other countries. Permission is granted by DCGI to conduct Phase 1 trials in India, if the drug has special relevance to a health problem in India, like malaria or tuberculosis.

Bioavailability and bioequivalence (BABE) studies should be conducted as per BABE guidelines. The comprehensive information on the marketing status of the drug in other countries is also required other than the information on safety and efficacy. The information regarding the prescription, samples and testing protocols, product monographs, labels must also be submitted. It usually takes 3 months for clinical trial approval in India. The clinical trials can be registered in the Clinical Trials Registry of India (CTRI) giving details of the clinical trials and the subjects involved in the trials [6]. The rules to be followed under The Drugs and Cosmetics Rules 1945 are:

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

The changes in the Drugs and Cosmetics Act includes, establishing definitions for Phase I- IV trials and clear responsibilities for investigators and sponsors. The clinical trials were further divided into two categories in 2006. In one category (category A) clinical trials can be conducted in other markets with competent and mature regulatory systems whereas the remaining ones fall in to another category (category B) Other than A. Clinical trials of category A (approved in the U.S., Britain, Switzerland, Australia, Canada, Germany, South Africa, Japan and European Union) are eligible for fast tracking in India, and are likely to be approved within eight weeks. The clinical trials of category B are under more scrutiny, and approve within 16 to 18 weeks. An application to conduct clinical trials in India should be submitted along with the data of chemistry, manufacturing, control and animal studies to DCGI. The date regarding the trial proto col, investigator's brochures, and informed consent documents should also be attached [2,3]. A copy of the application must be submitted to the ethical committee and the clinical trials are conducted only after approval of DCGI and ethical committee.

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.

Most countries have adopted the CTD format. Hence, CDSCO has also decided to adopt CTD format for technical requirements for registration of pharmaceutical products for human use (Figure 2).

Drug Approval Process in Europe

The European Medicines Evaluation Agency (EMA) was established in London, in the year 1995, to coordinate the European Union (EU) member states for evaluating and supervising the medicinal products for both human and veterinary use [2]. It introduced a transparent procedure for the development, consultation, finalization and implementation of pharmaceutical guidelines. The drug approval process in European countries is accomplished in two phases:

1. Clinical trial.
2. Marketing authorization.

A clinical trial application (CTA) is filed to the competent authority of the state to conduct the clinical trial within European Union (EU). The competent authority of that member state evaluates the application. The clinical trials are conducted only after the approval. Marketing authorization application is filed only after all the three phases of clinical trials are completed. The European Legislation containing the pharmaceutical directives has been published in the following volumes entitled The Rules Governing Medicinal Products in the European Union.

Volume 1: Pharmaceutical Legislation for Medicinal Products for human use

Volume 2: Notice to Applicants for Medicinal Products for human use

Volume 3: Scientific Guidelines for Medicinal Products for human use

Volume 4: Good Manufacturing Practices Guidelines for Medicinal Products for human and veterinary use

Volume 5: Pharmaceutical Legislation for Medicinal Products for veterinary use

Volume 6: Notice to Applicants for Medicinal Products for veterinary use.

Volume 7: Scientific Guidelines for Medicinal Products for veterinary use

Volume 8: Maximum Residue Limits

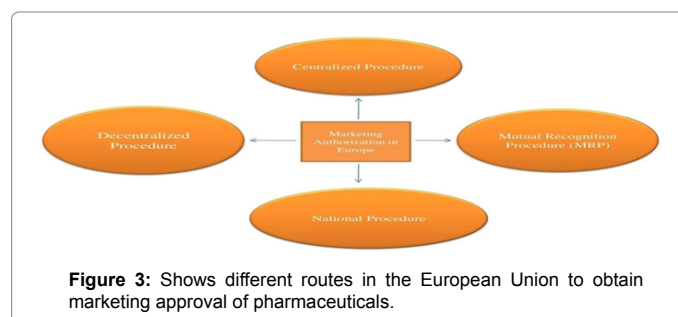
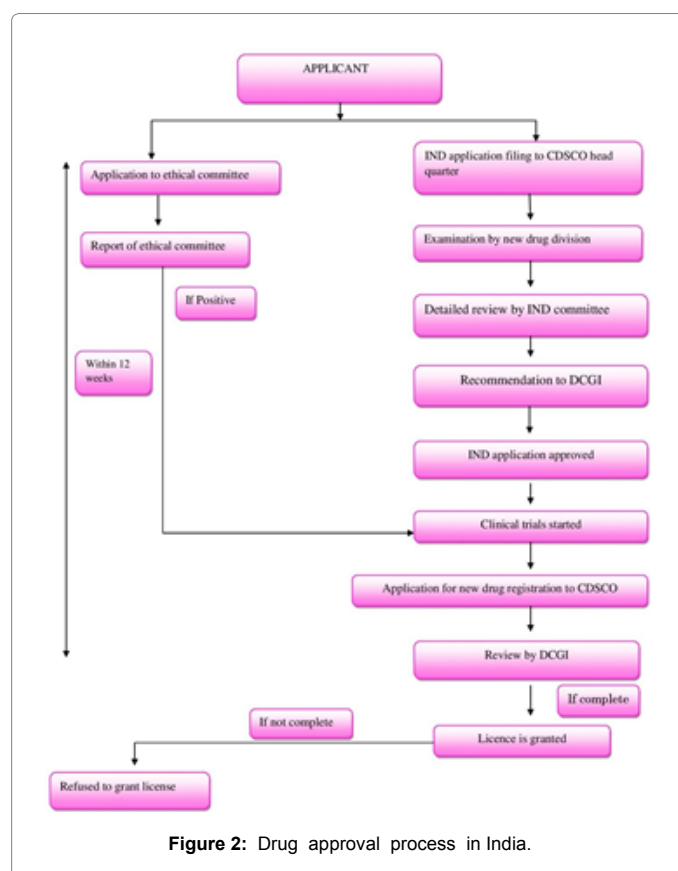
Volume 9: Pharmacovigilance Guidelines for Medicinal Products for human and veterinary use

Volume 10: Clinical Trials Guidelines.

Europe has multiple structures and administrative procedures for obtaining market authorization of pharmaceuticals. There are four different routes in the European Union to obtain marketing approval of pharmaceuticals (Figure 3).

Centralized Procedure

The centralized procedure is one which allows applicants to obtain a marketing authorization that is valid throughout the EU [7-9]. In



this procedure, applications are accepted with regards to products of bio-technological sciences and New Chemical Entities (NCEs). All the Biotechnological products are grouped as “List A” and NCEs are grouped as “List B”. According to this procedure, only a single marketing authorization is valid for entire European Union. The EMA staff, on receiving the Marketing Authorization Approval (MAA), checks the completeness and compliance of the application with EU guidelines. This appraisal must be completed within ten days from the date of filing the application. The sponsor pays the appropriate fees. Then, EMA has 210 days to consider the application. It can appoint rapporteurs, who assess the application and report Committee for Medicinal Products for Human Use (CHMP). CHMP gives an opinion whether to accept or reject the application; it is forwarded to the European Commission, which can take 90 days to arrive at a decision. The total time for approval is around 300 days (210+90) [5]. Under this product is recognized by all member countries through a single application to EMA. Example: CEP submissions, eDMF, CTD submission on special product such as all Orphans Medicinal Product. All biotechnology based product,

Specified Aids and cancer Medicines, Specified Antiviral Medicines, Specified Medicines for Neurodegenerative Disorder including diabetes and Specified Medicines for Auto immune Diseases/dysfunctions. The rejection of application under these schemes bans entry to EU.

- ◇ Results in a single authorization valid in EU, Norway, Iceland and Liechtenstein
- ◇ Application evaluated by assigned Reporters.
- ◇ Timeline: EMA opinion issued within 210 days, and submitted to European Commission for final approval.

Centralized process is compulsory for:

- ◇ Those medicines which are derived from any biotechnology processes, such as genetic engineering
- ◇ Those medicines which are intended for the treatment of Cancer, HIV/Aids, diabetes, neurodegenerative disorders or autoimmune diseases and other immune dysfunctions.
- ◇ Medicines officially designated 'orphan medicines' (medicines used for rare diseases) (Figure 4).

Decentralized Procedure

Under this, a product is recognized by a group of member's countries simultaneously. It is considered as very efficient procedure. Decentralized procedure is followed to obtain marketing authorizations in several member states. The sponsor submits to a national regulatory authority, the application and a list of all Concerned Member States (CMSs), specifying a Reference Member State (RMS). The RMS must validate the application and Summary of Product Characteristics (SPCs); prepare a draft assessment report within 210 days and send a copy to the CMSs; this report can be approved within 90 days. If a medicinal product is supposed to cause potential serious risk to public health. CMSs can raise any objections and then the CHMP intervenes and takes a final decision within 30 days [2]. However, a negative decision can affect the registration in many countries under this scheme also following product cannot be registered: Orphans Medicinal Product, All biotechnology based product, Specified Aids and Cancer Medicines,

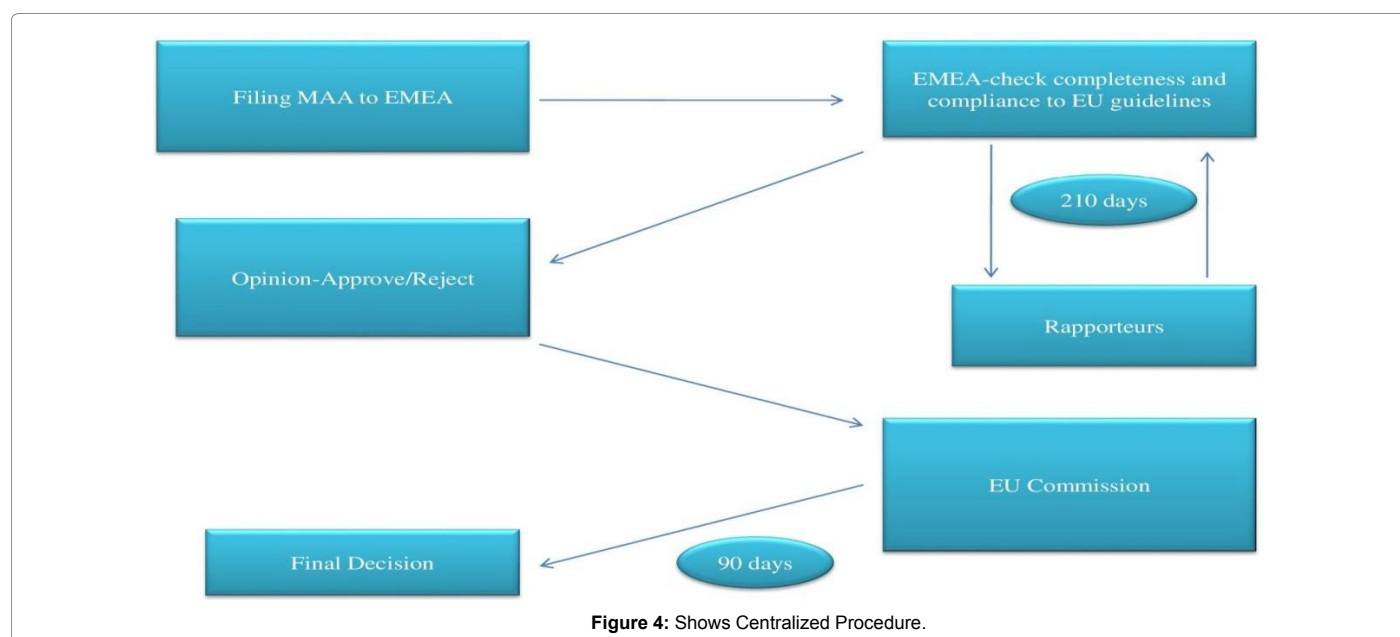
Specified Antiviral Medicines, Specified Medicines for Neurodegenerative Disorder including diabetes and Specified Medicines for Auto immune Diseases/dysfunctions (Figure 5).

National Procedure

In Europe each nation has its own regulatory body. National procedure is procedure adopted by each nation independently of other nations. The fees are affordable even for small firms. It saves on translation cost to English or regional languages. It creates a base for Mutual recognition Procedure Biotechnical procedures cannot be registered through national procedure. The Centralized filing through EMA is compulsory for the same. The application, submitted by the sponsor under the national rules to the national competent authority, is reviewed and a marketing authorization is granted [2]. Under this scheme also following product cannot be registered: Orphans Medicinal Product, All Biotechnology Based Product, Specified Aids and Cancer Medicines, Specified Antiviral Medicines, Specified Medicines for Neurodegenerative Disorder including diabetes and Specified Medicines for Auto immune Diseases/dysfunctions (Figure 6).

Mutual Recognition Procedure (MRP)

Under this a product registered in one country is mutually recognized by the other country. The application is required to make application only once for initial registration. The same application with some regional changes is accepted by another member country. Assessment Report of medicinal Product by Member Countries in EU: During Mutual recognition process the assessment report of Reference member state is reviewed before granting approval. The submission can be made to any number of the other member states and the RMS sends a copy of the assessment report to the CMSs, who can raise any objections within 90 days. Each CMS issues a national marketing authorization with an identical SPC. Under this scheme following product cannot be registered: Orphans Medicinal Product, All biotechnology based product, Specified Aids and cancer Medicines, Specified Antiviral Medicines, Specified Medicines for Neurodegenerative Disorder including diabetes and Specified Medicines for Auto immune Diseases/dysfunctions (Figure 7).



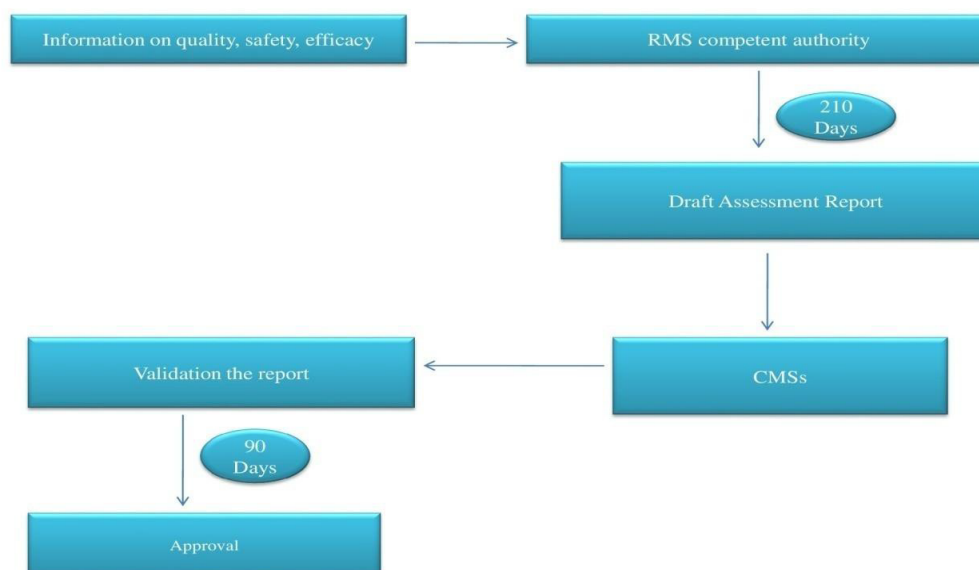


Figure 5: Decentralized Procedure.

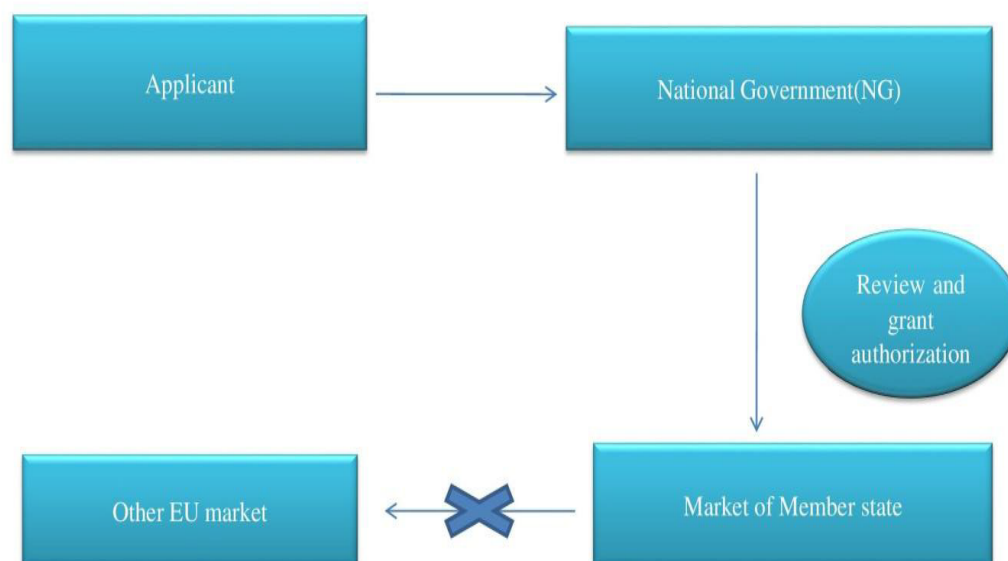
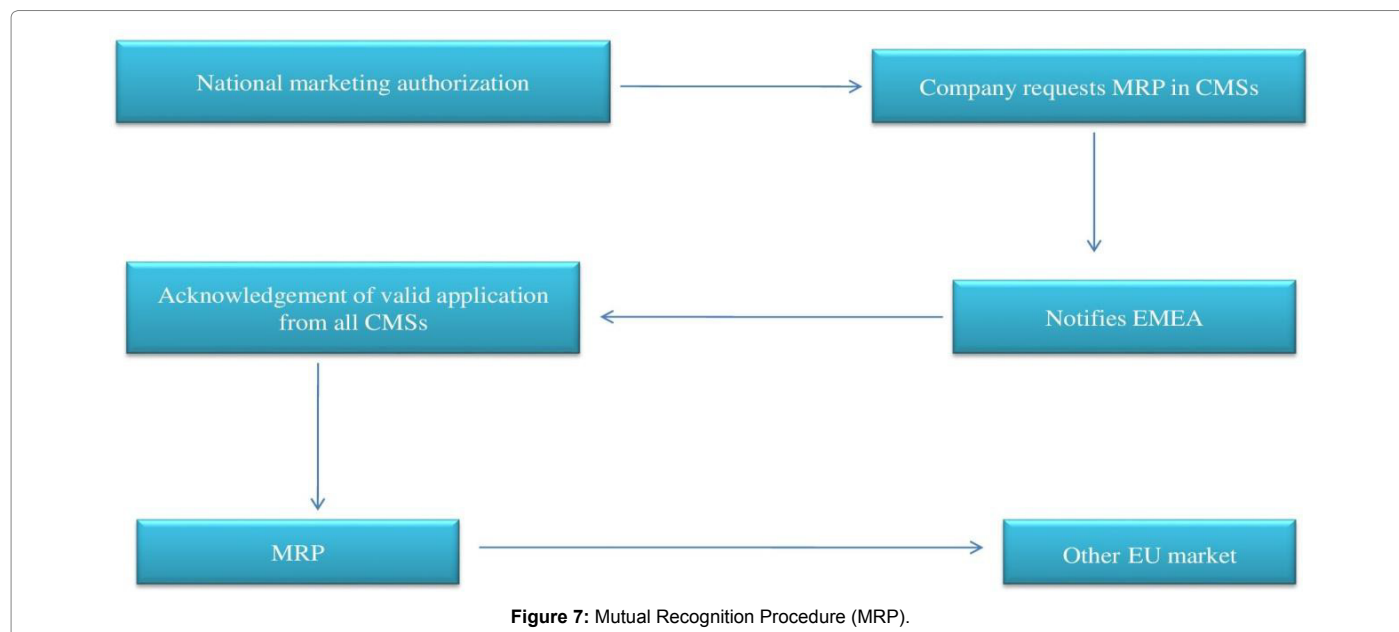


Figure 6: National Procedure.

Drug Approval Process in United States

The United States has perhaps the world's most stringent standards for approving new drugs. Drug approval standards in the United States are considered by many to be the most demanding in the world. In 1820, the new era of USA drug regulation was started with the establishment of U.S. Pharmacopoeia. In 1906, Congress passed the original Food and Drugs Act, which require that drugs must meet official standards of strength and purity. However, in 1937, due to sulphanilamide tragedy, the Federal Food, Drug and Cosmetic Act (of 1938) was enacted and added new provisions that new drugs must be shown safe before marketing [3]. Further, in 1962, the Kefauver-Harris

Amendment Act was passed which require that manufacturers must prove that drug is safe and effective (for the claims made in labelling). The Food and Drug Administration (FDA) is responsible for protecting and promoting public health. Like general drug approval process, FDA's new drug approval process is also accomplished in two phases: Clinical Trials (CT) and New Drug Application (NDA) approval. The new drug product are controlled through an new drug application (NDA). Currently such applications are accepted for review in eCTD format. The major concern about NDA is that the product shall be safety and effective. FDA approval process begins only after submission of investigational new drug (IND) application. The US Drug Law and Regulations United States Pharmacopoeia (USP) were started in 1820



to set standards for strength and purity of drugs. Major milestones in the evolution of US drug law are:

- ◇ Food and Drugs Act (1906): It requires that the drugs must meet official standards of strength and purity.
- ◇ Federal Food, Drug and Cosmetic Act (1938): It was enacted after sulfanilamide tragedy, to prove the safety of a drug before being marketed.
- ◇ Kefauver- Harris Amendment (1962): It was passed after the thalidomide disaster. It requires the manufacturers to prove that drug is safe and effective. All the firms should send adverse effect reports to FDA.
- ◇ Orphan Drug Act (1973): This allows tax deductions for drug companies to develop orphan drugs.
- ◇ Generic drug enforcement Act (1992): It deals with convictions related to ANDA approvals.
- ◇ FDA Modernization Act (1997): It contains some changes in Federal Food, Drug and Cosmetic Act regarding collection and assessment of user fees and accelerated approval processes.

Investigational New Drug Application (INDA)

It is an application filed to FDA prior to human testing [10,11]. It gives a full description of chemistry, manufacturing and controls, pharmacology and toxicology information, any previous human experience.

Types of IND

- ◇ An Investigator IND: It is submitted by a physician who both initiates and conducts an investigation and under whose immediate direction the investigational drug is administered or dispensed. A physician might submit a research IND to propose studying an unapproved drug, or an approved product for a new indication or in a new patient population.
- ◇ Emergency Use IND: This allows the FDA to authorize use of an experimental drug in an emergency situation that does not allow time for submission of an IND.

- ◇ Treatment IND: It is submitted for experimental drugs showing promise in clinical testing for serious or immediately life-threatening conditions while the final clinical work is conducted and the FDA review takes place.

The two IND categories are commercial and research (non-commercial) types. The IND application must contain information in three broad areas: (1) Animal Pharmacology and Toxicology Studies (2) Manufacturing Information and (3) Clinical Protocols and Investigator Information. Once the IND is submitted, the sponsor must wait 30 calendar days before initiating any clinical trials. During this time, FDA has an opportunity to review the IND for safety to assure that research subjects will not be subjected to unreasonable risk.

IND Content and Format

The requirements for the content and format of IND application are given in the 21 Code of Federal Regulations (CFR), Section 312. A sponsor (commercial organization) or an investigator who intends to conduct a clinical investigation should submit an “Investigational New Drug Application” in the following order (Figure 8):

1. Form FDA 1571
2. Table of contents
3. Introductory statement and investigational plan
4. Investigator's brochure
5. Protocols
6. Chemistry, manufacturing and control (CMC) information
7. Pharmacology and toxicology information
8. Previous human experience
9. Additional information.

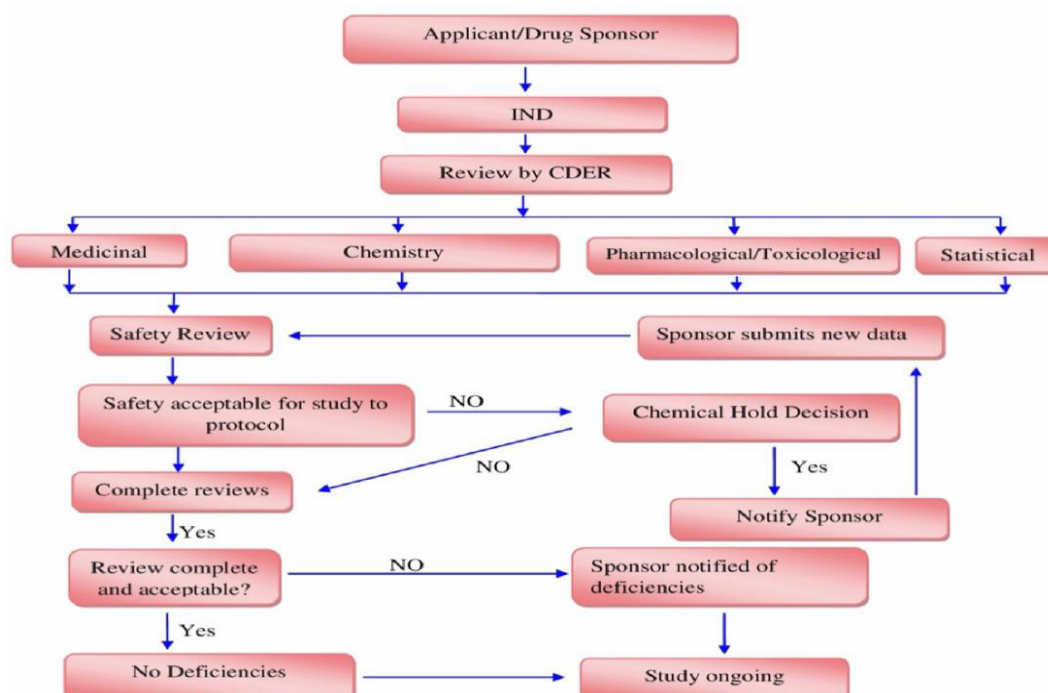


Figure 8: Investigational New Drug Application.

New Drug Application (NDA)

A New Drug Application is filed to get approval for marketing a new drug in the USA. An NDA contains information included in the IND, as well as the results of clinical studies proving safety and efficacy. The FDA shall start the review process within 60 days from the submission of an NDA [11]. Contents and Format of NDA Two copies of the application are: (a) Archival copy and (b) Review copy.

α) Archival Copy: It serves as a reference source for FDA reviewers to locate information not contained in the review copy; and it contains copies of tabulations and clinical study case report forms. It contains the following elements:

- β) Application form FDA 356
- χ) Index
- δ) Summary
- ε) Technical sections: further typed to-
- φ) Chemistry, manufacturing and controls section
- γ) Non-clinical pharmacology and toxicology section
- η) Human pharmacokinetics and bioavailability section
- ι) Microbiology section
- φ) Clinical data section
- κ) Statistical section
- λ) Pediatric use section
- μ) Samples and Labeling
- ν) Case report forms

b.) Review Copy: Each technical section is separately bound in each folder. Each technical section should contain:

1. Index
2. Copy of FDA Form 356 h
3. Copy of cover letter
4. Letters of authorization
5. Copy of application summary.

The FDA can conduct meetings with the sponsor at least two times; once at the end of Phase 2 clinical trials and another before an NDA is submitted i.e., a pre- NDA meeting. The review team shall analyze the study results and make a decision whether or not to approve the application (Figure 9).

Abbreviated New Drug Application (ANDA)

ANDA is applied for products with same or closely related active ingredients, dosage form, and strength, route of administration, use and labeling as product already shown to be safe and effective. It is used when the patent has expired for a product, and a company wants to market its copy. Such drugs are called generic drugs, which should meet bio and pharmaceutical equivalent standards [2]. An ANDA is submitted to Center for Drug Evaluation and Research, Office of Generic Drugs, where it is reviewed and approved.

Content and Format of ANDA

1. Application form
2. Table of contents
3. Basis for ANDA submission
4. Conditions of use

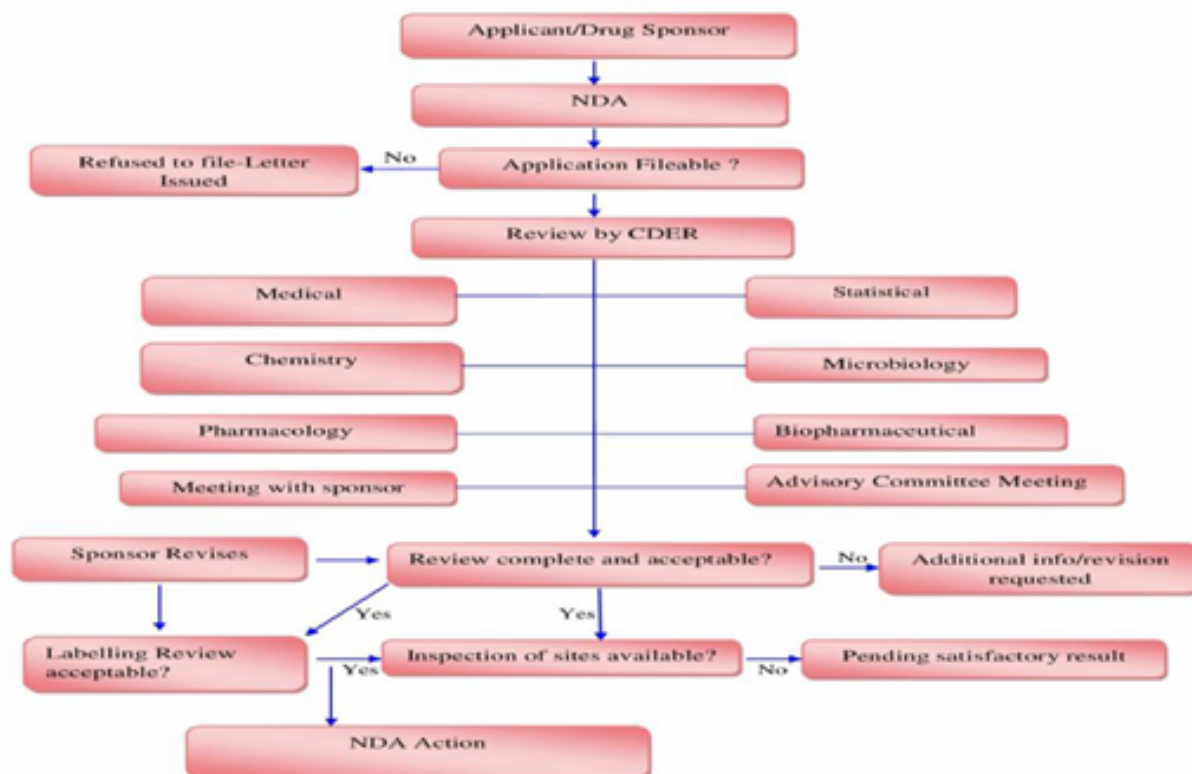


Figure 9: New Drug Application.

Requirements	India	EU	US
Agency	Single agency DCG I (CDSCO)	Multiple agencies <ul style="list-style-type: none"> ◊ EMEA ◊ CHMP ◊ National health agencies 	Single agency USFDA
Registration process	Single registration process	Multiple registration process <ul style="list-style-type: none"> ◊ Centralised (European community) ◊ Decentralised (at least 2 member states) ◊ Mutual recognition (at least 2 member states) National member state) 	Single registration process
TSE/BSE study data	Required	Required	Required
Braille code	Braille code is not required on labelling	Braille code is required on labelling	Braille code is not required on labelling
Post approval changes	Post approval changes: <ul style="list-style-type: none"> ◊ Major ◊ Moderate 	Post variation in the approved drug: <ul style="list-style-type: none"> ◊ Type IA ◊ Type IB ◊ Type II 	Post approval changes in the approved drug: <ul style="list-style-type: none"> ◊ Minor ◊ Moderate ◊ major

Table 1: Difference between India, EU and US.

Requirements	India	EU	US
Number of batches	1	3	1
Packaging	Not addressed	Not required	A minimum of 1,00,0000
Process validation	Required	Required	Not required at the time of submission
Batch size	Pilot scale batch	2 pilot scale plus 1 lab batch or minimum of one lakh units whichever is higher	1 pilot scale or minimum of one lakh units whichever is higher

Table 2: Manufacturing and control requirements.

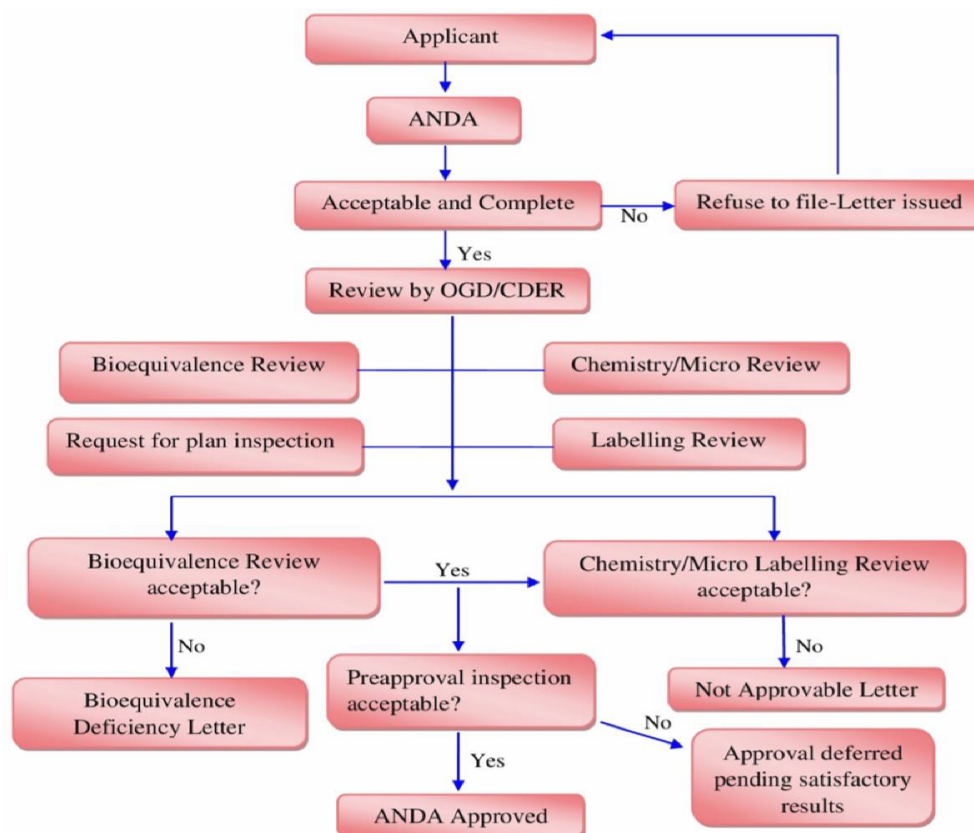


Figure 10: Abbreviated New Drug Application (ANDA).

5. Active ingredients
6. Route of administration, dosage form, strength
7. Labeling
8. Chemistry, manufacturing and control
9. Human pharmacokinetics and bioavailability
10. Samples
11. Analytical methods
12. Case report forms and tabulations.

The Division of Bioequivalence's Office of Generic Drugs of CDER issued "Guidance on statistical Procedures for Bioequivalence Studies Using a Standard Two Treatment Crossover Design" published in July 1992, which gives regulations on valid statistical analysis for bioequivalence assessment. This ensures the validity of bioequivalence assessment. The FDA has later given a draft guidance entitled "*in vivo* bioequivalence studies based on population and bioequivalence" that provides recommendations to sponsors of INDs, NDAs, ANDAs, who intend to perform studies based on a comparison of pharmacokinetic metrics. All approved drug products, including branded and generic drugs are listed in FDA's "Approved Drug Products with Therapeutic Equivalence Evaluations", called Orange Book. It includes products that are reviewed by FDA for both safety and effectiveness and for which NDAs or ANDAs have been approved. It also provides therapeutic

equivalence evaluations for multisource prescription drug products that contain the same active ingredients (Figure 10) [2,3].

Supplemental New Drug Application (SNDA)

After approval of NDA or ANDA, all significant changes in the conditions described in the applications must be approved, by filing a supplemental NDA or ANDA. Such changes like those in packing or ingredients should be approved by the CDER. New-uses approvals of already approved drugs coming under this category are a better innovation as they need lesser resources to review than that needed for original-use approvals (Tables 1 and 2).

Discussion

Generally, the drug approval process to be composed mainly in the two steps, application to conduct clinical trial and application to the regulatory authority for marketing authorization of drug. The new drug approval process of different countries is similar in some of the aspects where as it differs in some aspects. In most of the countries, sponsor firstly files an application to conduct clinical trial, and only after the approval by the regulatory authority, the applicant conducts the clinical studies and further submits an application to the regulatory authority for marketing authorization of drug. In all countries, information submitted to regulatory authorities regarding the quality, safety and efficacy of drug is same; however, the time, fees and review process of clinical trials and marketing authorization application different. For the purpose of harmonisation, the International Conference on Harmonisation (ICH) has taken major steps for recommendations in

the uniform interpretation and application of technical guidelines and requirements. Through The International Conference on Harmonization (ICH) process, the Common Technical Document (CTD) guidance has been developed for Japan, European Union, and United States. Hence, India also follows the same. This step will ultimately reduce the need to duplicate work carried out during the research and development of new drugs. Therefore, harmonization of drug approval processes either by ICH or WHO may be initiated at global level. The regulatory agency for INDIA and US is a single agency i.e. CDSCO [7,10] and USFDA respectively, whereas in EU, there are three regulatory agencies, they are EMEA, CHMP and NATIONAL HEALTH AGENCY. Europe also has multiple regulatory procedures when compared to US and INDIA. The approval time in all the countries is almost the same i.e., 12 to 18 months. The fee for the new drug approval in US is very high when compared to EUROPE [12] and INDIA.

Conclusion

The Drug approvals in the India, Europe & US are the most thought due in the world. The primary purpose of the rules governing medicinal products in India, Europe & US 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.

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