



A Review on Drug Approval in Regulated and Non-Regulated Markets

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ABSTRACT

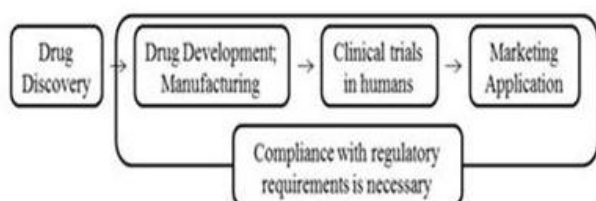
This topic aims to explain and compare the different regulations and processes for approval of drugs in regulated and non-regulated market. The pharmaceutical industry is one of the highly regulated industries, to protect the health and well being of the masses. The overall objective of a stringent drug approval system is to ensure that medicinal products of acceptable quality and efficacy are manufactured. By law; all new drugs must first be shown to be safe and effective before they can be approved for marketing. A regulated market is the provision of services that is regulated by a government approved body. Drug approval standards in regulated countries are considered by many to be the most demanding in the world. Discovering a new drug, and shepherding it through various review process, can take many years. To a large degree, these costs are mostly associated with the clinical testing. Coming to approval of drugs in typical non-regulated markets, they are becoming an important player in drug manufacture, in particular, the production of generics. Many of the generics produced are now found in all parts of the world. In conclusion, this study deals with the comparison of drug approval requirements between various regulated and non-regulated markets that could result in a clear understanding of the market positions of different countries and most importantly revise regulations for a healthier tomorrow.

Keywords: Generics, Non-Regulated Markets, Regulated Markets.

INTRODUCTION

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, having an overall objective of a stringent drug approval system is to ensure that medicinal products of acceptable quality and efficacy are manufactured.¹⁻⁵

METHODS¹



Drug Approval 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.

Investigational New Drug (IND) Application

It's an application filed to the FDA in order to start clinical trials in humans if the drug was found to be safe from the reports of Preclinical trials. The IND application is not a request for permission to market a new drug; instead, it is

an exemption from the statutory prohibition against shipping experimental drugs in interstate commerce without FDA approval. Drugs with approved INDs, however, can be legally shipped and administered to patients enrolled in clinical investigations.

New Drug Application (NDA)

If clinical studies confirm that a new drug is relatively safe and effective, and will not pose unreasonable risks to patients, the manufacturer files a New Drug Application (NDA), the actual request to manufacture and sell the drug in the United States. The NDA must include all data from animal and laboratory testing, comprehensive information about the drug's chemistry and pharmacology, and the complete results of all clinical investigations

Abbreviated New Drug Application (ANDA)⁴

It's an application made for approval of Generic Drugs. An ANDA is considered "abbreviated" because the sponsor is not required to reproduce the clinical studies that were done for the original, brand name product. Instead, generic drug manufacturers must demonstrate that their product is the same as, and bioequivalent to, a previously approved brand name product.

Drug Approval process in Europe³

Similar to the US requirements, there are two regulatory steps to go through before a drug is approved to be marketed in the European Union. These two steps are clinical trial application and marketing authorization application. There are 27 member states in the European Union (as of August 2007); clinical trial applications are



approved at the member state level, whereas marketing authorization applications are approved at both the member state or centralized levels.

Market Authorization Procedures in Europe

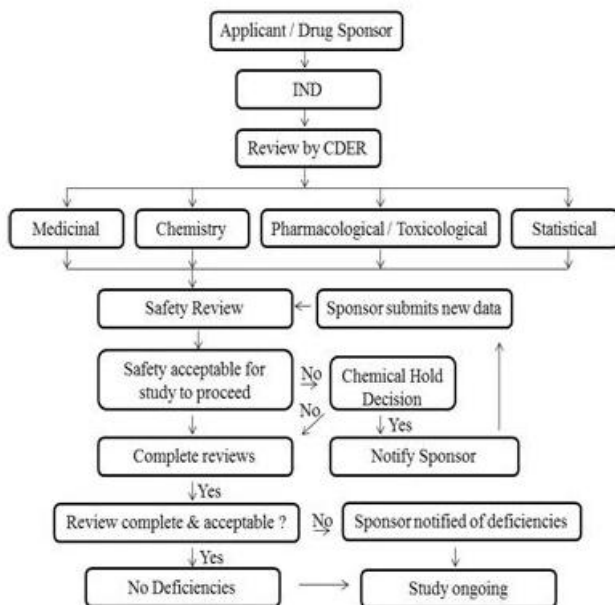
The National Procedure - 1 member state only

The centralized procedure - all member states simultaneously

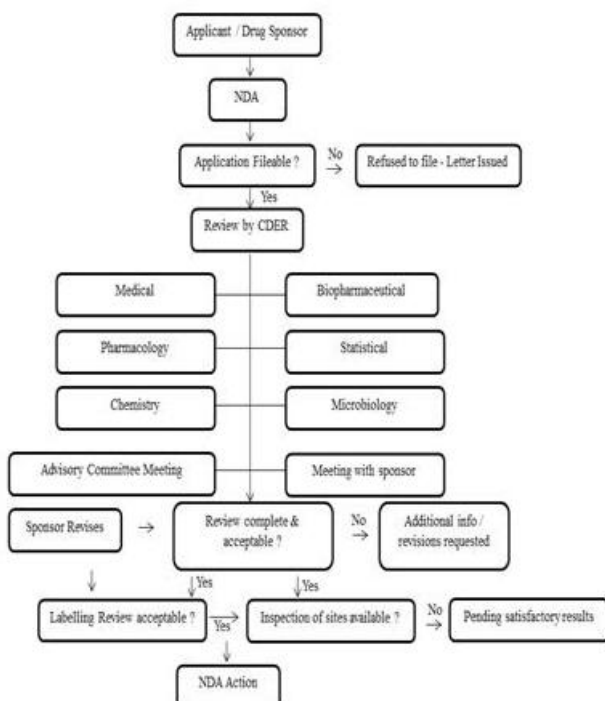
Mutual recognition process - a selected number of member state > 1(chosen by applicant)

Decentralized Procedure - a selected number of member states > 1 (chosen by applicant)

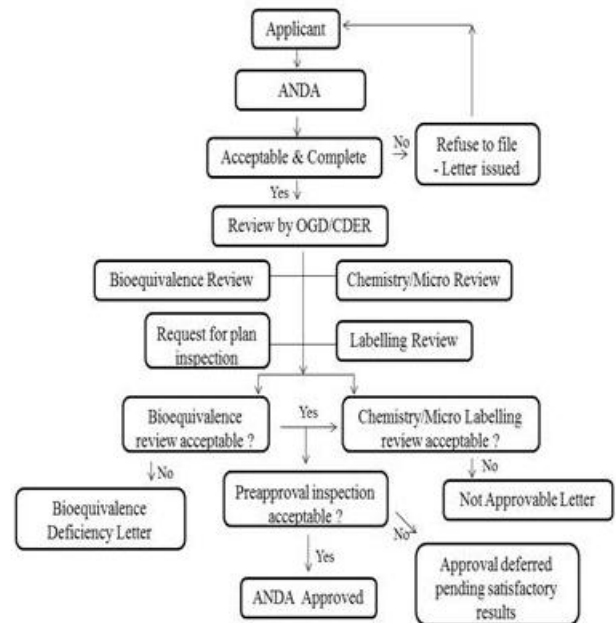
Investigational New Drug Application (IND)



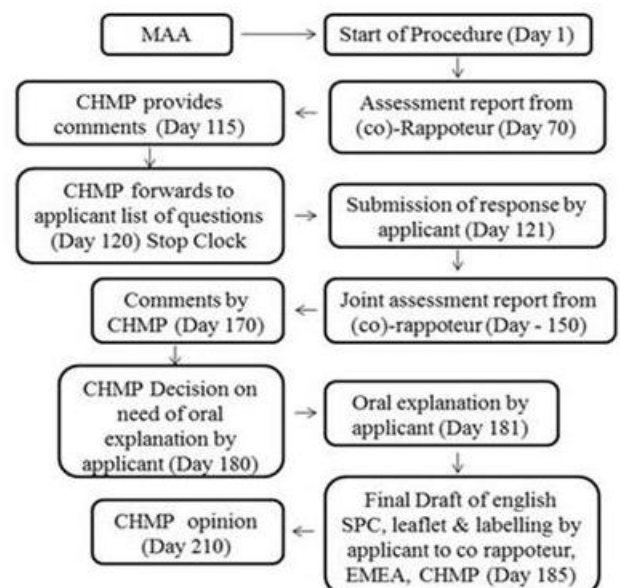
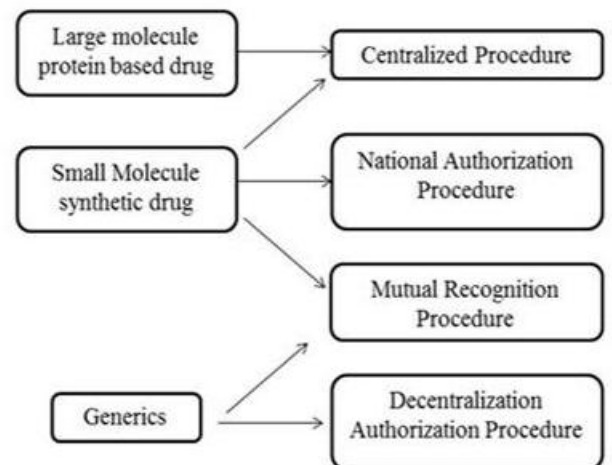
New Drug Application (NDA)⁴



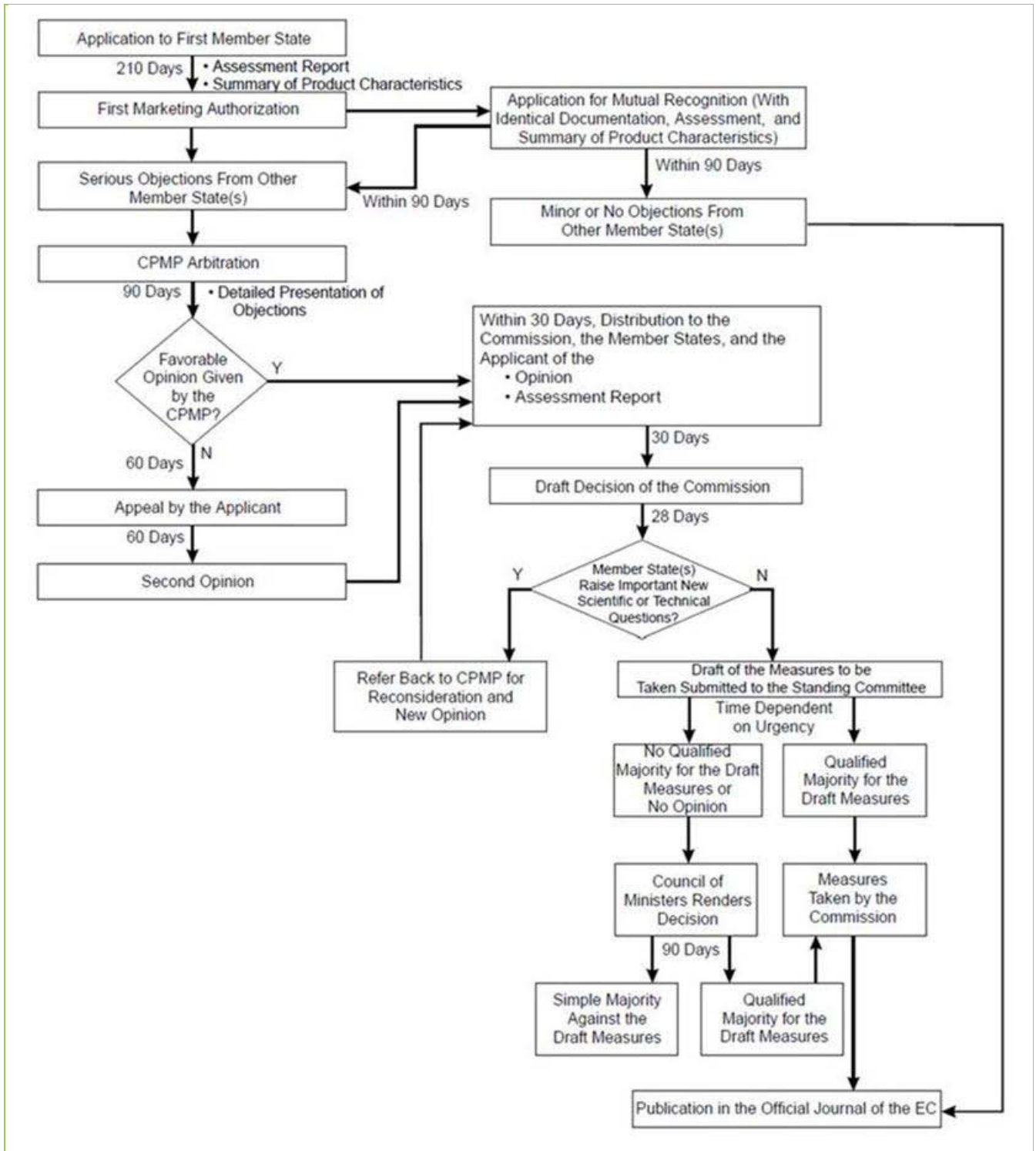
Generic Drugs Approval (ANDA Approval)



Centralized Procedure – EU



Decentralized Procedure - EU



Drug Approval in China

China’s Pharmaceutical market is growing at a very fast pace. The current data shows that the total market is around US\$20 billion & is the 9th largest pharmaceutical country in the world. China’s market is expected to be the world’s largest market by 2020.

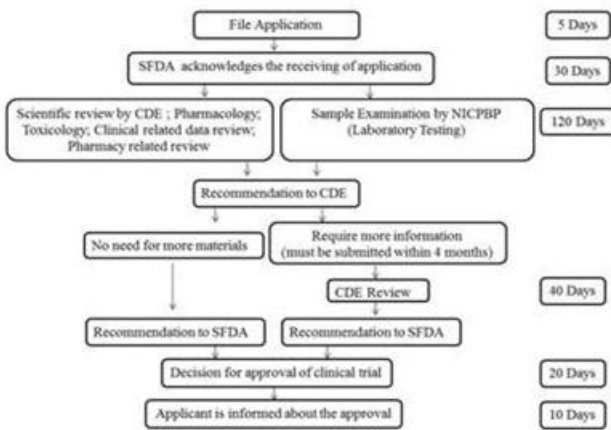
The regulation of drugs in china is under the jurisdiction of State Food & Drug Administration (SFDA) which is under control of the state council. The SFDA manages the regulation for “Western” drugs and Traditional Chinese

Medicine (TCM) under the Division of Pharmaceuticals, Division of Biological Products, and Division of TCM of the DDR.

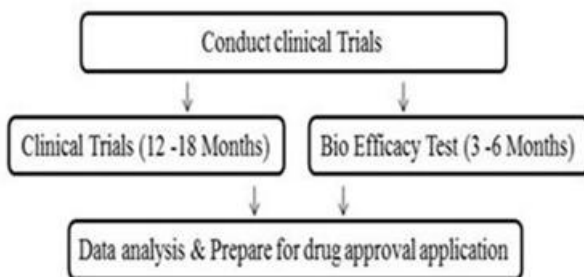
China offers a large pool of treatment naive patients for clinical trials. Clinical trials are one - third the cost of that in the United States and recruitments are expected to be rapid.

Step 1 - Application for approval of Clinical Study (Clinical / Bio-efficacy Study)

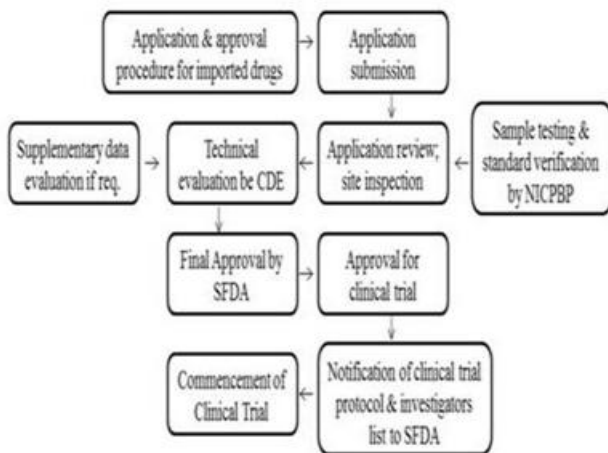




Step 2 - Clinical Trials



Imported “Western drug approval process” in China



Drug Approval in India

Increasingly, India is becoming an important player in drug manufacture, in particular, the production of generics. Many of India’s generics are now found in all parts of the world, challenging the dominance once held by the large pharmaceutical companies in Western countries.

Under India’s Drugs & Cosmetics act, Central Drugs Standard Control Organization (CDSCO) controlled by DCGI, is the Central Drug Regulating Agency responsible for approving new drugs, clinical trials, & maintenance of standard of drugs, jurisdiction of importation of foreign drugs, approval of manufacturing licenses & coordination of activities of the State Drug Control Organizations.

The central government is also responsible for the testing of drugs by the central drug labs, whereas the state authorities are responsible for the regulation of the manufacture, sale & distribution of drugs. Schedule Y of D&C rules sets up the requirements for clinical trials & that of schedule M for GMP compliance system.

The Approval process in India



- The drug approval process varies from one country to another. Other issues where the difference appears are, time taken for the approval of a CTA application, time taken in evaluation of marketing authorization application, registration fee, registration process & marketing exclusivity.
- Globally clinical trials are classified into 2 categories
- Category A: It includes clinical trials whose protocols have been approved by USA, UK, Switzerland, Australia, Germany, Canada, South Africa, Japan & Europe for which DCGI will reach to a decision whether to approve the trial within 2 - 4 weeks
- Category B: It includes clinical trials whose protocols have been approved in other countries which are not listed in Category A for which the DCGI turnaround time for these applications will be 8 - 12 weeks.
- Some countries have two review processes as normal review process & accelerated review process as in USA, China etc. & some countries have only a single review process as in India.

RESULTS





CONCLUSION

Today, the United States & Europe has perhaps the toughest drug approval standards in the world. Before new drugs can be sold, pharmaceutical manufacturers are required by law to produce large amounts of clinical data demonstrating that products are both safe and effective. In addition, safety and efficacy have to be proven through rigorous, well-controlled clinical trials, investigations that

are scientifically demanding and expensive to conduct. Although the drug regulation Act in regulated countries requires that all drugs be proven safe and effective, it doesn't specify just how safe and effective they have to be. For this reason, the FDA has a lot of discretion in deciding whether a drug's clinical data are sufficient to meet the statutory requirements for marketing approval. New & regulating countries like India & China are developing the best standards for regulating the drugs in order to demonstrate that products are both safe & effective.

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