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## **DRUG APPROVAL PROCESS IN US, EUROPE, INDIA, AND CANADA**

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### **ABSTRACT**

The existing limitations of regulatory affairs make it clear that various nations must adhere to various regulatory standards in order to approve marketing authorization Applications (MAA) for novel drugs. According to the US Food and Drugs Administration (UDFDA), the European Medical Agency (EMA), the Central Drug Standard Control Organization (CDSCO), and Health Canada, the study in this effort represents the medication approval procedure and regulatory standards. In the United States, FDA is the regulatory agency responsible for drug approval. The process typically involves multiple phases of clinical trials, rigorous data collection, and analysis to demonstrate the safety and effectiveness of the drug. The FDA may approve the drug for marketing and sale if it judges the advantages outweigh the hazards. In Europe, EMA is the central regulatory authority responsible for drug approval. The EMA follows a similar process to the FDA, but the approval is granted through a centralized procedure that allows for marketing authorization across multiple European Union (EU) member states. Health Canada is the regulatory body in charge of approving drugs in Canada. The process involves a thorough review of the drug's safety, efficacy, and quality data, and may also require additional studies or information before approval is granted. In India, the CDSCO is the regulatory agency responsible for drug approval. The process involves multiple stages of scrutiny, including pre-clinical and clinical trials, to ensure the safety and efficacy of the drug. Despite some similarities, the drug approval processes in these regions also have differences in timelines, requirements, and documentation.

**Keywords: Marketing Authorization Application (MAA), NDA, Clinical Trials, Drug Approval, Clinical Trail**

## INTRODUCTION:

To authorize the new drug in each of their individual nations, all nations must adhere to the regulatory standards. The hardest element is having a single regulatory strategy for Marketing Authorization Applications (MAA) for different nations. Thus, it is important to comprehend the regulatory criteria for MAA in each country. Each nation has its regulatory standards that must be met before a new medicine may be approved there. It is challenging to use a single regulatory strategy for the approval of a novel medicine in many nations [1, 2, 3]. Many companies focus on their regulatory frameworks in this field since it is well known that the United States of America (USA) and the European Union (EU) are the two most promising markets in the entire world for pharmaceutical products. As a

result, this article emphasizes the regulatory approaches used by the US, EU, India, and Canada. First, once a lead molecule for a certain illness has been found, it has to be improved. Pre-clinical tests are carried out on animals once a medicine is discovered to ensure its safety and effectiveness. To obtain approval for carrying out clinical research, a request should be made to the relevant country's responsible authorities. Clinical studies are carried out in four stages to ensure safety and efficacy before the medicine dose in humans is optimized. If the medicine meets the criteria for safety and efficacy and demonstrates that its advantages exceed its dangers, a Marketing Authorization Application (MAA) is then filed and authorized by the appropriate authorities.

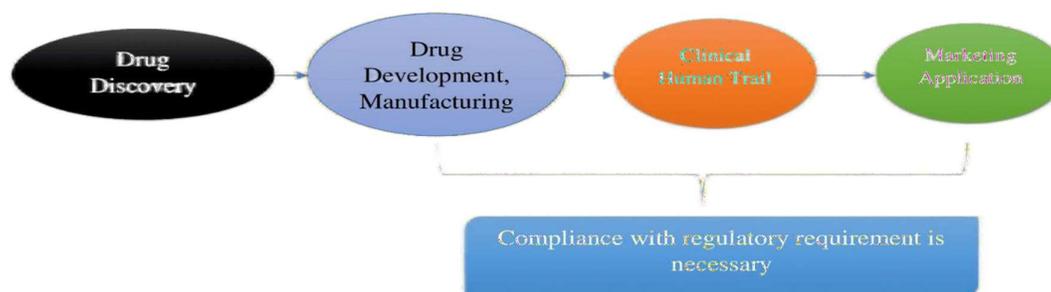


Figure 1: Regulations of Drug Approval Process

A request for authorization to commercialize a novel drug or innovative product is known as a new drug application, or NDA, and it is made to the relevant regulatory agency. To acquire this approval,

a sponsor must submit preclinical and clinical test findings, along with descriptions of manufacturing trials, for examination of the drug information. There are various phases of Clinical trial. They are:

Phase 0	Pre-Clinical Study	Conduct on Animals
Phase 1	Clinical Trial	20 to 80 Healthy Volunteers
Phase 2	Exploratory Trial	100 to 300 Volunteers
Phase 3	Confirmatory Trail	300 to 3000 Volunteers having that diseasefor what drug is discovered to treat
Phase 4	Post -Marketing Surveillance	Include n numbers of participants

NDA is subjected to a technological check after being received by the agency. This assessment makes sure that there is enough data and information in each section to support "filing" the application. Following the evaluation of an NDA, the sponsor may get one of three possible actions:

- Not approvable
- Approvable
- Approval [4]

### 1. Drug Approval Process in India:

The Indian Parliament passed the Drug and Cosmetic Act 1940 and Rules 1945 to control the importation, production, distribution, and sale of medications and cosmetics. The Central Drugs Standard Control Organization (CDSCO) and the Office of the Drugs Controller General (DCGI) were established. The Drug and Cosmetics Rules of 1945 were amended by the Indian government by including Schedule Y in 1988. The specifications and standards for clinical investigations are included in Schedule Y. A firm in India must complete Form 44 and supply the information required by Schedule Y of the Drugs and Cosmetics Act 1940 and Rules 1945 in order to obtain permission from the licensing authority (DCGI) to manufacture

or import a new pharmaceutical [5]. Clinical studies must be conducted in accordance with Schedule Y's requirements, and the findings must be submitted in the appropriate way, in order to demonstrate the drug's effectiveness and safety in the Indian population [6].

### Rule

According to section 122A of the Drug and Cosmetics Act, new medications that have been licensed and used for a number of years in other countries are exempt from the requirement for clinical research. All phases of clinical trials are necessary for therapeutic compounds created in India, according to Section 2.4 (a) of Schedule Y's Drugs and Cosmetics Act of 1940 and Rules of 1945. According to Section 2.4(b) of Schedule Y of the Drugs and Cosmetics Act 1940 and Rules 1945, applicants for drug substances discovered in nations other than India are required to submit data from those nations, and the licensing authority may either demand that he repeat all the studies or grant him permission to move on to Phase III clinical trials. The drug product must first demonstrate that it is safe and effective for use in humans in order to receive a license from the Central pharmaceuticals Standard

Control Organization (CDSCO) for importation or the development of new pharmaceuticals by the applicant. The information needed to approve a request to import or create a novel medicine for commercialization is outlined in the Drugs and Cosmetics Act of 1940 and its regulations 1945, 122A, 122B, and 122D [4]. The sponsor must provide the DCGI with full information on the following for an experimental new medication:

1. Generic name
2. Patent status
3. Brief description of physio-chemical/biological
4. Technical information
5. Stability
6. Specification
7. Manufacturing process
8. Worldwide regulatory status
9. Published Clinical trial Report
10. Proposed protocol and pro format
11. Trial Duration
12. During Master File
13. Undertaking to Report Serious or Life-threatening Adverse drug reaction.

Depending on how well the drug is accepted abroad, regional clinical trials may be necessary in India. Phase III studies are usually necessary when a medicine has previously received approval in another nation. India does not let phase I trials unless

data from other nations is supplied. Phase 1 studies may be carried out in India if a drug has a special connection to a disease affecting Indians, such as TB or malaria.

Bioavailability and bioequivalence (BABE) investigations should be conducted in accordance with BA/BE guidelines. Complete information on the drug's marketing situation in other countries is also required, in addition to the specifics on safety and efficacy. The prescription information, samples, testing procedures, product monographs, and labels must all be provided. A clinical study is normally approved in India after 3 months. When registering clinical studies with the Clinical TrialsRegistry of India (CTRI), participants and trial information must be provided [7]. The rules to be followed under The Drugs and Cosmetics Rules 1945 are:

**Rule 122 - A:** Request for authorization to Import New Drug

**Rule 122 - B:** A request for authorization to produce novel medications other than those listed in Schedules C and C (1).

**Rule 122 - D:** Authorization to produce or import a fixed-dose combination.

**Rule 122 - DA:** Request for authorization to carry out clinical studies for experimental or new drugs.

**Rule 122 - DAB:** Compensation in the case of injury or death during clinical trials.

### Approval Processes

- A. Submission of Clinical Trial application for evaluating safety and efficacy.
- B. Requirements for permission of new drugs approval.
- C. Post-approval changes in biological products: quality, safety, and efficacy documents
- D. Preparation of the quality information for drug submission for new drug approval.

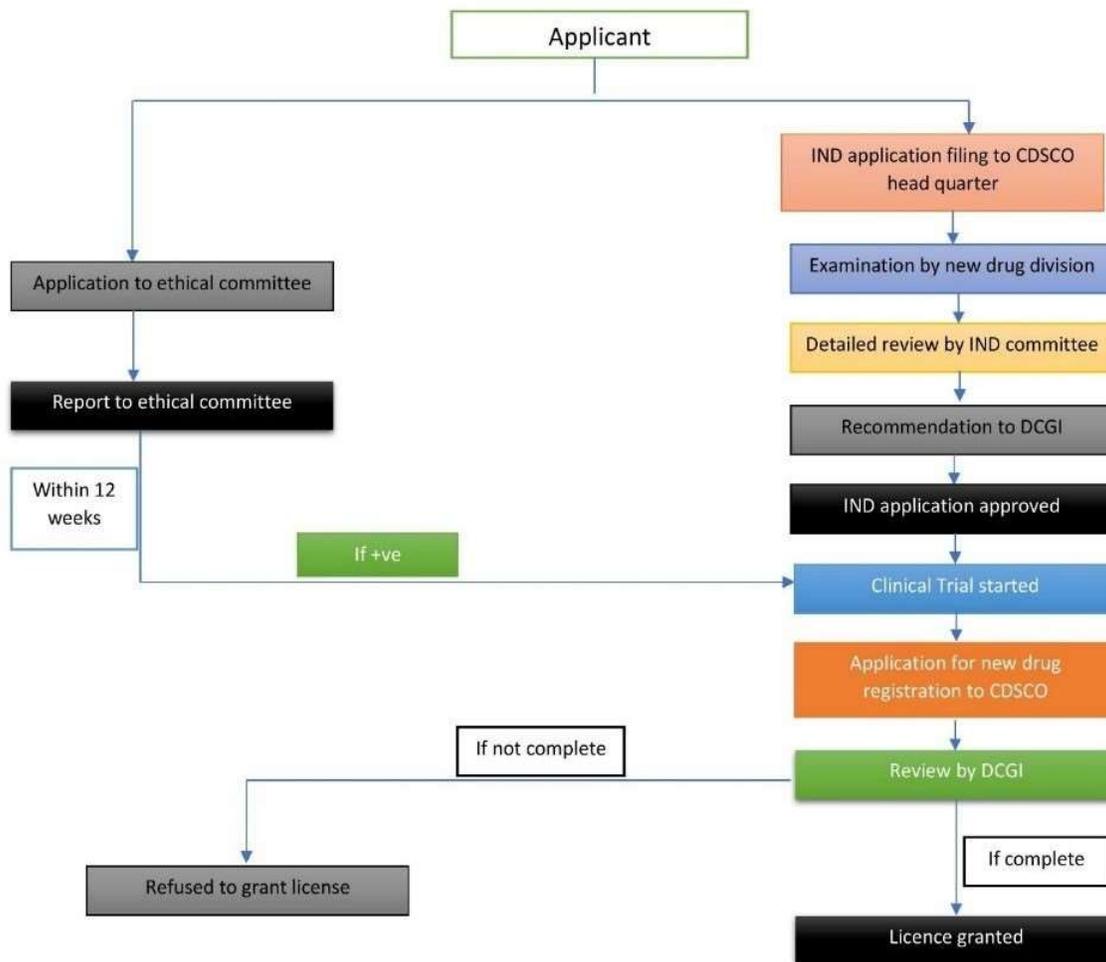


Figure 2: Drug approval process in India

**2. Drug Approval Process in Europe:**

The European Medicines Assessment Agency (EMA) was founded in London in 1995 to coordinate the evaluation and oversight of medications for both human and

veterinary use by the member states of the European Union (EU) [3]. It defined a detailed process for the creation, review, approval, and application of pharmacological recommendations. In

European nations, the approval procedure for pharmaceuticals is performed in two stages:

1. Clinical Trail Application
2. Marketing Authorization Application

The state's relevant authority receives a clinical trial application (CTA) that must be filed in order to conduct the clinical research within the European Union (EU). The

application is evaluated by the member state's appropriate authorities. Clinical research is only done with permission.

Only after having successfully completed all three clinical trial phases is a marketing authorization application made. The following volumes, whose titles are The Rules Governing Medicinal Products in the European Union, include the European Law including the pharmaceutical directives.

Volume 1	Pharmaceutical Laws for Human Use Medicinal Products.
Volume 2	Notice to Applicants for Human Medicinal Product.
Volume 3	Scientific Recommendations for Human Medicinal Products.
Volume 4	GMP Guidelines for Pharmaceuticals for Human and Animal Use.
Volume 5	Pharmaceutical Regulations for Veterinary Pharmaceuticals.
Volume 6	Notice to Applicants for Veterinary Medicine Products.
Volume 7	Scientific Recommendations for Veterinary Pharmaceuticals.
Volume 8	Limits on Maximum Residue.
Volume 9	Pharmacovigilance Recommendations for Drugs Used in Human and Veterinary Medicine.
Volume 10	Guidelines for clinical trials.

The market authorization of medicines is obtained through a variety of administrative processes and organizational structures

throughout Europe. The European Union offers four methods for obtaining marketing authorization for drugs [9, 10].



Figure 3: Different routes of EU to obtain marketing approval for pharmaceuticals

**Centralized Procedure**

Applicants can get a marketing authorization through the centralized approach that is accepted throughout the EU. Applications for biotechnological goods and New Chemical Entities are accepted via this approach (NCEs). NCEs

are classed as "List B," whereas all biotechnological products are grouped as "List A." According to this procedure, only one marketing authorization is legitimate for the entire European Union. The EMEA team reviews the application after receiving the Marketing Authorization Approval (MAA)

to make sure it is accurate and conforms with EU standards. Within ten days of the application's filing date, this review must be finished. The expenses are paid for by the sponsor. EMEA has 210 days to review the application after that. It may designate rapporteurs to examine applications and report findings to the Committee for Medicinal Products for Human Use (CHMP). The European Commission may have 90 days to decide whether to approve or reject the application after receiving a recommendation from CHMP. The entire approval process requires (210 + 90) days, or 300 days [8, 6]. Through a single application to EMA, this product has been approved by all of the participating nations. Centralized processes are required for

1. Drugs produced using any technological procedure, such as genetic engineering.
2. Drugs used to treat autoimmune illnesses, diabetes, cancer, HIV/AIDS, neurological disorders.
3. Drugs used to treat uncommon disorders that have been formally categorized as "orphan medicines"

### **Decentralized Procedure**

This allows for the simultaneous recognition of a product by a number of member countries. It is said to be a highly powerful tactic. A decentralized procedure is utilized in a few of the member states to obtain

marketing authorizations. A national regulatory body (RMS) receives the application from the sponsor along with a list of all CMSs and a reference member state. The Summary of Product Characteristics (SPCs) and application must be verified by the RMS, whomust also provide a draught assessment report within 210 days, send a copy to the CMSs, and approve the report within 90 days. However, a poor judgement may have an impact on registration in many nations [3].

### **National Procedure**

Each country in Europe has its own regulatory body. National process is a set of rules that each country has individually enacted. Even tiny businesses can afford the expenses. The expense of translation into English or other regional languages is reduced. It builds the foundation for mutual recognition. Procedure National procedure cannot be used to register biotechnological techniques. For the same, centralized filing via EMA is required. Marketing permission is given upon consideration of the application that the sponsor submits to the national competent body in accordance with national regulations [3].

### **Mutual Recognition Process (MRP)**

A product that has been registered in one nation is recognized in another under this. For the first registration, just one application has to be submitted. After some local

changes, another member country approves the same application. Pharmaceutical Product Evaluation Report by EU Member Countries: Before granting approval, the Mutual Recognition Process examines the Reference Member State's evaluation report.

The proposal may be sent to as many more member states as desired, and the CMSs have 90 days to protest upon receipt of a copy of the RMS's assessment report. A nationwide marketing permit with a comparable SPC is issued by each CMS.

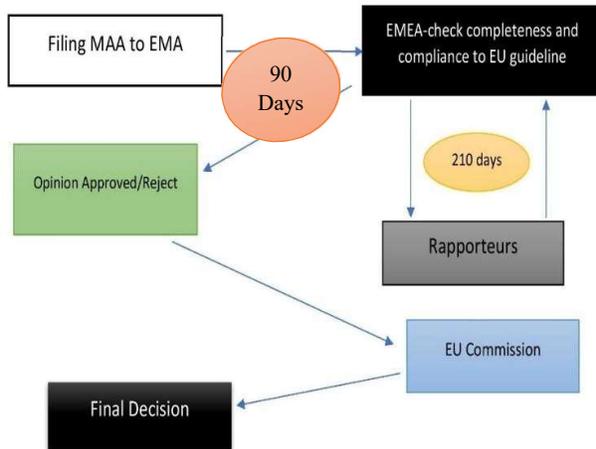


Figure 4: Centralized Process [9, 10]

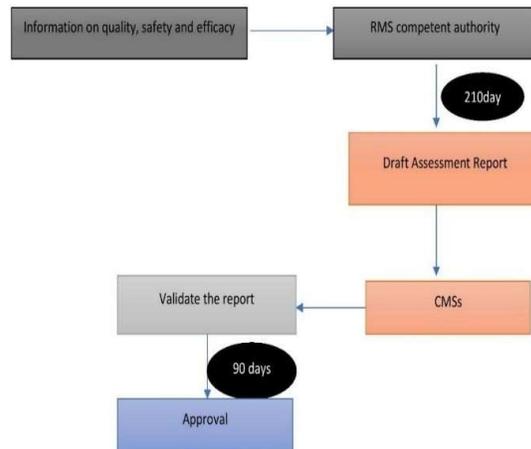


Figure 5: Decentralized Process [9,10]

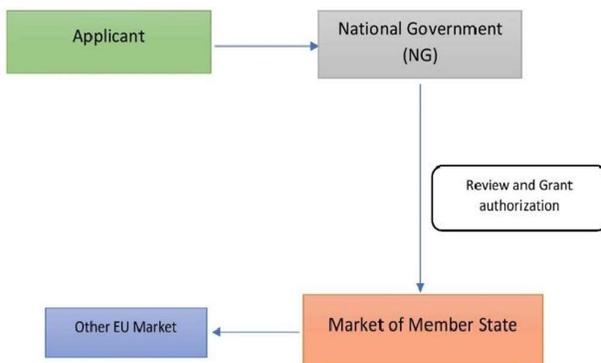


Figure 6: National Process [9,10]

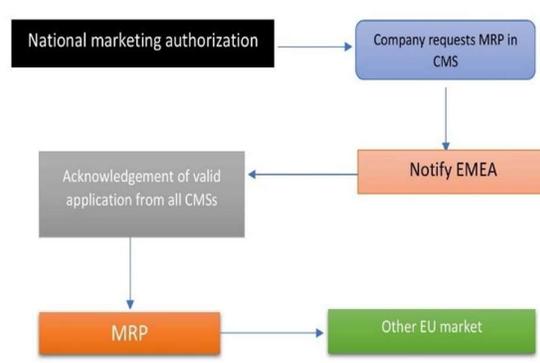


Figure 7: Mutual Recognition Process [9,10]

### 3. Drug Approval Process in USA

The United States may have the tightest regulations in the world for approving new medications. Many people think that American drug approval standards are the strictest in the world. The U.S. Pharmacopoeia's establishment in 1820

marked the start of a new era in American drug regulation. Congress adopted the first Food and Drugs Act in 1906, which formalized standards for drug potency and purity. The Federal Food, Drug, and Cosmetic Act (of 1938), which enacted new regulations mandating that new

pharmaceuticals be proven to be safe before being marketed, was nonetheless brought about by the sulphanilamide disaster in 1937 [4]. The task of preserving and enhancing the welfare of society is under the purview of the Food and Drug Administration (FDA). Clinical trials (CT) and new drug application (NDA) approval are the two steps in the FDA's new drug approval process, which is similar to the generic medication approval procedure. A novel drug application (NDA) controls the new drug product (NDP). These applications are accepted in eCTD format for evaluation. The NDA's primary subjects are the product's efficacy and safety. only after an investigational new drug (IND) application has been submitted to the FDA. Drug laws and policies in the US In 1820, the United States Pharmacopoeia (USP), which set criteria for medicine purity and potency, was created.

### **Investigational New Drug Application**

Prior to human testing, the FDA received an application [11]. Information on chemistry, production and controls, pharmacology, and toxicity, as well as any prior human experience, is described.

### **Types of IND**

- ✓ **An Investigational IND:** It is filed by a physician who also controls the administration or distribution of the

experimental drug as well as plans, organizes, and conducts the research. An authorized pharmaceutical, an unapproved medication, or both may be the subject of a study IND submitted by a physician to examine them for a new indication or in a new patient group [12].

- ✓ **Emergency IND:** In an emergency situation where there isn't enough time to submit an IND, the FDA can utilize this to allow the use of an experimental drug.
- ✓ **Treatment IND:** While the FDA examination is continuing, it is filed for investigational drugs that have showed promise in clinical trials for conditions that are severe or urgently life-threatening.

Commercial and research (non-commercial) kinds make up the two IND classifications. The IND application must include information in the following three categories: 1. Animal pharmacology and toxicological studies, 2. Manufacturing data, 3. Details on clinical researchers and their techniques. The sponsor must wait 30 calendar days after submitting the IND before starting any clinical study. The FDA can assess the IND during this period to ensure that study participants won't be exposed to an unacceptable high risk [12].

### IND Content and Format

21 Code of Federal Regulations (CFR), Section 312 specifies the specifications for the content and presentation of IND applications. When planning to undertake clinical research, a sponsor (commercial business) or investigator should file an "Investigative New Drug Application" in the manner described below:

1. Cover Letter
2. Form FDA 1571
3. Form FDA 1572
4. Table of contents
5. Letter of authorization
6. Clinical Protocol
7. Informed Consent
8. Investigational brochure
9. Statement about product development
10. Additional information [13]

### New Drug Application (NDA)

To get authorization for the commercialization of a new medicine in the USA, a New medicine Application must be submitted. The NDA contains both the data from the IND and the findings of clinical trials demonstrating effectiveness and safety. After obtaining an NDA, the FDA must begin the review process within 60 days [11].

NDA Contents and Format The application is in two copies and is:

1. Archival copy
2. Review copy [14]

**Archival Copy:** It comprises copies of tabulations and clinical study case report forms, which FDA reviewers can use as a reference tool to find material not included in the review copy.

**Review Copy:** Each folder has a different binding for each technical aspect.

The FDA can consult with the sponsor at least twice, once after the conclusion of Phase 2 clinical trials and once before to the filing of an NDA, known as a pre-NDA meeting. The review panel will evaluate the research's results and decide whether or not to approve the proposal after doing so [14].

### 4. Drug Approval Process in CANADA

The Food and Medications Act, which was created to safeguard the public by regulating the sale of food, pharmaceuticals, medical equipment, and cosmetics, applies to marketing requests for pharmaceutical items in Canada [15, 17]. The Health Protection Bureau (HPB), a division of Health Canada, is in charge of monitoring this pharmaceutical approval process.

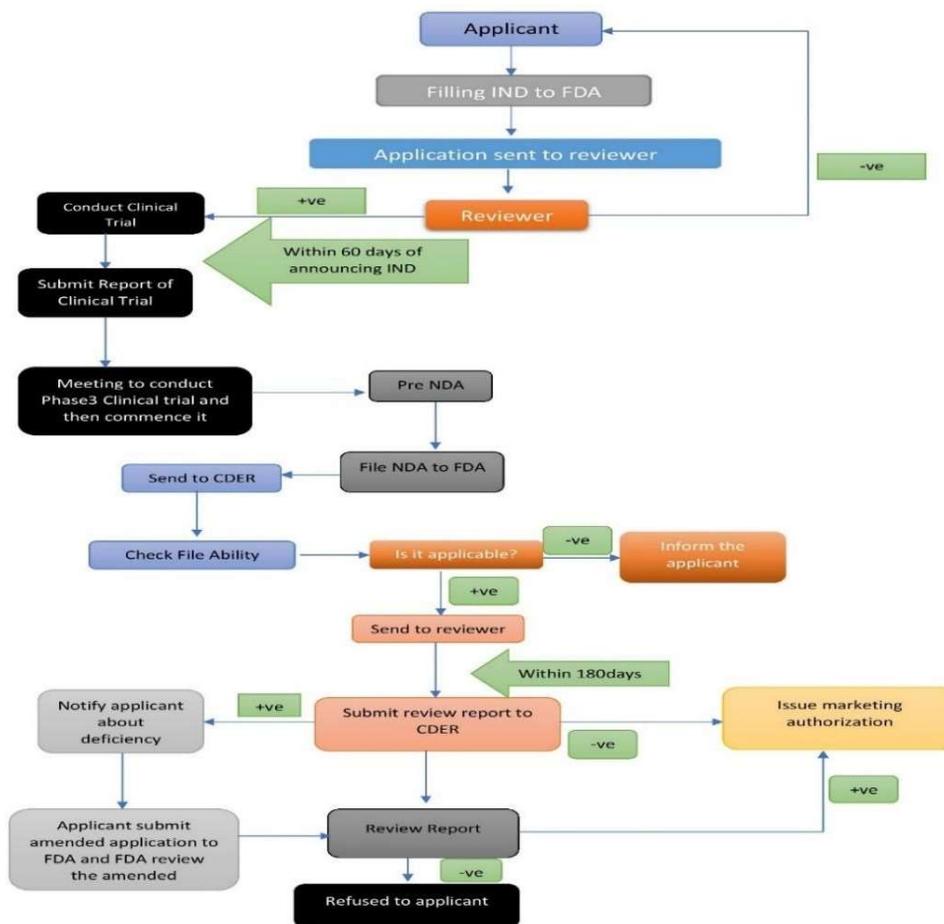


Figure 8: Drug approval process in US

**Preclinical development**

The HPB requires the findings of non-human experiments to be submitted before any new pharmaceutical product may be tested on humans. This data may have been acquired via in vitro research, in vivo animal studies, further (foreign) human trials, or data gathered in earlier Canadian studies for various purposes. The required information is frequently composed of the findings of toxicological and pharmacological tests.

**Investigational New Drug (IND)**

Pharma companies must submit an investigational new drug (IND) application

prior to starting human clinical research, same like in the US. However, before submitting the formal IND application, the manufacturer must deliver a bundle of data to the HPB. An overview of the planned clinical protocols, the reason for the proposed Canadian clinical trials, the manufacturer's worldwide clinical development strategy, and a synopsis of the chemistry and manufacturing information for the medicine must all be included in this data package. In order to resolve any ambiguities in the information package, the HPB examines this data and speaks with the

manufacturer. The drug producer sends a formal IND comprising the aforementioned information along with a submission certificate attesting that all of the information included in the IND is correct and complete after the HPB accepts the information package. Clinical trials may start if the IND properly indicates that the drug is generally safe for human use and that the intended clinical trial method won't put human subjects in needless danger. The HPB's Drugs Directorate (DD) clearance is quiet, much like the FDA's, and the drug developer may begin performing clinical research as long as the clearance is not rescinded. The reason(s) the DD rejected the IND must be disclosed to the drug manufacturer. If the maker of the medicine feels that it has sufficiently allayed the DD's concerns in the meantime, it may submit a new IND for the impacted drug.

### **Clinical Trails**

The four stages of clinical trials in Canada are relatively equivalent to those in the US. Canada's clinical trials include:

- 1) Phase I: designed to gather information about the drug's clinical pharmacology and human safety
- 2) Phase II: aimed to gather information on the drug's safety and clinical efficacy
- 3) Phase III: designed to gather

information on the human dosage as well as to confirm and improve the clinical safety and efficacy data already gathered.

- 4) Phase IV trials are carried out after a medicine has been given permission to be sold in Canada.

The manufacturer of the medication is required to inform the Minister of National Health and Welfare of any serious adverse drug reactions and other side effects. Clinical trials conducted after a product has been marketed, which are usually more extensive than Phase I-III trials and may not be subject to the same regulations as pre-approval studies, are a crucial approach for drug manufacturers to learn more about their products. Clinical trial data from other countries may be accepted by the HPB [15, 17].

### **New Drug Submission (NDS)**

The company submits an NDS after the successful conclusion of clinical trials in an effort to give the HPB enough data to permit the new drug to be commercialized in Canada. After contacting internal experts to review the NDS, the DD may also consult external experts if the burden is too large or more knowledge is needed. These professionals assess the quantity and caliber of the supplied data to make sure that:

- The medicine in issue satisfies the requirements for safety and

effectiveness set out in the Food and medicine Act and Regulations.

- The controls and manufacturing processes used to make the medicine are effective.
- The suggested labelling for the medicine is sufficient.

The company submits an NDS after the

successful conclusion of clinical trials in an effort to give the HPB enough data to permit the new drug to be commercialized in Canada. If the burden is too great or additional knowledge is required, the DD may turn to external experts after consulting with internal experts to assess the NDS [16, 17].

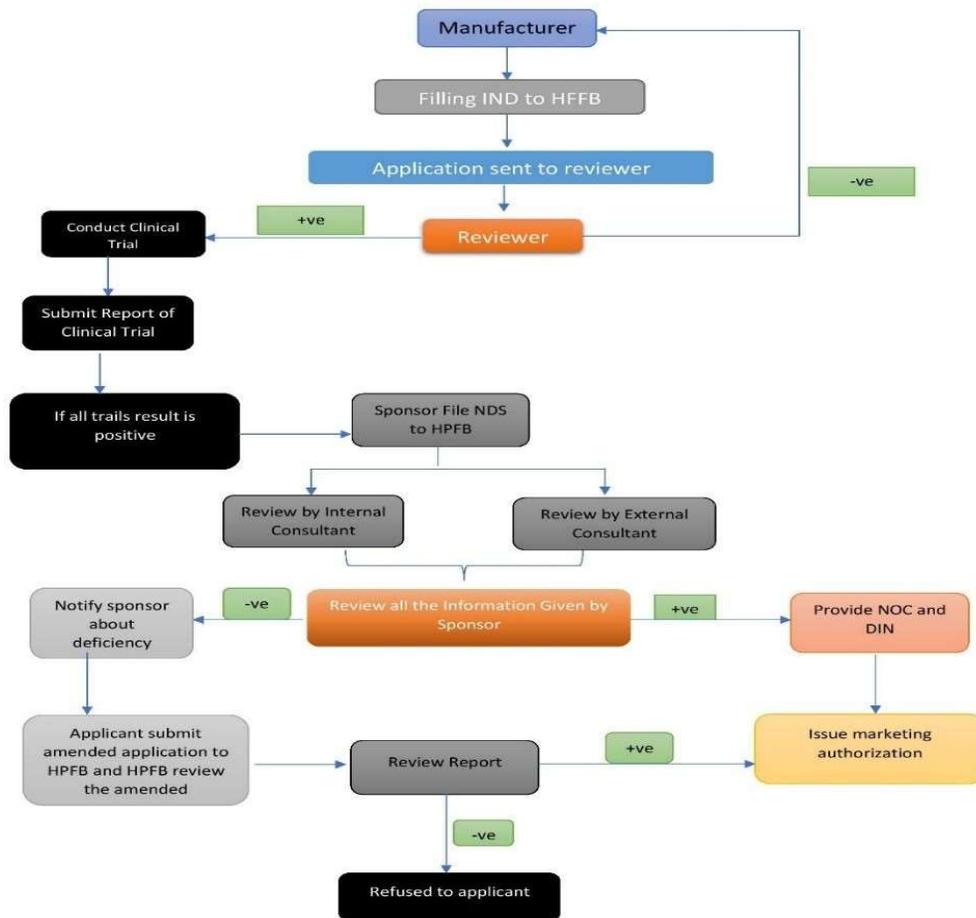


Figure 9: Drug approval process in Canada

**CONCLUSION:**

India, Europe, the United States, and Canada all have rigorous and complicated drug approval processes in place to make sure new medications are safe and effective

before they are made accessible to the general public. Preclinical testing, clinical trials, and regulatory review are often only a few of the steps that are included in the process. Depending on the nation, it might

take anything from a few months to many years to approve a new medicine. These four nations all have the same objective of assuring the safety and efficacy of new medications before they are made available to the general public, despite the variances in their respective drug approval procedures. This procedure includes a crucial step for safeguarding the public's health, the medication approval process. As new technology and scientific advancements are created, the medication approval procedure is always changing. The regulatory bodies in these four nations are dedicated to keeping abreast of the most recent advances in medication research and are always looking for ways to streamline the drug approval procedure. By doing this, it is made sure that patients have access to new medications as soon as they are both safe and effective.

#### REFERENCE:

- [1] Ng R. Drugs: From discovery to approval. 3rd ed. Nashville, TN: John Wiley & Sons; 2015. <https://www.wiley.com/onus/Drugs:+From+Discovery+to+Approval,+3rd+Edition+on-p-9781118907276> [Access Date: 30 Dec. 22]
- [2] Chakraborty R, Yadav K (2018) Drug approval process in US, Europe, and India and its regulatory requirements: A Review 6: 31-39.

- [3] Mahapatra AK, Sameeraja NH, Murthy PN (2014) Drug Approval Process in United States of America, European Union and India: A Review. *AcrcTra* 1: 13-22.
- [4] Pharmainfo.in  
<https://www.jpsr.pharmainfo.in/Documents/Volumes/vol9Issue10/>  
[Access Date: 30 Dec. 22]
- [5] Gupta NV, Reddy CM, Reddy KP, Kulkarni RA, Shivakumar, et al. (2012) Process of Approval of New Drug in India with Emphasis on Clinical trials 13: 17-23.
- [6] U.S. Government Accountability Office. European Union drug approval: Overview of new European medicines evaluation agency and approval process *Gao.gov.*:  
<https://www.gao.gov/products/HEHS-96-71> [Access Date: 5 Jan. 23]
- [7] A / B noc for export division B. Guidance document for BA/BE noc for export. *Gov.in.* Available from: [https://cdsco.gov.in/opencms/export/sites/CDSCO\\_WEB/Pdf-documents/BA\\_BE/guidance\\_doc\\_BABE\\_NOC1\\_1Jan2018.pdf](https://cdsco.gov.in/opencms/export/sites/CDSCO_WEB/Pdf-documents/BA_BE/guidance_doc_BABE_NOC1_1Jan2018.pdf)  
[Access Date: 10 Jan. 23]
- [8] Van Norman GA. Drugs and devices: Comparison of European and U.S. approval processes. *JACC*

- Basic Transl Sci. 2016;1(5):399–412.:  
<https://www.sciencedirect.com/science/article/pii/S2452302X16300638>  
[Access Date: 10 Jan. 23]
- [9] EUR-Lex - 52013XC0802(04) - EN - EUR-Lex. Europa.eu.: [https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:52013XC0802\(04\)](https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:52013XC0802(04)) [Access Date: 20 Jan. 23]
- [10] Europa.eu.:[https://www.ema.europa.eu/en/documents/leaflet/applying-european-union-marketing-authorization-medicinal-products-human-use\\_en.pdf](https://www.ema.europa.eu/en/documents/leaflet/applying-european-union-marketing-authorization-medicinal-products-human-use_en.pdf) [Access Date: 20 Jan. 23]
- [11] About FDA [Internet]. U.S. Food and Drug Administration. FDA: <https://www.fda.gov/about-fda> [Access Date: 21 Jan. 23]
- [12] Investigational new drug (IND) application [Internet]. U.S. Food and Drug Administration. FDA: <https://www.fda.gov/drugs/types-applications/investigational-new-drug-ind-application> [Access Date: 23 Jan. 23]
- [13] IND applications for clinical treatment: Contents and format. U.S. Food and Drug Administration. FDA: <https://www.fda.gov/drugs/investigational-new-drug-ind-application/ind-applications-clinical-treatment-contents-and-format> [Access Date: 23 Jan. 23]
- [14] eCFR :: 21 CFR part 314 -- applications for FDA approval to market a new drug [Internet]. Ecf.gov.<https://www.ecfr.gov/current/title-21/chapter-I/subchapter-D/part-314> [Access Date: 24 Jan. 23]
- [15] Appel WC. Post-marketing surveillance in Canada. Drug. Information Journal. 1996;30(3):655–9.
- [16] Canada.ca.:<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/health-canada-clinical-trials-database.html> [Access Date: 30 Jan. 23]
- [17] Canada.ca.:<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/fact-sheets/drugs-reviewed-canada.html> [Access Date: 30 Jan. 23]