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"A Review Role Of Regulatory Agencies In The World For Controlling The Quality Of Medicines"

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Abstract: Drugs are crucial for saving lives, preserving health, preventing diseases, halting epidemics, and boosting a nation's economy. As a result, the cost of pharmaceuticals is borne by the general public, government, pharmaceutical industry, and research institutions. However, for this to happen, the medicine must be high-quality, reliable, and safe. In order to ensure that medications are developed, produced, imported, exported, and distributed in accordance with established standards, there are regulations in place. Governments create powerful National Regulatory Authorities (NRAs) to ensure that pharmaceutical products are adequately regulated, thereby preserving and advancing public health. Global pharmaceutical rules are essential for ensuring the efficacy, quality, and safety of the medicines. The responsibility for enforcing laws and issuing guidelines for medication development, licencing, registration, production, labelling, storage, marketing, distribution, drug pricing, import, and post-marketing research on pharmaceutical products falls on the shoulders of the pharmaceutical regulatory agency. Pharmaceutical businesses that are interested in the global market must adhere to the various regulatory requirements of other nations' pharmaceutical laws. It is challenging to develop a single regulatory strategy for a drug product's Marketing Authorization Application (MAA) that is relevant to numerous nations. As a result, the Common Technical Document (CTD) was created to offer a standard structure for electronic filing of applications for the registration of pharmaceuticals. This review article provides an outline of the pharmaceutical regulatory bodies in India, the United States, and Europe.

Keywords: WHO, Regulatory Agency ,CDSCO, US FDA, EMA, MHRA, TGA, ICH guidelines

1. Introduction

The main objective of Regulatory Agency is to provide the basis for the assurance of high quality of drug products which can increase consumre's interest for ensuring the efficacy, quality, and safety. Regulatory frameworks vary from region to region. The Committee on Herbal Medicinal Products in Europe is an excellent model for how scientfic evalution of herbal medicines can be harmonized and accepted through science-based standards to ensure public health. As the pharmaceutical industries worldwide becoming much competitive, authorities are reaponsible in effective drug regulation required to ensure the safety, efficacy and quality of durgs, as well as the accuracy and approtriateness of the durg information and support for working within regulation. This expedites the development and delivery of safe effective healthcare products to individuals around the world.

Additionally, regulatory authorities act as a guardian to ensure the safety, efficacy and quality of drugs available to the public, to identify the strength and weakness of drug regulation and to purpose strategies for improving drug regulation. These authorities also play a vital role in ensuring and expanding regularly implementation in parts of the world. The international regular organisation Play essentials role of the all aspects of pharmaceutical regulations releted to drug product registration, manufacturing, distribution, price control, marketing, R and D, and IPR protection. The major challenges of these regulatory bodies are to promote the public health and protect the public from harmful and dubious drugs, to establish proper legal issues covering all products claim and to increase worldwide regulatory growth to ensure safety of public.Every counties has their own regulatory authorities, which are responsible for enforcing the rules and regulations and issue guidelines for drug development, licensing, registration, manufacturing, marketing and labelling of pharmaceutical products.[1]

Pharmaceutical regulations are a set of legal, administrative, and technical measures that governments implement to make sure the safety, efficacy, and quality of medicines, as well as the relevance and accuracy of product data available to the public. The term "regulation" includes a variety of texts such as guidelines, recommendations, procedures, policies, etc. that have different legal bases and authority. Regulatory agencies provide strategic, tactical and operational guidance as well as support for working within regulations to accelerate the

development and delivery of safe and effective medicines or healthcare products to public. Current pharmaceutical industry is very organized, systematic and compliant to international regulations. Multiple tragedies like sulphanilamide elixir, vaccine tragedy and thalidomide tragedy led to the need for a well-controlled regulatory framework. This has resulted into efficient manufacturing and marketing of safe, effective and quality healthcare products.[2]

Table No1. Regulatroy Agencies in world

Sr. No	Country	Regulatory Agencies
1	India	Central Drug Standard Control Organization (CDSCO)
2	USA	Food and Drug Administration (FDA)
3	UK	Medicines and Healthcare products Regulatory Agency (MHRA)
4	Europe	European Medicines Agency (EMA)
5	Australia	Therapeutic Goods Administration (TGA)
6	Canada	Health Canada
7	Italy	Italian Pharmaceutical Agency (IPA)
8	China	State Food and Drug Administration (SFDA)
9	Thailand	Ministry of Public Health
10	Japan	Ministry of Health, Labour & Walfare (MHLW)
11	South Africa	Medicines Control Council (MCC)
12	Malaysia	National Pharmaceutical Control Bureau, Ministry of Health
13	Pakistan	Drugs Control Organization, Ministry of Health
14	Hong kong	Department of health: Pharmaceutical Services
15	Singapore	Centre for Pharmaceutical Administration health Sciences Authority

2. World Health Organization

2.1 Introduction

Health according to WHO " Health is state that complete physical, mental and social well being, and not merely the absence of disease or infirmity."

- The World Health Organization (WHO) is specialized agency of the United Nations that concerned with international public health.
- It was established on 7 April 1948, which is celebrated every has world health day. Headquartered in Geneva, Switzerland.
- It is responsible for providing leadership on global health matters.
- WHO's logo was chosen by the first world health assembly in 1948. The logo consists of united nations symbol surmounted by a staff with a snake coiling around it. The staff with the snake has long been a symbol of medicine and the medical profession.

2.2 History

- The first global health organization. In latter half of 19th contrary, sver cholera epidemics was occurred. Are that time, series of international sanitary confarance were held in Europe to co- ordinate policy and practice around quarantine and disease management.
- The league of Nations established a health organization in 1920.

2.3 Establishment

- Establishment of United Nations is in 1945 marked as a period of aggressive internationalism and international organisations building and though health was not intially through to be under the U.N.
- After its motion started by Brazilian and chainse delegates establish an international health organization and was generally accepted.
- A group of health experts, working on emergency relief in world II were changed with task of drifting a constitution to define the structure and mandet of the would become known as the world health organization.

2.4 Objective of WHO

- The develop and implement multiple sectoral public for health, integrated gender to facilitate the community empowerment, together with action with action for health promotion, self care and health protection.
- To attain a level of health that will permit them to lead a socially and economically productive life in the whole world.

2.5 WHO Works

- Prevention and control specific diseases.
- Development of comprehensive health services.
- To improve the family health.
- Environmental health.
- Health statistics.
- Bio-medical research.
- Assembly of health literature and information.
- Cooperation with organisation to get the equilibrium in improved status.

2.6 Function of WHO

- To determine international health public programme.
- To remove the work past years.
- To approve the Budget.
- To elect member states designate a person serve for 3 years on expensive board.
- To supervisor the financial policies of the organisation and rewives and approves the proposed programme budget.[21]

3. Defination of Regulatory Agencies

A regulatory agency (regulatory body, regulator) or independent agency (independent regulatory agency) is a government authority that is responsible for exercising autonomous dominion over some area of human activity in a licensing and regulating capacity.[2]

4. Major National Regulatory Agencies World Wide

4.1 Drug Regulatory Agency in India

4.1.1 Central Drugs Standard Control Organization (CDSCO)

CDSCO is the National Regulatory Authority (NRA) of India. It works under the Directorate General of Health Services (DGHS), Ministry of Health & Family Welfare; Government of India. The CDSCO is the central drug regulatory authority for execution of functions assigned to the central government under the Drugs and Cosmetics Act. CDSCO head office is located in New Delhi. CDSCO and state regulatory bodies are jointly responsible for grant of licenses of blood and blood products, intravenous fluids, vaccines and sera. Within the CDSCO, Drug Controller General of India (DCGI) is responsible for regulation of pharmaceutical products and medical devices. The Drug Technical Advisory Board (DTAB) and the Drug Consultative Committee (DCC) advise the DCGI. Licensing and classification of Medical devices is the function of the Central Licensing Approval Authority (CLAA). It is also responsible for setting and enforcing safety standards, performing post-market surveillance, issue of warnings and recall of pharmaceutical products for adverse events.[3-5]

4.1.1.1 Functions of CDSCO

Central licensing authorities are responsible for

- New drugs approval.
- Performing clinical trials.
- Establishing standards for drugs.
- Quality Control of imported drugs, import registration and licensing.
- Coordination of the activities of state drug control authorities by giving expert opinion to uniformly enforce the D&C Act.

State licensing authorities are responsible for

- Regulation of production, sale and marketing of drugs.

Other Functions

- Grant of license for blood banks, Large Volume Parenteral (LVP), vaccines, recombinant DNA products and some.
- medical devices Amendment of D & C Act rules.
- Ban of old drugs and cosmetics.
- Grant of test license, personal license, No Objection Certificate (NOC) for export.
- Testing of new drugs and cosmetics.

Functions of Central Drug Testing Laboratories

- Acts as an appellate authority in drug quality related disputes.
- Procurement, preservation and distribution of international reference standard pharmaceutical substances.
- Preparation of national reference standard pharmaceutical substances and microbial cultures useful in pharmaceutical analysis. And also distribution of standard drugs and cultures to state QC laboratories and pharmaceutical manufacturing establishments.
- Training of analysts appointed by state drug control laboratories and other institutions.
- Training of WHO personnel from abroad on advanced analytical methods.
- Advises the central drug control authorities with respect to quality and toxicity of drug awaiting license.
- To work out analytical specifications for monograph preparation for the Indian Pharmacopoeia and the Indian Homoeopathic Pharmacopoeia.
- Additionally the CDL also associates with the WHO in preparing standards and specifications for InternationalPharmacopoeia.
- Research and analysis of drug and cosmetics.
- Registration samples analysis for site registration approval as per Good Manufacturing Practices (GMP).
- To take up analytical research on standardization of drugs.[6]

4.1.1.2 Schedule Y of D&C Act 1940 and Rules 1945

- Section 2.4 (a) of Schedule Y says for those drug substances which are discovered in India all phases of clinical trials must be performed.
- Section 2.4 (b) of Schedule Y says that for those drug substances which are discovered in foreign countries; the applicant should submit the data available from those countries and the licensing authority may ask him to repeat all the studies or may permit him to proceed from Phase III.
- Section 2.8 of Schedule Y says that the licensing authority may require Pharmacokinetic studies (Bioequivalence studies) first to confirm that the data generated in Indian population is equal to data generated abroad and then require him to proceed with Phase III.

The exact requirements of clinical trials may vary from case to case and depending on the extent to which licensing authority is satisfied about its safety and efficacy. New drug approval in India is a very complicated process, which should meet necessary requirements along with New Drug Application to Food and Drug Administration (FDA).[4-5]

4.1.1.3 There is provision in Rule 122A of D&C Act 1940, that certain trails may be waived off if

- the licensing authority considers that in the interest of public.
- may grant permission for import of drugs based on the data of the clinical trials conducted in other countries.
- in the case of drugs which are approved and being used for many years in other countries.[7]

4.2 Drug Regulatory agency in USA

4.2.1 United States Food and Drug Administration (USFDA)

The Food and Drug Administration (FDA) is an agency of United States Department of Health and Human Services. It consists of 6 product centers, 1 research center, and 2 offices. The Center for Drug Evaluation and Research (CDER) ensures that safe and effective drugs are available to enhance the health of the people.

4.2.1.1 Food and Drug Modernization Act states that the USFDA has 4 roles.

- To improve health by reviewing research and new products approval.
- To assure that foods and drugs are safe and properly labelled.
- To work with other countries to decrease the burden of regulation.
- To cooperate with scientific experts and consumers to properly implement these obligations.

The Commissioner of Food and Drugs, who is appointed by the President, leads the FDA. The FDA was empowered by the US Congress to enforce the Federal FD&C Act. The FDA has its headquarters in unincorporated White Oak, Maryland. The agency also has 223 field offices and 13 laboratories throughout the 50 states.

4.2.1.2 Functions of USFDA

- Protecting and improving public health by control and supervision of Food (dietary supplements, food additives etc.,)

- Drugs including both prescription and over the counter (non-prescription) drugs.
- Biological products like vaccines, blood & blood products.
- Cellular & gene therapy products.
- Allergenic, tissue and tissue products.
- Medical devices and Electromagnetic Radiation Emitting Devices (ERED).
- Cosmetics, animal foods and veterinary medicines.
- Tobacco products.

➢ Protecting the public health by ensuring that foods are safe and wholesome.
➢ Helping to fasten product discovery or innovations.[8]

4.3 Drug Regulatory Agency in Europe

4.3.1 European Medicines Agency (EMA)

EMA is a European Union (EU) agency which evaluates and supervises medicinal products. Before 2004, it was known as the European Agency for the Evaluation of Medicinal Products or European Medicines Evaluation Agency (EMEA). The EMA was established in 1995 with funding from the EU and the pharmaceutical industry, as well as indirect subsidy from member states, in order to harmonize the work of existing national regulatory bodies for medicines. The EMA is a decentralized body located in London, before UK's withdrawal from the EU. It was relocated to Amsterdam in March 2019. The EU is presently the source of about 1/3rd of the new drugs brought onto the international market each year.[9]

4.3.1.1 Functions of EMA

- Provides timely patient access to new medicines.
- Scientific suggestions and protocol assistance.
- Orphan designation of medicines for rare diseases.
- Developing scientific guidelines on needs for the safety, efficacy and quality testing of medicines and setting standards.
- Promotes research and development of new medicines in the pharmaceutical industry by European small and medium sized enterprises.
- Continuous monitoring and supervision of the safety of medicines.
- Assessment of pharmaceutical manufacturing companies compliance with their Pharmacovigilance (PV) obligations.
- Contributes to international PV activities with other authorities outside the EU.
- Provides information on the safety of medicines to the public.
- Publishes impartial and clear information about medicines and their approved uses.[10]

4.4 Drug Regulatory Agency in United Kingdom

4.4.1 Medicines and Healthcare products Regulatory Agency (MHRA)

The Medicines and Healthcare products Regulatory Agency (MHRA) is an executive agency of the Department of Health and Social Care in the United Kingdom which is responsible for ensuring that medicines and medical devices work and are acceptably safe.

The MHRA was formed in 2003 with the merger of the Medicines Control Agency (MCA) and the Medical Devices Agency (MDA). In April 2013, it merged with the National Institute for Biological Standards and Control (NIBSC) and was rebranded, with the MHRA identity being used solely for the regulatory centre within the group. The agency employs more than 1,200 people in London, York and South Mimms, Hertfordshire.

MHRA is divided into three main centres namely: MHRA regulatory (the regular and pharmaceutical and medical devices industries,) clinical practice research Datalink (CPRD)and NIBSC.

4.4.1.1 The MHRA has following roles.

- Operate post-marketing surveillance – in particular the Yellow Card Scheme – for reporting, investigating and monitoring of adverse drug reactions to medicines and incidents with medical devices.
- Assess and authorise of medicinal products for sale and supply in the UK.
- Oversee the Notified Bodies that ensure medical device manufacturers comply with regulatory requirements before putting devices on the market.
- Operate a quality surveillance system to sample and test medicines to address quality defects and to monitor the safety and quality of unlicensed products.
- Investigate internet sales and potential counterfeiting of medicines, and prosecute where necessary.
- Regulate clinical trials of medicines and medical devices.
- Monitor and ensure compliance with statutory obligations relating to medicines and medical devices.
- Manage the Clinical Practice Research Datalink and the British Pharmacopoeia.[1

4.5 Drug Regulatory Agency in Australia

4.5.1 Therapeutic Goods Administration (TGA)

- The TGA is responsible for conducting assessment and monitoring activities to ensure that therapeutic goods available in Australia are of acceptablestandards.
- Established on 15 February1991.

The Therapeutic Goods Administration (TGA) is the medicine and therapeutic regulatory agency of the Australian Government. As part of the Department of Health and Aged Care, the TGA regulates the quality, supply and advertising of medicines, pathology devices, medical devices, blood products and most other therapeutics. Any items that claim to have a therapeutic effect, are involved in the administration of medication, or are otherwise covered by the Therapeutic Goods Act 1989, the Therapeutic Goods Regulations 1990, or a ministerial order, must be approved by the TGA and registered in the Australian Register of Therapeutic Goods.[11]

4.5.1.1 Objective Of TGA

- To provide a national framework for the regulation of therapeutic goods in Australia to ensure the quality, safety and efficacy of medicines and ensure the quality, safety and performance of medical devices.
- Essentially therapeutic goods must be entered on the. Australian Register of Therapeutic Goods (ARTG) before they can be supplied in Australia.

4.5.1.2 Role of the TGA

- The TGA carries out an overall control through five main processes.
- Pre-market evaluation and approval of registered products intended for supply in Australia.
- Development, maintenance and monitoring of the systems for listing of medicines.
- Licensing of manufacturers in accordance with international standards of GMPs.
- Post-market monitoring, through sampling, adverseevent reporting, surveillance activities, and response to public inquiries.
- The assessment of medicines for export.

4.5.1.3 Structure Of TGA

The TGA's offices are grouped into following core groups.

a. TGA Executives.
b. Market Authorization Group (MAG).
c. Monitoring and Compliance Group (MCG).
d. Regulatory Support Group.
e. Office of Regulatory Integrity (ORI).

a. TGA Executives

The TGA Executives has overall responsibility for the management of the TGA's regulatory functions and activities.

- The TGA Executives comprises.
- TGA National Manager.
- Principal MedicalAdviser.
- Principal LegalAdviser.
- Chief Regulatory Officer.
- Chief Operating Officer.

b. Market Authorization Group (MAG)

The Market Authorization Group is responsible for undertaking evaluations of applications to approve new therapeutic products for supply in Australia. The MAG makes decisions whether to approve or reject market authorization of medicines, medical devices and blood and tissues that are imported, exported, manufactured and supplied in Australia.

c. Monitoring and Compliance Group (MCG)

The Monitoring and Compliance Group is responsible for ongoing monitoring of therapeutic products approved for supply in Australia to ensure they meet the necessary standards throughout their lifecycle.

d. Regulatory Support Group

Provides regulatory support services to the TGA, this includes technology communications, the legal, finance, and information parliamentary information management, and human resource management services.

e. Office of Regulatory Integrity (ORI)

The Office of Regulatory Integrity (ORI) provides an independent and objective review and advisory service to provide assurance to the National Manager of the TGA that the TGA's financial and operational controls are operating in an efficient, effective and appropriate manner and that its regulatory controls are operating in an efficient, effective and appropriate manner and are consistent with relevant legislative requirements.[12]

5 Drug approval process of regulatory agencies in world

5.1 Drug approval process in India

For manufacture or import of a new drug, the company should obtain permission from the licensing authority (DCGI) by filing in Form 44 and submitting the necessary data according to Schedule Y of D&C Act 1940. Fig. 1 shows the drug approval process in India. To prove the efficacy and safety of imported drug in Indian population, clinical trials are conducted as per the Schedule Y guidelines and the report is submitted in specified format. DCGI reviews the application and approves if acceptable.[4]

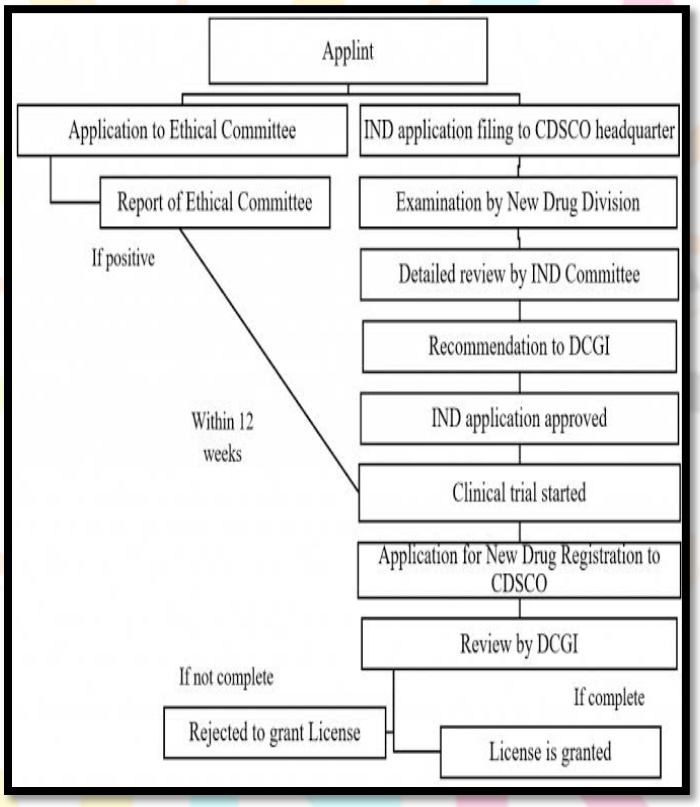

Fig. No.1:- Flow chart of drug approval process in India.

5.2 Drug approval process in United States

5.2.1 Investigational New Drug (IND) Application

After drug discovery, preclinical trials are performed and results are reported. If the drug is found to be safe the drug developer (or) sponsor files IND application to the FDA in order to initiate clinical trials in humans volunteers. IND applications require information regarding animals used for pre-clinical studies, toxicological studies, and data including the composition, manufacturer, stability and clinical protocols of the trial. After approval of IND application, the investigators of the clinical trial can distribute a drug to multiple study locations across the US. IND application approval process is represented. A pre -IND meeting can be arranged with the FDA to discuss on issues like design of animal studies, intended study protocol for conducting the trials and chemistry, production & control of the IND. Such a meeting will help the drug developer or sponsor to organize animal research, gather information, and design the study protocol based on recommendations by the FDA. There are three types of IND applications: Investigator IND, Emergency Use IND (EIND), and treatment IND.

The Investigator IND

A physician, sometimes on behalf of an institution/sponsor, files an investigator IND application. The investigator must wait minimum one month after submission of an IND application, in order to start any clinical trials. If the FDA does not have any objection, within that time Phase-I clinical trials can be started.

The EIND

An EIND application requests for FDA approval to utilize an experimental drug in an emergency when there is no sufficient time for following a standard IND process.

Treatment IND

Treatment IND applications are filed for approval to make use of an investigational new drug that shows promise in clinical trials prior to study completion, FDA review and final approval. These are also called Expanded use INDs.[13-16]

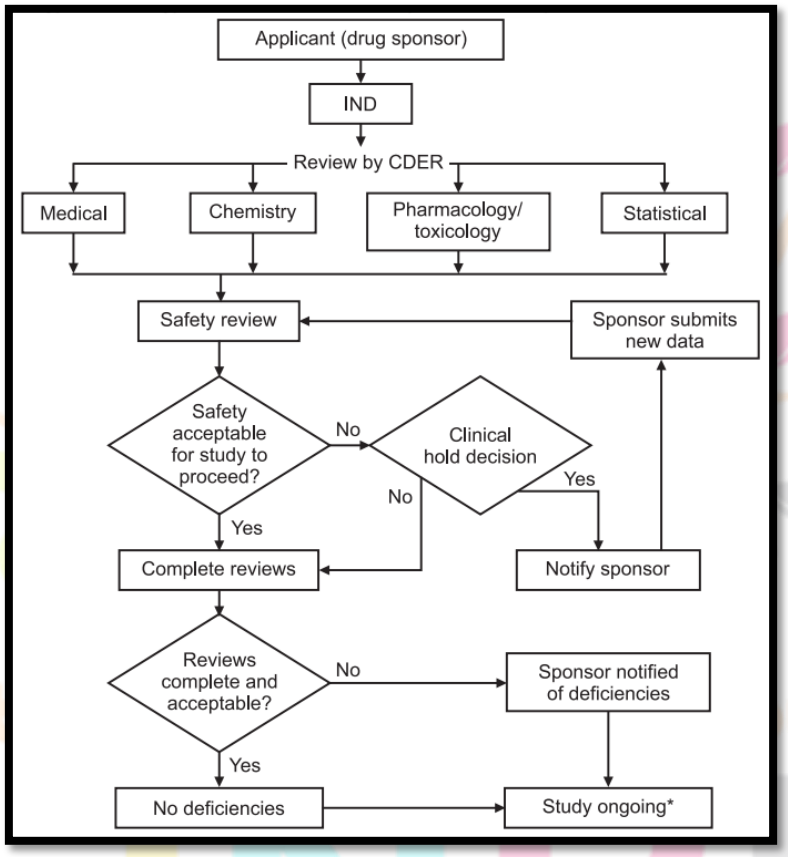

Fig No.2:- Flow chart of Investigational New Drug Application.

5.2.2.New Drug Application (NDA)

The manufacturer files a NDA, if the clinical studies prove that a new drug is safe (without any unwanted or toxic effects) and effective. It is the actual request to produce and sell the drug in the US. NDA is submitted based on FD&C Act 505(b). NDAs are submitted for:

- New molecular entity (NME).
- New formulation of previously existing approved drug.
- New combination of multiple drugs.
- New indication (claim) for existing drug.

The NDA application requires all data regarding the drug, manufacturing process, facilities, quality control & quality assurance, product description, packing and labeling. FDA personnel will assess clinical data, tests drug samples, audit the manufacturing facilities, and check labelling. FDA review completes within 180 days of receipt of application. describes NDA application approval process. If FDA denies approval of the NDA, it sends a response letter including specific deficiencies and recommendations for the applicant in order to make the application viable. Unsuccessful applicants can request a hearing. Post approval of the NDA, the applicant can manufacture and market the drug.

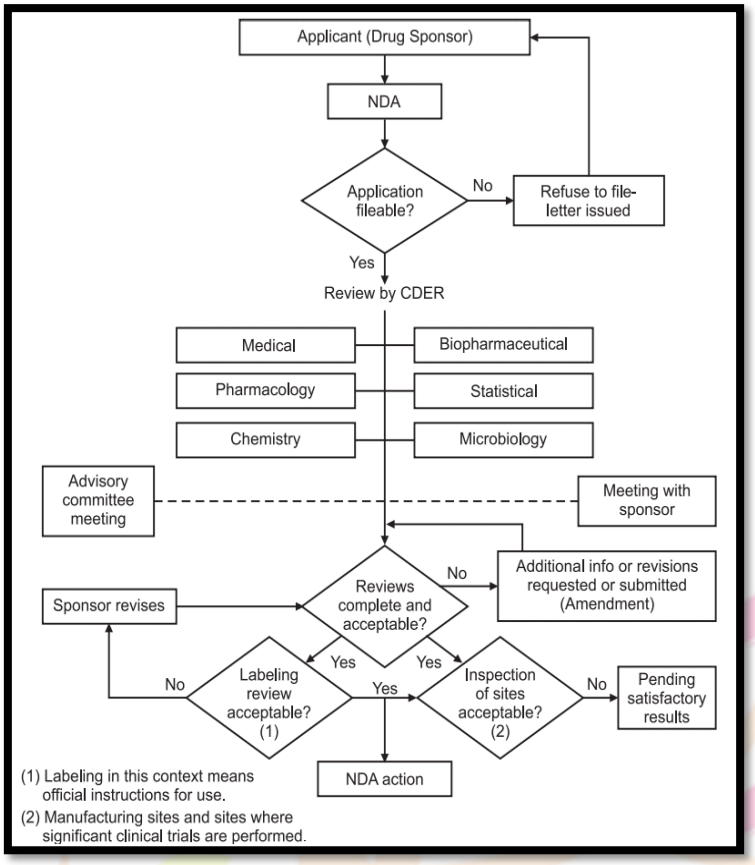

Fig.No.3:- Flow Chart of New Drug Application.

5.2.3. Abbreviated New Drug Application (ANDA)

ANDA is an application filed for approval of generic drug product. The sponsor is not required to repeat the clinical studies that were done for the original/brand name drug product. Instead of this, generic drug product manufacturers must prove that their product is bioequivalent to, an already approved brand name product. Therefore, the generic drug applications are termed "abbreviated". Based on FD&C Act 505(j) ANDA is submitted.

ANDAs are submitted for generic drugs to which NDA must be approved previously and listed (known as the Reference Listed Drug). ANDA may not be submitted up to five years after the date of the approval of the NME. After approval, an applicant may produce and market the generic drug product to provide a safe, effective and lower cost alternative medicine to the public. All approved drug products (innovator and generic) are listed in Orange Book (FDAs Approved Drug Products with Therapeutic Equivalence Evaluations).

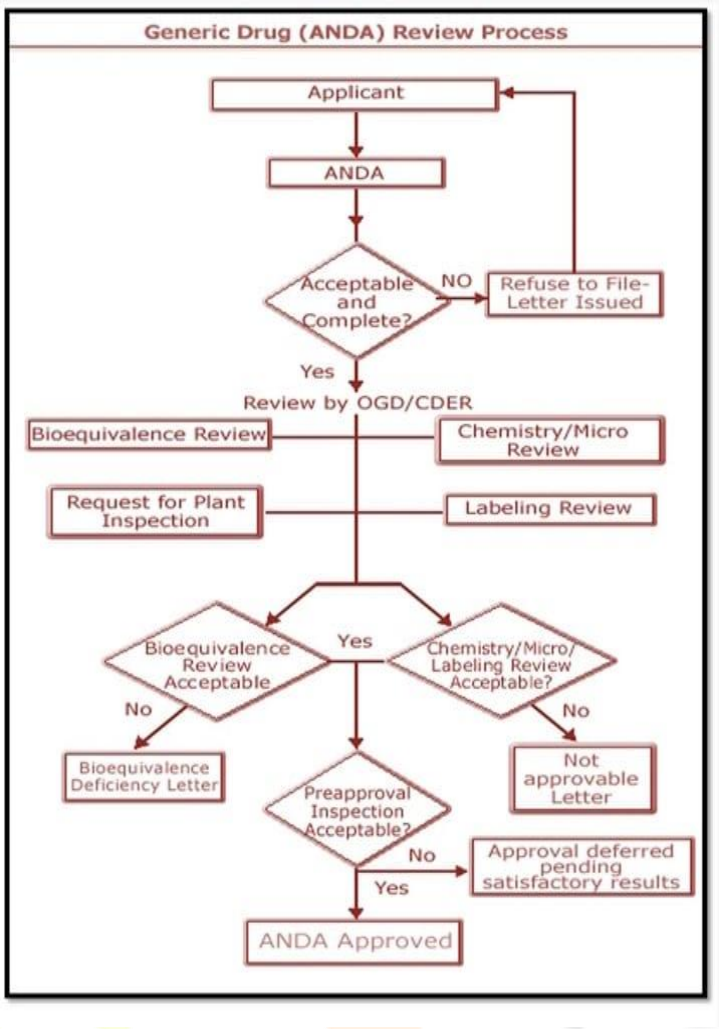

Fig.No.4:- Flow chart of Abbreviated New Drug Application.

5.3 Process of drug approval in EU

Similar to the US FDA requirements, there are two regulatory steps to go through prior to approval of a drug for marketing in the EU. These two steps are clinical trial application and marketing authorization application. In the EU there are 28 member states; clinical trial applications approval is done at the member state level, whereas MAA are approved at both the member state and centralized levels. Approval for manufacture and marketing of a drug can be obtained by any of the following four procedures, depending on the drug class and the preference of the manufacturer:

A. Centralized process.
B. National process.
C. Mutual recognition.
D. Decentralized procedure.

A. Centralized process

This process allows applicants to obtain a marketing approval that is valid in all the EU member states. EMA opinion issued within 210 days after filing application, and submitted to European Commission for final approval. Centralized process is mandatory for the medicines that are:

- derived from biotechnology processes (genetic engineering).
- used for the treatment of cancer, HIV/AIDS, diabetes, neuro-degenerative disorders/autoimmune diseases and immune system dysfunctions.
- officially designated 'Orphan medicines' which are used for rare diseases.
  This process is controlled through the EMA. Every EU member state is represented on the EMA Committee for Medicinal Products, which provides a single license valid in all EU member states.

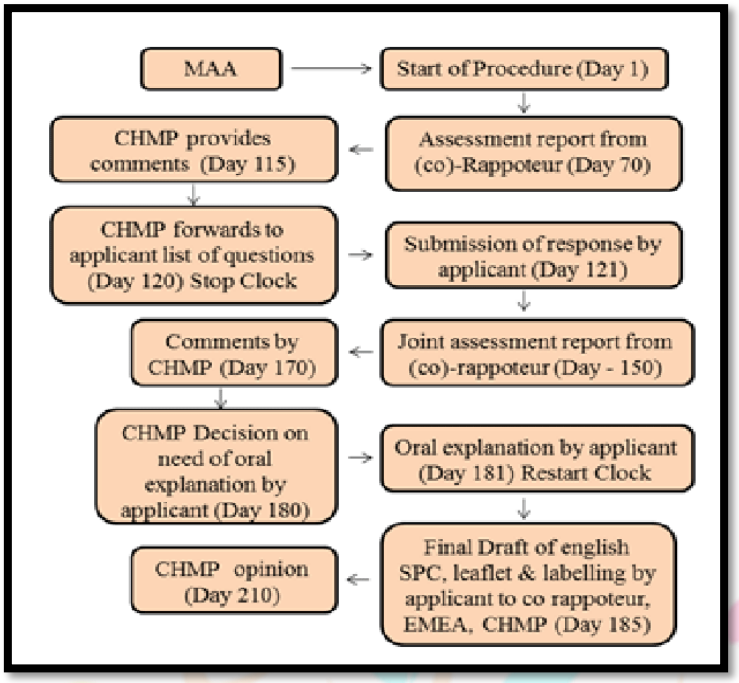

Fig.No.5:- Flow chart of Centralized Procedure

B. National process

This procedure allows applicants to attain a marketing authorization in only one member state. To obtain a marketing authorization in a country, an application must be submitted to the competent authority of the Member State. New active substances, which are not mandatory under centralized procedure, can obtain marketing approval under this procedure. Timeline for issue of EMA opinion is 210 Days. Each EU state can have its own procedures for approving drugs that fall outside of those needed to undergo the centralized process.

C. Mutual recognition

This process permits applicants to get a marketing authorization in the Concerned Member States (CMS) other than the Reference member state (RMS), where the drug is already approved. Applicant must submit identical dossier to all the EU member states in which they want to obtain marketing approval, along with required information.

As soon as one of the member states decides to evaluate the medicinal product (at which point it will become the RMS), it will inform this decision to other member states (which then will become the CMS), to which applications have also been submitted. RMS issues a report to other states on its own findings after completion of evaluation. Generic drug industry is the major user of this type of drug approval process. Time line for issuing the EMA opinion is 390 days.

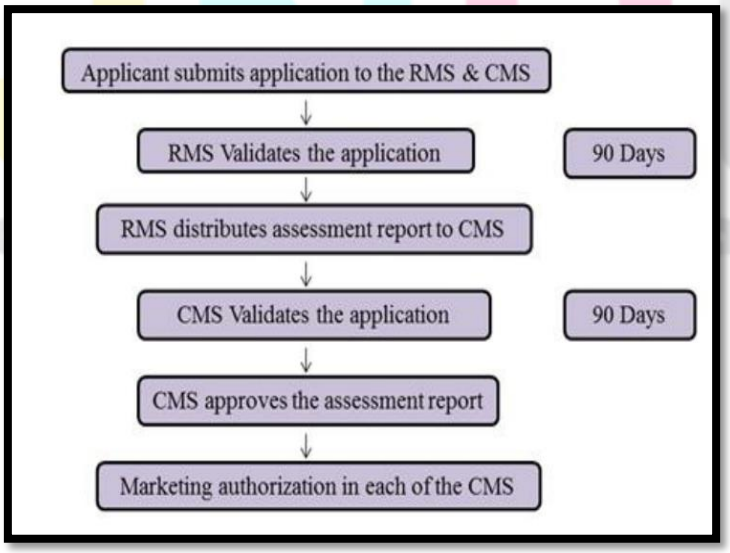

Fig.No.6:- Flow chart of Mutual Recognition Procedure

D. Decentralized procedure

Using this procedure, pharmaceutical industry may apply for marketing authorization at a time in more than one EU country for medicinal products that have not yet obtained authorization in any EU country and essentially do not fall within the centralized procedure's essential list of drugs. In this decentralized procedure, according to the decision taken by the RMS & CMS the marketing authorization should be granted. Generally used for those medicinal products that did not receive any authorization in an EU country. Time taken for issue of EMA opinion is 210 days.[16-19]

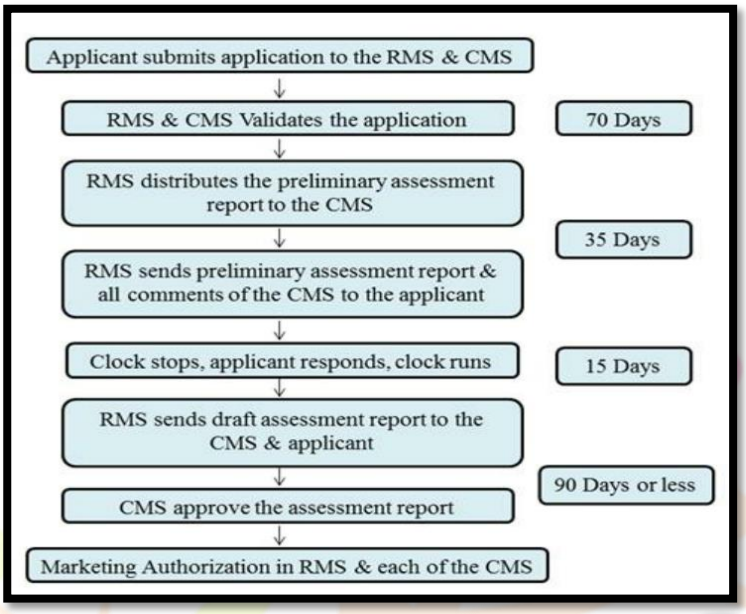

Fig.No.7:- Flow chart of Decentralized Procedure

6 International Council for Harmonisation (ICH)

- It is a joint associaion which involves indutry and regulatory boies together as equal partner in scientific and technical dissussion of testing procedure which is required to ensure the quality safety and efficacy of medicines.
- It is started in 1990.
- It is non-profit organisation.

6.1 Objective

- To make the recommendation towards achieving greater harmonization.
- To improve the efficiency of new drug development and registration process.
- To prevent the public health and prevent the duplication of trails in humans and the minimize the use of animals testing without compromising with safety, quality, and effectiveness.

6.2 Pupose

Tragedy in Europe in 1965 with thalidomide.

In 1960s and 1970s, thre is rapid increase in law and gudlines for the evaluating the data on quality, safety and efficacy of new medicinal products.

6.3 Process Of Harmonization

a) **Formal ICH Procedur**: It deals with topic for harmonisation.
b) **Quality Assurance**: clasification for an existing ICH guidliness.
c) **Revision Procedure**: When any existing ICH guidelines is invalid or when a new dada it to be added.
d) **Maintainance Procedure**: Applicable only for alteration to the Q3 guidelines on impurities.

6.4 ICH GUIDELINES

The ICH topics are divided into four categories and ICH topic codes are assigned according to these categories.

1. Quality guidelines (Q)

2. Safety guidelines (S)
3. Efficacy guidelines (E)
4. Multidisciplinary guidelines (M)

1. Quality Guidelines

Harmonisation achievements in the Quality area include pivotal milestones such as the conduct of stability studies, defining relevant thresholds for impurities testing and a more flexible approach to pharmaceutical quality based on Good Manufacturing Practice (GMP) risk management.

Q1- Stability

Q2- Analytical Validation

Q3- Impurities

Q4- Pharmacopoeias

Q5- Quality of Biotechnological Products

Q6- Specifications

Q7- Good Manufacturing Practice

Q8- Pharmaceutical Development

Q9- Quality Risk Management

Q10- Pharmaceutical Quality System

Q11- Development and Manufacture of Drug Substances

Q12- Lifecycle Management

Q13- Continuous Manufacturing of Drug Substances and Drug Products

Q14- Analytical Procedure Development

2. Safety guidelines (S)

ICH has produced a comprehensive set of safety Guidelines to uncover potential risks like carcinogenicity, genotoxicity and reprotoxicity. A recent breakthrough has been a non-clinical testing strategy for assessing the QT interval prolongation liability.

S1 - Carcinogenicity Studies

S2- Genotoxicity Studies

S3- Toxicokinetics and Pharmacokinetics

S4- Toxicity Testing

S5- Reproductive Toxicology

S6- Biotechnological Products

S7- Pharmacology Studies

S8- Immunotoxicology Studies

S9- Nonclinical Evaluation for Anticancer Pharmaceuticals

S10- Photosafety Evaluation

S11- Nonclinical Paediatric Safety

3. Efficacy guidelines (E)

The work carried out by ICH under the Efficacy heading is concerned with the design, conduct, safety and reporting of clinical trials. It also covers novel types of medicines derived from biotechnological processes and the use of pharmacogenetics /genomics techniques to produce better targeted medicines.

E1- Clinical Safety for Drugs used in Long-Term Treatment

E2 - Pharmacovigilance

E3- Clinical Study Reports

E4- Dose-Response Studies

E5- Ethnic Factors

E6- Good Clinical Practice

E7- Clinical Trials in Geriatric Population

E8- General Considerations for Clinical Trials

E9- Statistical Principles for Clinical Trials

E10- Choice of Control Group in Clinical Trials

E11- Clinical Trials in Pediatric Population

E12 -Clinical Evaluation by Therapeutic Category

E14- Clinical Evaluation of QT

E15- Definitions in Pharmacogenetics / Pharmacogenomics

E16- Qualification of Genomic Biomarkers

E17- Multi-Regional Clinical Trials

E18- Genomic Sampling

E19- Safety Data Collection

E20- Adaptive Clinical Trials

4. Multidisciplinary guidelines (M)

Those are the cross-cutting topics which do not fit uniquely into one of the Quality, Safety and Efficacy categories. It includes the ICH medical terminology (MedDRA), the Common Technical Document (CTD) and the development of Electronic Standards for the Transfer of Regulatory Information.

M1- MedDRA Terminology

M2- Standards

M3- Nonclinical Safety Studies

M4- Common Technical Document

M5- Data Elements and Standards for Drug Dictionaries

M6- Gene Therapy

M7- Mutagenic impurities

M8- Electronic Common Technical Document

M9- Biopharmaceutics Classification System-based Biowaivers

M10- Bioanalytical Method Validation

M11- Clinical electronic Structured Harmonised Protocol.[20]

7 Conclusion

The drug approvals in the US, Europe and India are the most demanding in the world. The primary purpose of the rules governing pharmaceutical products is to safeguard public health. It is the role of regulatory authorities to ensure that pharmaceutical companies comply with regulations so that the drugs developed and manufactured will be safe, effective and thus the patient's well-being is protected.

Scientifically based ICH guidelines that remove redundant studies will reduce development costs, improve safety, and allow global drug distribution based on single compliance.

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