Sushma K. et al. / Vol 10 / Issue 1 / 2020 / 1-5.

International Journal of
Innovative Drug Discovery
e ISSN 2249 - 7609
Print ISSN 2249 - 7617
www.ijidd.com

SIMILARITIES AND DIFFERENCES IN APPROVAL PROCEDURES FOR GENERIC DRUG APPLICATION IN USA AND EU

Sushma K*, Praveen Kumar J, Jayachandra Reddy P

Department of Regulatory Affairs,
Krishna Teja Pharmacy College, Chadalawada Nagar, Tirupati-517506, Andhra Pradesh, India.

ABSTRACT
Presently different countries must follow different regulatory requirements for sanction of new drug. Marketing Authourization Application (MAA) is a single. Every country has its own regulatory authourity which is responsible to enforce the rules and regulations and issue the guidelines to regulate the marketing of the drugs. A generic drug is a medication created to be the same as an already marketed brand-name drug in dosage form, safety, strength, route of administration, quality, performance characteristics and intended use. USFDA is the regulatory agency which is responsible for safety regulations of the food and drug products in U.S. EMA is the regulatory agency/decentralized body which is responsible for safety regulation of the food and drug products in Europe.

KEY WORDS: MAA, EMA, USFDA.

INTRODUCTION

The Drug approvals in the United states & Europe are the most demanding in the world. The primary purpose of the rules governing medicinal products in US & Europe 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.

Drug Approval Process in United States

Investigational New Drug Application (INDA)

It is an application filed to FDA prior to human testing. It gives a full description of chemistry, manufacturing controls, pharmacology and toxicology, any previous human experience [1,2].

New Drug Application:

It is filed to get approval for marketing a new drug in USA. It 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 [2].

Abbreviated New Drug Application

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 [3].

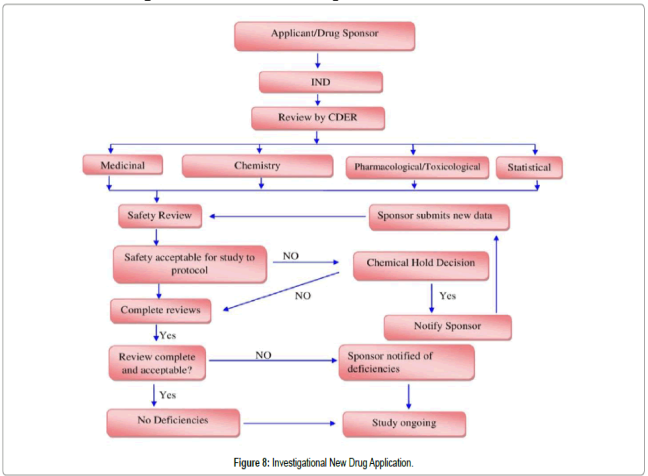

Figure 8: Investigational New Drug Application.

Corresponding Author:- **Sushma K** E-mail: kasiralasushma@gmail.com

An ANDA is submitted to Center for Drug Evaluation and Research, Office of Generic Drugs, where it is reviewed and approved.

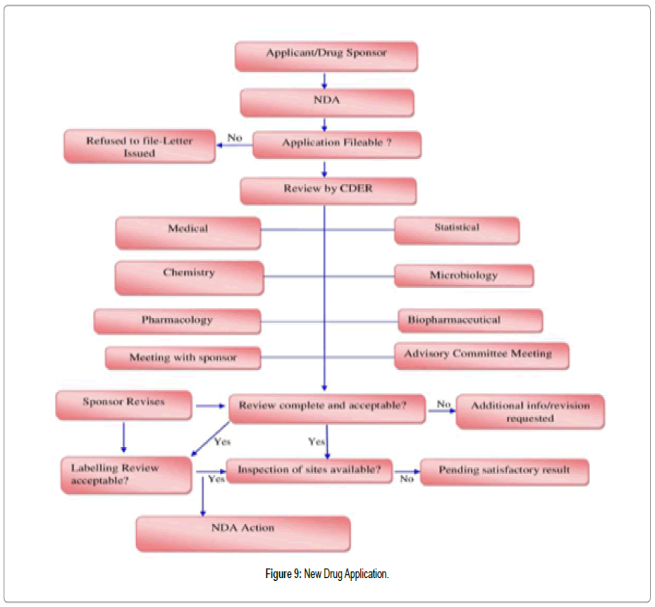

Figure 9: New Drug Application.

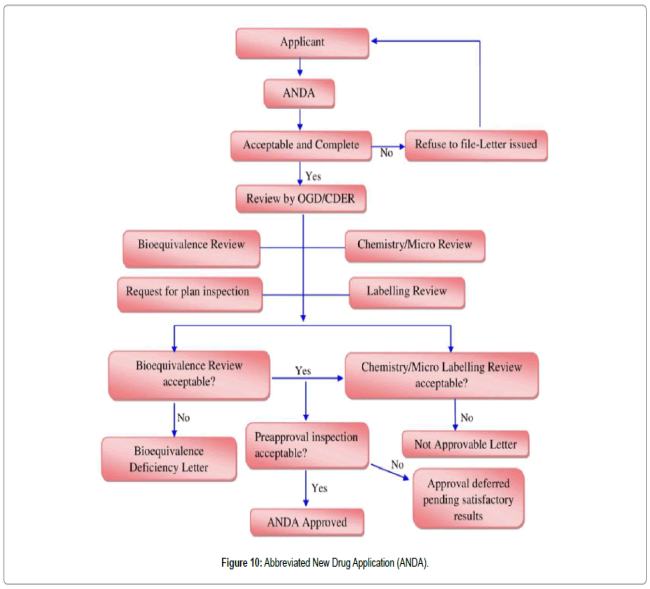

Figure 10: Abbreviated New Drug Application (ANDA).

Drug Approval process in Europe

The European Medicines Agency (EMEA) is a decentralized body of the European Union. The EMEA was established in London, in the year 1995, to coordinate the European Union member states for evaluating and supervising the medicinal products for both human and veterinary use [3]. 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 filled 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

There are four different in the European Union to obtain marketing approval of Pharmaceuticals.

Centralized Procedure

The centralized procedure is one which allows applicants to obtain a marketing authorization that is valid throughout the EU [4-6]. In this procedure, applications are accepted with regards to products of bio-technological sciences and New Chemical Entities (NCEs).The total time for approval is around 300 days(210+90) [7]. The 210 days is to consider the application from the date of filing. CHMP gives an opinion whether to accept or reject the application, which can take 90 days to arrive at a decision.

This process is compulsory for biotechnological processes, genetic engineering, treatment of cancer, HIV/AIDS, diabetes, neurodegenerative disorders or autoimmune diseases.

Decentralized Procedure

Decentralized procedure is followed to obtain marketing authorizations in several member states. The sponsor submits to a national regulatory authority, the applications 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 [3]. The following products cannot be registered under this scheme: Orphan Medicinal Product, All biotechnological based product, specified Aids and cancer medicines, Specified Antiviral medicines for Neurodegenerative Disorder including diabetes and Specified Medicines for Auto immune Diseases/dysfunctions.

National Procedure

National procedure is procedure adopted by each nation independently of other nations. In order to obtain a national marketing authorization, 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 authorization under this procedure. Timeline for this procedure is 210 Days [3]. In this procedure following products cannot be registered: Orphan 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.

Mutual Recognition Procedure (MRP)

Under this a product registered in one country is mutually recognized by the other country. The submission can be made to any number of the other member states and the RMS send a copy of the assessment report to the CMSs, who can raise any objections within 90 days. Each CMS issue a national marketing authorization with an identical SPC.

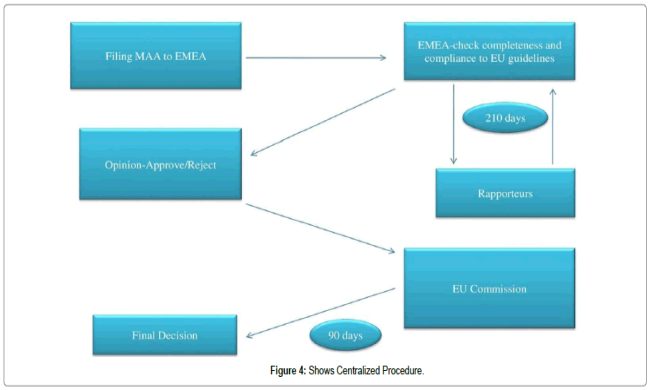

Figure 4: Shows Centralized Procedure.

The following products cannot be registered under this scheme: All biotechnological based product, specified Aids and cancer medicines, Specified Antiviral medicines for Neurodegenerative Disorder including diabetes and Specified Medicines for Auto immune Diseases/dysfunctions.

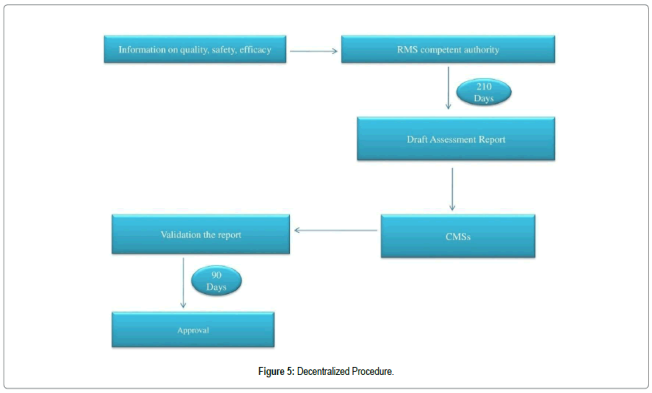

Figure 5: Decentralized Procedure.

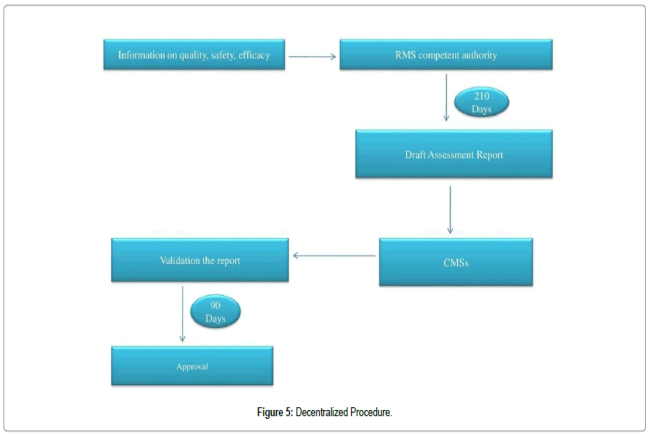

Figure 5: Decentralized Procedure.

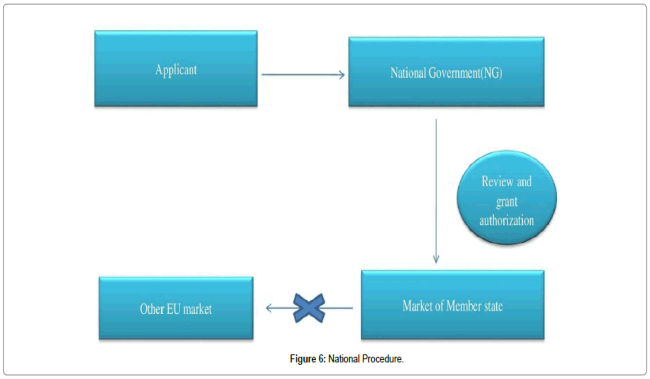

Figure 6: National Procedure.

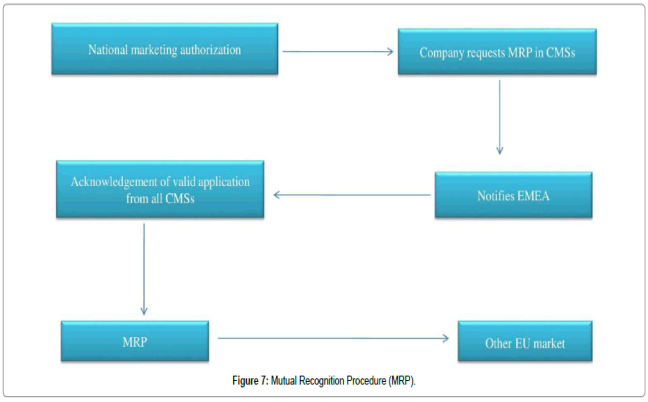

Figure 7: Mutual Recognition Procedure (MRP).

RESULTS AND DISCUSSION

Requirements	**EU**	**US**
Agency	Multiple agencies EMEA CHMP National health agencies	Single agency USFDA
Registration process	Multiple registration process Centralized (European community) Decentralized (at least 2 member states) Multiple recognition (at least 2 member states) National member state	Single registration process
TSE/BSE study data	required	required
Braille code	Braille code is required on labelling	Braille code is not required on labelling
Post approval changes	Post variation in the approved drug: Type I A Type I B Type II B	Post approval changes in the approved drug: Minor Moderate Major

Difference between EU and US

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

Manufacturing differences between USFDA & EU

Requirement	**USFDA**	**EU**
Application	ANDA/NDA	MAA
Debarment classification	Required	Not Required
Number of copies	3	1
Approval Timeline	18 Months	12 Months
Fees	No fees	10-0 Lakh
Presentation	eCTD & Paper	eCTD

Administrative Requirements

Requirement	**USFDA**	**EU**
Justification	ICH Q6A	ICH Q6A
Assay	90-100%	95- 105%
Disintegration	Not Required	Required
Color Identification	Not Required	Required
Water Content	Required	Not Required

Finished Product Control Requirements

Requirement	**USFDA**	**EU**
Number of batches	1	2
Condition	25/60 – 40/75	25/60 – 40/75
Date & Time of Submission	3 Months Accelerated & 3 Months long term	6 Months Accelerated & 6 Months long term
Container orientation	Inverted & Upright	Do not address
Clause	21 CFR Part 210 & 211	Vol 4 EU Guidelines for medicinal products
QP Certification	Not Required	Required

Stability Requirements

Requirement	**USFDA**	**EU**
CRO	Audited by FDA	Audited by MHRA
Reserve Sample	5 times the sample required for analysis	No such requirement
Fasted/Fed	Must be as per OGD recommendation	No such requirement
Retention of samples	5 years from date of filling the application	No such requirement

CONCLUSION

The Drug approvals in the Europe & US are the most thought due in the world. The primary purpose of the rules governing medicinal products in Europe & US is to safeguard public health. It is the role of public regulatory authorities to ensure that pharmaceuticals 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.

ACKNOWLEDGEMENT

We would like to thankful to Krishna Teja Pharmacy College for making this article a success.

REFERENCES

1. http://www.cdsco.nic.in/
2. https://www.fda.gov/
3. Mahapatra AK, Sameeraja NH, Murthy PN. Drug Approval Process In United States of America, European Union and India: A Review. *AcrcTra*, 1, 2014, 13-22.
4. http://www.cdsco.nic.in/writereaddata/Guidance_for_New_Drug_Approval-23.07.2011.pdf
5. http://citeseerx.ist.psu.edu/viewdoc/download?doi=10.1.1.375.519&rep=rep1&type=pdf
6. Norman GA Van. Drugs and Devices. *JACC Basic to Transl Sci*, 1, 2016, 399-412.
7. https://www.gao.gov/products/HEHS-96-71