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CHALLENGES IN REGULATORY FILING OF GENERIC PRODUCTS IN EUROPE AND MALAYSIA

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ABSTRACT

The main aim of this topic is facing challenges and overcoming when filling Generic Products. The objective of this topic is to review and compare generic drug filing process along with their challenges in different countries. Examples: Generic drug filling process in USA is ANDA(Abbreviated New Drug Application). Generic drugs are filled seperately through EMA (European Medical Agency) in Europe. In India generic drugs are filled to Drug Controller General of India (DCGI). Regulatory Challenges facing in Europe and Malaysia. Access to healthcare professionals and services tends to be concentrated in urban areas and it can be difficult for those residing in remote and rural areas to get access to quality pharmaceuticals and treatment. The majority of pharmaceutical products in the region are imported, either as the final product, or as base materials which are then manufactured into the finished product locally. There are serious problems with high volumes of counterfeit products making their way onto the market. One of the biggest challenges when entering the European market is the multitude of languages, which results in a large number of associated country-specific pack formats. Within the 28 member states of the EU, there are 150 regional and minority languages, of which 23 are recognized working languages. The purpose of the study is to compare generic drug registration and requirements in ASEAN countries & to find out the differences in guidelines. The focus on countries like Indonesia and Thailand is because of high population rate, maximum share of ASEAN pharmaceutical market, low income. But these countries are ranked after Vietnam and Philippines because of some restriction by countries government for foreign players.

Singapore and Malaysia are the only countries in ASEAN, who have well established pharmaceutical regulations and more strict to quality & safety of drugs.

KEYWORDS: Challenges, Europe, Malaysia, CTD, ACTD.

INTRODUCTION

The pharmaceutical industry is one of the highly regulated industries, with many rules and regulations enforced by the government to protect the health and well-being of the public. Therefore, the aim of the pharmaceutical industry is to identify and develop a generic drug product which can be tailor made to meet the diverse market requirements. As per global market trend, it is estimated that approximately $150 billion worth of drugs will be off-patented during the period 2010 to 2017, which will serve as a platform for pharmaceutical companies to develop generic drugs. The pharmaceutical industry in India has shown a remarkable growth which in turn has risen the economy of India. After the introduction of the product patent regime in India, there was a need for pharmaceutical companies both in India and abroad to explore newer markets. Indian pharma majors are entering new markets with global ambitions, mergers and acquisitions are in focus with a reason to enter new market. For sustained growth over the next few decades, firms have to concentrate on generic drug products. “Diseases that cannot be cured, diseases that have to be managed, provide great opportunities for generic drugs.” Government has the responsibility to protect their citizens. It is the responsibility of national governments to establish regulatory authorities with strong guidelines for quality assurance and drug regulations in the respective territories. Somewhat parallel with the ongoing harmonization and movement toward creating a common market for medicines inside the EU, the need for wider harmonization was felt by officials from Japan, EU, and US during International Conference of Drug Regulatory Authorities (ICDRA) organized by world health organization (WHO). The informal discussions had led to a need of the harmonization of requirements relating to the new innovative drugs and also subsequently paved the way to the establishment of International Conference on Harmonization of Technical Requirements for the Registration of Pharmaceuticals for Human Use (ICH), a collaborative initiative between the EU, Japan, and the United States with observers from WHO, EFTA, and Canada. Efforts to harmonize various elements of drug regulatory activities have been initiated by various inter-governmental organizations at regional and inter-regional level in the past decade. The driving force behind these efforts has been the increase in global trade in pharmaceutical products, and growth in the complexity of

technical regulations related to drug efficacy, safety, and quality.

Status as of today: Due to the emerging regulatory needs of pharmaceutical sector, the drug evaluation for the control of drug quality and trade has become highly sophisticated. Regulatory guidelines and standard tools provide a basis for implementation of laws, whereas laws provide a legal basis for drug control. The world covers more than 100 countries, where most of them have established pharmaceutical legislations and regulatory requirements. For worldwide regulatory dossier submissions, it is a pre-requisite requirement to have a knowledge of country specific guidelines and norms. Therefore, it is very important to analyze the differences and commonness between the regulatory requirements and pharmaceutical legislations of different countries of the world. The Pharmaceutical market based on the diversity in the regulation region and marketing interest can be divided into two groups: Regulated and emerging markets. The regulated market involves those countries where there are defined regulatory requirements set by the regulatory bodies of that country and the emerging market countries are those who still lag behind in putting forward the well defined regulations for drugs. United States (US) and the EU are the biggest and the most potential markets for in the world and are categorized under the regulated markets, whereas ROW (Rest of the World) market includes all the emerging markets like Brazil (LATAM), Tanzania (Africa), Russia (CIS), Hong Kong (ASIA), etc.

Innovator product

An innovator drug is the first drug created containing its specific active ingredient to receive approval for use. It is usually the product for which efficacy, safety and quality have been fully established. When a new drug is first made, drug patent usually will be acquired by the founding company.

Generic Product

A generic drug is a pharmaceutical drug that is equivalent to a Innovator product in dosage, strength, route of administration, quality, performance and intended use, but does not carry the brand name. A generic drug must contain the same active ingredients as the original brand-name formulation.

Generic drugs are filled in CTD format for Europe, US and Japan countries. Generic Drugs are approved under ***ANDA*** (Abbreviated New Drug Application) in ***USA*** and ***MAA*** (Marketing Authorization Application) in ***Europe.***

Difference between Innovator & Generic Product

Innovator Product

Initially Marketed as New Chemical Entities

First version sold by the innovator manufacturer is known as the reference product. Ex. IND (Investigational New Drug Application), NDA (New Drug Application) etc.

Generic Product

Copies of Innovator.

Produced after the original patent Expires. Ex. ANDA for USFDA, MAH (Marketing Authorization Holder) for Europe and JANDA for Japan etc.

Generic Drug Requirments

It must be same active Ingredient(s), same route of administration, same dosage form, same strength, same indication, same container, same pharmacological action in terms of efficacy with the already approved drug product.

A suitable manufacturing site/plant to manufacture the drug product and with a suitable clinical laboratory for conducting clinical trials. Both sites must hold site approvals from regulatory authorities.

Generic Drug Development

To make a generic product, formulator must know in detail the exact regulatory requirements of each concerned country where the drug is intended to be filed. Generic drug product development uses a different approach and strategy compared to that used to develop an innovator drug product containing a new chemical entity. Generic drug product manufacturers must formulate a drug product that will have the same therapeutic efficacy, safety, and performance characteristics as of its branded counterpart. The key factor is that the generic drug product must meet all the necessary criteria to be therapeutically equivalent to the innovator drug product. Therapeutically equivalent means that the drug product shows pharmaceutical equivalence as well as bioequivalence.

Therapeutic Equivalence

Therapeutic Equivalence includes:

♦ **Pharmaceutically Equivalent (PE)**

- Same active ingredient(s)
- Same dosage form
- Same route of administration
- Identical in strength or concentration
- May differ in characteristics such as shape, excepients, packing.

♦ **Bioequivalent (BE)**

- Two drugs demonstrate same rate and extent when they become available at the site of the drug action.

A generic drug is considered to be bioequivalent to the brand name drug if:

- The rate and extent of absorption do not show a significant difference from the innovator drug,
- The extent of absorption does not show a significant difference and any difference in rate in intentional or not medically significant.

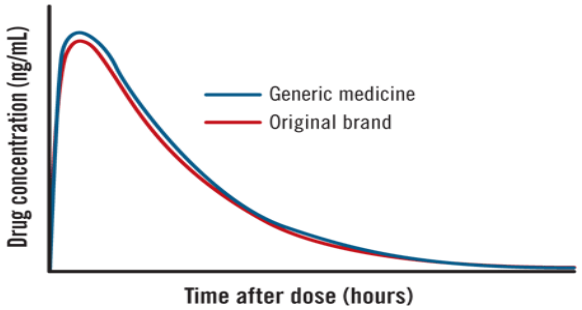


Figure 1: Indicate difference between Generic Medicine And Original Brand.

A GENERIC PRODUCT DEVELOPMENT PROCESS

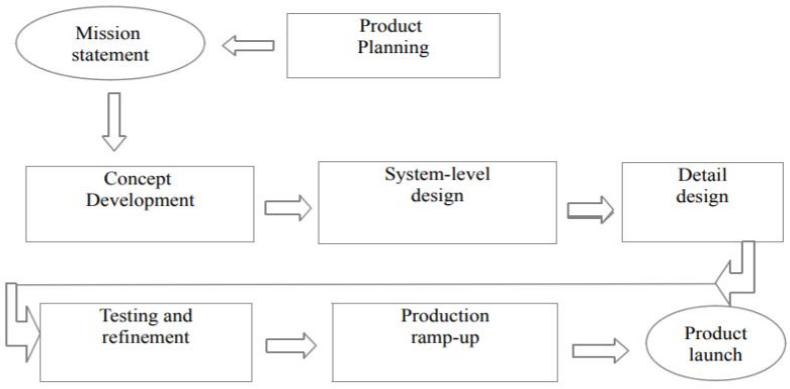


Figure 2: Generic Product development Process.

Filing A Generic DrugApplication

When a dossier is ready as per the regulatory requirement of the respective country, it is submitted to the regulatory agency of that country. Various regulatory agencies worldwide are tabulated in the Table 1.

Table 1: Various Regulatory Agencies are listed Below.

Name of Country/ Group	Regulatory authority
USA	FDA
EU	EMA
Canada	HPFB
Japan	PMDA
Australia	TGA
South Africa	MCC
AFRICA (Tanzania)	Independent regulatory agencies/TFDA
LATAM (Brazil)	Independent regulatory agencies/ANVISA
CIS (Russia)	Independent regulatory agencies/ ROSZDRAVNADZOR
ASIAN (Hong Kong)	Independent regulatory agencies/DOH
GCC	Independent regulatory agencies/National filling

Legal basis for applications in Europe

The eligibility and the requirements are set in the commission regulation (EC) No 726/2004 and defined in articles 8 and 10 are of the Directive 2001/83/EC.

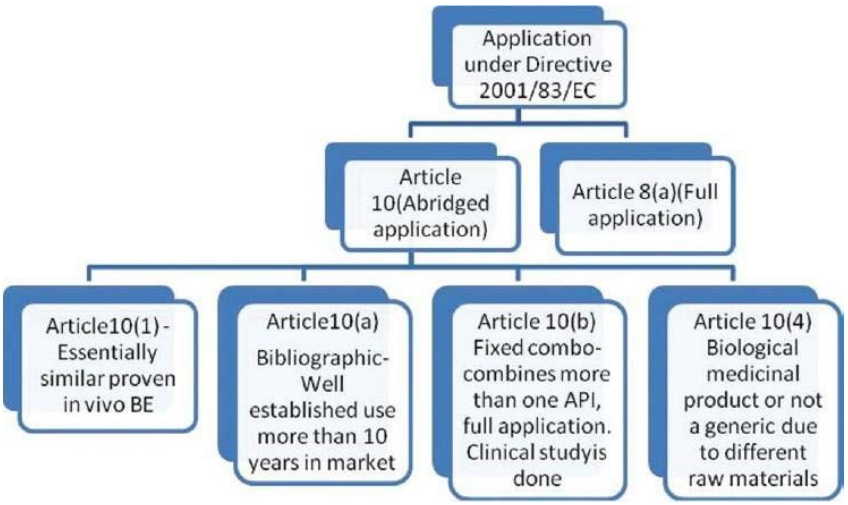


Figure 3: Represents the types of application filed in Europe.

Types of submission procedure

To market a generic medicinal product in European Economic Area (EEA) which consists of 27 member states and 3 EFTA countries, a marketing authorization has to be issued. European medicines Agency (EMA formerly known as EMEA) regulates the medicinal

products marketing authorization through various committees. Different types of submissions for receiving Marketing authorization in Europe are given below in Table 2.

Table 2: Different types of submissions for receiving Marketing authorization in Europe.

Agencies responsible	Procedure type	Summary
EMA	Centralized procedure	It is for single application, single evaluation and authorization allowing direct access to the single market of the member countries.
Reference member state (RMS)	Decentralized procedure (DCP)	Application is submitted to all member states where intended and choose one of them as reference member state. The assessment report is prepared by RMS including the concerned member states and based on both comments MA is granted.
Reference member state (RMS)	Mutual recognition procedure (MRP)	It is followed where an applicant having MA in one member state, wishes to obtain the same in other member states. It is based on mutual recognition of concerned member states, granted by the reference member states.
Member states	National authorization	MA is granted by Member states and hence an application must be submitted to the particular member state.

The EU has one of the most highly regarded regulatory systems in the world. The system comprises of European parliament, the council of ministers, and the European Commission. EU consists of 27 member states:

Austria, Belgium, Bulgaria, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxemburg, Malta, Netherlands, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, and the United Kingdom and three countries which are member of European Free Trade Agreement (EFTA) Iceland, Norway, and Liechtenstein. These EFTA members are those countries which were unable to join rest of the 27 member states as common market.

The Agency is responsible for the scientific evaluation of medicines developed by pharmaceutical companies for use in the European Union and applications for European marketing authorizations for both human and veterinary medicines (centralized procedure). Under the centralized procedure, companies submit a single marketing-authorization application to the Agency. Once granted by the European Commission, a centralized (or "Community") marketing authorization is valid in all European Union (EU) and EEA-EFTA states (Iceland, Liechtenstein and Norway). The European parliament approves the laws together with the council of ministers. The council of ministers is the voice of Member states and is responsible for enactment of directives.

EUROPE

Marketing Authorization Application (Europe)

European Filing Procedure

EU establishes 4 different drug approval processes Centralized procedure

Decentralization procedure National Procedure

Mutual Recognition Procedure

All medicines must be authorized before they can be marketed and made available to patients

In European union (EU) there are two main routes for authorized medicines

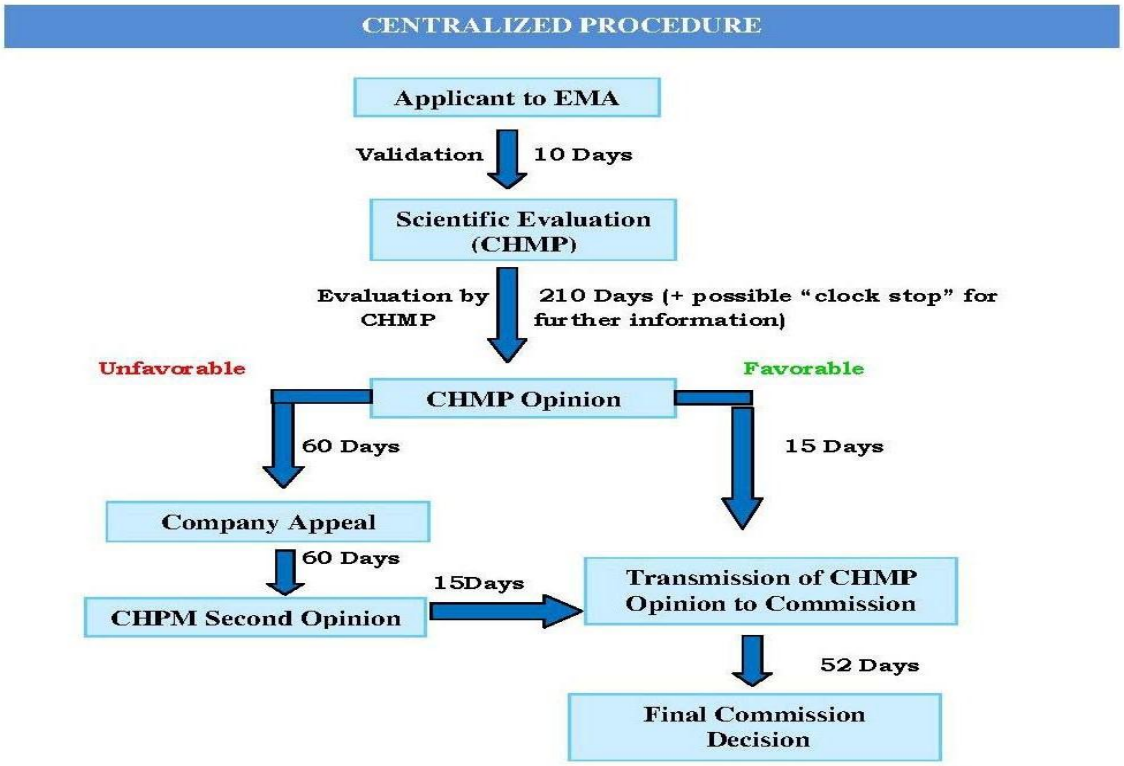
A centralized route. A national route

Centralized Procedure

Those medicines which are intended for the treatment of Cancer, HIV/Aids, diabetes, neurodegenerative disorders or autoimmune diseases and other immune dysfunctions.

The European Medicines Agency (EMA) organises the process of evaluation using scientific expertise from the Member States. The centralised procedure is compulsory for some products and optional for others. Some products are not eligible for the centralised procedure.

Timeline: EMA opinion issued within 210 days, and submitted to European Commission for final approval.

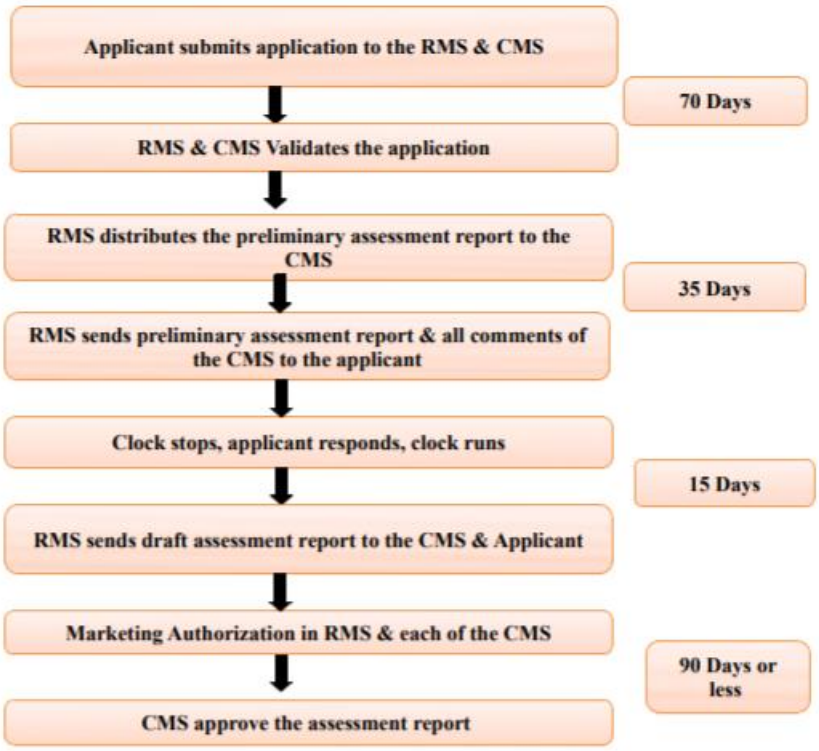


Decentralization procedure

The decentralised procedure (DCP) is a European authorisation route resulting in a mutually recognised product (MRP).

The difference between MRP and DCP is that a product must already be authorised in at least one Member State on a national basis in order for MRP to be used. DCP may be used if the product is not already authorised in any Member State, but does not want to use the centralised procedure, or the product is not eligible for the centralised procedure.

Decentralization procedure



Mutual Recognition Procedure

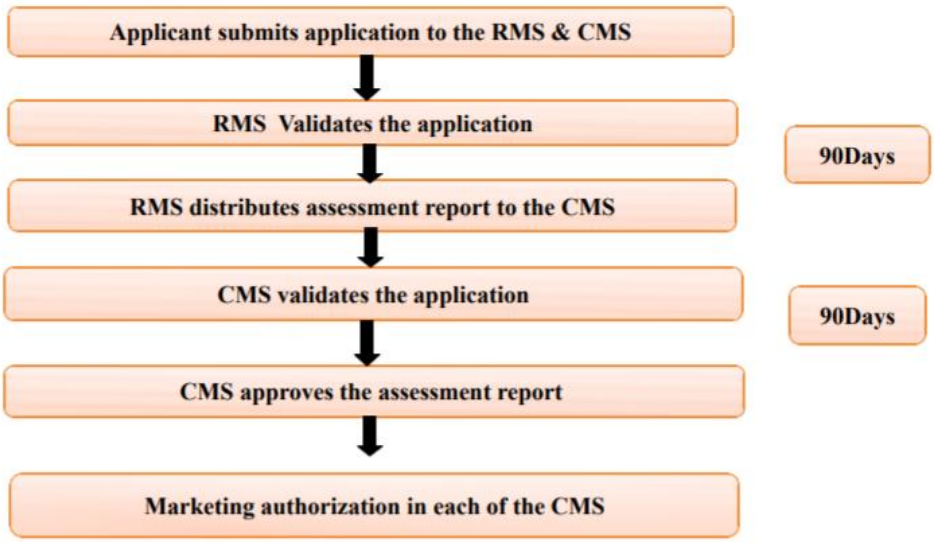
The mutual recognition procedure (MRP) is a European authorisation route resulting in a mutually recognised product.

Mutual recognition must be used when a product is already authorised in at least one Member State on a national basis and the Marketing Authorisation Holder wishes to obtain a Marketing Authorisation (MA) for the same product in at least one other Member State.

The Member State that has already authorised the product is known as the Reference Member State (RMS). The RMS submits their evaluation of the product to other Member State/s, these

are known as Concerned Member States (CMS). The CMS is asked to mutually recognise the MA of the RMS. If the applicant is successful, the CMS will then issue a MA for that product permitting the marketing of that product in their country.

Flow Chart for Mutual Recognition Procedure



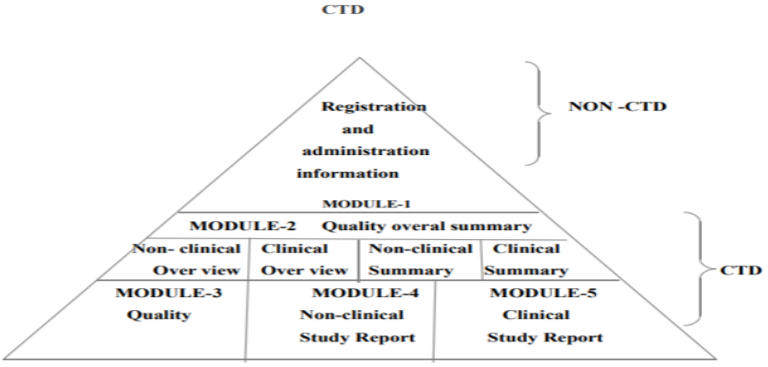
Nationalized Procedure

The National procedure is one which allows applicants to obtain a marketing authorization in one member state only.

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.



ASEAN

The Association of Southeast Asian Nations (ASEAN) contains the following 10 countries like Indonesia, Malaysia, Philippines, Singapore, Thailand, Brunei Darussalam, Vietnam, Laos, Myanmar and Cambodia was establish in 1967 to promote pharmaceutical market in ASEAN countries.

ASEAN region is considered as "Emerging market" for pharmaceutical export and bilateral trade. The understanding of the registrations & regulatory requirements of this region can be beneficial for pharmaceutical export.

The regulations of ASEAN countries are encouraging the import of quality generic products.

ASEAN member countries

1. Thailand
2. Vietnam
3. Indonesia
4. Philippines
5. Malaysia
6. Singapore
7. Myanmar (Burma)
8. Cambodia
9. Laos
10. Brunei

Current status of generics in Asean countries

a. Southeast Asia, with its fast-growing, young population and uninsured majority represent a great opportunity for generics in the pharmaceutical industry.
b. Although the generic market is currently quite small, improved access to medicines in the region means that it is growing rapidly and is expected to reach US$3.9 billion by 2016.
c. This fact is expected to both intensify competition and attract multinational pharma companies to the area.

Dossier requirements

- The dossier requirements for the ASEAN countries are in principle very similar to the requirements for the ICH countries.

- ASEAN Common Technical Dossier ACTD is common application format that will be submitted to ASEAN regulatory authorities for the registration of pharmaceutical products for human use.
- Even though some of the Individual ASEAN Countries have their own drug registration formats, all ASEAN countries accept the ACTD.

CTD & ACTD - DOSSIERS

Common Technical Document (Product Dossier) is an integral Part of any registration application for Marketing Authorization. Dossier in CTD Format/ ACTD Format or local country format is submitted to Food & Drug Authority or Ministry of health or any other equivalent authority along with other required technical documents and legal manufacturing permissions.

Perfect Pharmaceutical Consultants can help you prepare entire technical document for drug product registration in various countries all over the world. PPC Provides following consulting service in regards to Technical Document.

Dossier Compilation and writing as per CTD Format – Common Technical Document

- Module 1 – Administrative Information
- Module 2 - CT Overview
- Module 3 – Drug & Product Part /CMC
- Module 4 – Non Clinical
- Module 5 – Clinical

CTD Format Dossier is widely used in semi regulated & regulated market like CIS Countries, Middle Eastern countries, European Union, USA, Australia, Canada, Japan, etc.

- Dossier writing and compilation as per ACTD Format – Asian Common Technical Document
- Part I – Administrative Documents
- Part II – Quality Documents
- Part III – Non Clinical Documents
- Part IV – Clinical Documents.

ACTD Format is Asian harmonization for Common Technical Document used in Asian Countries like Vietnam, Thailand, Singapore, and Malaysia etc.

ASEAN COMMON TECHNICAL DOCUMENT[ACTD]

INTRODUCTION

The Association of South-East Asians Nations (ASEAN) is a regional organization consisting of ten member countries, namely, Brunei Darussalam, Cambodia, Indonesia, Laos, Myanmar, Malaysia, Philippines, Singapore, Thailand and Vietnam.

ASEAN was established in n8 August 1967 by the governments of five countries - Indonesia, Malaysia, Philippines, Singapore and Thailand. In 1984, Brunei Darussalam joined its neighbours in the association. As a group, these early participants are dubbed the ASEAN6. Vietnam has become member since 1995, Laos and Myanmar since 1997 and Cambodia since 1999. These four new members are usually referred to as the CLMV group.

In 1992, the governments of ASEAN member countries agreed to create the ASEAN Free Trade Area (AFTA) to set common tariff scheme. The agreement on Common Effective Preferential Tariff Scheme (CEPT) has been effective since 2003. Pharmaceutical trade among the members now enjoy import duties of 0-5% under CEPT, provided that the products has no less than 40% local content.

A Pharmaceutical Product Working (PPWG) was established to work on the details in the development of harmonization guidelines for technical procedures and requirements partially applicable to the ASEAN pharmaceuticals have been identified for harmonization - quality, efficacy, safety and administrative data.

Key documents resulted from work of PPWG include

- ASEAN Common Technical Requirements (ACTR) for pharmaceutical product registration (for human use).
- ASEAN Common Technical Dossier (ACTD) for pharmaceutical product registration (for human use).
- ASEAN Guidelines on the following areas: analytical validation, bioavailability and bioequivalence studies, process validation, stability.

While ASEAN was working on its harmonized pharmaceutical registration, another international collaboration for harmonization of pharmaceutical registration was taking place in parallel called the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH). It was established in 1990 and

works for development for technical guidelines for registration of pharmaceutical products to achieve greater harmonization.

ACTD

Table 3: Difference of ACTD & ICH CTD.

Documents	Location	
	ICH CTD	ACTD
Administrative Documents and Product Information	Module-1	Part-I
Common Technical Document Overview and Summaries	Module-2	Incorporated in parts II, III, & IV
Quality Documents	Module-3	Part-II
Non-Clinical documents	Module-4	Part-III
Clinical Documents	Module-5	Part-IV

Table 4.General comparison of Asean countries.

S. No.	Country	Validity	Format Followed	Format Included In This Sis
1	Singapore	5yrs	ACTD	ACTD
2	Malaysia	5yrs	ACTD	ACTD
3	Thailand	5yrs	ACTD	ACTD
4	Philippines		Country specific &ACTD	Country Specific
5	Indonesia	5yrs	ACTD	ACTD
6	Vietnam	5yrs	ACTD	ACTD
7	Brunei Darussalam	5yrs	ACTD	ACTD
8	Myanmar	5yrs	Country specific & ACTD	Country specific
9	Cambodia	5yrs	ACTD	ACTD
10	Laos	5yrs	Country Specific & ACTD	Country specific

Table 5: List Of Countries And Their Regulatory Authority (ACTD).

Country	Regulatory Agencies
Indonesia	National Agency of Drug & Food Control
Malaysia	Drug Control Authority, NCE Unit
Philippines	Department of Health
Thailand	Thai FDA Drug Control Division
Singapore	Health Sciences Authority (HSA)
Brunei	Ministry of Health
Vietnam	Drug Administration of Vietnam
Myanmar	Food and Drug Administration
Cambodia	Department of Drug, Food and Cosmetics
Laos PDR	Ministry of Health, Food And Drug Department (FDD)

Table 6: ASEAN Storage Conditions.

Parameter	Storage Condition
Product in Containers Permeable to Water Vapors	30°C±2°C/75%RH±5%RH
Product in Containers impermeable to Water Vapors	30°C±2°C/RH not Specified
Accelerated Studies	40°C±2°C/75%RH±5%RH
Stress studies for analytical process validation	40°C±2°C/75%RH±5%RH

The Asean Common Technical Dossier (Actd) For The Registration Of Pharmaceuticals For Human Use Organization Of The Dossier

PREAMBLE

This ASEAN Common Technical Dossier (ACTD) is a guideline of the agreed upon common format for the preparation of a well-structured Common Technical Dossier (CTD) applications that will be submitted to ASEAN regulatory authorities for the registration of pharmaceuticals for human use. This guideline describes a CTD format that will significantly reduce the time and resources needed to compile applications for registration and in the future, will ease the preparation of electronic documental submissions. Regulatory reviews and communication with the applicant will be facilitated by a standard document of common elements. This guideline merely demonstrates an appropriate write-up format for acquired data. However, applicants can modify, if needed, to provide the best possible presentation of the technical information, in order to facilitate.

Part I. Table of Contents, Administrative Data and Product Information

Part I contains initially the overall Table of Contents of the whole ACTD to provide basically the information that could be looked through respectively. Secondly, the next content is the Administrative Data where required specific documentation in details is put together such as application forms, label, and package insert etc. The last section of this part is Product

Information where necessary information includes prescribed information, mode of action, side effects etc. A general introduction to the pharmaceutical, including its pharmacologic class and mode of action should be included.

Part II. Quality Document

Part II should provide the Overall Summary followed by the Study Reports. The quality control document should be described in details as much as possible.

Part III. Nonclinical1 Document

Part III should provide the **Nonclinical** Overview, followed by the Nonclinical Written Summaries and the Nonclinical Tabulated Summaries. The document of this part is not required for Generic Products, Minor Variation Products and some Major Variation Products. For ASEAN member countries, the Study Reports of this part may not be required for NCE, Biotechnological Products and other Major Variation Products if the Original Products are already registered and approved for market authorization in Reference Countries. Therefore, the authority who requires specific Study Reports should ask for the necessary documents.

Part IV. Clinical Document

Part IV should provide the Clinical Overview and the Clinical Summary. The document of this part is not required for Generic Products, Minor Variation Products and some Major Variation Products. For ASEAN member countries, the Study Reports of this part may not be required for NCE, Biotechnological Products and other Major Variation Products if the Original Products are already Registered and approved for market authorization in Reference Countries. Therefore, the authority who requires specific Study Reports should ask for the necessary documents.

Malaysia Introduction

In 2016, Malaysia's economy expanded 5% and the population was at 30 million. The country also has the third highest GDP per capita adjusted for purchasing power parity (PPP) in ASEAN at $27,000, behind only Singapore and Brunei (International Monetary Fund, 2016). Malaysia's pharmaceutical market is estimated to be worth $3 billion, more than two times that of Singapore. Malaysia's pharmaceutical market is expected to grow at approximately 10% annually, double the Asia-Pacific average.

Malaysia's national spending on healthcare has increased more than two and a half times

during the last twenty years, and is expected to continue rising alongside the longevity and affluence of its population. The Malaysian government has allocated 10% of its national budget to healthcare in 2017, a level on par with many western countries.

Malaysia's healthcare is regulated by the government's Ministry of Health. The healthcare system is structured in a two-tier system consisting of a public universal healthcare system and a private system. In recent years, the private sector has seen immense growth and caters to one- third of Malaysia's wealthier population, as well as a growing number of medical tourists. Malaysia's National Pharmaceutical Regulatory Agency (NPRA) is also a member of the Pharmaceutical Inspection Co-operation Scheme (PIC/S), which guarantees that the country's Good Manufacturing Practice (GMP) is aligned with international standards.

Pharmaceutical Regulations

The National Pharmaceutical Regulatory Agency (NPRA), formerly known as the National Pharmaceutical Control Bureau (NPCB), is the main regulatory body for pharmaceutical products in the country. The NPRA is an organization under the Pharmaceutical Services Division (PSD) of the Ministry of Health (MOH). The Drug Control Authority (DCA) is the executive branch of the NPRA, and is responsible for drug registration, licensing for importers and manufacturers, as well as drug quality monitoring.

Disease Trends

In recent decades, Malaysia's population has seen a dramatic surge of non-communicable diseases (NCDs) due to the prevalence of unhealthy diets, increasingly sedentary lifestyles, as well as the use of tobacco and alcohol. NCDs currently account for 70% of all deaths in the country.

Myths of Generic Drugs

Some myths that are often associated with generic drugs:

- Generic drugs are not as safe as innovators.
- Generics drugs are not as effectives as innovator
- Generics drugs take longer time to act in the body.

Generic drugs use the same active ingredients as innovator drugs and work the same way. So they have the same risks and benefits as the innovator drugs.

Generic drugs may look different because of certain inactive ingredients, such as colours and

flavouring agents, may be different. These ingredients do not affect the safety, effectiveness or performance of the generic drug.

So, there's no truth in the myths that generic drugs are inferior in quality as compared to innovator drugs.

Generic Drug Issues

Innovator drugs are more expensive because the company who first manufactures the drug spends large amount of money in research to develop the new drug which includes clinical trials, marketing and promotion of the drugs.

Generics drugs are cheaper as their manufactures are not required to demonstrate their efficacy and safety through clinical trials as these have also been established by the innovators.

However, generics drugs still needs to conform to same standard of quality, safety and efficacy required of the innovators. In addition, when the patent of a drug expired, there will be more company produce generic drugs which create competition and may reduce the cost of a drug.

Innovator Vs Generic

Table 7: Table.14 Innovator Vs Generic.

Criteria	Innovator	Generic
Registration by DCA	Yes	Yes
Procedures	Online/Manual	Online
Processing Fee	RM4000-RM5000	RM2200-RM3000
Requirements	Quality, Safety Efficacy (Animal And Clinical Study)	Quality, Safety, Efficacy (BE Study)
Processing Time	245 W.D.	210 W.D.
Validity of Registration	5 Years	5 Years
PMS & ADR Monitoring	Yes	Yes
GMP Facilities	Yes	Yes
Finished Product QC	Yes	Yes
Stability Data	Yes	Yes

Types of Generic Applications

Generic Pharmaceutical Products

A) Full Evaluation

- Scheduled Poison Time line: 210 Days.

B) Abridged Evaluation

- OTC/Non Scheduled Poison Categories Time line: 80 Days

Scheduled Poison(s) Products

Pharmaceutical products which contain scheduled poison(s) as defined in the First Schedule under POISON ACT 1952.

E.g. Atenolol, Ibuprofen, Lisinopril, Cimetidine, Dextromethorphan, etc.

Non-Scheduled Poison(s) Products (Over-the-Counter (OTC))

Pharmaceutical products which do not contain scheduled poison(s), other than health supplements or natural medicines or cosmetics.

E.g. Paracetamol, Simethicone, Aspirin, Clotrimazole, etc.

Non-Scheduled Poison(s) Products (Over-the-Counter (OTC))

Includes, but not limited to the following:

- Antiseptics / skin disinfectants
- Locally-acting lozenges / pastilles
- Topical analgesics / counter-irritants
- Topical nasal decongestants
- Emollient / demulcent / skin protectants
- Keratolytics
- Anti-dandruff
- Oral care
- Anti-acne
- Medicated plasters / patch / pad
- Topical antibacterial

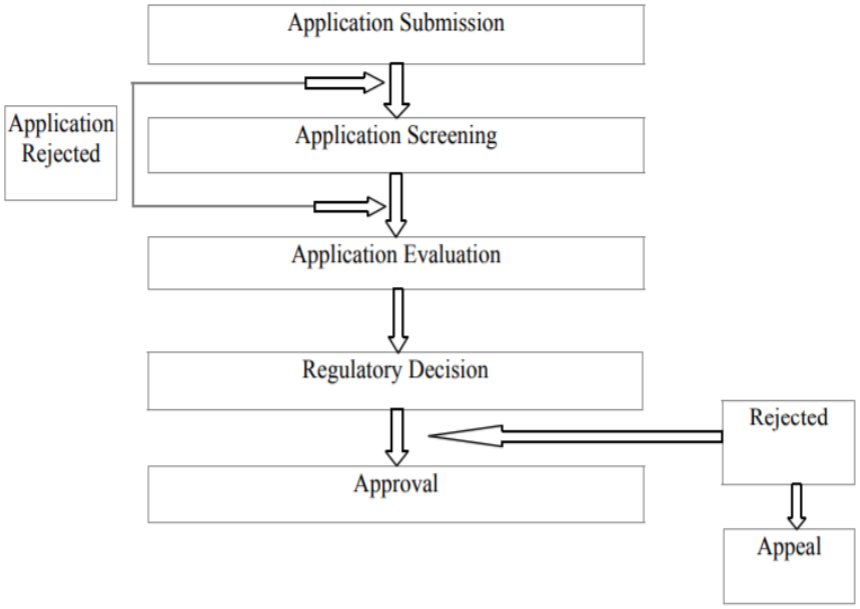
REGISTRATION AND APPROVAL PROCESS

The Drug Control Agency (DCA), under Malaysia's Ministry of Health (MOH), oversees drug registration.

In Malaysia, many high-end drug products are imported. Robust government spending on healthcare and attractive government tax incentives for foreign drug companies operating in Malaysia leads to increased growth and opportunities for prospective foreign pharmaceutical companies.

Applications can be submitted to the DCA online via the Quest 2 system. There are 4 categories of pharmaceuticals in Malaysia: biologics, new drug products, over the counter (OTC) generics and generics. Although certain types of OTC products are eligible for an abridged evaluation, all other pharmaceutical products must undergo an entire evaluation via the DCA prior to approval. The estimated timeline for abridged evaluations is around 180 days; full evaluations can extend up to a year or more. Registrations are valid for 5 years and can be renewed.

Registration Process Flow chart



REGISTRATION CONDITIONS

Registration no: MAL07021234A

- Product registration is for a period of 5 years.
- Updating of product information / amendments / variations is allowed through proper application - any changes that would affect the quality, safety and efficacy of product will not be allowed.
- Renewal of registration is required for maintenance on the register (to be notified by holder within 6 months before registration expires).

- Post Market Surveillance, Adverse Drug Reaction Monitoring and investigation on complaints AT ALL TIME.
- The DCA wishes that all medical practitioners, health professionals, consumers and the public report any complaints regarding the quality of medicines particularly if they experience adverse reactions or any other problems with these medicines.
- DCA will not hesitate to suspend, cancel, and Recall unsafe or substandard products from the market.

Challenges in Malaysia and Europe

Malaysia

Desirable healthcare products and services vary by country and are also impacted by the region's uneven distribution of wealth. For example, branded pharmaceuticals with a higher price tag may be more popular in the wealthier states of Singapore or Brunei than in the lower income member states, where generic products would be preferable.

Access to healthcare professionals and services tends to be concentrated in urban areas and it can be difficult for those residing in remote and rural areas to get access to quality pharmaceuticals and treatment.

The majority of pharmaceutical products in the region are imported, either as the final product, or as base materials which are then manufactured into the finished product locally. There are serious problems with high volumes of counterfeit products making their way onto the market.

Intellectual property (IP) rights are another challenge within the ASEAN region. patents are only extended to products that have been manufactured within the country; therefore, any foreign products that have been registered in Indonesia are at risk of local companies manufacturing the same product and marketing it at a reduced price as a generic under a new name**.**

Europe

Impact of Multiple Languages on Packaging Requirements One of the biggest challenges when entering the European market is the multitude of languages, which results in a large number of associated country-specific pack formats. Within the 28 member states of the EU, there are 150 regional and minority languages, of which 23 are recognized working

languages.

To ensure all drug products reach the end user in optimum condition, the CMO should conduct a full validation of shipping and packaging configurations. For example, our validation and logistics teams work with the client company, the packaging supplier, and distribution partners to design a customized configuration for the drug product being shipped.

CONCLUSION

Although there is a continuous process of harmonization taking place all around the world, still we see a huge challenge, which is yet to be overcome by the Pharmaceutical industry in case of generic drug development and filing. This is due to the heterogeneity in the regulatory landscape of the various countries. Therefore, to meet these challenges, a lot of strategic planning is required before the development of any generic drug product.

The purpose of the study is to compare generic drug registration and requirements in ASEAN countries & to find out the differences in guidelines. The focus on countries like Indonesia and Thailand is because of high population rate, maximum share of ASEAN pharmaceutical market, low income. But these countries are ranked after Vietnam and Philippines because of some restriction by countries government for foreign players. Singapore and Malaysia are the only countries in ASEAN, who have well established pharmaceutical regulations and more strict to quality & safety of drugs. These countries believe on innovation and give full protection to them. Hence there may not be many opportunities for small and medium scale generic companies in these countries unless their manufacturing procedures are well to do with regulatory requirements. This article gives a simplified overview of the Drug Regulatory Authority of 10 countries (ASEAN) and in detail registration requirements for filing a dossier for a generic drug product in the markets selected.

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