"COMPARATIVE STUDY OF HONGKONG, MALAYSIA & INDIA REGULATORY FRAMEWORK AND REGISTRATION REQUIREMENTS FOR GENERIC DRUGS"

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REGULATORY AFFAIRS & QUALITY ASSURANCE

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CERTIFICATE

This is to certify that the dissertation work entitled "Comparative study of Hongkong, Malaysia and India regulatory framework and registration requirements of generic drugs" submitted by Ms. Arti S. Chauhan with Regn. No. (15mph801) in partial fulfillment for the award of Master of Pharmacy in"Regulatory Affairs and Quality Assurance" is a bonafide research work carried out by the candidate at the Department of Regulatory Affairs and Quality Assurance, Institute of Pharmacy, Nirma University and at Finecure Pharmaceutical Pvt. Ltd. Ahmedabad under our guidance. This work is original and has not been submitted in part or full for any other degree or diploma to this or any other university or institution.

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DECLARATION

I hereby declare that the dissertation entitled "Comparative study of Hongkong, Malaysia and India regulatory framework and registration requirements of generic drugs", is based on the original work carried out by me under the guidance of Mrs. Devanshi Patel, Executive Regulatory Affairs, Finecure Pharmaceutical Pvt. Ltd. And Dr. Priti J. Mehta, Professor, Department of Pharmaceutical Analysis, Institute of Pharmacy, Nirma University. I also affirm that this work is original and has not been submitted in part or full for any other degree or diploma to this or any other university or institution.

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List of Abbreviations

ACTD	ASEAN Common Technical Dossier
ACTR	ASEAN Common Technical Requirement
ACCSQ	ASEAN Consultative Committee for Standards and Quality
AMV	Analytical Method Validation
ASEAN	Association of Southeast Asian Nations
BA	Bioavailability
BE	Bioequivalence
BSE	Bovine Spongiform Encephalopathy
CDCR	Control of Drugs & Cosmetics Regulations 1984
CDSCO	Central drug standard control organization
CEP	Certificates of Suitability
CFDA	China Food and Drug Administration
CFS	Certificate of Free Sale
CMC	Chemistry, Manufacturing And Controls
COA	Certificate of Analysis
COS	Change of manufacturing site
CPP	Certificate of Pharmaceutical Product
DH	Department of Health
DMF	Drug Master File
DP	Drug Product
DPS	Department of Pharmaceutical Services
DS	Drug Substance
DRGD	Drug Registration Guidance Document
FDA	Food and Drug Administration
GDA	Generic Drug Application
GDP	Good Distribution Practice
GMP	Good Manufacturing Practice
HSA	The Health Sciences Authority
ICH	International Comission on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use
IEC	Independent Ethics Committee
INN	International Nonproprietary Names
ISO	International Organization for Standardization

LOA	Letter of Authorization
LOD	Loss On Drying
Ma V	Major Variation
MHRA	Medicine and Healthcare product Regulatory Authority
Mi V	Minor Variation
MiV-N	Minor Variation Notification
MOA	Method of Analysis
NCE	New Chemical Entity
NDP	New Drug Products
NPRA	National Pharmaceutical Regulatory Agency
PIC/S	Pharmaceutical Inspection Co-operation Scheme
PI	Package Insert
PK/ PD	Pharmacokinetic / Pharmacodynamic
PMF	Plasma Master File
PSUR	Periodic Safety Update Report
QOS	Quality Overall Summary
RiMUP	Consumer Medication information Leaflet
RM	Malaysian Ringgit
SFDA	State Food and Drug Administration
SPC	Summary of Product Characteristics
TGA	Therapeutic Goods Administration
TSEs	Transmissible spongiform encephalopathies
WHO	World Health Organisation
US FDA	United States Food & Drug Administration

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CHAPTER-1

INTRODUCTION

1. INTRODUCTION

1.1 Regulatory Affairs

Regulatory is involved in the development of innovator product, by regulatory principles and by preparing and submitting the regulatory dossiers of the authorities. Regulatory Affairs is dynamically involved in all stage of development of a innovator and in the post-marketing activities with the medicinal products.

The Regulatory Affairs are essentially to the overall success for the development drugs, both at early pre-marketing stages and for the post-marketing. The pharmaceutical industry deals with an rising number of drug candidates, all of which require the involvement of the Regulatory Affairs' department.

Regulatory affairs professionals are occupied for the development for the product from the starting. The Regulatory requirements need to be careful for drafting the preclinical pharmaceutical, and clinical development study.

Regulatory professionals make sure that the information and data to be discussed with the regulatory bodies. The regulatory strategy developments, meetings with the agencies, prepare and collect the questions and documents with the agencies**.**

1.2 What are Generics?

A generic drug is a that is equivalent to a brand-name product in dosage, strength, route of administration, quality, performance, and intended use. A generic drug must contain the same

In most cases, generic products become available after the afforded to a drug's original developer expire. Once generic drugs enter the market, competition often leads to substantially lower prices for both the original brand-name product and its generic equivalents. In most countries, patents give 20 years of protection.

1.3 Regulation of Generic Drugs

In the present scenario, the pharmaceutical market has been widespread across the world as a result of varied collaborations and development of national regulatory authorities.

According to worldwide pattern, it is accepted that $150 billion medications are going off-patent in the times of 2010-2017 which additionally demonstrates the open door for generics. Subsequently, the administrative needs are upgraded to keep up such an outpouring of market deal without influencing the patient's wellbeing. Administrative rules and standard devices help in development of laws which at last gives tranquilize control. For an organization to build up a generic medication advertise at various nations, it is critical to comprehend administrative dossier entries rules of particular nations and in this manner it is imperative to investigate the similarities & dissimilarities between administrative prerequisites and generic pharmaceutical laws crosswise over different regions. Generic drug registration is being regulated by different regulatory agencies like USFDA, EU, TGA, PMDA which has their own set of generic regulations and other authorities like CIS,LATAM,ASEAN which has adapted ICH and USFDA,EU guidelines for generics.

Although every one of these specialists work towards giving straightforward administrative process a reliable approach is yet to be kept up. For e.g. Filing a generic drug application requires much more time in USFDA and EU rather than in emerging markets. Moreover filing of ANDA is necessary for marketing authorization of generics in US while in Europe 4 types of registration process is being followed to obtain MAA: 1) Centralized Process, 2) Decentralized Process, 3) National authorization 4) Mutual Recognition Procedure. In ASEAN region, GDA should be carried out according to ACTD-ACTR guidelines while CIS countries follow their own country specific guidelines.

1.4 PIC/S

The Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme are two universal instruments amongst nations and pharmaceutical review specialists working together in parallel, which give together a dynamic and valuable co-operation in the field of GMP. PIC was established in 1970.

Its mission is "to lead the international development, implementation and maintenance of harmonized Good Manufacturing Practice (GMP) standards and quality systems of inspectorates in the field of medicinal products."

This is to be accomplished by creating and advancing orchestrated GMP benchmarks and

direction archives for industry; preparing of capable specialists, specifically auditors; evaluating (and reassessing) inspectorates; and encouraging the co-operation and systems administration for skilled experts and universal associations.

At present, there are in PIC/S. 32 out of 34 OECD member countries are PIC/S members.

The PIC/S has recently undergone new organizational structure on 1st January 2014, which includes seven sub committees. Each subcommittee chairman is a member of PIC/S governing body.

The Pharmaceutical Inspection Co-operation Scheme (PIC/S) . PIC/S plans to harmonize investigation techniques worldwide by creating basic measures in the field of GMP and by giving preparing chances to controllers and inspectorates. It additionally plans to encouraging co-operation and systems administration between capable experts and universal associations, in this manner expanding common certainty and encouraging the acknowledgment of review results.

Table 1.1: Difference between PIC (convention) and the PIC/S (Scheme)

PIC (Convention)	PIC/S (Scheme)
It is a formal treaty between states (Countries)	It is an informal arrangement between health regulatory authorities.
With internationally recognized legal status (international treaty)	Without internationally recognized legal status
Legally binding	Non-binding
Mutual recognition of inspections:	Exchange of information:
Exchange of GMP certificates	Exchange of mainly GMP inspection reports
Each party recognizes that GMP certificates of the other party are equivalent to its own national certificates.	The exchange is on a purely voluntary basis. PIC/S Participating Authorities may rely on these reports in order to facilitate the GMP approval of medicinal products and establishments.
No possibility of re-inspection	Re-inspection is possible
Exceptions are possible	-

It is not applied to veterinary product.	It is applied to the Veterinary product.

1.4.1 Principles

PIC/S is an absolutely specialized association in the field of GMP where new thoughts identified with GMP are discussed by profoundly equipped specialists.

All individuals from PIC/S have level with rights and commitments as indicated by understanding. Common trust is a key an incentive in PIC/s which relies on upon willful co-operation and every part being surveys for identicalness before being conceded so individuals think that its less demanding to trade data on GMP on a deliberate premise.

PIC/S is a part determined association which implies that each taking an interest specialists are required to add to either PIC/S occasions or working, for example, official obligations and leading gatherings.

1.4.2 Benefits of membership

- PIC/S gives a stage to the preparation of GMP controllers by going to classes and by taking an interest in the PIC/S joint visits program.
- By partaking in the meeting Participating Authorities are included in the advancement and harmonization of worldwide GMP aides and rules. Advisory group additionally advances the uniform understanding of GMP and Quality Systems for GMP Inspectorates.
- Participants are profited from individual contacts with different offices, regardless of whether they are a piece of PIC/S or not. This make simple trade of GMP related data.
- PIC/S guarantees consistence of the GMP measures that strengths GMP investigation framework and methodology. These outcomes in expanded effectiveness of the GMP inspectorate. PIC/s additionally permits deliberate sharing of GMP assessment report.
- PIC/s has a quick ready and review framework for quality imperfections of batches of the medicinal items, which gives their review for arrangement of EU/EEA/MRA.
- PIC/S enrollment promotion is one of the basic criteria for MRA. (e.g. ASEAN MRA Australia-Canada MRA, EU-Switzerland MRA).

- Some non PIC/S specialists like Colombia and South Africa acknowledges GMP testament from PIC/S taking an interest expert.
- Benefits for industry:

  Reduced duplication of examination

  Cost reserve funds

  Export help

  Enhanced advertise get to

1.4.3 PIC/S GMP

PIC/S GMP guide is created to guarantee of elevated requirements in the advancement, manufacture and control of drug products, to evacuate in exchange, to advance consistency in permitting choices, to advance consistency and consistency of assessment.

Guidance document consist of 2 parts.

Part 1: GMP principles for the manufacturing of medicinal product
Part 2: GMP for active substances

1.5 ASIA Region

Asia is world's biggest and most populated which is situated in the eastern and northern half of the globe. Because of its huge size it comprises of tremendous differing qualities in culture, atmosphere, and government framework.

1.6 ASEAN Region

South East Asia is a sub locale of Asia comprises of nations that are topographically south of China, east of India, and north of Australia. From this sub locale 10 nations involve the Association of South East Asian Nation (ASEAN), a political and monetary gathering which was established in 1967 to advance shared financial improvement and intensity. ASEAN part nations are Indonesia, Malaysia, Philippines, Singapore, Thailand, Brunei, Myanmar, Cambodia, Lao PDR, and Vietnam. It has political social and financial differences; alongside that it has changing medicinal services framework extending from profoundly created Singapore to the moderately immature human services arrangement of Cambodia, Laos and Myanmar. ASEAN nations have a more than 620 million

populace which is about twofold than US and 100 million higher than Europe.

Figure 1: Map of ASIA

Harmonization of ASEAN pharmaceutical direction was started in 1992 with foundation of ASEAN Consultative Committee for Standards and Quality (ACCSQ).

Extent of the ACCSQ PPWG exercises:

- Development of Quality Guideline and discourse on existing administrative rule and specialized necessity.
- Exchange of data on existing administrative prerequisite and harmonization of administrative necessity relevant to ASEAN part states.

- The improvement of Common Technical Documents with a view to landing at Mutual Recognition Arrangement (MRAs).

Table 2: Drug Regulating Authorities of ASIA

Sr No.	Country	Regulatory Authority
1	Malaysia	National pharmaceutical regulatory authority (NPRA)
2	Hongkong	Department of health (DH)
3	India	Central Drug Standard Control Organization (CDSCO)

CHAPTER-2

AIM
&
OBJECTIVES

2. AIM and OBJECTIVES

- In Asia a large portion of the nations are developing nations. Pharmaceutical administrative system is likewise making strides. Administrative prerequisites are less stringent than other developed nation.

- The main goal of this dissertation work is to carry out a detailed study regarding registration requirements of generic drugs and the regulatory framework in Hongkong, Malaysia and India. Also, comparative study has been carried out for these countries to help broaden the essential requirements for the generics.

- The main objective of the current dissertation work is to study the regulatory guidelines of Hongkong, Malaysia and India and to carry out the comparison of the regulatory pathways for registration of drugs in respective nations taken into consideration.

CHAPTER-3

LITERATURE REVIEW

3. LITERATURE REVIEW

Shweta Handoo at el has reported that administrative regulatory requirements for enrolling generic medications in various nations differ from each other and the part of administrative experts is critical, to recognize how to screen the medication's quality wellbeing and viability as indicated by administrative necessities. Creator has depicted the wide variety in administrative procedures between U.S, Europe, CIS and Africa by demonstrating examination among steadiness conditions, BE prerequisites, number of bunches tried inside these regions. Creator by demonstrating the contrasts between control of different districts, clarified the nearness of heterogeneity inside specialists and the need of harmonization for less demanding non specific medication improvement and recording.

P. Nagaraju et al has showed the generic market is developing quickly over Southeast Asia because of quickly developing populace and enhanced directions over the area. Significant distinction between ICH-CTD and ACTD organization is described with a short review of specialized archive necessities in ASEAN area. The Singapore and Malaysia are the main nations in ASEAN which contain all around organized controls and the ones who have confidence in advancement of new medications. Different nations like Vietnam, Thailand, and Philippines are the objectives for little and medium scale of the generic company , which has less difficult directions.

Jitendra Badjatya reported that emerging markets like LATAM, ASEAN, GCC, and CIS are more prone to pharmaceutical development rather than developed markets due to high population rate and varied health care issues. Developed countries have harmonized their regulation through ICH standards but emerging markets are yet to establish uniform standards. Author has described regulatory barriers and challenges which hinder the pharmaceutical exports, like pricing approval, GMP inspections, COPP, varied time duration for evaluation of dossiers which are not seen in western approval processes.

Department of health drug office for the drug registration and import/export contron division guidance notes provide understanding on registration requirements of pharmaceutical product , registration fees, stability data, labeling requirements, renewal of registration.

Bindhu Madhavi has reported that comparitive study of dossier submission process for drug product in USA, EU & INDIAN regulatory.The individually study about rule & regulations1 which are followed for drug approval process in USA, Europe & India. Quality must ensure consistency of safety and efficacy during the shelf life of all batches Produced. This comparative study of dossier compilation given a brief idea about the difference in regulatory requirements for drug approval process among USA, EU & India.

Prajapati Vishal has showed that a review on drug approval process for us, europe and india. Developing a new drug requires great amount of research work in chemistry, manufacturing, controls, preclinical science and clinical trials. Drug reviewers in regulatory agencies around the world bear the responsibility of evaluating whether the research data support the safety, effectiveness and quality control of a new drug product to serve the public health. Every country has its own regulatory authority, which is responsible to enforce the rules and regulations and issue the guidelines to regulate the marketing of the drugs.

Drug registration guidance documents has showed that Parts of documents submission in ACTD-dossier format, Registration process flow chart, Specific labelling requirement, Requirement of actd part on the basis of route of evaluation along with approval timeline, documents require for change of site, variation **,** Registration fees, renewal of registration.

Dr. Dilip Maheshwari has reported that the documentation Requirements for Generic Drug Application to be Marketed in India. Branded drugs play an important role in medications, but generics are their cost effective alternatives. Generics are similar to branded drugs in terms of purity, efficacy and are perceived to be safer as compared to new drug molecules. Indian pharmaceutical market of generic drugs is increasing day by day.. A regulatory affair is a somewhat new profession which has developed from the desire of governments to defend public health. Substantial documentation and data are required in these types of submissions, resulting in large, complex applications. The International Conference on Harmonization (ICH) process, the Common Technical Document (CTD) which is helpful for the marketing application for generic drugs in India.

V. Prabhakaran has reported that drug regulation has developed over the past 50 years in response to crises in relation to pharmaceutical products. Current drug regulation was the comprehensive multi-country study undertaken by the World Health Organization (WHO). In order to register a NDA & ANDA molecules globally, a pharmaceutical company develops a dossier that describes the pharmaceutical quality, safety and efficacy of the product for a specified indication. This drug was filed in Kenya, Tanzania, Uganda, Malaysia, Bahrain, Kuwait, Oman, Qatar, Mexico, Peru, and Venezuela. After studying the regulatory requirements to register a pharmaceutical product for human use and after analysing the communications received from respective regulatory authorities filing strategy has been developed to improve the quality of the submission file and also helps to reduce the product registration lead time which allows commercial team to launch the product at the earliest.

CHAPTER-4

COUNTRY SPECIFIC REQUIREMENTS IN HONGKONG

4. COUNTRY SPECIFIC REQUIREMENTS IN HONGKONG

Drug Regulatory Authority: Department of Health (DH)

4.1 Introduction

DH is responsible agency to market drugs in Hong Kong. According to the Pharmacy and Poisons Ordinance Drug should be registered in Hong Kong before sale.

Drug Product is classified into three categories:-

- Product that requires doctor's prescription.
- Product that requires its sale under registered pharmacist.
- Product which might be sold without resident pharmacist.

4.1.1 Criteria For Registration

Formulation will only get approved for its registration provided it meets the criteria of safety, quality and efficacy related to it.

4.1.2 Eligibility to Apply Pharmaceutical Product

If the pharmaceutical product is manufactured in Hong Kong, the individual in charge of acquiring enrollment of the product is the authorized maker, or the authorized discount merchant contracting with the authorized producer. If the pharmaceutical product is manufactured outside Hong Kong, the individual in charge of acquiring enrollment is the authorized discount merchant who imported the pharmaceutical item, or the Hong Kong branch, backup, delegate, operator or wholesaler of the abroad producer.

4.1.3 Pharmaceutical Products which are not Applicable to Registration

(A) products having only proprietary Chinese medicines as defined in the Chinese Medicine Ordinance;

(B) drug substances that are imported by licensed manufacturers in order to manufacture their own pharmaceutical products

(C) products that are imported for re-export purpose only;

(D) products which are manufactured in Hong Kong for the purpose of export by only licensed manufacturer;

(E) products which are given to carry out a clinical trial/medicinal test according to its certificate issued under the Pharmacy and Poisons Regulations.

4.2 Registration Requirements

a) A separate dossier is needed for various dosage forms and strength but not for diverse pack size.
b) 1 set of prototype sales pack having full labeling requirement.
c) In package insert cross referencing is required to be done with relevant part & page number of the reference.
d) Scanned image in PDF format/photograph image in JPEG format of sales pack.
e) Pocket printing is required on every blister.

- Category one and two drug should be labelled with "Poison"

- Stability data of any 1of the below mentioned conditions:-

Real Time Testing Conditions:-

(i) 30°C±2°C / 75%±5% RH
(ii) 30°C±2°C / 65%±5% RH
(iii) 25°C±2°C / 60%±5% RH
Three months' real time stability data is to be provided.

Accelerated Testing Conditions

40°C±2°C / 75%±5% RH for six months

f) BE study is to be conducted according to the WHO guidance document.
g) Separate dossier is needed for each strength.
h) Completed check list of the documents required should be submitted with the registration application.

Table 3: List of Documents Required in HongKong

NO.	CONTENTS
1	Letter of Authorization for Product
2	Certified true copy of the valid Pharmaceuticals Manufacturer's License issued by the national control authority of the origin country
3	Certified true copy of the valid GMP Certificate of the manufacturer
4	Certified true copy of the FSC of Product issued by the origin country of the Manufacturer
5	Completer Master Formula (Active and Inactive Ingredients) and Manufacturing Process.
6	Finish Product Specification
7	Method of Analysis of the finished Product
8	COA of a representative batch of the product
9	Stability Data
10	A copy of Site Master File
11	Bioequivalence (BE) study for Anti – Epileptic Drugs.
12	One set of prototype Sale Pack, Pack insert and Container Label of every pack size of the product complying entirely with the suitable labelling requirements.
13	Package Insert
14	Package Insert references
15	The Scanned image or photograph of the product sample including sale pack – inner container / packing and image of the drug sample.

4.3 Registration Fee

Application fees: $ 1100

Registration fees: $ 1370

Re registration fees: $ 575

Change in registered particular: No fees are charged. For change of name or address of the registration certificate holder $155 per certificate will be charged for each registration

certificate.

4.4 Registration Renewal

Registration certificate validity is 5 years.

Renewal notice will be sent to the holder of registration certificate around 3 to 4 months prior to certificate expiry. Renewal applications should file in Form FPRN01 within 30 days of issuance of renewal notification**.**

CHAPTER-5

ACTD - ASEAN COMMON TECHNICAL DOSSIER IN MALAYSIA

5. ACTD- ASEAN COMMON TECHNICAL DOSSIER IN MALAYSIA

Drug Regulatory Authority: National Pharmaceutical Regulatory Authority (NPRA)

5.1 Introduction

The National Pharmaceutical Regulatory Authority (NPRA) is a main regulatory authority responsible for quality, safety, and efficacy of pharmaceutical product. Registration of product in Malaysia is done by an online submission via quest system.

ASEAN guideline is a common format for the well- structured common technical dossier (CTD) that will be submitted to the regulatory authority of ASEAN for the registration of pharmaceutical products. This guideline represents dossier format that will reduce the time and resources required to compile application of registration and ease the preparation of electronic submission.

ACTD organized into 4 parts:

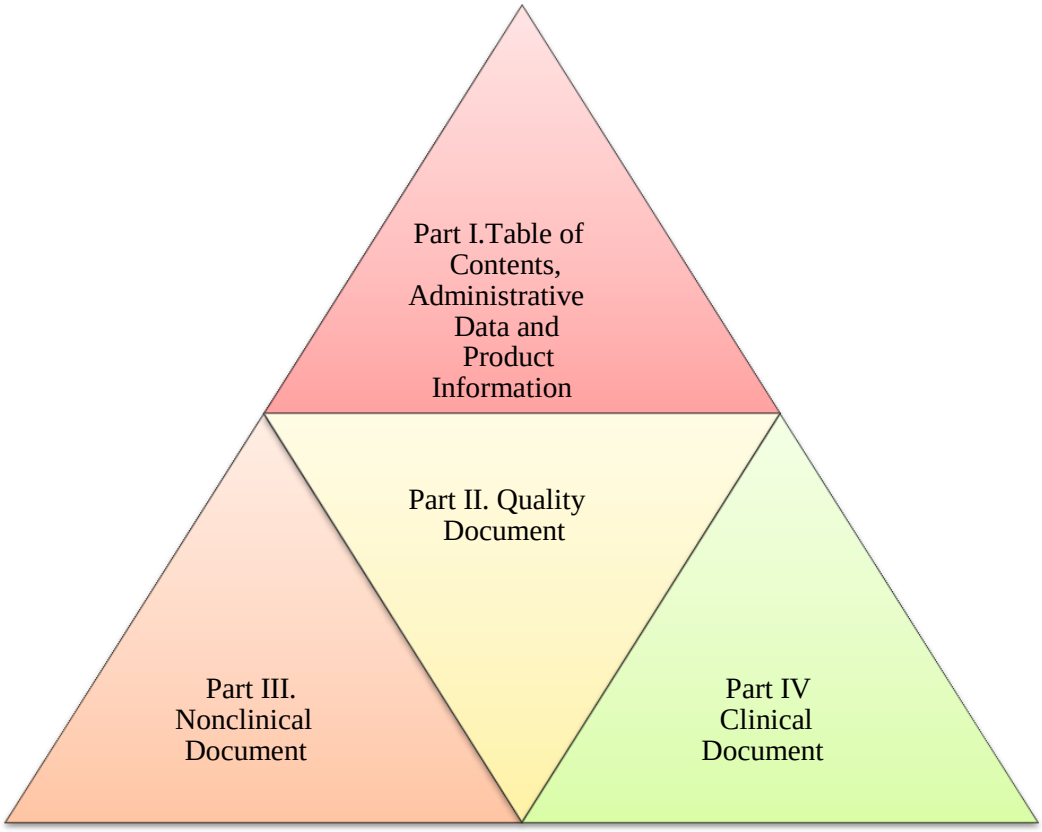
Part I : Administrative Data and Product Information

Part II : Quality Document

Part III: Non-Clinical Document

Part IV: Clinical Document

Figure 2: Organization of ACTD parts



5.2 List Of Documents In Actd-Dossier Submission

5.2.1 Part I:- Administrative Data and Product Information

Section A- Product Particulars

Section B- Product Formula & attachment of Batch manufacturing formula

Section C- Particular of Packing

Section D- Proposed Label (Mock-up)

Specific labeling requirements

- Qualitative and quantitative composition of preservatives
- The words "Keep medicine out of reach of children "should be stated
- The words "Controlled Medicine"/ "*Ubat Terkawal*"

- Security label or hologram
- substance specific labelling requirement is to be mentioned wherever applicable

Types of Labels

- D1-Immediate container
- D2-Outer Carton
- D3-For Package Insert

Section E- Supplementary Documentation

LOA from product owner

Types of Documentation

- E 6 - COPP (Malaysia specific)
- E12 - CFS
- E 16 - Certificate of GMP
- E 20 - SPC
- E 21 - Consumer Medication information Leaflet (RiMUP)
- E 22 - FP specification and MOA with chromatograms
- E23 - Summary of AMV which involves all the related validation characteristics, its acceptance criteria & results.
- E 24 - COA for active drug substance (one batch) & recent batches of finished product (three different batches).
- E 25 – Other supporting document

5.2.2 Part II :- Quality Document

Part II is required to be given with the Overall Summary followed by the Study Reports. The quality control document should be described in details as much as possible.

Section A: TOC

Section B: QOS

Section C: Body of Data

Table 4: Module 3-List of Quality Documents

Quality Overall summary: Drug Substance		
S Drug Substance		
S1	**General Information**	
	S.1.1	Nomenclature
	S.1.2	Structure and Attachment for Structure of Drug Substance
	S.1.3	General Properties
S2	**Manufacturer**	
	S.2.1	Manufacturer Name and Address
	S.2.2	Description of Manufacturing process and process Controls
	S.2.3	Control of Materials
	S.2.4	Control of Critical Steps and Intermediate
	S.2.5	Process Validation and/or Evaluation
	S.2.6	Manufacturing Process Development
S3	**Characterization**	
	S.3.1	Elucidation of Structure and Characteristics
	S.3.2	Impurities
S4	**Control of Drug Substance**	
	S.4.1	Specification
	S.4.2	Analytical Procedure
	S.4.3	Validation of Analytical Procedure
	S.4.4	Batch Analysis
	S.4.5	Justification of Specification
S5	**Reference Standards or Materials**	
S6	**Container Closure System**	
S7	**Stability**	
P	**DRUG PRODUCT**	
P.1	**Description and Composition**	
P.2	**Pharmaceutical Development**	
	P.2.1	Information on Development
	P.2.2	Components of Drug Product

	P.2.3	Finished Products
	P.2.4	Manufacturing Process Development
	P.2.5	Container Closure System
	P.2.6	Microbiological Attributes
	P.2.7	Compatibility
P.3	**Manufacture**	
	P.3.1	Batch Manufacturing Formula
	P.3.2	Manufacturing Process and Process Control
	P.3.3	Manufacturing Process Flowchart
	P.3.4	Control of Critical Steps and Intermediates
	P.3.5	Process validation/or Evaluation
P.4	**Control of Excipients**	
	P.4.1	Specification
	P.4.2	Analytical Procedures
	P.4.3	Validation of Analytical Procedures
	P.4.4	Justification of Specifications
	P.4.5	Excipients of Human or Animal Origin
	P.4.6	Novel Excipients
P.5	**Control of Finished Products**	
	P.5.1	Specification
	P.5.2	Analytical Procedures
	P.5.3	Validation of Analytical Procedures
	P.5.4	Batch Analysis
	P.5.5	Characteristics of Impurities
	P.5.6	Justification of Specifications
P.6	**Reference Standards or Materials**	
P.7	**Container Closure System**	
P.8	**Product Stability**	
P.9	**Product interchangeability/equivalence evidence**	

Section D: Key Literature References

5.2.3 Part III: - Non-Clinical Document

For registration of generic drugs, only TOC of Non Clinical Part is needed if the original product has already been registered in other reference nations.

Major sections of Part III are:

Section A: TOC

Section B: Non Clinical Overview

Section C: Non-Clinical Tabulated and Written Summaries

Section D: Non Clinical Study Reports.

5.2.4 Part IV :- Clinical Document

ASEAN nations registration does not need Part IV for Generics, Minor or Major Variation product dossier registration. Study Reports portion of Part IV is not needed for New Chemical Entity, Biotechnological products if the product has market authorization of reference nations.

Major sections of Part IV include:

Section A: TOC

Section B: Clinical Overview

Section C: Clinical summary

1) Bio-pharmaceutics and Associated Analytical Methods summary
2) Clinical Pharmacology Studies summary
3) Clinical efficacy summary
4) Clinical safety summary
5) Individual Studies summary

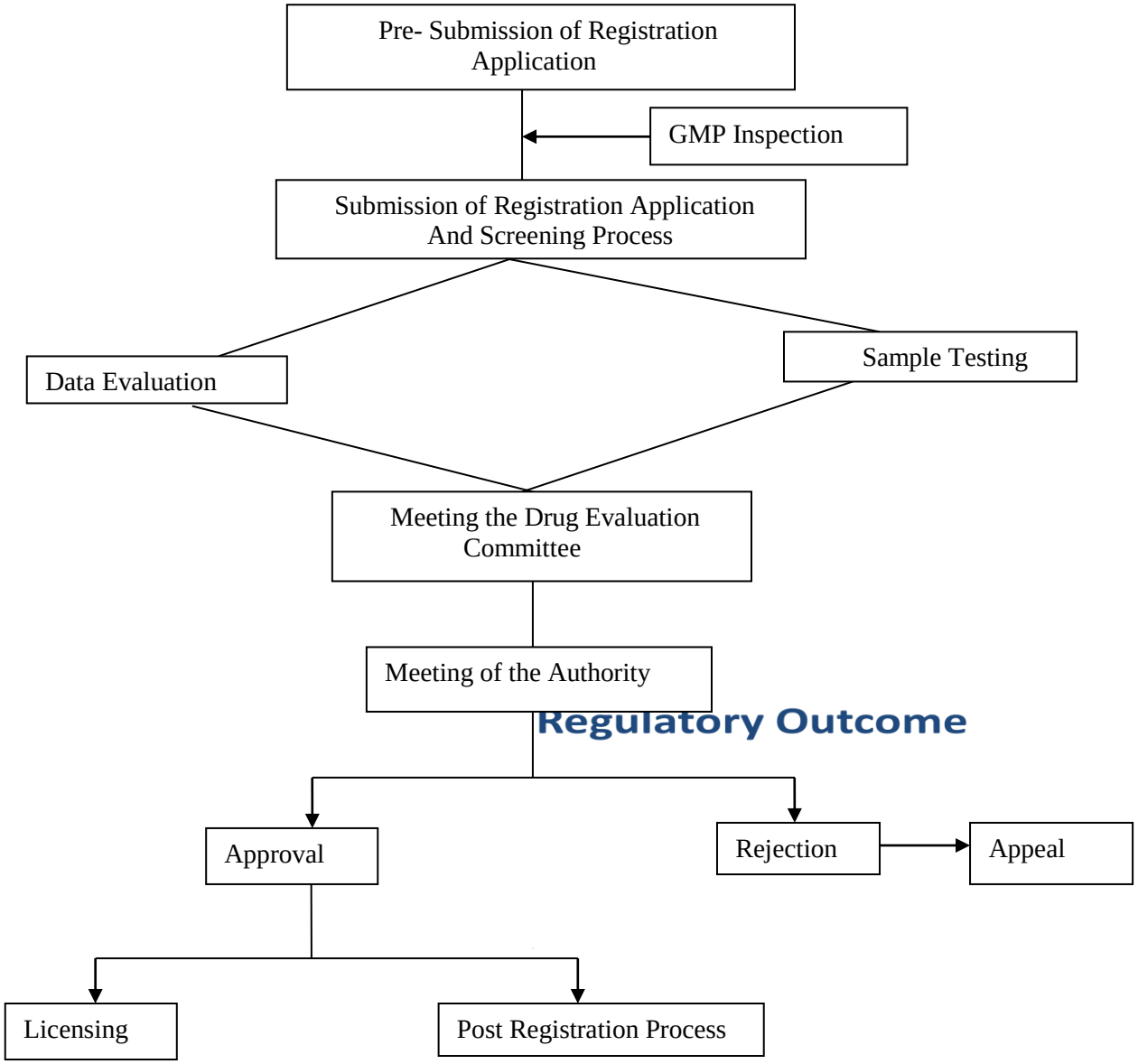
Section D: Tabular Listing of All clinical

Section E: Clinical Study Reports

Section F: List of Key Literature Reference

5.3 Registration Process Flow Chart

Figure 3: Registration Process Flow Chart in Malaysia



5.3.1 PRE-SUBMISSION OF APPLICATION

5.3.1.1 The Category of the Product

e.g. GENERICS

a. Poison medicine

b. Non- Poison medicine

5.3.1.2 Method of Evaluation

a. Full Evaluation

b. Abridged Evaluation.

5.3.1.3. Requirements for Product Registration

A. General requirements

i. Full Evaluation;

Part I:- product information & Administrative data

Part II :- Quality Documents for product quality

Part III:- Nonclinical Document for product safety

Part IV:- Clinical Documents for the product safety and efficacy

ii. Abridged Evaluation

iii. Additional Information on Requirement of BA and BE study.

B. Requirements for specific product

5.3.1.4 MULTIPLE APPLICATIONS

Separate application for registration of the product is required for the following conditions:

- Products having similar ingredients but made to different specifications, or
- When the manufacturer is different.

5.3.1.5 VARIANTS

- The variants should differ only in terms of fragrance & color.
- Product name of the variants is required to remain the same, alongwith the addition of an identifying variant name.
- Each variant is required to be registered as 1 product with a diverse registration number.

5.3.1.6 LANGUAGE

All the information as well as data involving supporting documents for registration of

product like certificates, letters and product labels are needed to be in English.

5.3.2 SUBMISSION OF APPLICATION

Product registration application is to be submitted through online QUEST system.

5.3.3 SCREENING OF APPLICATION

a. Satisfactory

Only a complete application is required to be accepted and to be approved for payment.

b. Non-satisfactory

If the application has found to be incomplete during the screening procedure, the application is to be rejected & the applicant is to be notified via system..

5.3.4 EVALUATION OF APPLICATION

a. Initiation of review

Upon confirming payment, application alongwith the submitted data is to be evaluated.

b. Correspondence

Application is to be rejected if the applicant fails to respond to the correspondence from NPRA regarding the submission of supplementary data/ information within 6 months from first correspondence date.

c. Timeline for product registration

Table 5: Timeline for product registration

Evaluation type	Parts of ACTD	Timeline for approval
Full Evaluation ▪ New Drug Product ▪ Generic (Scheduled poisons/Non Scheduled poisons)	Part I, II, III, IV Part I, II	245 days 210 days
Abridged Evaluation Generic (Non Scheduled poisons/OTC Product)	-------	Single API: 116 days two or more API: 136 days

5.3.5 POST-REGISTRATION PROCESS

Product registration is to be valid for 5 years or such period as mentioned in the database of authority.

Application for re-registration of a product shall be submitted within 6 months before expiry of the validity period of the product registration. A letter of reminder for product re-registration will be issued to the product registration holder 3 months prior to the expiry date of a product registration.

5.3.6 REJECTED APPLICATION

Any individual distressed by the choice of the Authority or the Director of Pharmaceutical Services, a composed interest might be made to the Minister of Health Malaysia. All notice of claims might be made inside fourteen (14) days from the date of notice from the Authority; Any choice of the Minister made on an interest might be last.

5.4 FEES

Table 6: Processing And Analysis Fee For Product Registration

No.	Category of Product	Processing Fees	Analysis Fees	Total Fees
1.	New Drug Product	RM 1,000.00	Single active ingredient : RM 3,000.00	RM 4,000.00
			Two or more active ingredients : RM 4,000.00	RM 5,000.00
2.	Generic (Scheduled Poison) Generic (Non- Scheduled Poison)	RM 1,000.00	Single active ingredient : RM 1,200.00	RM 2,200.00
			Two or more active ingredients: RM 2,000.00	RM 3,000.00

Table 7: Charges For Application Of Licenses

License	Processing fee	Timeline	Validity
Manufacturer	RM 1,000.00	4 working days upon receipt of complete application	1 year
Import	RM 500.00	4 working days upon receipt of complete application	1 year
Wholesale	RM 500.00	4 working days upon receipt of complete application	1 Yea r

Table 8: Charges For Amendments to Particulars of a Registered Product

Types of Amendment	Processing fee	
	Pharmaceutical	Natural Product
Change of Manufacturing Site (Type II, III, IV, V)	RM 1,000.00	RM 500.00
Change of Product Registration Holder	RM 1,000.00	RM 500.00

Table 9: Fee For Certificates

Certificates	Fee	Validity
Issuance of one (1) Certificate of Pharmaceutical Product	RM 50.00	2 years
Issuance of one (1) Certificate of Good Manufacturing Practice	RM 50.00	2 years

(GMP)		

5.5 Documents require for change of site

Table 10: Documents require for COS

No.	Documents to be Submitted	Type I	Type II	Type III	Type IV	Type V
1	LOA	√	√	√	√	√
2	Letter explaining need for change of site	√	√	√	√	√
3	Declaration that manufacturing process & Specifications of product are same as already approved. / If minor change then justification for change.	√	√	√	√	√
4	Release & Shelf life specifications from new site	√	√	√	√	√
5	CPP/ CFS/ GMP certificate of new site	√	√	√	√	√
6	Specification of the drug substance	√	√	√	√	√
7	Product formula/ batch manufacturing formula	√	√	√	√	√
8	Original COA from new manufacturing site	√	√	√	√	
9	Comparative batch analysis data of 2 production batches (or 1 production batch/ 2 pilot batches) from proposed site and last three batches from current site.	√	√	√	√	
10	Accelerated and real time stability data (Zone IVb)	√	√	√	√	
11	Amended label or PI	√	√	√	√	√
12	Process validation report	√	√	√	√	
13	Hold time stability testing of bulk pack	√	√	√	√	

	during storage and transportation.					
14	Letter of commitment to submit stability data, PVR, COA, and sample for testing within 6 months of approval of site change					√
15	A written plan for assessing the quality of the product at new site	√	√		√	
16	CDP between current and proposed site for the product applicable for biowaiver or report for BABE study.	√	√	√		
17	Commitment letter to submit CDP between current and proposed site for the product applicable for biowaiver or report for BA-BE study.					√

Change of manufacturing site

It refers to the change in manufacturing site or certain part or all of the manufacturing process. It doesn't cover changes that are related to the new site. There are five types of manufacturing site changes.

Type I –Manufacturing site change within Malaysia

Type II - Manufacturing site change from foreign country to Malaysia

Type III - Manufacturing site change located outside Malaysia

Type IV - Manufacturing site change for sterile the formulations

Type V - Manufacturing site change in crisis situation

5.6 Variation

Three sorts of variety Major Variation (MaV), Minor variety Notification (MiV-N), Minor Variation Prior Approval (MiV-PA). Variety application ought to be according to Malaysian Variation Guideline. Variety not recorded in rule ought to make suitable reference with the ACTD, SUPAC, EMA order or WHO direction. Endorsed variety ought to be submitted inside 6 months.

5.7 Registration renewal

Product registration validity is of 5 years. Product registration renewal should be carried out 6 months before expiry of the product registration.

CHAPTER-6

CTD - COMMON TECHNICAL DOSSIER IN INDIA

6. CTD - Common Technical Dossier In India

Drug Regulatory Authority: Central Drugs Standard Control Organization (CDSCO)

6.1 Introduction

The Central Drugs Standard Control Organization (CDSCO) is the national administrative body for Indian pharmaceuticals and therapeutic gadgets. Inside the CDSCO, the Drug Controller General of India directs pharmaceutical and medicinal gadgets, under the Ministry of Health and Family Welfare. The DCGI is exhorted by the Drug Technical Advisory Board and the Drug Consultative Committee. It is separated into zonal workplaces which do pre-authorizing and post-permitting investigations, post-advertise observation, and reviews when required.

CTD is an institutionalized basic arrangement shaped by International Conference of Harmonization for specialized documentation of the considerable number of assets methodically to lessen time length for enlistment of restorative items.

CTD includes 5 Modules which incorporates assist granularity area containing all the pertinent documentation identified with enlisting drug item.

Module 1: Regional Administration Information

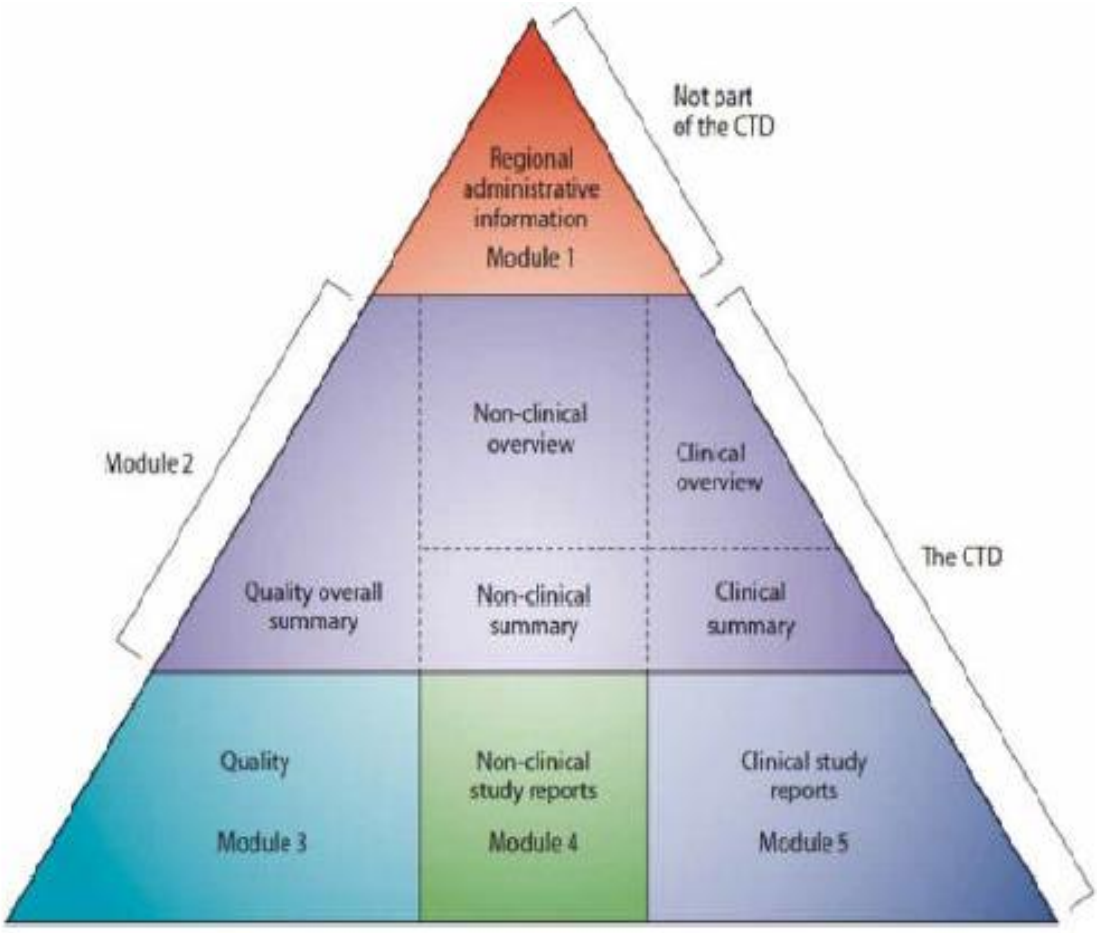
Module 2: Quality Overall Summary

Module 3: Quality

Module 4: Non Clinical Study Reports

Module 5: Clinical Study Reports

Figure 5: Organization of Common Technical Document



6.2 List of Documents in CTD-Dossier Submission

6.2.1 Module 1:- General Information

This module should contain region specific documents for India where applicant is registering the drug. So, they are not considered to be a part of CTD and differ according to the requirements of specific regulatory authorities.

Table 11: Module-1: General Information in India

Module-1: General Information	
1.1	Covering Letter & Comprehensive Table Of Contents (Modules 1 To 5)
1.2	Administrative Information
1.2.1	Brief Introduction About The Applicant Company
1.2.2	Duly Filled And Signed Application In Form 44 And Treasury Challan
1.2.3	Legal And Critical Documents
1.2.4	Coordinates Related To The Application
1.3	General Information On Drug Product
1.3.1	A Brief Description Of The Drug And The Therapeutic Class To Which It Belongs
1.3.2	Non-Proprietary Name Or Generic Name Of Drug
1.3.3	Composition
1.3.4	Dosage Form
1.3.5	Strength Per Dosage Unit
1.3.6	Dispensing Requirements
1.3.7	Route Of Administration
1.3.8	Commercial Presentation
1.3.9	Conditions Of Storage Or Conservation
1.3.10	Full Prescribing Information (Package Insert)
1.3.11	Product Labelling: Proposed Draft Labels And Cartons Have To Be Provided.
1.3.12	Summary Of The Packaging Procedures
1.4	Summary Of Testing Protocol(S) For Quality Control Testing
1.5	Regulatory Status In Other Countries
1.5.1	List Of Countries Where Proposed Drug Is Marketed
1.5.2	List Of Countries Where Proposed Drug Is Approved For Marketing
1.5.3	List Of Countries Where Proposed Drug Is Approved As Ind
1.5.4	List Of Countries Where Proposed Drug Is Withdrawn
1.5.5	Details Of Any Restrictions On Use, In Any Country Where It Is Marketed /Approved
1.6	Domestic Price Of The Drug Followed In The Countries Of Origin In Inr.

1.7	A Brief Profile Of The Manufacturer's Research Activity
1.8	A Brief Profile Of The Manufacturer's Business Activity In Domestic As Well As Global Market
1.9	Information Regarding Involvement Of Experts, If Any
1.10	Samples Of Drug Product
1.11	Promotional Materials

6.2.2 Module 2:- Quality overall summary

It has summary in tabular format, related to the quality, non-clinical and clinical documents to be involved in Module 3-5 respectively. It must not contain data that aren't included in Module 3-5.

6.2.3 Module 3:- Quality

Detailed information of Quality Documents of drug development are required to be placed in specific format as mentioned below.

Table 12: Module 3: List of Quality Documents

3.1	**TABLE OF CONTENT OF MODULE 3**	
3.2	**BODY OF DATA**	
3.2.S	**DRUG SUBSTANCE**	
3.2.S.1	General Information	
	3.2.S.1.1	Nomenclature
	3.2.S.1.2	Structure
	3.2.S.1.3	General Properties
3.2.S.2	Manufacture	
	3.2.S.2.1	Manufacturer(s)
	3.2.S.2.2	Description of Manufacturing Process and Process Controls
	3.2.S.2.3	Control of Materials
	3.2.S.2.4	Controls of Critical Steps and Intermediates
	3.2.S.2.5	Process Validation and/or Evaluation
	3.2.S.2.6	Manufacturing Process Development
3.2.S.3	Characterization	

	3.2.S.3.1	Elucidation of Structure and other Characteristics
	3.2.S.3.2	Impurities
3.2.S.4	Control of Drug Substance	
	3.2.S.4.1	Specification
	3.2.S.4.2	Analytical Procedures
	3.2.S.4.3	Validation of Analytical Procedures
	3.2.S.4.4	Batch Analyses
	3.2.S.4.5	Justification of Specification
3.2.S.5	Reference Standards or Materials	
3.2.S.6	Container Closure System	
3.2.S.7	Stability	
	3.2.S.7.1	Stability Summary and Conclusions
	3.2.S.7.2	Post-approval Stability Protocol and Stability Commitment
	3.2.S.7.3	Stability Data
3.2.P	**DRUG PRODUCT**	
3.2.P.1	Description and Composition of the Drug Product	
3.2.P.2	Pharmaceutical Development	
	3.2.P.2.1	Components of the Drug Product
	3.2.P.2.1.1	Drug Substance
	3.2.P.2.1.2	Excipients
3.2.P.2.2	Drug Product	
	3.2.P.2.2.1	Formulation Development
	3.2.P.2.2.2	Overages
	3.2.P.2.2.3	Physicochemical and Biological Properties
3.2.P.2.3	Manufacturing Process Development	
3.2.P.2.4	Container Closure System	
3.2.P.2.5	Microbiological Attributes	
3.2.P.2.6	Compatibility	
3.2.P.3	Manufacture	
	3.2.P.3.1	Manufacturer(s)
	3.2.P.3.2	Batch Formula
	3.2.P.3.3	Description of Manufacturing Process and Process Controls

	3.2.P.3.4	Controls of Critical Steps and Intermediates
	3.2.P.3.5	Process Validation and/or Evaluation
3.2.P.4	Control of Excipients	
	3.2.P.4.1	Specifications
	3.2.P.4.2	Analytical Procedures
	3.2.P.4.3	Validation of Analytical Procedures
	3.2.P.4.4	Justification of Specifications
	3.2.P.4.5	Excipients of Human or Animal Origin
	3.2.P.4.6	Novel Excipients
3.2.P.5	Control of Drug Product	
	3.2.P.5.1	Specification(s)
	3.2.P.5.2	Analytical Procedures
	3.2.P.5.3	Validation of Analytical Procedures
	3.2.P.5.4	Batch Analyses
	3.2.P.5.5	Characterization of Impurities
	3.2.P.5.6	Justification of Specification(s)
3.2.P.6	Reference Standards or Materials	
3.2.P.7	Container Closure System	
3.2.P.8	Stability	
	3.2.P.8.1	Stability Summary and Conclusion
	3.2.P.8.2	Post-approval Stability Protocol and Stability Commitment
	3.2.P.8.3	Stability Data
3.2.A	**APPENDICES**	
	3.2.A.1	Facilities and Equipment
	3.2.A.2	Adventitious Agents Safety Evaluation
	3.2.A.3	Excipients
3.2.R	**REGIONAL INFORMATION**	

6.2.4 Module-4:- Non-Clinical Reports

Non-Clinical Reports including Pharmacology, Pharmacodynamics, Pharmacokinetics, Toxicology, Carcinogenicity and Geno-lethality are given in this area. Generics Drugs do exclude Module 4 information, because of settled non-clinical reports accessible by the

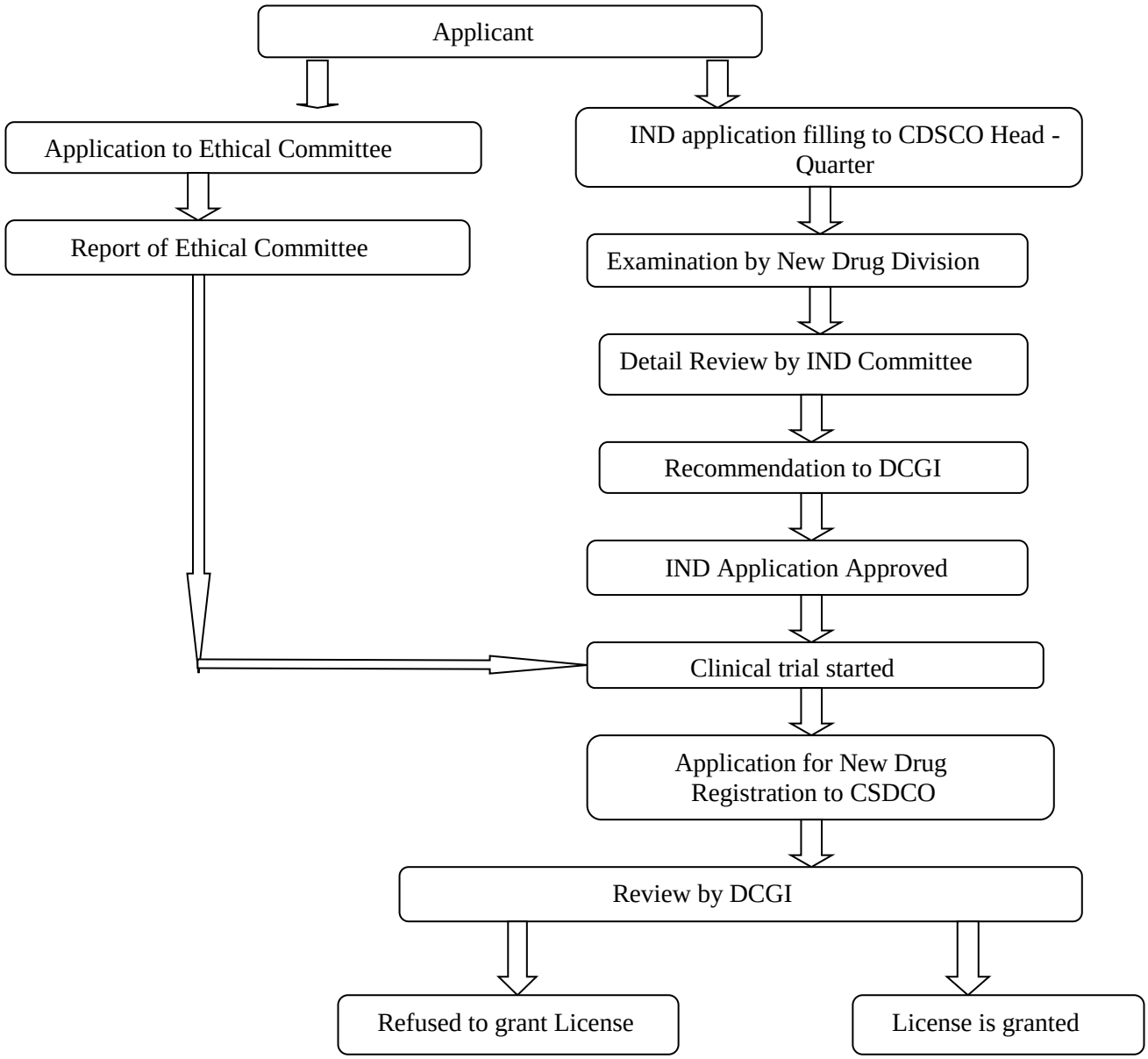
reference items.

6.2.5 Module-5:- Clinical Study Reports

Clinical Documents mainly involve the Biopharmaceutical studies having BA study reports showing clinical equivalence of test drug with that of reference listed innovator drug product. It also involves in-vitro dissolution tests for comparison of test and reference product.

6.3 Chart of Drug Approval Process in India

Figure 6: **Chart of Drug Approval Process in India**



6.4 Guidance document on grant of license in form 11for the purpose of examination testing and analysis

6.4.1 Procedure for obtaining Form 11

- The following conditions to be considered by the applicant:
- No drug shall be imported for any other commercial purpose.
- The license shall use the substances imported for the purpose of test analysis.
- Drug Inspector authorized by the licensing authority will inspect the premises with or without prior notice.
- The license shall keep a record and will report to the licensing authority.
- Technical literature /package inserts of drugs.

6.4.2 Documents required for filling the Form 11 application

1. Covering letter

A covering letter is a significant part of the application and is attached alongwith an application which clearly specifies the submission purpose of an application.

A cover letter must contain the following points:

- Name and Address of the firm.
- Purpose of submission.
- List of documents attached with the application.
- Duly signed and stamped by authorized signatory.
- Application Reference number.

2. Form 12

An application for a licence for examination, test or analysis shall be made in Form 12 and shall be made or countersigned by the head of the institution, or by a proprietor or director of the company or firm by which the examination, test or analysis will be conducted.

3. T.R 6 challan

The Amount should be paid in T.R 6 Challan (duly signed and stamped by the Bank Officer) alongwith the application. A challan of Rs 100/- for first product and Rs 50/- for of each additional product must be submitted along with the Application.

4. Form 29

Form 29 is a license for manufacturing drugs for the purpose of Examination Testing and Analysis. Every application in Form 29 is to be accompanied by a fee of 250/-..

Conditions of license:

(a) The licensee might utilize the medications fabricated under the permit solely for motivation behind examination, test or investigation, and should bear on the produce and examination, test or investigation at the place determined in the permit;

(b) the licensee should permit any 4 Inspector selected under the Act to enter, with or without notice, the premises where the medications are made and to fulfill himself that lone examination, test or investigation work is being led;

(c) the licensee should keep a record of the amount of medications fabricated for examination, test or investigation and of any individual or people to whom the medications have been provided.

5. Utilization/Justification

Utilization/justification submitted by includes the following points:

- Utilization/justification is required to be duly signed by the Authorized Signatory.
- Details of each testing parameters mentioning the quantity are needed for each tests.
- If the firm wants to conduct bioequivalence studies then detailed bioequivalence studies are to be submitted.

6. Bioequivalence NOC

Applications of Test Licence for importing drug for bioequivalence studies under form 11 licence are to be submitted alongwith bioequivalence protocol.

7. Notarized agreement

When firm applies for grant of licence in form 11 & utilize testing facility of another firm then firm is required to submit copy of notarized agreement between 2 firms duly authenticated by applicant.

8. DSIR approval

Applicant is required to submit a copy of valid DSIR approval certificate.

9. Replies in response to queries

When any deficiency is found in application & query letter is already issued then in response to the query the firm is required to submit the reply in a proper manner.

10. Authority letter at the time of collection of approvals/query letters

A valid authority letter should be presented at the time of collection of approval/query letters by the person who collects the letters. Authority Letter should be duly signed and stamped by the authorized signatory.

11. Form 25/form 28

Form 25 is a Licence to manufacture for sale or for distribution of drugs other than those specified in Schedules C and C(1) and X.

Form 28 is a Licence to manufacture for sale or for distribution of drugs specified in Schedules C and C (1) excluding those specified in Schedule X.

6.4.3 Form 11 licence renewals

No test licence is renewed; the firm has to submit fresh application in Form 12 with T.R 6 challan and documents as per checklist.

6.4.4 Rejection

1. No test licence to be issued for banned drugs
2. No test licence to be issued for starting material
3. No test licence to be issued for herbal/agricultural products
4. No test licence to be issued for recipients.

6.5 Bioequivalence Study Requirements In India

1. Application in Form-44 duly signed, by the competent authority with name and designation.
2. 25,000 rupees /- as per Drugs & Cosmetic Rules.
3. Undertaking by the Principal Investigator (PI) as per appendix VII of schedule "Y" of Drugs and Cosmetic Rules.
4. A copy of the approval granted to the BE study centre by CDSCO.
5. Sponsor's Authorization letter duly signed by the competent authority on their letterhead.
6. The study protocols and synopsis.
7. Pre-clinical single dose data and repeated dose toxicity data.
8. Clinical study data.

9. Regulatory status of the drug.

10. Names of the countries where the drug is currently being marketed .

11. Package literature on the international product.

12. Complete Certificate of Analysis of same batches to be used in the BE study.

13. Case of multiple dose BE study.

14. In the case of Injectable preparation the sub-acute toxicity should be submitted on the product of the sponsor, generated in two species for adequate duration.

15. Depending on the nature of the drug like cytotoxic agent, hormonal preparations etc. Proper justification for conducting studies on healthy volunteers/patients or male/ female should be submitted.

6.5 Checklist For Grant Of Permission To Import Or Manufacture New Drugs Going To Be Introduced For The First Time In The Country For Sale Or To Undertake Clinical Trials.

Table 13: Checklist For Grant Of Permission To Import Or Manufacture New Drugs

1	Application
2	Name of the applicant
3	Name of the new drug
4	Application in form 44 complete with signed and stamped
5	Treasury challan of INR 50,000 for phase-I
6	Copy of manufacturing license in form 25/28
7	Source of bulk drug
8	Chemical & Pharmaceutical information
9	Animal Pharmacology
10	Animal toxicity data
11	Human / Clinical Pharmacology
12	Therapeutic exploratory trials
13	Therapeutic confirmatory trails
14	Regulatory status in other countries
15	Proposed Draft specimen of the carton & label.

CHAPTER-7

COMPARATIVE SUMMARY

7. Comparative Summary

Table 14: Comparative Study of Dossier format

Country	Drug Regulatory Authority	Dossier Format
Malaysia	National Pharmaceutical Regulatory Agency (NPRA)	ACTD
Hongkong	Department of health (DH)	Country specific
India	Central Drug Standard Control Organization (CDSCO)	CTD

Table 15: Comparative Study of Submission Requirements

Documents	CTD (India)	ACTD (Malaysia)	Country specific (HongKong)
Administrative Documents and Product Information	Module 1	Part I	General Index
CTD 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 16: Differences between MALAYSIA, HONGKONG and INDIA Requirements

Parameters	Malaysia	Hongkong	India
Certificate of Pharmaceutical product	Required	Required	Required
Free Sale Certificate	Required	Required	Required
GMP Inspection	PIC/S GMP Inspection	PIC/S GMP Inspection	GMP Certificate Required

Mfg License	×	(√)	Required in Form 25 /26 / 28
Letter of Authorization	Required from product owner	Required from the overseas manufacturer	Required
FP and MOA	Required with chromatograms	Required	Required
Working Standard COA	Required	Required	Required
TSE-Certificate of Suitability for ingredient origin from animal	Required	Required	Required
Process Validation Report/Protocol	Required	Required	Required
QOS	(√)	×	(√)
DMF	Not Required	Not Required	Required
Site Master File	Not Required	Required	Required
CEP	N/A	N/A	N/A
Non clinical Report Summary	Not Applicable for Generics		
Clinical Overview	Not Applicable for Generics		

Table 17: Comparative Study of Renewal of Registration

Country	Validity
Malaysia	Registration certificate is valid for 5 years
Hongkong	Registration certificate is valid for 5 years
India	Registration certificate is valid for 5 years

Table 18: Comparative Study of Fees

Country	Applicable fees
Malaysia	**Registration Fees** New Drug Product – RM 4000.00 Generics (single API) – RM 2200.00

	(Two or More API) - RM 3000.00
Hongkong	**Registration fees:** $ 1370
India	**Registration fees:** 50,000 INR

Table 19: Comparative Study of Stability Requirements

Region	**Climatic zone**	**Long Term Conditions**	**Accelerated Conditions**
MALAYSIA	IVb	30°C ± 2°C 75% RH ± 5% RH	40°C ± 2°C 75% RH ± 5% RH
HONGKONG	IVa	30°C ± 2°C 65% RH ± 5% RH	40°C ± 2°C 75% RH ± 5% RH
INDIA	IVb	30°C ± 2°C 75% RH ± 5% RH	40°C ± 2°C 75% RH ± 5% RH

CHAPTER-8

CONCLUSION

8. CONCLUSION

- Regulatory situation in this day and age has isolated the entire pharmaceutical markets over the world in two fundamental segments Developed very much controlled market and also Developing/or developing business sector including the Rest of the world (ROW). Emerging nations are the ones which are demonstrating a speedier advancement in advancing different pharmaceutical fares and consequently they depends to a great extent on non specific restorative items instead of advancing new pioneer drugs. The explanation behind this may depend on the certainties that creating nations contains bigger populace and less logical development comparatively& therefore they require less expensive pharmaceuticals in bigger scale, and this is a motivation behind why creating nations rely on upon outside non specific speculators.
- Lawful necessities of the documentation for enrollment utilization of non specific medications are fit. Harmonization permits dossier accommodation ACTD organize in Malaysia, CTD design in India and nation particular prerequisites in Hongkong. It can be concluded that MALAYSIA, HONGKONG and INDIA has not wide diversity in Dossier format, Registration required documents, stability, renewal process, fees etc.
- FDA requires all DMF submissions to be in electronic common technical document (eCTD) format beginning May 5, 2018**.**

CHAPTER-9

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