ACCSQ-PPWG

ASEAN Consultative Committee for Standards and Quality - Pharmaceutical Product Working Group

by

Patharavan Chimvong, M.Sc.

Bureau of Drug Control

Thai Food and Drug Administration (Thai FDA)

August 3, 2017

Outline

- Introduction
- ASEAN Harmonization on Pharmaceutical Registration
  - Objective
  - Scope
  - Strategies
  - Impact of Harmonization
- New Drug Registration (ASEAN Harmonization)
- Current status

What is ASEAN?

ASEAN = Association of Southeast Asian Nations

Members (10 countries)

ASEAN HARMONIZATION ON PHARMACEUTICAL REGISTRATION

1992 **ACCSQ**

(ASEAN Consultative Committee on Standards and Quality)

1999 **ACCSQ - PPWG**

ASEAN HARMONIZATION ON PHARMACEUTICAL REGISTRATION

Objective of ACCSQ-PPWG

- **To develop harmonization schemes of pharmaceutical regulations of the ASEAN member countries to complement and facilitate the objective of ASEAN Free Trade Area (AFTA)**
- **To eliminate of technical barriers to trade posed by these regulations, without compromising on drug quality, efficacy and safety**

Scope of PPWG

- Discussion of existing technical guidelines and regulatory requirements
- Study of harmonized procedures and regulatory systems currently implemented in other regions relating to technical guidelines and regulatory requirements
- Harmonization of technical guidelines and regulatory requirements applicable to the ASEAN pharmaceutical industry
- Development of Common Technical Documents with a view to arriving at Mutual Recognition Arrangement (MRAs)

The scope of pharmaceutical products covered by the PPWG includes New Chemical Entities (NCEs), biotechnological products, major and minor variation products, and generics.

Strategies

- Comparative study on existing product registration requirements and regulations for pharmaceuticals
- Identification of key areas on requirements for harmonization
- Development of common technical requirements (CTR) for pharmaceutical product registration
- Development of common technical dossier (CTD) towards MRA
- Implementation of harmonized ASEAN Pharmaceutical Product Dossier

Impact of Harmonization

- **Public Health - Improve Quality, Safety & Efficacy**
- **Patients & Consumers - Improve access & availability**
- **Industry - Improve compliance to GMP, GSP, GCP, GLP**
- **Regulatory - Confidence building & Mutual understanding**

ASEAN HARMONIZATION ON PHARMACEUTICAL REGISTRATION

Present Outcomes

- ASEAN Common Technical Requirement (ACTR)
- ASEAN Common Technical Dossier (ACTD)

- 5 ASEAN Guidelines :
  - BA/BE Studies
  - Process Validation
  - Stability Study
  - Analytical Method Validation
  - Variation
- Adopted ICH Guideline – Only Safety and Efficacy
  Delete Quality

ASEAN HARMONIZATION ON PHARMACEUTICAL REGISTRATION

Glossary of ACTR

A set of written materials intended to guide applicants to prepare application dossiers in a way that is consistent with the expectations of all ASEAN drug regulatory authorities

Glossary of ACTD

The part of marketing authorization application dossier that is common to all ASEAN member countries

4 Parts : Administrative, Quality, Safety, Efficacy

ASEAN HARMONIZATION ON PHARMACEUTICAL REGISTRATION

Thai FDA Notification 28 Dec 2008: Implementation of ASEAN Harmonized Product on Pharmaceutical Registration

Date started: 1 Jan 2009

- Manual/Guidance on New Drug Registration (ASEAN Harmonization)
- Requirements and Documents to be submitted for New Drug Registration (ASEAN Harmonization)
- Manual/Guidance on New Generic Drug Registration (ASEAN Harmonization)
- Manual/Guidance on Generic Drug Registration (ASEAN Harmonization)
- Manual/Guidance on Biological Product Registration (ASEAN Harmonization)

4 Guidelines

- Guidelines for the conduct of Bioavailability and Bioequivalence Study
- Process Validation Guidelines
- Analytical Validation Guidelines
- Stability Guidelines

New Drug Registration (ASEAN Harmonization)

Documents to be submitted (ACTD) 4 Parts

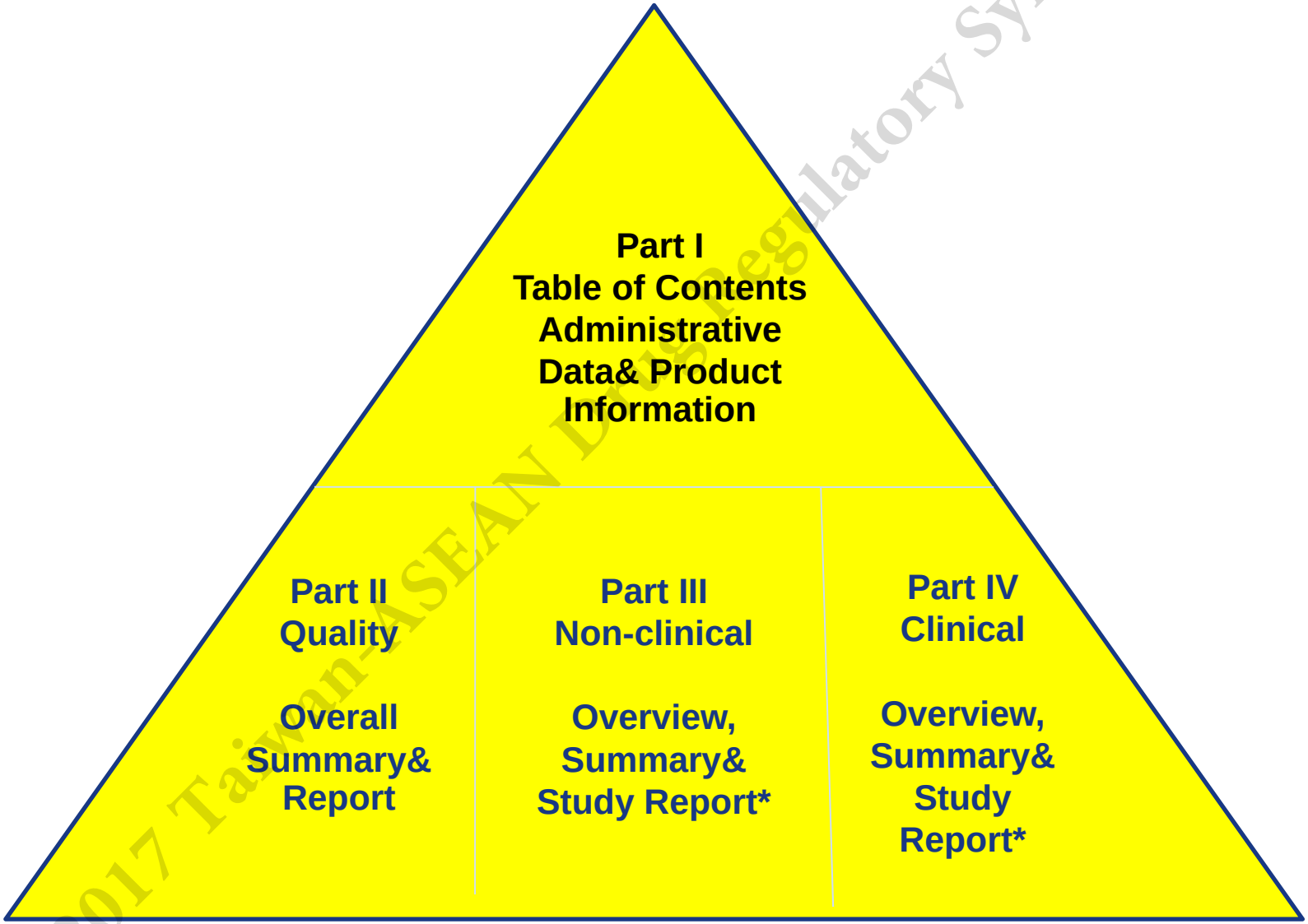
Part 1: Administrative Data and Product Information

Part 2: Quality Document

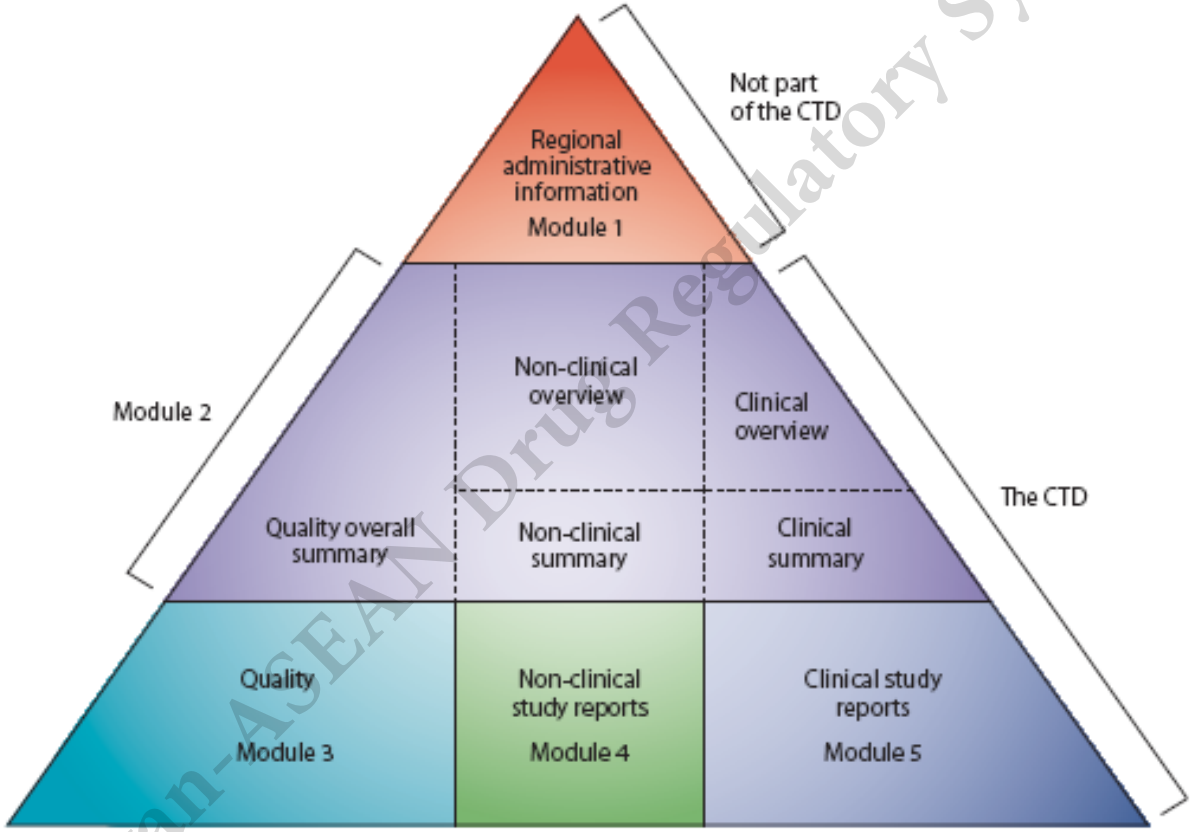
Part 3: Nonclinical Document

Part 4: Clinical Document

Organization (Diagram) of Application Dossier (ACTD)



CTD Triangle



The CTD triangle. The Common Technical Document is organized into five modules. Module 1is region specific and modules 2, 3, 4 and 5 are intended to be common for all regions.

http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/CTD/CTD_triangle.pdf

Part 1: Administrative Data and Product Information

3 Sections:

Section A: Introduction

Section B: Overall Table of Contents

Section C: Documents required for registration

- **Application form(Yor1)**
- **Certifications: License to manufacture/import, GMP Certificate, Certificate of Pharmaceutical Product(CPP)/Certificate of Free Sales(CFS)**
- **Labeling**
- **Product Information:**
  - **Package Insert (PI)**
  - **Summary of Product Characteristics (SPC): required for NCE**
  - **Patient Information Leaflet (PIL)**
- **Por Yor 8/Nor Yor 8**
- **Photograph of drug product**
- **Comparative data between new drug and existing drugs**

Part 1: Administrative Data and Product Information
Labeling

16 sections required for Unit Carton, Inner Label:

1. Product Name 2. Dosage Form* 3. Name of Active Ingredient(s)
4. Strength of Active Ingredient(s) 5. Batch Number 6. Manufacturing Date * 7. Expiration Date 8. Route of Administration 9. Storage Condition*
10. Country's Registration Number*
11. Name and Address of Marketing Authorization Holder*
12. Name and Address of Manufacturer* 13. Special Labeling (if applicable)*
14. Recommended Daily Allowance(For Vitamins and Minerals)*
15. Warning (if applicable)* 16. Pack sizes (unit/volume)

*exempted for small ampoule and vial

7 sections required for Blister/Strips:

1. Product Name 2. Name of Active Ingredient(s)
3. Strength of Active Ingredient(s) 4. Batch Number
5. Expiration Date
6. Name/Logo of Manufacturer/Product Owner/ Marketing Authorization Holder (country specific)
7. Country's Registration Number (country specific)

Part 1: Administrative Data and Product Information
Summary of Product Characteristics (SPC)

1. **Name of Medicinal Product:** Product Name, Strength, Pharmaceutical Dosage Form
2. **Quality and Quantitative Composition:** Active substance and quantity per dosage unit
3. **Pharmaceutical Form:** Description of the product
4. **Clinical Particulars:** Therapeutic Indication. Posology and method of administration, Contraindication, Special warning and precaution for use, Interactions, Pregnancy and lactation, Effects on ability to drive and use machine, Undesirable effects, Overdose
5. **Pharmacological Properties:** Pharmacodyamic/Pharmacokinetic properties, Preclinical safety data
6. **Pharmaceutical Particulars:** List of excipients, Incompatibilities,Shelf life, Special precautions for storage, containers
7. **Marketing Authorization Holder**
8. **Marketing Authorization Numbers**
9. **Date of first authrization/renewal of the authorization**
10. **Date of revision of the text**

Part 1: Administrative Data and Product Information
Package Insert (PI)

1. Product Name
2. Name and Strength of Active Ingredient(s)
3. Product Description
4. Pharmacodynamics/Pharmacokinetics
5. Indication
6. Recommended Dose
7. Mode of Administration
8. Contraindication
9. Warnings and Precautions
10. Interactions
11. Pregnancy and Lactation
12. Undesirable Effects
13. Overdose and treatment
14. Storage Condition
15. Dosage Forms And packaging available
16. Name and Address of Manufacturer/Marketing Authorization Holder
17. Date of Revision of Package Insert

Part 1: Administrative Data and Product Information
Patient Information Leaflet (PIL)

1. Name of Product 2. Description of Product 3. What is in the medicine?
4. Strength of the medicine 5. What is this medicine used for?
6. How much and how often should you use this medicine?
7. When should you not take this medicine? 8. Undesirable effects
9. What other medicine or food should be avoided whilst taking this medicine?
10. What should you do if you miss a dose?
11. How should you keep this medicine?
12. Signs & Symptoms of over dosage
13. What to do when you have taken more than the recommended dosage?
14. Name/Logo of manufacturer/importer/Marketing Authorization Holder
15. Care that should be taken when taking this medicine?
16. When should you consult your doctor?
17. Date of Revision of PIL

Part 2: Quality Document

ACTD 4 Sections:

- Section A: Table of Contents
- Section B: Quality Overall Summary: Drug Substance, Drug Product
- Section C: Body of Data: Drug Substance, Drug Product
- Section D: Key Literature References

ACTR:

S Drug Substance

- S1 General Information
- S2 Manufacture
- S3 Characterization
- S4 Control of Drug Substance
- S5 Reference Standards
- S6 Container Closure System
- S7 Stability

P Drug Product

- P1 Description/Composition
- P2 Pharmaceutical development
- P3 Manufacture
- P4 Control of excipients
- P5 Control of Finished Product
- P6 Reference Standards
- P7 Container Closure System
- P8 Stability
- P9 Interchangeability

Part 2: Quality Document

No.	Parameters	Components	Requirements						
			NCE	NI	NCO	ND	NR	NDOS	NS
	Section A Table of content		/	/	/	/	/	/	/
	Section B Quality Overall Summary								
S	Drug Substance								
S1	General Information								
	1.1 Nomenclature								
	1.2 Structure		/ /		/ /	/	/	/	/

Part 3 : Nonclinical Document

ACTD 5 Sections:

- **Section A: Table of Contents**
- **Section B: Nonclinical Overview**
- **Section C: Nonclinical Summary(Written and Tabulated)**
- **Section D: Nonclinical Study Report (as requested)**
- **Section E: List of Key Literature References**

Part 3 : Nonclinical Document
ACTR

1. Pharmacology

-Primary Pharmacodynamics

-Secondary Pharmacodynamics

-Safety Pharmacology

-Pharmacodynamics Drug Interactions

2. Pharmacokinetics

-Absorption

-Distribution

-Metabolism

-Excretion

-Pharmacokinetics Drug Interactions

-Other Pharmacokinetics Studies

3. Toxicology

- Single dose toxicity
- Repeat dose toxicity
- Genotoxicity
- Carcinogenicity
- Reproductive and developmental toxicity
- Local tolerance
- Other toxicity studies, if available

Part 3 : Nonclinical Document

Parameters	Requirements						
	NCE	NI	NCO	ND	NR	NDOS	NS
Section A Table of content	/	/	/	/	/	/	/
Section C Nonclinical Summary	/						
1.Nonclinical Written Summaries							
1.1 Pharmacology							
1.1.1 Primary Pharmacodynamics	/						
1.1.2 Secondary pharmacodynamics	/						
1.1.3 Safety Pharmacology	/						
			*		*		

Part 4: Clinical Document

ACTD 6 Sections:

- **Section A: Table of Contents**
- **Section B: Clinical Overview**
- **Section C: Clinical Summary**
- **Section D:Tabular Listing of All Clinical Studies**
- **Section E: Clinical Study Reports (If applicable)**
- **Section F: List of Key Literature References**

Part 4: Clinical Document
Section B: Clinical Overview

- **Provide information on**
  - **critical analysis of the clinical data**
  - **strengths and limitations of the development program and study results**
  - **benefits and risks analysis**
- **Concise tables and graphs**
- **Contents:**
  - **Product Development Rational**
  - **Overview of Biopharmaceutics**
  - **Overview of Clinical Pharmacology**
  - **Overview of Efficacy**
  - **Overview of Safety**
  - **Benefits and Risks Conclusions**

Part 4: Clinical Document
Section C: Clinical Summary

- **Provide a detailed, factual summarisation of all of the clinical information**
- **Include information provided in clinical study reports, information obtained from any metaanalyses or other cross-study analysis and post-marketing data for products that have been marketed in other regions**

Contents:

- Summary of biopharmaceutic studies and associated analytical methods

- Summary of clinical pharmacology studies

- Summary of clinical efficacy

- Summary of clinical safety

- Synopses of individual studies

Part 4: Clinical Document

Parameters	Requirements						
	NCE	NI	NCO	ND	NR	NDOS	NS
Section A Table of content	/	/	/	/	/	/	/
Section C Clinical Summary	/	/	/	/	/	/	/
Section E Clinical Study Report							
5. Report of Efficacy and Safety Studies							
5.1 Controlled Clinical Studies							
5.2 Uncontrolled Clinical Studies	/ /	/ /	/	/ /	/ /	/	/ /

Latest Update on 24th ACCSQ-PPWG meeting

- **Held in Bangkok, Thailand from 24th to 28th JULY 2017**
- **~400 participants from ASEAN regulatory agencies and pharmaceutical industry**
- **Paperless meeting - all participants can download e-document**

Latest Update on 24th ACCSQ-PPWG meeting

Issues

- The JSC GMP- MRA
- ASEAN BE Task Force
- Joint Assessment Coordinating Group (JACG)
- Technical Working Group (TWG)
  - Quality
  - Biologics
- Implementation Working Group meeting (IWG)

Thank you for your attention