



ASEAN Harmonization

by

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Co-Chair of ACCSQ/PPWG

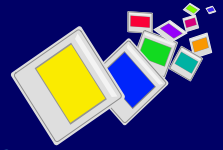
Drug Control Division, FDA, THAILAND

The 2006 Symposium of APEC Network on Pharmaceutical Regulatory Science

Royal Park Hotel, Tokyo, Japan

12-13 October 2006

Outline:



- **International & Asian Pharmaceutical Harmonization**
- **ASEAN**
- **ACCSQ**
- **High Level Task Force (HLTF)**
- **The PPWG**
- PPWG : Agreement / Outcomes
- PPWG : ASEAN Harmonized Products
- ***My Perspective on Global Drug Development & ASEAN***

International & Asian : Pharmaceutical Harmonization Environment

Scope - Technical, Guideline, Procedure

Coverage - NCEs, Generic, Herbal med.,...

Topic - GMP Inspection, Drug Evaluation, etc...

WHO
(>190 countries)

PANDRH
(Pan American)

SADC
(South Africa)

GCC
(Middle East)

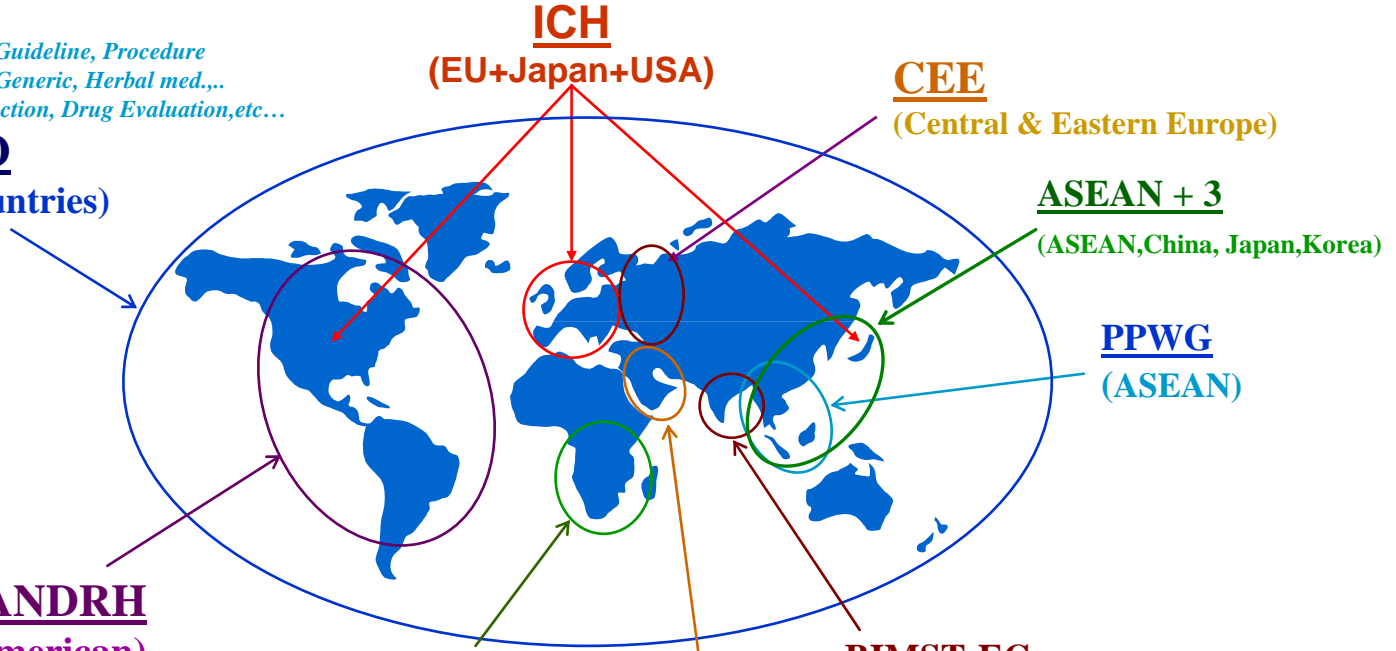
BIMST-EC
(South Asia)

ICH
(EU+Japan+USA)

CEE
(Central & Eastern Europe)

ASEAN + 3
(ASEAN, China, Japan, Korea)

PPWG
(ASEAN)





ASEAN



Symbol of ASEAN



ASEAN

= Association of Southeast Asian Nations

Member



- Brunei Darussalam
- Cambodia
- Indonesia
- Lao PDR
- Malaysia
- Myanmar
- Philippines
- Singapore
- Thailand
- Vietnam

Total population ~ 520 million



ASEAN-Major Cooperation





Economic Cooperation in ASEAN

ASEAN Summit



AEM

← HLTF



SEOM



ACCSQ



WGs



PWGs

- WG1** on Mutual Recognition Arrangements (MRAs) & Standards –
WG2 on on Accreditation and Conformity Assessment –
Scientific/Industrial Metrology Sub-WG –

- ACC (ASEAN Committee on Cosmetic)
- PPWG (Pharmaceutical PWG)
- EE PWG (Electrical and Electronic PWG)
- Pf PWG (Prepared Foodstuff PWG)
- TMHD PPWG (Traditional Medicine & Health Supplement PWG)
- Medical Devices&Equipment PWG
- Automotive PWG
- Rubber-based PWG
- Wood-based PWG



Ultimate Goal of the ASEAN

ASEAN Summit

ASEAN Leader



ASEAN Economic Community (AEC)
“by the year 2020..... ASEAN will be
Single Market and Single Production Base

- Free flow of Goods
- Free flow of Services
- Free flow of Investment
- Free flow of Capitals
- Free flow of Skilled Labour

AEC → year 2015



ACCSQ



ACCSQ



ASEAN Consultative Committee for Standards and Quality



Mandate from ACCSQ

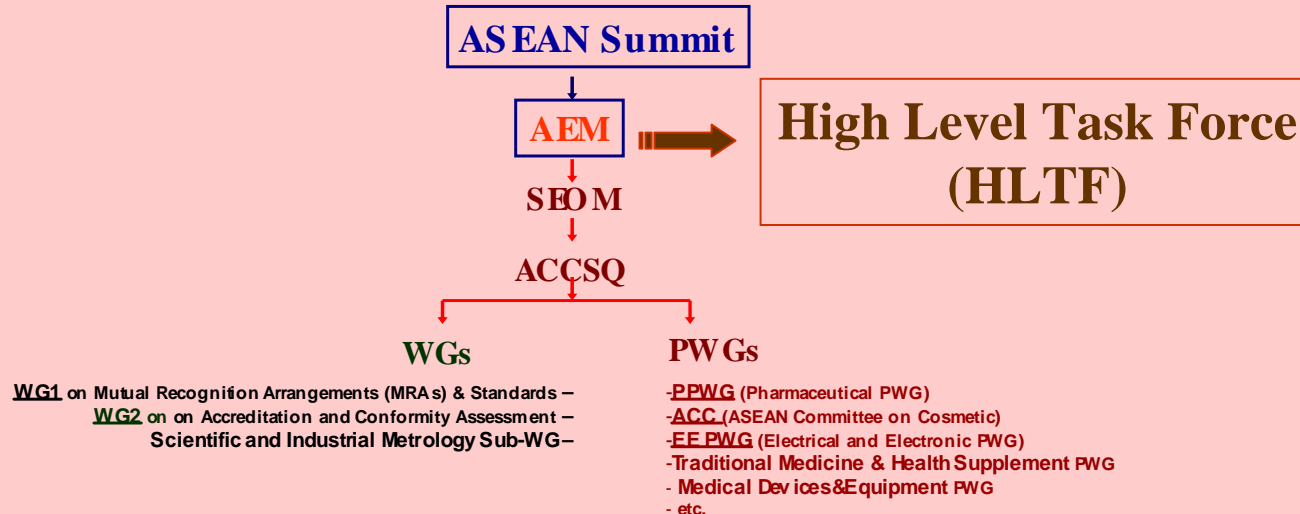
- Harmonizing “Standard & Requirement” posed by Regulation
- Working to Facilitate the “ASEAN Free Trade Area-AFTA”
- Establishing “Mutual Recognition Agreement-MRA”
- Comply to “HLTF-Recommendation”



High Level Task Force - HLTF



Establishment





Objective

*To accelerate ASEAN Harmonization
towards ASEAN Economic Community*

for 11 Priority Products

now → 12 priority products



Priority products vs. Coordinators

- **Wood-based product & Automotives** (*Indonesia*)
- **Healthcare & e-ASEAN sectors** (*Singapore*)
- **Rubber-based products & Textiles and apparels** (*Malaysia*)
- **Agro-based products & Fisheries** (*ASEAN Secretariat*)
- **Electronics** (*Philippines*)
- **Air travel & Tourism** (*Thailand*)
- **Logistic** (*Vietnam*)



HLTF – Major Recommendations on Healthcare (1)

Harmonization of Labeling Standards & Requirement
for Drug in ASEAN (31 Dec.06)

Develop Common Submission Dossiers Template
for Product Approval in ASEAN (31 Dec.05)



HLTF – Major Recommendations on Healthcare (2)

**Explore the Feasibility of Implementing
a Flexible Twinning system**

to cooperate in enhancing capacity and resource development (on going)

Formalization of a Post-marketing Alert System

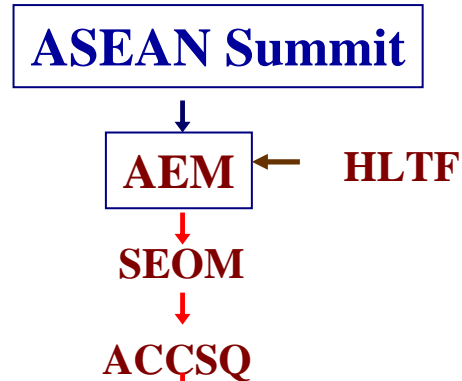
for Defective or Unsafe Medicine and Drugs (31 Dec.05)



The PPWG



Establishment



WG1 on Mutual Recognition Arrangements (MRAs) & Standards –
WG2 on on Accreditation and Conformity Assessment –
 Scientific and Industrial Metrology Sub-WG-

PWGs

-PPWG (Pharmaceutical PWG)

- **ACC** (ASEAN Committee on Cosmetic)
- **EE PWG** (Electrical and Electronic PWG)
- **Pf PWG** (Prepared Foodstuff PWG)
- **TMHD PPWG** (Traditional Medicine & Health Supplement PWG)
- **Medical Devices&Equipment PWG**



PPWG



ACCSQ/PPWG

**ASEAN Consultative Committee
for Standards and Quality /
Pharmaceutical Product Working Group**



1. Beginning and Objective of ASEAN Harmonization

1.1 Establishment :

- 1992 AEM ---> ACCSQ
 - > Working Groups (WGs)
 - > Product Working Groups (PWGs)
- 1998 ACCSQ---> initiated the PPWG
- 1999 ACCSQ--->endorsed the PPWG
 - PPWG --->finalized the 'TOR'
 - >started to function !!!
- 2003 & 2005 ACCSQ--->endorsed “2nd & 3rd Term of the PPWG”
with same Chair & Co-Chair country



1.2 TOR (Term of Reference) :

Article 1: Establishment

Article 2: Objective

Article 3: Scope

Article 4: Structure

Article 5: The Meeting and Correspondance

Article 6: Term



Article 2: Objective

“To develop harmonization scheme of Pharmaceuticals regulations of the ASEAN member countries

to complement and facilitate the objective of AFTA, particularly, the elimination of Technical Barriers to Trade posed by the regulations,

without compromising on drug quality, efficacy, and safety”



1.3 Principle /Scope / Output of the PPWG

Principle --> to promote “Registration”, “Trade”, & “Co-operation”

--> to eliminate “TBT”

Scope --> to harmonize “ASEAN Pharmaceutical Registration”

Output -->ASEAN Harmonized Product
(ACTR, ACTD, Glossary of Terms, GLs)



1.4 Aim & Target of the ASEAN Harmonization

For....**Generic, Modified, and NCEs & Bio.**product

‘ASEAN Harmonized Product’ **by 2002 !**



‘**Trial Period**’



Full Implementation **by Dec. 2008 !**



PPWG Agreement / Outcomes



Agreement :- topics

1. Harmonized Key Areas → *Agreed!*
2. Format for ACTR & ACTD → *Agreed!*
3. Content of ACTR / ACTD / Glossary of Term → *Agreed!*
4. Guidelines to ACTR ⇒ *Agreed!*
5. Implementation -Trial period
6. Full Implementation



Agreement:-



Guideline to ACTR-*Quality*

- adopted *the WHO's GLs*
- adopted *the existing International Pharmacopoeias*
- adopted *ICH-Quality Guideline (12 GLs)*
- drafted *4 ASEAN Quality GLs*



Agreement:

ASEAN Quality gls

- (1) **Analytical Validation guideline**
- (2) **BA/BE Studies guideline**
- (3) **Process Validation guideline**
- (4) **Stability Study guideline**



Agreement:-



Guideline to ACTR-*Safety*

→ adopted ICH-Safety guideline (15 GLs)



Agreement:-



Guideline to ACTR-*Efficacy*

- adopted 11 GLs (E1, E2A, E2C, E3, E4, E6-E11)
- accepted as Ref.gl. 4 gls (E2C(A), E2D, E2E, E12A)
- not adopted 2 gls (E2B(M), E5)



Agreement :- topics

1. Harmonized Key Areas → *Agreed!*
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4. Guidelines to ACTR → *Agreed!*
5. Implementation - Trial period ⇒ *Sep. 2003 onwards*
6. Full Implementation



Agreement :- topics

1. Harmonized Key Areas → *Agreed!*
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4. Guidelines to ACTR → *Agreed!*
5. Implementation - Trial period → *Sep. 2003 onwards*
6. Full Implementation ⇒ *by 31 Dec. 2008*



PPWG ASEAN Harmonized Products

ACTR / ACTD / Glossary of Term / GLs



Glossary of Term / Others :-

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*



ACTR Format

No.	Parameter	Components	Requirement						
			NCE	Bio.	MaV			MiV	GP
					Rt.	S/P	Ind.		

- Note:**
- NCE** = New Chemical Entity
 - Bio.** = Biotechnological product
 - MaV** = Major Variation (*variation affecting 1 or MORE of following aspect: Rt., S/P, Ind., or other Non-MiV*)
 - Rt.** = Route of Administrative
 - S/P** = Strength & Posology
 - Ind.** = Indication
 - MiV** = Minor Variation (*variation not affecting 1 or MORE of following aspect: Rt., S/P, Ind., API*)
 - GP** = Generic Product



Content of ACTR

ACTR - *Quality*

Drug Substance

- General info.
- Manufacture
- Characterisation
- Control of Drug Substance
- Ref. Std. or Materials
- Container Closure System
- Stability

Drug Product

- Description and Composition
- Pharmaceutical Development
- Manufacture
- Control of Excipients
- Control of Finished Product
- Ref. Std. or Material
- Container Closure System
- Stability
- Product Interchangeability/Equivalence evidence



Content of ACTR

ACTR - *Safety*

Pharmacology

- Primary P'dynamics
- Secondary P'dynamics
- Safety P'cology
- P'dynamic Drug Interaction

Pharmacokinetics

- Absorption
- Distribution
- Metabolism (inter-species comparison)
- Excretion
- P'cokinetic Drug Interaction(Non-clinical)
- Other P'cokinetic Studies

Toxicology

- Single Dose Toxicity
- Repeat Dose Toxicity
- Genotoxicity
- Carcinogenicity
- Reproductive & Development Toxicity

Local Tolerance

Other Toxicity Studies

List of Key Literature Ref.



Content of ACTR

ACTR - *Clinical Data*

BA & BE Studies

- BA Studies
- Comparative BA or BE Studies

Studies Pertinent to P'cokinetics

Using Human Biomaterials

Human P'cokinetic Studies

Human P'codynamic Studies

Efficacy and Safety

Post Marketing Data (if available)

References



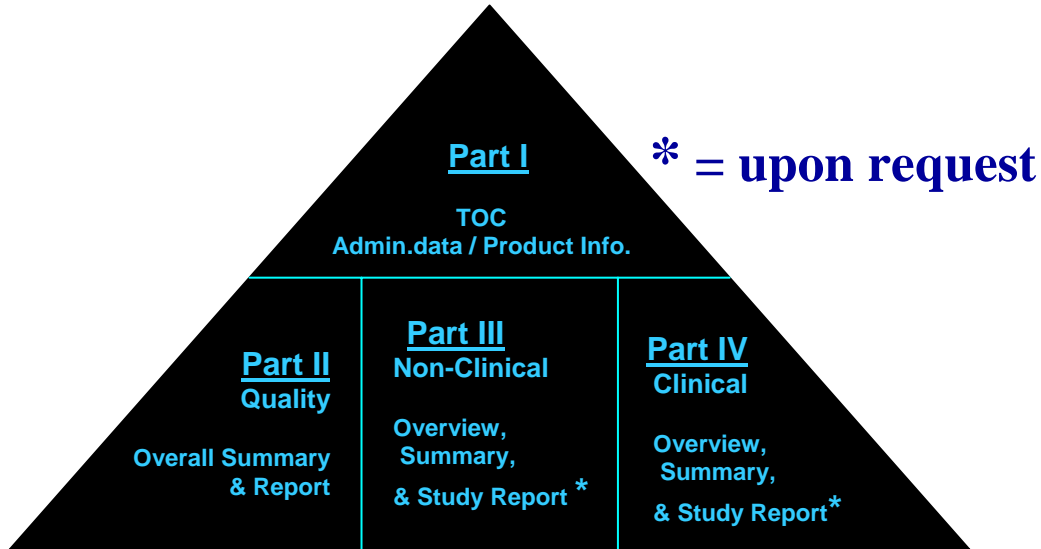
Glossary of Term / Others :-

ACTD

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



ACTD Organization





Content of ACTD

Part 1: ToC Admin.Data&Product Info.

- Section A: Introduction
- Section B: Overall ACTD-ToC
- Section C: Doc. Required for Registration

Part 2 : Quality Document

- Section A: ToC
- Section B: Quality Overall Summary
- Section C: Body of Data

Part 3 : Non-clinical / Safety Document

- Section A: ToC
- Section B: Non-clinical Overview
- Section C: Non-clinical Written & Tabulated Summaries
- Section D: Non-clinical Study Reports*

Part 4 : Clinical / Efficacy Document

- Section A: ToC
- Section B: Clinical Overview
- Section C: Clinical Summaries
- Section D: Tabular Listing of All Clinical Studies
- Section E: Clinical Study Reports*
- Section F: List of Key Literature References

Note:

ToC = Table of Content

* = Upon REQUEST



Content of ACTD

Part I: Administrative Data & Product Information

- Application Form
- Letter of Authorisation
- Certification
- Labeling
- Product Information
- Language



My Perspective on *Global Drug Development & ASEAN*



My Perspective on :

Global Drug Development & ASEAN

- **Standards & Requirement *to be a Player***
- **Advantage *to NDA Approval & Access to Medicine of Patients***
- **Affordable ?**
- **Individual vs. Regional?**
- **Impact ?**
 - **Pharmaceutical Registration**
 - **ASEAN Framework Agreement on Product Integration**
 - **ASEAN Economic Community (AEC)**



Thank You





Myself :

Name : *Yuppadee Javroongrit, Ph.D.*

Education :

B.S. in Pharmacy-Thailand (*Major-Cosmetic*)

M.S. in Industrial Pharmacy- USA

(Evaluation of Calcium Polycarbophil As a Disintegration Agent in Direct Compression Tableting)

Ph.D. in Industrial Pharmacy-USA

(Modification of Residence Time-Concentration Profile of IgA at Nasal Mucosal Surface)

Work : *Inspector-Inspection Div., ThaiFDA*

Pharmacist- Drug Control Div., ThaiFDA

Head of International Affairs and IND Section-Drug Control Div., ThaiFDA

Assistant Director- Drug Control Div., ThaiFDA

Designation to ASEAN : *Co-Chair of PPWG*



Abbreviation :

ACCSQ = *ASEAN Consultative Committee for Standards and Quality*

ACTD = *ASEAN Common Technical Dossier*

ACTR = *ASEAN Common Technical Requirement*

DRA = *Drug Regulatory Authority*

GLs = *Guidelines*

IWG = *Implementation Working Group*

MRAs = *Mutual Recognition Arrangements*

PPWG = *Pharmaceutical Product Working Group*

NTB = *Non Tariff Barrier*

TBT = *Technical Barrier to Trade*

ASEAN Harmonized Product = ACTR, ACTD, Glossary of Term, Technical guidelines



Abbreviation on ASEAN

ACCSQ	= ASEAN Consultative Committee for Standards and Quality
AEC	= ASEAN Economic Community
AEM	= ASEAN Economic Ministers
AFAS	= ASEAN Framework Agreement on Services
AFTA	= ASEAN Free Trade Area
AIA	= ASEAN Investment Area
AICO	= ASEAN Industrial Cooperation Scheme
HLTF	= High Level Task Force
PPWG	= Pharmaceutical Product Working Group
MRA	= Mutual Recognition Arrangement
SEOM	= Senior Economic Officials Meeting