ASEAN Harmonization

by
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Drug Control Division, FDA, THAILAND

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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)

**ICH**
(EU+Japan+USA)

**CEE**
(Central & Eastern Europe)

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

**PPWG**
(ASEAN)

**PANDRH**
(Pan American)

**SADC**
(South Africa)

**GCC**
(Middle East)

**BIMST-EC**
(South Asia)
ASEAN Harmonization
Symbol of ASEAN
ASEAN
= Association of Southeast Asian Nations
Member
- Brunei Darussalam
- Cambodia
- Indonesia
- Lao PDR
- Malaysia
- Myanmar
- Phillippines
- Singapore
- Thailand
- Vietnam

Total population ~ 520 million
ASEAN-Major Cooperation

ASEAN Summit
The Leader (Presidents, Prime Minister)

- Economic Cooperation-AEM
  Minister of Economic/Trade Ministry

- Political & Security Cooperation
- Socio-cultural Cooperation
  Minister of Foreign Affairs Ministry
Economic Cooperation in ASEAN

ASEAN Summit

AEM

SEOM

ACCSQ

WG1 on Mutual Recognition Arrangements (MRAs) & Standards

WG2 on Accreditation and Conformity Assessment

Scientific/Industrial Metrology Sub-WG

PWGs

- ACC (ASEAN Committee on Cosmetic)
- PPWG (Pharmaceutical PWG)
- EE PWG (Electrical and Electronic PWG)
- PT 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 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

ASEAN Summit

AEM

SEO M

ACCSQ

WGs

PWGs

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

High Level Task Force (HLTF)

PPWG (Pharmaceutical PWG)
ACC (ASEAN Committee on Cosmetic)
EE PWG (Electrical and Electronic PWG)
Traditional Medicine & Health Supplement PWG
- Medical Devices & Equipment PWG
- etc.

ASEAN Harmonization
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)_
Explore the Feasibility of Implementing a Flexible Twining 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

ASEAN Summit

- AEM
- SEOM
- ACCSQ

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

HLTF

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!
2. Format for ACTR & ACTD → Agreed!
3. Content of ACTR / ACTD / Glossary of Term → Agreed!
4. Guidelines to ACTR → Agreed!
5. Implementation - Trial period → Sep. 2003 onwards
6. Full Implementation
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 → Sep. 2003 onwards
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

<table>
<thead>
<tr>
<th>No.</th>
<th>Parameter</th>
<th>Components</th>
<th>Requirement</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>NCE</td>
<td>Bio.</td>
</tr>
<tr>
<td></td>
<td>Rt.</td>
<td>S/P</td>
<td>Ind.</td>
</tr>
</tbody>
</table>

**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 Adminstrative
  - **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

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

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

**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’cokinetrics**
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

Part I
TOC
Admin.data / Product Info.

Part II
Quality
Overall Summary & Report

Part III
Non-Clinical
Overview, Summary, & Study Report*

Part IV
Clinical
Overview, Summary, & Study Report*

* = upon request
   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

<table>
<thead>
<tr>
<th>Abbreviation</th>
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<tbody>
<tr>
<td>ACCSQ</td>
<td>ASEAN Consultative Committee for Standards and Quality</td>
</tr>
<tr>
<td>AEC</td>
<td>ASEAN Economic Community</td>
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<td>AEM</td>
<td>ASEAN Economic Ministers</td>
</tr>
<tr>
<td>AFAS</td>
<td>ASEAN Framework Agreement on Services</td>
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<tr>
<td>AFTA</td>
<td>ASEAN Free Trade Area</td>
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<tr>
<td>AIA</td>
<td>ASEAN Investment Area</td>
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<tr>
<td>AICO</td>
<td>ASEAN Industrial Cooperation Scheme</td>
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</tr>
<tr>
<td>SEOM</td>
<td>Senior Economic Officials Meeting</td>
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</tbody>
</table>