ASEAN Pharmaceutical Harmonization Updates

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Presentation Outline

- About ASEAN
- Background
- Economic Integration
- Current Status
- Issues & Challenges
- Efforts by Malaysia
- Conclusion
History of ASEAN

ASEAN = Association of Southeast Asian Nations

- 10 member countries

- Indonesia, Malaysia, Philippines, Singapore and Thailand (1967)
- Brunei Darussalam (1984)
- Vietnam (1995)
- Lao PDR and Myanmar (1997)
- Cambodia (1999)
ASEAN

STRENGTHENING REGIONAL REGULATORY FRAMEWORKS THROUGH PARTNERSHIP
Facts

- As of 2006, ASEAN region has a population of about 560 million
- Total area of 4.5 million square kilometers
- Combined gross domestic product almost US$ 1,100 billion
- Total trade of about US$ 1,400 billion
Intra ASEAN Trade

- AFTA is a collective effort by ASEAN to reduce/eliminate tariffs in intra-ASEAN trade in the goods sector.
- Objective of AFTA is primarily to enhance ASEAN’s position as a competitive production base for regional and global markets.
- The ASEAN population provides enormous potential for market expansion.
- Trend of increasing intra-ASEAN trade
1992:
- The ASEAN Consultative Committee for Standards and Quality (ACCSQ) formed to facilitate and complement the ASEAN Free Trade Area (AFTA).

1997
- ASEAN regulatory bodies authorized to achieve mandate of eliminating technical barriers to trade.

1998
- Efforts to harmonize regulatory requirements amongst ASEAN was initiated through the (ACCSQ)

1999
- Concept of ASEAN pharmaceutical harmonization was presented by Malaysia and agreed upon by the Senior Economic Officials Meeting (SEOM)
ACCSQ Agenda

- Facilitation of the realization of the ASEAN economic community
- Working Groups and Product Working Groups
- Cooperation with dialogue partners and other organizations on standards and conformance
- ASEAN FTA negotiations
The Pharmaceutical Product Working Group (PPWG) was formed in 1999
- Malaysia hosted the 1st PPWG meeting and was appointed the Chair and Thailand the Co-Chair.
Objective of PPWG

To develop harmonization schemes of pharmaceutical regulations of the ASEAN member countries to complement and facilitate the objective of AFTA, particularly the elimination of technical barriers to trade posed by regulations without compromising product quality, efficacy and safety.
Scope of PPWG

- Exchange of information on existing requirements and regulations
- Review requirements and regulations
- Conduct comparative studies
- Study other harmonized procedures and regulatory system
- Develop technical requirements
- Establish common technical documents towards achieving MRA
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 by December 2008
Technical Cooperation

- **ACTR/ACTD**
  - Quality – Indonesia
  - Safety – Philippines
  - Efficacy – Thailand
  - Administrative Data, Product Information and Glossary – Malaysia

- **Guidelines**
  - Analytical Validation – Thailand
  - Process Validation - Singapore
  - Stability Studies – Indonesia
  - BA/BE Studies - Malaysia
ASEAN Harmonized Product

- ASEAN Common Technical Requirements and Dossier (ACTR/ACTD) on Quality, Safety and Efficacy plus Administrative Data and Glossary

- Guidelines on
  - Analytical and Process Validation
  - Stability Studies
  - Bioavailability/Bioequivalence
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
Harmonization Milestones


- PPWG
- IWG
- GMP MRA TF
- BA/BE TF
- ACTD Implementation

- ACTD development
- ACTR & technical guidelines development
- Regulatory capacity building
- Post-Market Alert System development
- GMP Inspection MRA development
- Training scheme development
- ACTD implemented
- ACTR & technical guidelines established (maintenance and enhancement of common interpretation ongoing)
- Post-Market Alert System established
- GMP Inspection MRA finalized
- Training identified
- Pan-ASEAN registration
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

ACTD
The part of marketing authorization application dossier that is common to all ASEAN member countries
Content of ACTR - Quality

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

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

Pharmacology
- Primary P’dynamics
- Safety P’cology
- Secondary P’dynamics
- Drug Interaction

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

Pharmacokinetics
Local Tolerance
Other Toxicity Studies
List of Key Literature Ref.
Content of ACTR – Clinical Data

BA & BE Studies

Studies Pertinent to P’cokinetics

Human P’cokinetic Studies

Human P’codynamic Studies

Efficacy and Safety

Post Marketing Data (if available)

References
Technical guidelines to ACTR - Quality

- adopted the WHO’s GLs
- adopted the existing International Pharmocopoeia
- adopted ICH-Quality Guideline (12 GLs)
- drafted 4 ASEAN Quality GLs
  1. Analytical Validation guideline
  2. BA/BE Studies guideline
  3. Process Validation guideline
  4. Stability Study guideline
Technical guidelines to ACTR

Safety

→ adopted 15 ICH-Safety GLs

Efficacy

→ adopted 11 ICH-Efficacy GLs
  (E1, E2A, E2C, E3, E4, E6-11)
→ accepted as Ref.gls. 4 ICH-Efficacy GLs
  (E2C(A), E2D, E2E, E12A)-->
→ not adopted 2 ICH-Efficacy GLs
  (E2B(M), E5)
Content of ACTD

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

- Part 2: Quality Document
  - Section A: ToC
  - Section B: Quality Overall Summary
  - Section C: Body of Data

- Part 3: Non-clinical / Safety Doc
  - 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 Doc
  - 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
Current Situation

Situation :-

Implementation \textit{ASEAN Harmonized Product}

- Trial period \textit{Sep.03 onwards}
- Full implementation
  - for new submission \textit{by 31 Dec.08}
  - for existing registered product \textit{by 01 Jan.12}

- Maintenance/Amendment \textit{the adopted Technical guidelines}
- Strengthening Capacity of \textit{the DRAs, as well as Industries}
Current Situation

Cooperation with others

**with International**

- ICH-GCG (as observer)
- WHO (Vaccine Chapter, IMPACT)

- with ASEAN Dialogue Partners
  - on going cooperation project with EU
  - drafting Cooperation project with USA
Latest Update – 14th PPWG

- Implementation Working Group - new TOR
- GMP & BA/BE Task Force - MRA
- Technical Discussion Groups - Technical Guidelines, Q&A
- ACTD implementation - Readiness Survey
- Recommendations by APC & APRIA
- Post Marketing Alert System
- Collaboration with WHO - Vaccines & Counterfeits
- Training needs - Regulators & Industry
Follow Up Actions

- **MRA on GMP Inspection** - Amendments, Further consultations, Technical assistance
- **BA/BE** - Q&A, revised BE Study Report
- **ACTD/ACTR Implementation** - Focus on Quality documents, Strengthen capacity building, Survey after implementation
- **IWG** - Mechanism, Impact Assessment Study
- **PMAS** - Circulate information to ACC & TMHS
- **Technical Cooperation** – Country specific technical assistance, CLMV
Way Forward

- Streamlined structure of PPWG
- Technical collaboration - APC & APRIA
- Monitoring of Implementation of ACTD & Technical Guidelines
- Sectoral MRA on GMP Inspections
- Sectoral MRA on BA/BE studies
- Structured training schemes
- Global partnership - ICH GCG, USA, EU, Japan, Australia, China
ASEAN Healthcare Integration

- Healthcare is one of eleven priority sectors identified for fast-tracked integration.

- Roadmap related to pharmaceuticals:
  - Study feasibility of an ASEAN MRA for pharmaceutical products
  - Implement ASEAN Common Technical Dossier (ACTD)
  - Harmonise labelling standards
  - Explore feasibility of adopting a harmonised placement system for pharmaceutical products
  - Facilitate approval process after full implementation of the ACTD
  - Explore the feasibility of twinning systems to enhance regulatory capacity and resource development
  - Formalise a post-marketing alert system for defective and unsafe pharmaceutical products
ASEAN Economic Community Blueprint

- A single market and production base
- A region of equitable economic development
- A fully integrated region into the global economy
- A highly competitive economic region
- Commitment to implement measures and actions listed in the AEC Blueprint by 2015
Issues

- Political will – reality
- Regulatory infrastructure – legal, physical, financial
- Human resource – capacity & capability
- Gaps
- Implementation – understanding & interpretation
- Scope of harmonization
- Country specific requirements
- Sectoral MRA
- Industry involvement – technical discussion groups
- Global cooperation – WHO, APEC, EU, USA, Australia, Japan, China
Challenges

- Current political situation
- Economic development
- Trade negotiations – FTA
- Legal framework
- Emerging public health issues
- Changing global environment
Future Horizon

- Pharmaceutical Joint Sectoral Committee (JSC)
- ASEAN Pharmaceutical Directives?
- Future initiative for integration of Pharmaceutical Sector?
- New sectoral MRAs?
- Harmonized placement system for pharmaceutical products into ASEAN market – Pan ASEAN Registration?
Harmonization Efforts by Malaysia

- ACTD/ACTR implemented
- On-line registration system
- Training programmes for regulators and industry
- Networking and sharing of information
- Regulatory reviews by WHO & CMR
- Twinning programmes with CLMV countries
- Audits of BA/BE centres
- GMP, GSP, GCP, GRP
Moving Ahead

- 9th Malaysia Plan – Enhancement of ICT
- Human capital development
- GCP inspections
- GLP – Mutual Acceptance of Data (OECD)
- Bilateral arrangements
- Ongoing FTA
Malaysia - Accolades

- Training and Reference Centre for Quality Assurance of Pharmaceuticals (AWGTCP)
- 30\textsuperscript{th} member WHO Drug Safety Monitoring Programme
- WHO Collaborating Centre for Regulatory Control of Pharmaceuticals
- 26\textsuperscript{th} member of Pharmaceutical Inspection Cooperation Scheme (PIC/S)
Conclusion

- Trade globalization has prompted the need for strategic partnership. Harmonized standards are important in facilitating and liberalizing trade and investment.
- Regional harmonization can only be achieved by bridging the gaps between ASEAN member countries in the establishment of regulatory systems and implementation of common requirements.
- Global co-operation provides opportunities for development and improvements, paving the way for international recognition. Establishing MRA is crucial to ensure effective harmonization.
- Despite challenges, PPWG has charted milestone achievements towards creating a single pharmaceutical market.
Thank You