COPING WITH INCREASING NEEDS FOR INSPECTIONS: ASEAN INITIATIVES

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Presentation Outline

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- Current Scenario
  - Acceptable GMP Evidence
  - Practice on GMP inspections
    - Malaysia & Singapore
- ASEAN MRA on GMP
- Issues & Challenges
- Recommendations
History of ASEAN

**Association of Southeast Asian Nations**

- **10 Member States**
  - Indonesia, Malaysia, Philippines, Singapore and Thailand (1967)
  - Brunei Darussalam (1984)
  - Vietnam (1995)
  - Lao PDR and Myanmar (1997)
  - Cambodia (1999)
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
- Establish Working Groups and Product Working Groups
- Cooperation with dialogue partners and other organizations on standards and conformance
- ASEAN Free Trade Agreement negotiations
Objective of Pharmaceutical Product Working Group (PPWG)

To develop harmonization schemes of pharmaceutical regulations of the ASEAN member countries to complement and facilitate the objectives 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
Harmonization Milestones

- 1999: PPWG
- 2002: IWG
- 2005: GMP MRA TF
- 2006: BA/BE TF
- 2009: ACTD Implementation

**1999 - 2009 Milestones:**

- ✔ ACTD development
- ✔ ACTR & technical guidelines development
- ✔ Regulatory capacity building
- ✔ Post-Market Alert System development
- ✔ GMP Inspection MRA development
- ✔ Training scheme development

**2009 Milestones:**

- ✔ ACTD implemented
- ✔ ACTR & technical guidelines established (maintenance and enhancement of common interpretation ongoing)
- ✔ Post-Market Alert System established

**Additional Milestones:**

- GMP Inspection MRA finalized
  - Training identified
  - Pan-ASEAN registration
Current Scenario in ASEAN

- Technical Requirements on Good Manufacturing Practices
  - WHO guidelines for GMP
  - Pharmaceutical Inspections Convention Scheme Membership (PIC/S) Guide to GMP for Medicinal Products
Acceptable Evidence of GMP

- Locally manufactured products
  - Evidence of GMP conformance through inspections of local manufacturers by GMP auditors in their respective countries

- Imported products
  - Acceptance of WHO Certificate of Pharmaceutical Product (CPP) with statement on GMP compliance issued by Drug Regulatory Agencies (DRA)
  - GMP certificates issued by relevant health/related agencies for certain categories of products e.g. traditional medicines, health supplements
Acceptable Code of GMP

Singapore and Malaysia

- Singapore attained membership to PIC/S in 2000 followed by Malaysia in 2002
- Implemented PIC/S Guide to GMP for local manufacturers of medicinal products
Other ASEAN Member States using WHO standards for GMP

Thailand in process of applying for PIC/S membership
- Underwent first inspection in January 2008

Indonesia and Philippines have expressed intention to join PIC/S

Brunei currently has no local manufacturers
Manufacturers located within Singapore subjected to licensing and periodic inspections by Health Sciences Authority (HSA)

For medicinal products exported to Singapore, overseas manufacturers are subjected to GMP conformity assessment

- Required to periodically provide acceptable evidence that the facility conforms to the acceptable GMP standard
- Otherwise, inspectors from HSA will conduct an on-site audit of the foreign facility
**Malaysia**

**Local Manufacturers**

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<th>Risk Compliance Rating</th>
<th>High</th>
<th>Medium</th>
<th>Low</th>
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<tbody>
<tr>
<td>Good</td>
<td>18 months</td>
<td>24 months</td>
<td>36 months</td>
</tr>
<tr>
<td>Satisfactory</td>
<td>12 months</td>
<td>18 months</td>
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</tr>
<tr>
<td>Poor</td>
<td>6 months</td>
<td>6 months</td>
<td>6 months</td>
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All newly licensed facilities will be scheduled for first routine audit not later than 1 year from the date of the pre-licensing inspection.
FOREIGN MANUFACTURERS

- **Sterile products, biosimilars**
  - Manufacturers from non-PIC/S member countries, USA, Japan subjected to audits
  - Exempted if facility has already been audited by any of these countries and manufacturer can provide the audit report

- **Foreign manufacturers of other categories of products not subjected to inspections**
  - Unless products found to be in non-conformance with regulatory requirements, frequent product complaints
ASEAN SECTORAL MUTUAL RECOGNITION ARRANGEMENT FOR GMP INSPECTIONS OF MANUFACTURERS OF MEDICINAL PRODUCTS
MRA on GMP

- Idea first mooted at the 10th PPWG meeting in 2005
- At 15th meeting held in Brunei Darussalam in July 2008, reached final draft stage
- Currently, under legal review in all Member States
- Targeted for acceptance by the ASEAN Economic Ministers by end 2008
OBJECTIVES

- Sets out arrangements under which each Party shall accept
  - The GMP certificates for manufacturers of medicinal products issued by the listed Inspection Service
  - The GMP reports which verify conformity of a manufacturer with the mandatory requirements issued by the listed Inspection Service
Pharmaceutical products in finished dosage form
- Includes both prescription and non-prescription medicinal products for human use
- Excludes
  - Biopharmaceuticals
  - Radiopharmaceuticals
  - Traditional medicines
  - Investigational medicinal products
Recognized GMP standard PIC/S Guide to GMP for Medicinal Products or its equivalent

- Effort to harmonise technical requirements for quality
- Should not be construed as a technical barrier to trade

Member States will have to establish an Inspection Service which will have to be accepted by the Joint Sectoral Committee tasked to oversee implementation of this MRA
Member States have a responsibility to ensure that their respective Inspection Services are capable of properly assessing manufacturers in their respective territories to ensure maintenance of confidence in the GMP inspection system.
AUDITS

- At the request of one NDRA to another, the listed Inspection Service will assess and where appropriate certify that the manufacturers complies with the established GMP code

- May involve joint participation in audits and inspections
MUTUAL RECOGNITION OBLIGATIONS

- Member States shall accept the GMP certificate and/or inspection report in respect of a manufacturing facility in the territory of those Parties which have their Inspection Services listed under this MRA.

- If there is suspension or withdrawal of the GMP certificate, a Party is obliged to notify the Parties which the manufacturer has exported its products to.
This MRA is a multilateral arrangement in which all Member States (MS) are required to participate in.

A MS not ready to fully implement this MRA may withhold from being listed in the Inspection Service.
IMPLEMENTATION

- If a Party decides not to accept the GMP Certificate or inspection report, it shall provide the necessary clarification of its reasons to the Party which Inspection Service furnished the report.

- A Member State may defer implementation of this MRA by notifying the ASEAN Secretary General in writing.

- Proposal that deferment will be no later than 1 January 2011.
IMPLICATIONS OF THE MRA

- Allows for an equivalent GMP code to be adhered to between manufacturers in PIC/S and non-PIC/S countries
- **Acceptance of GMP certificates and reports amongst ASEAN countries will reduce the number of inspections being conducted on manufacturers**
- Ensures the quality of products being traded in the region
- Increase acceptance of products manufactured in ASEAN
Issues

- Political will to make this MRA a reality
- Regulatory infrastructure – legal, physical, financial
- Human resource – capacity & capability
- Gaps
- Implementation – understanding & interpretation
- Scope of harmonization
- Country specific requirements
- Industry involvement
- Global cooperation – no implementation of other types of technical and non-technical barriers to trade
Challenges

- Current political situation
- Economic development
- Other trade negotiations
- Legal framework
- Emerging public health issues
- Changing global environment
RECOMMENDATIONS

- Work towards ensuring quality, efficacy and safety of drugs whilst trying to contain escalating costs of drug prices
  - Minimise duplication of inspection activities within WHO Member States through
    - Better networking
    - Improved information sharing
    - Enhanced collaboration
    - Increased mutual trust
Thank You

TERIMA KASIH