Pharmaceutical Regulation in the Philippines and the Impact of ASEAN Harmonization

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Presentation Outline

1. Mission, Vision and Quality Policy
2. Legal Basis for Regulation
3. Organizational Structure and Functions
4. Regulatory Reforms and Strategies
5. ASEAN Harmonization and its Impact
6. Moving Forward
Republic of the Philippines
Department of Health
Food and Drug Administration

FDA MISSION, VISION
and QUALITY POLICY
MISSION

To ensure the safety, efficacy, purity and quality of products we regulate through effective implementation of the national regulatory framework consistent with international best practices.
To be an internationally-recognized center of regulatory excellence safeguarding the health of the Filipinos
Our highest commitment is to ensure the safety, efficacy and quality of health products.
Toward this end, we commit to establish science-based standards as basis for regulatory policies, to continually improve and maintain our competencies, and to deliver quality public service with integrity.
LEGAL BASIS
for REGULATION
Legal Basis

- Republic Act No. 3720 (as amended) – Foods, Drugs, Devices and Cosmetics Act

- Republic Act No. 9711 – Food and Drug Administration (FDA) Act of 2009
Legal Basis


- Republic Act No. 7394 – Consumer Act of the Philippines
1. Licensing/Accreditation of Drug Establishments
   • Involves GxPs such as GMP, GDP, GSP, GCP and GLP

2. Pre-Marketing Assessment
   • Involves drug application dossier evaluation
   • Quality, Safety and Efficacy (for innovative medicines)
   • Quality + Product Interchangeability (for generics)

3. Post-Marketing Surveillance
   • Safety and Efficacy (drug benefit/risk balance)
   • Quality (quality testing and compliance monitoring)

Regulatory Framework Elements
Post-Marketing Surveillance

- Involves the active, systematic, scientifically-valid collection, analysis, and interpretation of data and other information about a registered/marketed drug product

- Aims to reduce public health risks associated with the use of a registered/marketed drug product

- Encompasses many regulatory activities and functions
1. **Pharmacovigilance**
   - Safety monitoring of drugs on the market for unexpected health risks and informing the public of risks posed by specific drugs and other health products
   - ADR reports from prescribers, manufacturers and consumers

2. **Quality monitoring, collection, sampling and laboratory testing of drug products**

3. **Inspection of drug establishments for continuous and consistent compliance to GxPs**

4. **Advertisements and claims monitoring**

5. **Product recall orders / Imposition of administrative sanctions**
FUNCTIONS of the CDRR DIVISIONS
1. Licensing of drug establishments
   • In coordination with the Field Regulatory Operations Office (FROO)

2. Oversight function over FROO inspectors in the conduct of inspection of drug establishments

3. Evaluation and registration of human and veterinary drugs
   • Clinical (Efficacy), Nonclinical (Safety) and Quality (CMC)
4. Post-approval changes
   • Variations

5. Establishment and product verification and certification

6. Issuance of Certificates of Pharmaceutical Product, Free Sale and Export Certificates, and other clearances
Product Research and Standards Development Division

1. Conduct of research and development of standards

2. Development of strategies for PMS

3. Compliance monitoring (analysis of field data)

4. Accreditation of CROs and other facilities engaged in the conduct of clinical research, and their oversight

- GCP, GLP, GTP
1. Conduct analysis and inspection of drug products

2. Establish analytical data to serve as basis for the preparation of drug product standards, and to recommend standards of identity, purity, quality, safety and efficacy
3. Conduct appropriate tests on all applicable drug products prior to the issuance of appropriate authorizations

4. Inspect centers conducting bioavailability and bioequivalence tests, as may be delegated

5. Accredit private analytical testing laboratories

Laboratory Support Division
1. Standards development including policies and guidelines

2. Provision of technical assistance in capacity building of stakeholders

3. Participation in ASEAN Harmonization meetings and other relevant international gatherings

4. Quality assurance through the development and maintenance of a Quality Management System (QMS)

Other Functions of CDRR
Commitment to Quality


- ISO 17025:2005 – Certification of Competence as a Testing Laboratory (awarded on 08 April 2010)
REGULATORY REFORMS and STRATEGIES
General Reforms

1. Improve Evaluation Process
2. Enhance the Inspectorate
3. Clarify Policies and Priorities
4. Increase Laboratory Capacity
General Reforms

**IMPROVE EVALUATION PROCESS**

- Activity-based divisions to product-oriented centers
- Paperless application system
- Electronic payment system
- Online publication of application guidelines
- Rationalized application forms

**ENHANCE THE INSPECTORATE**

**CLARIFY POLICIES AND PRIORITIES**
General Reforms

IMPROVE EVALUATION PROCESS

ENHANCE THE INSPECTORATE

CHECK PRIORITY

- Equip inspectors with tablets and other tools
- Set inspection protocols
- Equip REU with firearms backed by police and military training

INCREASE LABORATORY CAPACITY
General Reforms

- New laboratory equipment procurement
- Continuous training and skills acquisition
- Improvement of laboratory security

- ENHANCE THE INSPECTORATE
- INCREASE LABORATORY CAPACITY
- CLARIFY POLICIES AND PRIORITIES
General Reforms

- **IMPROVE EVALUATION PROCESS**
  - Review
  - Remove
  - Redundant Regulations
  - ISO accreditation and certification
  - IT administrative solutions in place
  - Rationalization of Clinical Trial approval process

- **CLARIFY POLICIES AND PRIORITIES**

- **INCREASE LABORATORY CAPACITY**
1. Work on improving the efficiency, clarity, and transparency of the CDRR work process

2. Review and update the existing policies and regulations to align with the international standards

3. Draft new policies to keep abreast with the new and emerging technology in the field of drug development

CDRR Strategies
4. Advocate a robust yet flexible and risk-based regulatory system

5. Enhance both the pre-market and post-market regulatory process in coordination with the FROO

6. Develop a coordinated approach with the FROO and other government agencies on safety and quality issues

CDRR Strategies
7. Continuous re-training and re-tooling of all technical and administrative personnel

8. Establish closer collaboration with other competent Drug Regulatory Authorities (DRAs)

9. Regular communication/dialogue with industry stakeholders

CDRR Strategies
Republic of the Philippines
Department of Health
Food and Drug Administration

REGULATORY UPDATES
Regulatory Updates

- **Administrative Order No. 2014-0040** (27 October 2014)
  - Revised Guidelines on the Need/Role of a Medical Director in the Pharmaceutical Industry

- **Administrative Order No. 2014-0034** (13 October 2014)
  - Rules and Regulations on the Licensing of Establishments Engaged in the Manufacture, Conduct of Clinical Trial, Distribution, Importation, Exportation, and Retailing of Drug Products, and Issuance of Other Related Authorizations
Regulatory Updates

- Administrative Order No. 2014-0016 (11 April 2014)
  - Adoption of the World Health Organization “Guidelines on Evaluation of Similar Biotherapeutic Products (SBPs)” for the Registration of Biosimilar Products

- Administrative Order No. 2013-0027 (02 October 2013)
Regulatory Updates

- **Joint DOH and DA Administrative Order No. 2013-0026** (24 September 2013)
  - Rules on the Regulation of Veterinary Drugs and Products, Veterinary Biological Products, and Veterinary Drug Establishments

- **Administrative Order No. 2013-0022** (13 August 2013)
  - Guidelines for Current Good Manufacturing Practice (cGMP) Clearance and Inspection of Foreign Drug Manufacturers
Regulatory Updates

- **Administrative Order No. 2013-0021** (01 July 2013)
  - Adoption of the Association of Southeast Nations (ASEAN) Common Technical Dossier (ACTD) and Common Technical Requirements (ACTR) for the Registration of Pharmaceutical Products for Human Use

- **Administrative Order No. 2013-0012** (18 March 2013)
  - Rules and Regulations Governing the Accreditation of Health Facilities Engaging in Human Stem Cell and Stem-Cell Based or Cellular Therapies in the Philippines
FDA Circular No. 2014-016 (30 May 2014)
  • Implementing Guidelines for Administrative Order No. 2013-0022 dated 13 August 2013 Re: Guidelines for Current Good Manufacturing Practice (cGMP) Clearance and Inspection of Foreign Drug Manufacturers

FDA Circular No. 2014-015
  • Manufacture, Sale, and Distribution of Traditional and Alternative Medicines
FDA Circular No. 2014-009 (15 March 2014)
- Filing and Submission of Applications for the Approval of Clinical Trial Protocol, Compassionate Special Permit (CSP), Import Permit for Investigational Drug Products, Pharmacovigilance, Adverse Events/Adverse Reaction Reports, and Other Related Documents

FDA Circular No. 2014-008 (28 February 2014)
- Application Process and Requirements for Post-Approval Changes of Pharmaceutical Products
  - Adoption of the ICH Harmonized Tripartite Guideline, Quality of Biotechnological Products: Stability Testing of Biotechnological/Biological Products Q5C

FDA Circular No. 2013-024 (05 September 2013)
  - The Adoption and Implementation of “The Mexico City Principles for Voluntary Codes of Business Ethics in the Biopharmaceutical Sector”
FDA Circular No. 2013-021 (15 August 2013)
- Comparator Drugs for Selected Pharmaceutical Products Containing Biopharmaceutics Classification System (BCS) Class 4 Drug Molecules

FDA Circular No. 2013-019 (12 August 2013)
- Organization of the ASEAN Common Technical Dossier (ACTD) for the Registration of Pharmaceutical Products for Human Use
FDA Circular No. 2013-018 (12 August 2013)
- Adoption of the International Conference on Harmonization (ICH) Safety and Efficacy Guidelines

FDA Circular No. 2013-014
FDA Circular No. 2013-008 (22 April 2013)
- Adoption of the Association of the Southeast Asian Nations (ASEAN) Post-Marketing Alert System (PMAS) for Defective or Unsafe Processed Food Products, Pharmaceutical Products, Traditional Medicines and Health Supplements, and Cosmetic and Household Hazardous Products and Devices

FDA Circular No. 2013-004 (22 February 2013)
- Post Market Surveillance (PMS) of Authorized Drug Products
Revised Labelling Requirements
Revised Brand Name Regulation
Revised Drug Registration Process
Revised Donations Regulations
Registration of Homeopathic Drugs
Registration of Radiopharmaceuticals
Expedited Review of Prequalified Vaccines

Upcoming Regulations
- Risk Management Plan
- Fixed-Dose Combination Products and Product Kits
- Loan Licensing
- Good Compounding Practices
- Good Regulatory Practices
- Dispensing Doctors for Special Products

Upcoming Regulations
ASEAN HARMONIZATION and its IMPACT
What is ASEAN?

Association of Southeast Asian Nations - established in 1967

Population: 603 million (2011)
GDP (Nominal): US$ 2.4 trillion (2013)
Objectives

1. To accelerate economic growth, social progress, and cultural development
2. To protect regional peace and stability
3. To give opportunities for member states to discuss differences peacefully

1995 – ASEAN Leaders reaffirmed that:
"Cooperative peace and shared prosperity shall be the fundamental goals of ASEAN"
Need for ASEAN Harmonization

10 ASEAN Member States have:

- Very diverse racial, religious, cultural, social, political, economic and geographical background

- Combined market of about 600 million people
<table>
<thead>
<tr>
<th>Target</th>
<th>Priority Products</th>
</tr>
</thead>
<tbody>
<tr>
<td>To create a single market by 2015</td>
<td>Agricultural, Fisheries, Wood, Rubber, Automotive, Textiles, Electronics, Tourism, Travel, Logistics, <strong>Healthcare</strong>, e-ASEAN</td>
</tr>
</tbody>
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<table>
<thead>
<tr>
<th>Principle</th>
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<tbody>
<tr>
<td>Elimination of technical barriers to trade posed by regulations, without compromising the quality, safety and efficacy</td>
</tr>
</tbody>
</table>
ASEAN Harmonization in the Pharmaceutical Sector

Timeline:

1992 – Initial efforts towards the harmonization of ASEAN regulations were initiated through the ASEAN Consultative Committee on Standards and Quality (ACCSQ).

1999 – To address specific harmonization issues on pharmaceuticals, the ACCSQ Pharmaceutical Product Working Group (PPWG) was formed.
# ASEAN Hierarchy

<table>
<thead>
<tr>
<th>Level</th>
<th>Function</th>
<th>Meeting, Output</th>
</tr>
</thead>
<tbody>
<tr>
<td>President Prime Minister</td>
<td>Highest decision-making body</td>
<td>Annual meeting</td>
</tr>
<tr>
<td>Minister of Economy, Trade, Foreign Affairs</td>
<td>Coordinate the work of the Association</td>
<td>Joint Ministerial Meeting (JMM)</td>
</tr>
<tr>
<td>ASEAN Consultative Committee on Standards and Quality</td>
<td>Facilitate the objectives of the Free Trade Area / Implement the Mutual Recognition Agreement</td>
<td>Harmonized sectors</td>
</tr>
<tr>
<td>Pharmaceutical Product Working Group</td>
<td>Develop harmonization scheme of pharmaceutical regulations</td>
<td>Harmonized format, requirements, guidelines, Glossary of Terms</td>
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ASEAN Harmonization in the Pharmaceutical Sector

Timeline:
2000-2003

– Key areas on Generics, NCEs, Biologics were harmonized.

– ASEAN Common Technical Dossier (ACTD) format (consisting of Administrative Data, Quality, Safety and Efficacy parts) and ASEAN Common Technical Requirements (ACTR) were developed.
ASEAN Harmonization in the Pharmaceutical Sector

Timeline:
2004-2007
- Trial period of ACTD/ACTR implementation

2009 to the present
- Full ACTD/ACTR implementation
- Development of further ASEAN technical guidelines on Quality, Safety and Efficacy, BA/BE and GMP
## ACTD Implementation

<table>
<thead>
<tr>
<th>Country</th>
<th>Date</th>
<th>Country</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brunei Darussalam</td>
<td>Oct 2008</td>
<td>Myanmar</td>
<td>Target Full: Dec 2014</td>
</tr>
<tr>
<td>Cambodia</td>
<td>Mar 2010</td>
<td>Philippines</td>
<td>Vol.: Jan 2005</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Full: Jul 2013</td>
</tr>
<tr>
<td>Indonesia</td>
<td>Jan 2009</td>
<td>Singapore</td>
<td>Full: Jan 2005</td>
</tr>
<tr>
<td>Lao PDR</td>
<td>Jan 2012</td>
<td>Thailand</td>
<td>Vol.: Jun 2004</td>
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<td></td>
<td></td>
<td></td>
<td>Full: Jan 2009</td>
</tr>
<tr>
<td>Malaysia</td>
<td>Jul 2003</td>
<td>Vietnam</td>
<td>Full: Nov 2009</td>
</tr>
</tbody>
</table>
ASEAN Common Technical Dossier (ACTD)

• Definition: Common format and content acceptable for an application in the ASEAN member states

• Benefits:
  • Uniformity of requirements
  • Reduction of time and complexity
  • Exchange of regulatory information
  • Facilitation of review
  • Quicker access of patients to safe and effective drugs
A set of written materials intended to guide applicants on how to prepare application dossiers in a way that is consistent with the expectations of all ASEAN Drug Regulatory Authorities.
ASEAN Common Technical Requirements

1. ASEAN Guidelines on Stability Study of Drug Product
2. ASEAN Guidelines for the Conduct of BA and BE Studies
3. ASEAN Guidelines on Submission of Manufacturing Process Validation Data for Drug Registration
ASEAN Common Technical Requirements

4. ASEAN Guidelines for the Validation of Analytical Procedures
5. ASEAN Variation Guidelines for Pharmaceutical Products

Other harmonized documents include:
- Glossary of Terms
- Nonclinical (Safety) Guidelines
- Clinical (Efficacy) Guidelines
✓ Rationalization of existing local technical regulations and requirements pertaining to marketing authorization of pharmaceutical products to be consistent with the rest of the ASEAN Member States with the implementation of the ACTD/ACTR

➢ Predominantly based on internationally-recognized standards on drug quality, safety and efficacy including ICH, WHO, US FDA and EMA

Key Benefits
As a result, the quality, safety and efficacy of every pharmaceutical product applied for local marketing authorization can be ensured.

Key Benefits
Although the concept of a Mutual Recognition Arrangement/Agreement (MRA) between ASEAN Member States in terms of marketing authorization has not been tackled yet at the ACCSQ-PPWG level, the harmonized application dossier (by virtue of the ACTD/ACTR) has already been developed and is currently being implemented region-wide.

Key Benefits
Given this, applicants need not prepare different technical dossiers (containing quality, safety and efficacy documentation) to suit the marketing authorization requirements of individual ASEAN Member States.

In effect, the complexity and timeframe of a pharmaceutical product’s marketing authorization process will expectedly be reduced and shorter, respectively.

Ultimately, the availability of/access to essential, critical and life-saving drugs will be faster.

Key Benefits
✓ The entry of new products from across the Southeast Asian region primarily multi-source pharmaceuticals (generics), that are deemed of quality, safe and effective as those currently available in the Philippine market, will mean more choices for consumers.

✓ Allowing market forces to take its due course, will also eventually result to lower costs.

Key Benefits
✓ For homegrown drug manufacturers who aim to establish their presence in 9 other ASEAN Member States, a regime of reduced trade barriers will bring about an expanded market of about 600 million ASEAN citizens.

✓ As previously cited, the same technical dossier for marketing authorization submitted for the Philippine drug regulatory authority’s approval shall be, in principle, considered acceptable by the rest of the ASEAN drug regulatory authorities.

Key Benefits
Republic of the Philippines
Department of Health
Food and Drug Administration

MOVING FORWARD
Moving Forward

• ASEAN Harmonization is inevitable and shall be part and parcel of the lives of Filipinos and the rest of the Southeast Asian region.

• There will be free flow of goods and services within the region by 2015.

• ASEAN Harmonization is generally beneficial for the region, although it poses certain challenges to the local pharmaceutical industry and the government.
Moving Forward

• In the face of the many opportunities and challenges presented by the looming ASEAN Harmonization, including a broader export market and a regime of reduced tariffs and technical barriers to trade, the local pharmaceutical industry needs all the support it can get to thrive in a highly competitive business environment amidst the anticipated influx of new players from ASEAN and beyond.
Moving Forward

• For its part, FDA Philippines has been and will continuously provide relevant information and technical assistance to the local pharmaceutical industry by way of workshops, fora and similar activities to ensure compliance with the harmonized requirements.
“As the national drug regulatory authority, the road ahead for the FDA Philippines may be difficult and challenging. Likewise, the same goes for the local pharmaceutical industry. However, with the strengthening of FDA’s institutional foundation in-line with its mandate, coupled with the close cooperation and shared commitment of all its stakeholders, the ultimate goal of ensuring that only safe, effective and quality drug products are made available in the Philippines is not a far-fetched one.”
Republic of the Philippines
Department of Health
Food and Drug Administration
THANK YOU!

Balancing Innovation

and Sound Regulation