Assessment Process of GMP Compliance in Taiwan

Current status & Future possibility

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5 April 2017
Outline

GMP Compliance of Medicinal Products in Taiwan

- Regulatory System
- Assessment of GMP Compliance
- Process for Foreign Manufacturers
- Moving Forward
GMP Compliance of Medicinal Products in Taiwan

Outline

Regulatory System

• Legislative Framework
• Competent Authority
• Adopt & Adapt the PIC/S GMP
Legislation Framework

Pharmaceutical Affair Act (PAA)

§57
Guide to GMP for MPs & MDs

The manufacturing of modern MPs shall comply with the PIC/S GMP Guide

§57
Regulations for Issuance of Manufacturing Licenses

§71
Regulations for Inspection

New GMP assessment, Routine inspection (2 to 4-year cycle) For-cause inspection

Article 57 of PAA
- The manufacturing of medicinal products (MPs) & medical devices (MDs) shall comply with the Good Manufacturing Practice requirements (including export only)
- The Manufacture of MPs & MDs must be authorized based on GMP inspections by Central Health Authority.
- these requirements apply to the foreign manufacturer of imported products.

Article 92 of PAA
- Health Authority has legal power to suspend, revoke or amend a manufacturing license.

Article 71 of PAA
- give Health Authority the legal power to inspect the sites....
Competent Authority – Taiwan FDA

A member of PIC/S starting on Jan. 1, 2013

Ministry of Health and Welfare

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**Taiwan Food and Drug Administration**

Inaugurated on Jan. 1 2010

**Vision / Missions**
- to safeguard food and drug safety
- to begin a new technology era
- to create a safe consumer environment

- **Pharmaceutical GMP Inspection and Licensing System** has been established based on:
  - PIC/S Recommendations (PI 002-3)
  - ICH Q10, ICH Q9

- **Competent inspectors**
  Qualification & training

- **Quality manual, SOPs, work instructions**
Adopt the PIC/S GMP

Publish bilingual version of PIC/S GMP Guide

- Current version: PE009-12, 1st October 2015.
Adapt the PIC/S GMP

Announced the timeframe to implementing the PIC/S GMP
- new facilities, expansion, new production line have to comply with PIC/S GMP

Dec. 2007

2010.1.1
PIC/S GMPs has been used for all of the inspections

2015.1.1
All manufacturers of modern medicinal products shall fully comply with PIC/S GMP

- For those facilities which are unable to comply with PIC/S GMPs, its manufacturing license had been revoked & importation of MPs was prohibited.

2016.1.1
All manufacturers of APIs shall fully comply with the PIC/S GMP

Training for Industry (free)
Outline

GMP Compliance of Medicinal Products in Taiwan

Assessment of GMP Compliance

• Domestic manufacturers
• Foreign manufacturers
Assessment of GMP Compliance

- Domestic Manufacturers -

Linked to issuance & renewals of Manufacturing License (has expiry date)

<table>
<thead>
<tr>
<th>Inspected On-Site</th>
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<tbody>
<tr>
<td>• Manufacturers of MPs</td>
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<tr>
<td>• Logistics company/ Wholesaler which involved packaging &amp; labeling of MPs</td>
</tr>
<tr>
<td>• APIs manufacturers</td>
</tr>
<tr>
<td>• Medical gases manufacturers</td>
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<tr>
<td>• Contract laboratories</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Types of Inspection</th>
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<tbody>
<tr>
<td>• GMP assessment of New facilities, relocation and expansion of existing facilities, resumption of operations, Addition of new dosage forms</td>
</tr>
<tr>
<td>• Routine inspection 2-4 years, adjusted based on risk</td>
</tr>
<tr>
<td>• For-cause inspection without notification</td>
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</table>
Authorized Pharmaceutical Manufacturers in Taiwan

- **208** sites in total
  - **127** manufacturers of MPs
  - **15** logistics companies involve in packaging & labeling of MPs
  - **10** pilot plants for IMPs
  - **32** Medicinal Gas manufacturers
  - **24** APIs manufacturers

Data collection until 2016.12.31
**Assessment of GMP Compliance**

- **Foreign Manufacturers** -
  
  - An **Official Letter of GMP compliance** (has expiry date) issued by the Taiwan FDA / MoHW is requested for product registration.
  - The application could only be submitted via the **Taiwan sponsor**, who must get a Drug Dealer License issued by Taiwan health authority.
  - Evidence documents may be sent to TaiwanFDA directly from manufacturer.

<table>
<thead>
<tr>
<th>Pathways for obtaining</th>
<th>MPs manufacturer &amp; active substance of biological product</th>
<th>APIs manufacturer</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Desk-top</strong> Inspection or NT$ 120,000~140,000</td>
<td>Verification the GMP Certificate issued by recognized Health Authority</td>
<td></td>
</tr>
<tr>
<td><strong>On-site</strong> Inspection (since 2002) &gt; NT$ 700,000 + travel expense</td>
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</table>

| Period of Validity (Site located) | | |
|-----------------------------------| | |
| **PIC/S** member countries: 2 to 4-year cycle | According to the expiry date of the GMP Certificate submitted | |
| **Non-PIC/S** member countries: 2 to 3-year cycle | | |
Qualified Foreign Manufacturers in Taiwan

Medicinal Products

data collection until 2017.2.28

- 926 sites in total from 48 countries
- 865 sites (93.4%) located in PIC/S member countries
- 215 sites (23.2%) has been on-site inspected.
Qualified Foreign Manufacturers in Taiwan

APIs

data collection until 2017.2.28

- **614** sites in total from **36** countries
- mostly from China (217, 35%) & India (180, 29%)
- **210** sites (34.2%) located in PIC/S member countries
Outline

GMP Compliance of Medicinal Products in Taiwan

Process for Foreign Manufacturers

• Issuance & Maintenance of the Official Letter of GMP compliance

• Application requirements
  - First submission (PMF review)
  - Renewal review
Issuance & Maintenance of the Official Letter of GMP compliance

Desk-top inspection or On-site inspection

First Submission (incl. Change in the scope of existing Letter of Compliance)

PIC/S Country

non-PIC/S Country

Desk-top

On-site

Inspect by

(PMF review)

Compliant

Official Letter of GMP Compliance

Expiry period: 2~4 years

Apply 6 months before expiration date

Decided by TaiwanFDA

Changes

Routine Inspection

International Rapid Alert

Continuously Monitoring

Site located at

First Submission

Continuously Monitoring

2017/4/5
Application requirements

First Submission - Plant Master File (PMF) review

- Request Documentation
  - ✓ Application form
  - ✓ Site Master File (English or Chinese)
  
  follow the PIC/S EXPLANATORY NOTES FOR PHARMACEUTICAL MANUFACTURERS ON THE PREPARATION OF A SITE MASTER FILE (PE008-4)

  ✓ Checklist of GMP Compliance & Evidence documents

  [Plant Master File, PMF]

  Where the original information is available in a language other than English or Chinese, the copy of the original information must be provide with an attestation on the accuracy of the translation.

- Application Fee
  - NT$120,000 for one dosage form/product per application;
  - NT$140,000 for maximum two dosage forms/products.
### Checklist of GMP Compliance & Evidence documents

<table>
<thead>
<tr>
<th>Full Package</th>
<th>Non-sterile</th>
<th>Sterile</th>
<th>Biological products</th>
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<tbody>
<tr>
<td><strong>Part I- General information</strong></td>
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<tr>
<td>• name, address, authorised manufacturing activities, lists of products &amp; its APIs manufactured;</td>
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<tr>
<td>• any production of biological and highly sensitising, high activity, toxic or hazardous, veterinary or non-medicinal products, and the prevention of cross-contamination.</td>
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<tr>
<td>• Dosage form(s) and process operation(s) already qualified, &amp; be registered in this application.</td>
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<tr>
<td><strong>Part II – GMP Compliance (64 indicators)</strong></td>
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<tr>
<td>1. Quality Management System (6)</td>
<td>Replaced by</td>
<td>Reduced by</td>
<td>As same as the full package</td>
</tr>
<tr>
<td></td>
<td>• the most recent inspection report issued by its Regulatory Authority, &amp; the CAPAs (must be applicable to the scope of the application)</td>
<td>• the most recent inspection report</td>
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<tr>
<td></td>
<td>• List of inspection in past 3 years.</td>
<td>• List of inspection in past 3 years.</td>
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<tr>
<td>2. Personnel (5)</td>
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<td>3. Premises and Equipment (17)</td>
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<td>4. Documentation (2)</td>
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<td>5. Production (8)</td>
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<td>6. Quality Control (5)</td>
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<td>7. Outsourcing Activities (3)</td>
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<tr>
<td>8. Complaints, Returned Products and Product Recall (3)</td>
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<td>9. Self Inspection (1)</td>
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<tr>
<td>10. Distribution (1)</td>
<td></td>
<td></td>
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<tr>
<td>11. Qualification &amp; Validation (13)</td>
<td>Replaced by:</td>
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</tr>
<tr>
<td></td>
<td>• CPP issued by reference countries (US, UK, DE, FR, JP, BE, CA, AU, SE, EMA)</td>
<td>• Summary report of Validation &amp; Declaration of Site</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Summary report of Validation &amp; Declaration of Site</td>
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<td>2017/4/5</td>
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Reduction to 34 indicators focus on the requirements of Annex 1 of PIC/S GMP Guide.
Application requirements

Renewal review

- Request Documentation
  - Application form
  - Site Master File
  - Summary reports of latest Product Quality Review
  - the most recent inspection report issued by its Regulatory Authority, & the CAPAs must be applicable to the scope of the application
  - Any major changes in the past 2 years
  - The periodical evaluation result of the effectiveness for the set procedures to prevent cross-contamination

- Application Fee: NT$120,000 per application

For sites located in PIC/S member countries, the inspection report may be replaced by the current GMP Certificate
GMP Compliance of Medicinal Products in Taiwan

Outline

Moving Forward

Consumer Protection
Good Drug Accessibility
Pharmaceutical Industry Development

Smart Administration

Leverage

Limited resources
Smart Administration

Leverage the resources & Work together

- Strengthen International Cooperation via PIC/S
- Networking & Trust building with other Regulatory Authority
- Conduct Joint inspection
- Agreement of Mutual Recognition of inspection result

- Keep upgrading & harmonizing the regulation system internationally

2017/4/5
Thank You for Your Attention

For more information: Website is at http://www.fda.gov.tw