Current GMP compliance assessment process and future possibility in Korea
Contents

I  Ministry of Food and Drug Safety
   - History
   - Organization

II  GMP Regulatory System in Korea
    - GMP Regulations
    - GMP System

III International Cooperation
Ministry of Food and Drug Safety
Ministry of Food and Drug Safety _History

1996
- Foundation of the Korea Food and Drug Safety Headquarters and 6 regional offices under the Ministry of Health and Welfare

1998
- Inauguration of the Korea Food and Drug Administration

2010
- Relocation of KFDA headquarters to Osong in Chungbuk from Seoul

2013
- Elevation to Ministry under the Prime Minister
  - 6 regional offices of KFDA (Regional FDAs: Seoul, Gyeongin, Daejeon, Daegu, Busan, Gwangju)
II GMP Regulatory system in Korea

- GMP Regulations
- GMP System
History of GMP regulations

- **1994**
  - Mandatory implementation of GMP for medicinal products

- **2002**
  - Mandatory implementation of GMP for Active Pharmaceutical Ingredients (APIs)

- **2008**
  - Introduction of pre-approval GMP inspection for medicinal products
  - Advancement of regulations through introducing Validation, Qualification, and Product quality review

- **2014~2015**
  - Harmonization with the PIC/S GMP guides
    (Ordinance of Prime Minister, July 2015/ MFDS Notification, July 2015 and January 2017)
  - Introduction of the system for renewing a Certificate of GMP Compliance of a Manufacturer
    (Ordinance of Prime Minister, October 2014)
GMP Regulations

- **Act**
  - Pharmaceutical Affairs Act

- **Presidential Decree**
  - Enforcement Decree on the Standards of Facilities of Manufacturers and Importers of Medicinal Products, etc.

- **Ordinance of Prime Minister**
  - Regulation on Safety of Medicinal Products, etc.
  - Enforcement Regulation of the Enforcement Decree on the Standards of Facilities of Manufacturers and Importers of Medicinal Products, etc.

- **MFDS Notification**
  - Regulation on Pharmaceutical GMP
GMP Standards equivalent to PIC/S’s

Regulation on Safety of Medicinal Products, etc.
(Ordinance of Prime Minister)

- [Annex 1] Medicinal Products GMP
- [Annex 1–2] API GMP
- [Annex 2] Biopharmaceutical Products GMP
- [Annex 3] Radiopharmaceuticals GMP
- [Annex 3–2] Medicinal Gases GMP
- [Annex 3–3] Investigational Medicinal Products GMP

Regulation on Pharmaceutical GMP
(MFDS Notification)

- Annex 1: Manufacture of Sterile Medicinal Products
- Annex 2: Manufacture of Biological Medicinal Substances and Products for Human Use
- Annex 3: Manufacture of Radiopharmaceuticals
- Annex 4: Manufacture of Medicinal Gases
- Annex 5: Manufacture of Herbal Medicinal Products
- Annex 6: Sampling of Starting and Packaging Materials
- Annex 7: Manufacture of Liquids, Creams and Ointments
- Annex 8: Manufacture of Pressurised Metered Dose Aerosol Preparations for Inhalation
- Annex 9: Computerised Systems
- Annex 10: Use of Ionising Radiation in the Manufacture of Medicinal Products
- Annex 11: Manufacture of Investigational Medicinal Products
- Annex 12: Manufacture of Medicinal Products Derived from Human Blood or Plasma
- Annex 13: Qualification and Validation
- Annex 14: Parametric Release
- Annex 15: GMP Guide for Active Pharmaceutical Ingredients
- Annex 16: Reference and Retention Samples
- Annex 17: GMP Guide for Final Products
Pre-approval GMP assessment is carried out by dosage form (domestic manufacturing site) and by medicinal product for marketing authorization (domestic or overseas manufacturing sites) requiring special attention to new drugs, biological products, sterile products, etc.

Periodic GMP assessment is carried out at least once every three years (approx.) in principle, and a Certificate of GMP compliance of a manufacturer to each domestic manufacturing site is issued.

GMP surveillance for domestic or overseas manufacturing sites
Process of pre-approval GMP assessment

- Manufacturer’s License or Registration of Importer
- Marketing Authorization for Medicinal products or APIs

GMP assessment

- Approval, Registration, DMF
- Marketing/Sale

- Period of GMP Assessment
  - (MP: 90 days, DMF: 120 days)
    - Except the period of document supplementation and discussion on inspection schedule

- Department of GMP Assessment
  - MFDS: Imported products, Biopharmaceuticals, New drugs, etc.
  - 6 Regional FDAs: Manufacturing products, Generic drugs, etc.
Pre-Approval GMP Assessment

On-site inspection may be substituted with Desk-top assessment, taking account of the results of previous GMP inspections to the site, the type of the product or manufacturing process to be audited, etc.

1. Pharmaceuticals

<table>
<thead>
<tr>
<th>Classification</th>
<th>Criteria</th>
<th>Effective Periods of Previous GMP inspection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sterile</td>
<td>Aseptic manipulation</td>
<td>Manufacturing site</td>
</tr>
<tr>
<td></td>
<td>Terminal Sterilization</td>
<td>Manufacturing site</td>
</tr>
<tr>
<td>Non-sterile</td>
<td></td>
<td>Manufacturing site</td>
</tr>
</tbody>
</table>

2. Biopharmaceuticals

<table>
<thead>
<tr>
<th>Classification</th>
<th>Criteria</th>
<th>Effective Periods of Previous GMP inspection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Process</td>
<td>Aseptic manipulation</td>
<td>Manufacturing site</td>
</tr>
<tr>
<td></td>
<td>Others</td>
<td>Manufacturing site</td>
</tr>
</tbody>
</table>
# Pre-Approval GMP Assessment

Some of the required GMP dossier for marketing authorization of medicinal products such as computerized system validation, utility and water system validation, and SOP (documentation, Warehousing, Personnel hygiene, Personnel Training, etc) may be substituted with the **Site Master Files** (only if the relevant contents are included) or **GMP inspection reports by the competent authority of a PIC/S’s member country** which support the valid GMP certificates as of the date of application.

* Reference document: Guidelines on Pre-Approval GMP Inspection of Medicinal Products, etc. (Dec. 2016)

## GMP dossier for marketing authorization

<table>
<thead>
<tr>
<th>Category</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Drawing of the manufacturing site</td>
<td>Each working area, laboratory, storage, and other ancillary facilities (utility, water, etc.) required for manufacturing process should be indicated.</td>
</tr>
</tbody>
</table>
| 2. Documents on the facilities of each working area | A) A drawing of the working area with cleanliness grade, pressure differences between working areas, and human/physical flow line indicated  
B) Details of machinery/equipment used in manufacturing/testing and equipment layout  
C) Diagrams of AHU, compressed air, and water treatment system |
| 3. Documents on the facilities and environment management | A) Water control status  
B) Control status of automated system, etc.  
C) Cleanliness grade control status |
| 4. Documents on GMP organization and quality control (assurance) system | |
| 5. Regulations on documentation and list of documents | |
| 6. Product Master File and a copy of batch production records/quality control records | |
| 7. Validation data | Qualification and Validation (Process, Analysis Method, Utility and Water, Computerized System, and Cleaning) |
Post – Approval GMP assessment (Periodic Inspection)

- Overall renewal of GMP Compliance by dosage form or manufacturing method (API) for Domestic manufacturing sites.
  - With an introduction of the system to issue a Certificate of GMP Compliance of a Manufacturer to each Manufacturing site in Oct 2014, periodic GMP evaluation has been carried out.
  - Periodic GMP evaluation has been carried out on dosage form of all manufacturing sites at least once every three years approximately in principle.

- In 2017, Law related registration of foreign manufacturing sites will be established.
  - Until now, GMP Surveillance has been carried out for some of overseas manufacturing sites based on risk assessment.
  - Going forward, periodic GMP evaluation will be also carried out for overseas manufacturing sites based on risk assessment.
GMP Surveillance

For-cause (triggered) Inspection is conducted:

• According to the MFDS order arising from any accusation, petition, and report, and other information;

• In the cases of detecting illegal online distribution of medicinal products, which are required to receive a direct inspection; and

• When cooperation with other agencies such as the Public Prosecutor’s Office, Police, or other related organizations is required.
International Cooperation
Accession of MFDS to the PIC/S

Officially recognized as a PIC/S Participating Authority from July 2014

- Application accepted at the 38th PIC/S Committee Meeting in Rome (Italy) 16 May 2014
- MFDS invited as a PA within 2 years only which was earlier than generally expected since the application in April 2012 (Only 2-year process period actually taken compared to 6 years of time limit)

Press release: PIC/S meetings in Rome (Italy)

From 15 to 21 May 2014, the meetings of the PIC/S Committee, the PIC/S Executive Bureau and the PIC/S Expert Circle on Active Pharmaceutical Ingredients (APIs) took place in Rome (Italy).

PIC/S Committee Meeting

The PIC/S Committee, preceded by the PIC/S Executive Bureau meeting, met on 15-16 May 2014 under the chairmanship of Dr Joey Gauthier (South Africa’s Medicines Control Council / MDC). The Chairperson said that it was a particular honour for Africa to chair PIC/S for the first time in history. The meeting was attended by 35 out of 44 PIC/S Participating Authorities (PA) as well as by a number of Applicants, Pre-Applicants and Associated Partners. For the list of Members and Partners (http://picsscheme.org/members.php)

South Korea’s Accession to PIC/S

South Korea applied for membership in April 2012 through the Korean Food & Drug Administration (KFDA). On 23 March 2013, the status of KFDA was elevated to ministerial level and the name was changed to "Ministry of Food and Drug Safety" (MFDS). A paper assessment was conducted in view of the accession of MFDS to PIC/S, followed by a pre-audit visit on 17-18 December 2013 and an on-site visit on 13-17 January 2014. Five PIC/S experts took part in the final audit team. At the Committee meeting of 15-16 May 2014, the audit team recommended to the Committee to accept the PIC/S membership application of South Korea. The Director General of the Pharmaceutical Safety Bureau of MFDS, Mr. Mokyoung Yoo, welcomed the accession of MFDS and thanked PIC/S for their access and the audit team for their help and support. He stated that since the introduction of GMP to Korea nearly 40 years ago, in 1977, Korean GMP has been continuously revised and updated to conform to international GMP standards. The PIC/S accession procedure had provided the opportunity for further revisions which would be completed by June 2014.
International Cooperation

Approval of accession to ICH (November 2016)

Membership / About ICH / Current Members and Observers

As of November 2016, the ICH Association comprises the following Members and Observers:

Founding Regulatory Members
- The European Commission (EC)
- The US Food and Drug Administration (FDA)
- The Ministry of Health, Labour and Welfare of Japan (MHLW) also represented by the Pharmaceutical and Medical Devices Agency (PMDA)

Founding Industry Members
- The European Federation of Pharmaceutical Industries and Associations (EFPIA)
- The Japan Pharmaceutical Manufacturers Association (JPMA)
- The Pharmaceutical Research and Manufacturers of America (PhRMA)

Standing Regulatory Members
- The Health Canada
- The Swedish Medic

Regulatory Members
- The Agência Nacional de Vigilância Sanitária (ANVISA, Brazil)
- The Ministry of Food and Drug Safety (MFDS, South Korea)
WHO Collaborating Center

- The National Institute of Food and Drug Safety Evaluation is designated as a 5th WHO Collaborating Center for Standardization and Evaluation of Biologicals. (Jan 2011)
  ** Following the US(FDA/CBER), the UK(NIBSC), Japan(NIID), and Australia(TGA)

GLO/Global Learning Opportunity)/GMP Training

1. Trainings of GMP inspectors from 22 foreign countries including the Indonesia, Malaysia, Thailand, etc. have been conducted 10 times since 2006
2. Attendance at WHO Guidelines Development Meetings (7 times in 2013)
3. Held the Meeting on 「building greater regulatory capacity of vaccine in the western pacific region」(2013)

WHO/ GLO Learning Centre

- The National Institute of Food and Drug Safety Evaluation has been accredited as that to conduct the “Lot Release/Laboratory Access” course for the period of Jan 2016 to Dec 2017.
  - First Training of the persons in charge of “Lot Release/Laboratory Access” from 5 foreign countries including the Malaysia, Saudi Arabia, Mongol, Sudan, etc. have been conducted for the period of 31 Oct 2016 to 9 Nov 2016.
APEC Harmonization Center (AHC)

The AHC was established at the MFDS to provide a platform to address and solve priority concerns of APEC member economies on regulatory convergence. (June 2009)

- Global Supply Chain Integrity (U.S.)
- Cellular Therapies (Singapore)
- Pharmacovigilance & Medical Device Vigilance (Korea)
- Biotherapeutics (Korea)
- Multi-Regional Clinical Trials & GCP Inspections (Japan, Thailand)
- Good Registration Management (Chinese Taipei, Japan)

AHC Organization

Priority Work Area

Major activities

1. APEC Training: Workshops & CoE (Center of Excellence) Pilots & On-line Training

   - GMP Validation Workshop ('09), QbD Workshop ('11) and sessions on GMP at other AHC Workshops on pharmaceuticals, biotherapeutics and medical device.
   - 33 trainings in total, about 8,500 participants from 45 economies

2. Reports of Pharmaceutical Regulatory Framework: Drug Approval system

   - A total of 11 finalized guidelines of APEC economies (Korea, Chinese Taipei, Hong Kong China, Japan, Singapore, USA, Australia, Chile, Malaysia, New Zealand, The Philippines)
THANK YOU

Ministry of Food and Drug Safety

Pharmaceutical Quality Division