Current GMP compliance assessment process and future possibility in Korea

5 May 2017

Ministry of Food and Drug Safety

Contents

I 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

KFDA 식품의약품안전청

2010

▸ Relocation of KFDA headquarters to Osong in Chungbuk from Seoul

KFDA 식품의약품안전청 Korea Food & Drug Administration

2013

▸ **Elevation to Ministry under the Prime Minister**

- 6 regional offices of KFDA(Regional FDAs : Seoul, Gyeongin, Daejeon, Daegu, Busan, Gwangju)

Ministry of Food and Drug Safety

Ministry of Food and Drug Safety _Organization

Ministry of Food and Drug Safety

- Minister
  - Spokesperson
  - Vice Minister
    - Criminal Investigation Office
    - Audit and Inspection Office
    - General Affairs Division
    - Director General for Planning and Coordination
    - Customer Risk Prevention Bureau
    - Food Safety Policy Bureau
    - Imported Food Safety Policy Bureau
    - Food Customer Safety Bureau
    - Pharmaceutical Safety Bureau
      - Pharmaceutical Quality Division
    - Biopharmaceuticals and Herbal medicine Bureau
      - Biopharmaceuticals Quality Management Division
    - Medical Device Safety Bureau

- National Institute of Food and Drug Safety Evaluation
  - Food Safety Evaluation Department
  - Drug Evaluation Department
  - Biopharmaceuticals and Herbal Medicine Evaluation Department
  - Medical Device Evaluation Department
  - Pharmaceutical and Medical Device Research Department
  - Toxicological Evaluation and Research Department

- 6 Regional Offices of FDS
  - Seoul Regional FDA
  - Busan Regional FDA
  - Gyeongin Regional FDA
  - Gwangju Regional FDA
  - Daegu Regional FDA
  - Daejeon Regional FDA

Ministry of Food and Drug Safety

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)

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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

PIC/S GMP Regulation and Annex

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 MEDICINALSUBSTANCES 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 DOSEAEROSOL PREPARATIONS FOR INHALATION
Annex 9	COMPUTERISED SYSTEMS
Annex 10	USE OF IONISING RADIATION IN THE MANUFACTUREOF MEDICINAL PRODUCTS
Annex 11	MANUFACTURE OF INVESTIGATIONALMEDICINAL PRODUCTS
Annex 12	MANUFACTURE OF MEDICINAL PRODUCTS DERIVEDFROM 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

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GMP system

Pre - Approval

Post - Approval

Approval

- **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.

Quality control

- **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

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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

Preriod 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

Classification		Criteria	Effective Periods of Previous GMP inspection
Sterile	Aseptic manipulation	Manufacturing site	3 year
	Terminal Sterilization	Manufacturing site	3 year
Non- sterile		Manufacturing site	5 year

2 Biopharmaceuticals

Classification		Criteria	Effective Periods of Previous GMP inspection
Process	Aseptic manipulation	Manufacturing site	3 year
	Others	Manufacturing site	3 year

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

Category	Details
1. Drawing of the manufacturing site	Each working area, laboratory, storage, and other ancillary facilities (utility, water, etc.) required for manufacturing process should be indicated.
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)

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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 oversea manufacturing sites based on risk assessment.
  - Going forward, periodic GMP evaluation will be also carried out for oversea manufacturing sites based on risk assessment.

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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.

III International Cooperation

Accession of MFDS to the PIC/S

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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)

PIC/S
PHARMACEUTICAL INSPECTION CO-OPERATION SCHEME

www.picscheme.org May 2014

Leading the international development, implementation and maintenance of harmonised GMP standards and quality systems of inspectorates in the field of medicinal products

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)

Dr Joey Gouws
PIC/S Chairperson

PIC/S Committee Meeting

The PIC/S Committee, preceded by the PIC/S Executive Bureau meeting, met on 15-16 May 2014 under the chairpersonship of Dr Joey Gouws (South Africa's Medicines Control Council / MCC). 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://picscheme.org/members.php)

Japan and South Korea to Join PIC/S

The Committee invited the competent authorities of Japan and South Korea to join PIC/S as of 1 July 2014. Japan will become the 45th PIC/S Participating Authority and will be represented by the Pharmaceutical & Food Safety Bureau of the Ministry of Health, Labour & Welfare (MHLW), the Pharmaceutical and Medical Devices Agency (PMDA) and the GMP Inspectorates of Japan's Prefectures. South Korea's Ministry of Food and Drug Safety (MFDS) will become the 46th PIC/S Participating Authority.

PIC/S
PHARMACEUTICAL INSPECTION CO-OPERATION SCHEME

www.picscheme.org May 2014

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. MooYoung Yoo, welcomed the accession of MFDS and thanked PIC/S for their accession 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 had 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

Ministry of Food and Drug Safety

Approval of accession to ICH (November 2016)

ICH
harmonisation for better health

About ICH | Work Products | Meetings | Training | Newsroom

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 Pharmaceuticals 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 Swissmedic

Regulatory Members

The Agência Nacional de Vigilância Sanitária (ANVISA, Brazil)
The Ministry of Food and Drug Safety (MFDS, South Korea)

International Cooperation

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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)

1. GLO(Global Learning Opportunity)/GMP Training

   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, Saudiarabia, Mongol, Sudan, etc. have been conducted for the period of 31 Oct 2016 to 9 Nov 2016.


World Health Organization

ACCREDITATION

This is to certify that

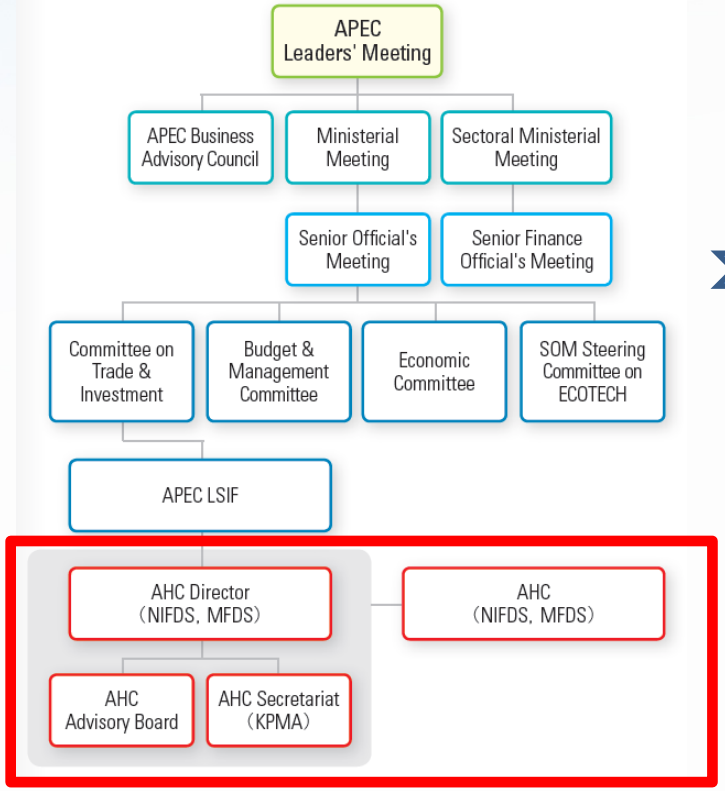
National Institute of Food and Drug Safety Evaluation

has been accredited as a WHO/Global Learning Opportunities learning centre to conduct the "Lot Release/Laboratory Access" course for the period of 1 January 2016 to 31 December 2017

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)

AHC Organization



Cooperation with APEC RHSC Priority Work Area

Priority Work Area

- 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)

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

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Pharmaceutical Quality Division