Preparation for PIC/S accession
Challenges and Prospects

April 13, 2012 (Friday)
Pharmaceuticals and Medical Devices Agency
(PMDA)
Office of GMP/QMS Inspection

Shingou SAKURAI, Ph.D
PIC/S加盟の必要性
Why is PIC/S accession necessary?

1. 使用者の保護（国民の安心・安全の確保）
   Due regard to public health
2. リソースの有効活用
   Utilization of resources
3. 日本の製薬業界の地位確保・サポート
   Secure the position of Japanese pharmaceutical Products
**GMP 調査体制**

GMP Inspection System

**Pharmaceutical and Food Safety Bureau, MHLW**
(manufacturing license, marketing license, marketing authorization, administrative order, pharmacovigilance, license withdrawal, seizure, penalty, etc.)

PMDA is partially vested with authority of MHLW (assessment, GMP inspection, information gathering)

Prefectures are vested with part of MHLW’s authority to have local autonomy.

**医薬品医療機器総合機構**

PMDA

**47都道府県**

Prefectures

**Inspectorate**

**47 Inspectoratorates**
### Inspection areas

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Domestic sites</th>
<th>Foreign sites</th>
</tr>
</thead>
<tbody>
<tr>
<td>New drugs, Biologics, Radiopharmaceuticals, etc.</td>
<td>PMDA</td>
<td>PMDA</td>
</tr>
<tr>
<td>Other drugs</td>
<td>Prefectures</td>
<td>PMDA</td>
</tr>
</tbody>
</table>

### Table: Number of GMP inspectors

<table>
<thead>
<tr>
<th></th>
<th>Mainly GMP</th>
<th>Mainly other operations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prefectures</td>
<td>116</td>
<td>271</td>
</tr>
<tr>
<td>PMDA</td>
<td>24</td>
<td>2</td>
</tr>
</tbody>
</table>

As of December, 2011
PMDA: Risk-based approach in selecting on-site inspection or desk-top inspection

Information
- Attached information at GMP application
  1. Information of the product (Attachment 1)
  2. Information of the site
     Inspections history (Attachment 2: domestic sites)
     (Attachment 3: foreign sites)
- Past inspection (Site profile)
  1. Rank of the site
  2. Each sub-system

Risk analysis
- Items to be evaluated at risk analysis
  - Kinds of product
  - Manufacturing process
  - Dosage form
  - Inspection history by foreign inspectorates
  - Past GMP non-compliance
  - Past recall history
  - Inspection by PMDA
  - Site information (Previous information)
  - Others

Data Accumulation

Selection sheet

Inspection
- On-site inspection
- Desk-top Inspection
Global Harmonization of GMP

GMPの国際整合化に向けての体制

Director-general, Pharmaceuticals and Food Safety Bureau of MHLW

GMP調査体制強化検討会
GMP Inspection System Review Committee
(Established in August, 2010)

●課題の抽出
To find issues to be attended
Study group for harmonization of GMP inspection method
(2009～2011)

●GMP調査機関の連携
Enhance cooperation among inspectorates
GMP Inspectorate Committee
(Established in July 2011)
Continue its activities

●GMPガイドラインの整合性
Harmonization of GMP Guidelines
Comparison and analysis of guidelines (2010~2011)

Study group for harmonization of GMP guidelines on pharmaceuticals and excipients (2011~)
1. Improvement of quality system at GMP inspectorates and enhance cooperation

2. Ensure qualification of each inspector

3. Ensure equivalence between Japanese GMP related regulations and PIC/S GMP Guide
Establishment of GMP Inspectorate Committee

- GMP Inspectorate Committee
  - (representatives from each block, PMDA, MHLW)

- MHLW
  - Committee to investigate harmonization

- Coordination is basically made within each block: training, internal audit, inspection support, etc.
  - Support from trainers at PMDA is available

- Secretariat in PMDA
  - Coordination

- Hokkaido and Tohoku block
  - (Pharmaceutical administration in each block)

- 7 blocks in total
GMP調査当局会議の活動
Activities of GMP Inspectorate Committee

1. 品質システムの共通化
Common quality system among inspectorates (Revision of SOP, Internal audit, etc.)

2. GMPガイドラインの継続的なアップデート
Continuous updates on GMP Guidelines

3. 継続的なトレーニングの立案、教育資料提供
Development of training plan, sharing of the training materials

4. 国際整合性に関する情報入手と提供
Information acquisition and information sharing on global harmonization

5. 全体会議の開催と密接な連携・情報交換
Holding of meeting among all the blocks for communication and information exchange

6. 指導内容に係る調査権者と業界双方の受付と解決
Consultation for inspectorates and industries
Recent revision of the Inspection Manual

Revision of Inspection Manual
(Notification from the director of Compliance and Narcotics Division, Pharmaceuticals and Food Safety Bureau, MHLW
February 16, 2012)

48 inspection authorities to improve the quality of GMP inspection in Japan

<Main revision points>

- Establishment of Quality Manual to create a common quality system at each inspectorate
- Establishment of qualifications of inspectors to ensure inspection quality
- Establishment of GMP Inspectorate Committee to maintain quality management systems at each inspectorate and facilitate communication among inspectorates
- Qualification of official medicines control laboratory for the analysis of samples
PMDAの品質マネジメントシステム

Quality management system

The first layer
- Quality manual

The second layer
- Common SOPs

The third layer
- SOPs of PMDA

Audit Check Points
- Solid products, Sterile products, APIs, Bio-derived product, Blood-center, Radio-pharmaceuticals, Vaccines, Plasma-derivatives, Contract Labs
進めている当局間の連携  
Enhanced cooperation of inspectorates

◆ 国内の４８調査権者間  
Cooperation among 48 inspectorates

○当局会議の開催（年3-4回）
  
  GMP Inspectorate Committee meeting (3-4 times a year)

○情報交換（教育資料、手順書等）
  
  Information Sharing (Training tool, SOPs etc.)

○模擬査察、自己点検の実施
  
  Mock inspection by each block, Internal Audit, etc.

◆ グローバルな連携  
Cooperation with other countries

○EudraGMPの設置
  
  Establishment of link with EudraGMP
Training program scheduled in this year

- Training program within each block
- Mock inspection within each block (several times/year in each block)
- Mock inspection sponsored by MHLW
- Training by NIPH ※ (in Wako City)
- Training by PMDA (3 days x 4 times/year, open to prefecture inspectors)
- On the job training ※ ※ (PMDA: 2 months × 2 times)

※ NIPH: National Institute of Public Health
※ ※ Training of manufacturing control and QC at a manufacturing site.
Link with EudraGMP

• GMP related community database in EU
• 100 NCAs (National Competent Authority) in EU countries (27 countries) and MRA partners with EU (8 countries) participated
• Input items: 「GMP Compliance (manufacturing sites for which GMP certificate are issued)」, and 「Manufacturing & Importation Authorization (corresponding to drug manufacturing license in Japan)」
• Information of manufacturing sites outside EU is included including US, India, China, and Japan. Non compliance information is included.
• Host computer is located in EMA main office and each participating authority connected through EudraNet can access to the system from their terminal
Situation of attendance to the PIC/S meetings

Outline of the situation of past two years (open circle indicate plan)

● 26—28 May, 2010  PIC/S Expert Circle on APIs 3rd meeting (Ireland)
● 9 September, 2010  PIC/S Expert Circle on Quality Risk Management (Poland)
● 28 September—1 October, 2010  PIC/S Expert Circle on Human Blood, Tissue and cells (France)
● 10—12 November, 2010  PIC/S Annual Seminar (Malaysia)
● 31 May—1 June, 2011  PIC/S 40th anniversary (Swiss)
● 26—30 September, 2011  PIC/S Expert Circle on Human Blood, Tissue and cells (Estonia)
● 12—14 October, 2011  PIC/S Expert Circle on API (Singapore)
● 9—11 November, 2011  PIC/S Annual Seminar (South Africa)
○ 7—8 May, 2012  PIC/S Committee, 9—10 PDA-PIC/S Workshop (Swiss)
○ 17—19 September, 2012  PIC/S Expert Circle on API (US-FDA)
○ 1—2 October, 2012  PIC/S Committee, 3—5  PIC/S Seminar (Kyiv)
○ 15—19 October 2012  PIC/S Expert Circle on Human Blood, Tissue and cells (Singapore)
Application to PIC/S by Japan

◆ Application letter, Questionair, Audit Check List and 12 supporting documents were sent to PIC/S secretariat on March 9, 2012
◆ The secretariat informed this to all the participating countries on the same day.
◆ Rapporteur will be appointed during the PIC/S committee meeting on 7-8 May, 2012, and assessment for accession will be started.