KGMP의 현재와 미래
식품의약품안전청의약품평가부
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Pharmaceutical Headquarter
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KGMP Overview
Guarantee on Policy Integrity

Elevating the Standard of Living

Scientific Progress

Harmonized GMP Rules
Constitution of Institutional Base for Quality Control

<QPolicy Quality Management Manual>
- Introduce Validation System
- Introduce International Standard

Quality Management System
GMP Steering Committee

Enhance Health Concept

Quality Assurance

Guarantee on Policy Integrity • Public Satisfaction
Milestone of KGMP

- KGMP was required by the law (mandatory)
- Established & Notified KGMP
- Recommended by WHO
- Established KGMP for Biologics

- 1969
- 1977
- 1992
- 2000
TOTAL : 359

Drug Product : 232

Drug Substance : 127

KGMP companies (August 2007)
Current Status

No Validation

Lack of GMP rules for herbal medicine

Lack of GMP rules for clinical trial medicine

Optional GMP education for manufacturer (Not mandatory)

GMP management by formulation (Not by product)

Authorization of GMP facility & operation system by document review & inspection

Lack of GMP rules for clinical trial medicine
<table>
<thead>
<tr>
<th></th>
<th>WHO, PIC/S</th>
<th>EU, Japan, Singapore</th>
<th>USA</th>
<th>India</th>
<th>Korea</th>
</tr>
</thead>
<tbody>
<tr>
<td>Validation</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>X</td>
</tr>
<tr>
<td>Automatic Equipment</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>X</td>
</tr>
<tr>
<td>Control</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Qualification</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>X</td>
</tr>
<tr>
<td>Out Of Specification</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>X</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Change Control</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>X</td>
</tr>
<tr>
<td>Annual Product</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Review</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Self Inspection</td>
<td>O</td>
<td>O</td>
<td>X</td>
<td>O</td>
<td>X</td>
</tr>
<tr>
<td>Contamination Control</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>Stability</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
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</tbody>
</table>
Considerable Issues
Backwardness of pharmaceutical Industry

**Issue Category**

- **Industry**
  - Small market
  - Small scale
  - Bottleneck of Accession to PIC/S & MRA planning
  - Lack of advanced GMP rules
  - Lack of development on product to profit items
  - Be short of experts for new drug development

- **Policy**
  - Lack of education for manufacturer
  - No product-based pre-approval GMP
  - No validation
  - Lack of herbal & IND (clinical) GMP rules

- **Technology**
  - Too many items in a company
  - Bottleneck of M&A
  - Lack of distribution system

**Why**
Lack of Advanced GMP Rules
- Formulation based GMP management
- No validation
- Low level GMP
- Lack of GMP rules for herbal & clinical trial medicine

Insufficient GMP Inspection System
- Lack of the wholly responsible structure for Inspection
- Be short of Professional inspectors

Issues

Solutions
- Adoption of product-based pre-approval GMP System
- Phase in Validation
- Harmonized with international GMP rules
- Establish GMP rules for herbal & clinical trial medicine
- Accession to PIC/S
- Enhancement of education for inspectors & authorized manufacturers
- Build a GMP inspection division
Revision of KGMP Regulation
Conduct study on the advanced model of KGMP for assuring International competition

September 2007
- Revision of Enforcement Ordinance of Pharmaceutical Affair Act

October 2006
- Notify the pharmaceutical industries regarding KGMP international harmonization through civil affair explanation meetings

July 2006
- The Presidential Commission Body decided to push ahead KGMP international harmonization

2003 ~ 2005
- Conduct study on the advanced model of KGMP for assuring International competition
1. Adoption of product based pre-approval KGMP
2. Mandatory validation by law
3. Adoption of change control
4. Adoption of annual product review
5. Control on Out of specification / Deviation
Pre-approval KGMP
(Product-based)

- Drug Substance
- Quasi-Drug (Oral Solid & Liquid Preparation)
- Non-prescription Drug
- Prescription Drug
- New Drug

On-going BE products since July 2006
: as a Study conducted by
The Presidential Commission on Healthcare Industry Innovation
<table>
<thead>
<tr>
<th>General-KGMP</th>
<th>Authorized manufacturer</th>
<th>IND-KGMP</th>
<th>Pharmacist or Non-pharmacist</th>
</tr>
</thead>
<tbody>
<tr>
<td>pharmacist</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Limited to Contract Unit</td>
<td>Range of quality unit</td>
<td>Not Limited</td>
<td></td>
</tr>
<tr>
<td>Mandatory</td>
<td>Validation</td>
<td></td>
<td>Optional</td>
</tr>
<tr>
<td>Mandatory</td>
<td>Qualification</td>
<td></td>
<td>Optional</td>
</tr>
<tr>
<td>3 Lot</td>
<td>Quantity</td>
<td></td>
<td>Not available</td>
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</tbody>
</table>
### KGMP Rules for Herbal Medicine

<table>
<thead>
<tr>
<th>General-KGMP</th>
<th>Herbal-KGMP</th>
</tr>
</thead>
<tbody>
<tr>
<td>A, B, C, ...</td>
<td>A, B, C, ...</td>
</tr>
<tr>
<td>Contamination control</td>
<td>Optional</td>
</tr>
<tr>
<td>Validation</td>
<td>Optional</td>
</tr>
<tr>
<td>Qualification</td>
<td>Optional</td>
</tr>
<tr>
<td>Annual Product Review</td>
<td>Optional</td>
</tr>
<tr>
<td>Compatibility</td>
<td>Optional</td>
</tr>
</tbody>
</table>

- Set up Facility Standard (Preprocessing/Storage Area etc) for Herbal Medicinal Materials
- Set up Manufacture & QC Standard for Extract and Powders of Herbal Medicinal Product
All who first desired to become an authorized manufacturer for KFDA’s approval or declaration (including any change of the manufacturer)

- Should complete the education designated by KFDA
- More than 16 hrs biennially

Anyone who have completed the same education designated by KFDA within 2 years
# GMP Review Range

in case of site changes within the same location of the facility

<table>
<thead>
<tr>
<th>Change</th>
<th>GMP Review</th>
<th>Document</th>
<th>Class</th>
</tr>
</thead>
<tbody>
<tr>
<td>New Building</td>
<td>O</td>
<td>GMP Application</td>
<td>License</td>
</tr>
<tr>
<td>Extension / Remodeling</td>
<td>O</td>
<td>Change Control Document</td>
<td>Filing Report</td>
</tr>
<tr>
<td>Air/Water System Change within the existing facility</td>
<td>O</td>
<td>Change Control Document</td>
<td>Filing Report</td>
</tr>
<tr>
<td>Transfer of major instrument/equipment, workroom</td>
<td>O</td>
<td>Change Control Document</td>
<td>Filing Report</td>
</tr>
<tr>
<td>Change of environmental conditions</td>
<td>X</td>
<td>-</td>
<td>Filing Report</td>
</tr>
<tr>
<td>Same environmental conditions</td>
<td>X</td>
<td>Change Control Document</td>
<td>Filing Report</td>
</tr>
<tr>
<td>Storage/Laboratory change</td>
<td>X</td>
<td>Change Control Document</td>
<td>Filing Report</td>
</tr>
</tbody>
</table>
Reinforcement on herbal medicine

- Quality control on manufacturing the herbal powders & extracts in separated working area and their batch records
- Storage of the records on chemicals and fumigants used for the prevention of insects and mold proliferation on the crude herbal medicine
- Obligation of detail quality control standards on the crude herbal medicine and control on the species and specimen of the herbal medicine
- Selection, discrimination, and cleaning of the herbal medicine should be proceeded at the separated preparation working area and stored in a separated storage facility
Main Reinforcement

- Sanitation by performing regular medical examination of the personnel and retaining the records of the cleaning, and the use record of the equipment and facilities

- Response to complaints such as investigating the content, finding the reason and corrective actions, etc.

- Mandatory stability test for the first three commercial batches (long-term storage)

- Review process of intermediate inspector beyond the person who performed the test and the authorized person in the quality control
Main Reinforcement

- Separation of the facility which manufacture the medicine including cephalosporin & cytotoxic anticancer materials

- In case of contract manufacture or quality control, the contract giver should perform self audit on the contract accepter sites

- Recommendation on the verification of suitability of all the testing methods in quality control

- Perform regular internal audits by the manufacturer in order to verify the manufacture and quality control
Main Reinforcement

Self audit by the manufacturing and quality control supervisor on the critical deviations or the failure in the standards of the manufacturing and quality control

Clarify the standard of detailed general laboratory facility

Quality management on the verification of the manufacturing and quality control of the annual manufactured products, and cause of rejected materials etc.

Detailed storage sample rules of the retaining samples for two or more tests for each unit of batch or lot number
Perspective
Future Activities

- Establishment of detailed education program for manufacturers
- Establishment of GMP inspection guideline
- Accession to PIC/S
- Better coordination between pre-market review and inspection and surveillance programs
Comprehensive Understanding of Manufacturing Process and Product Knowledge

Facilitation of Science-based Quality Assessment

Internationally Harmonized Quality System

Improvement of Pharmaceutical Quality System

Comply with KGMP

Risk-based Approaches

Quality by Design

Comprehensive Understanding of Manufacturing Process and Product Knowledge
Thank you

 Mercer

 Muchas Gracias

 Terima Kasih

 ขอบคุณ

 감사합니다

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