[S4-7] [10/22/2004(Fri) 14:00-14:30/Room 204]

KFDA Implementation Policy of KDMF

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• According to the change of pharmaceutical manufacturing & import control system into total GMP system, i.e., mandatory GMP for drug product (May 1994) and drug substance (BGMP, July 2002), Korea Food and Drug Administration (hereafter, KFDA) employed DMF system to ensure the quality assurance of drug substances.

• Pertaining to the drug substances that the Commissioner of KFDA designates to register, a comprehensive dossier on manufacturing and quality control should be submitted to KFDA, which includes manufacturing facility, manufacturing process, raw material at each process, control of degradates, packaging materials and stability data. Pharmaceutical manufacturers should not use other substances than those which were reviewed by and then notified on KFDA website.

• KFDA revised the relevant regulations in March 2004 and extend the DMF designation to 77 substances including 'Gliclazide' in addition to the active pharmaceutical ingredients (hereafter, API) of 'new drug', which is effective as of January 1st, 2005.

• The 77 extended substances were separated into 3 groups based on the therapeutic class and the dossiers were submitted in different schedules so as to facilitate the efficient review given the manpower. The results showed that the dossiers for approximately 570 substances were submitted and are under parallel review by Drug Safety Bureau and Drug Evaluation Division.

- Submission status: approx. 240 sites from 28 countries including Korea, China, India, Europe and US.

• So far, KFDA has posted on website 20 APIs of 'new drug' after thorough review and inspection of manufacturing sites (8 countries, 20 sites). Site inspection team consists of 1 official from Drug Safety Bureau and 1 official from Drug Safety Division. Inspection takes 3 days per each site.

• The issues pointed out most frequently on previous site inspections are as follows:

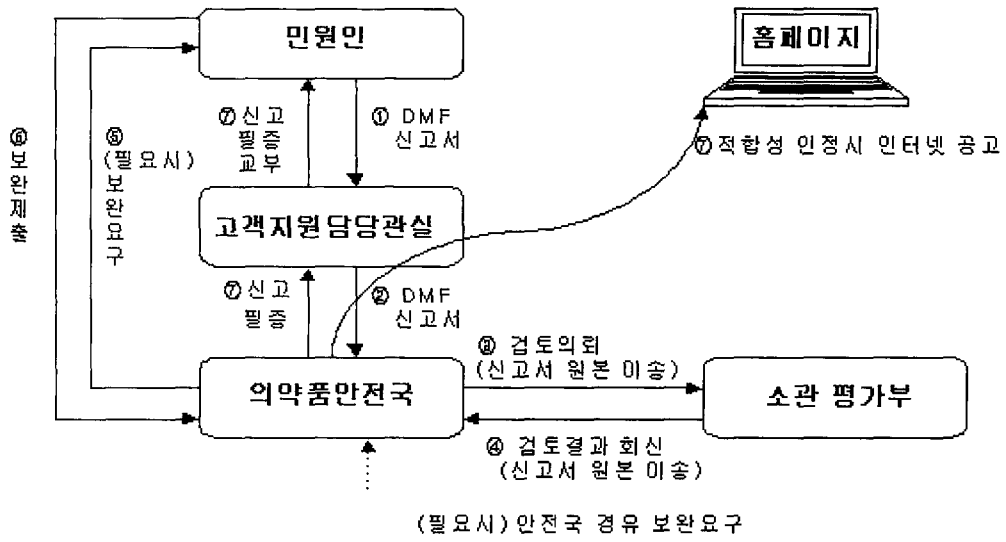
- Environment monitoring of the work area (e.g., filling and packaging area) where API is exposed in the air (suspended particle, microbiology test)
- Sampling method SOP
- Manufacturing process in details, including raw materials amount in each step
- SOP on the control of 'label's that should be discarded due to printing error.
- SOP on the cleaning of the packaging materials when they are brought into Controlled room.
- Specifications and Analytical method of key in-process materials in each step
- Periodic maintenance of Stability test data
- Maintenance of the Standard diary
- Calibration of scales used in IPC room in Production area
- Control of organic solvent used in manufacturing process and the residual solvent in final product.

• In addition, DMF guidance site (KFDA section) has been available to present the various information including submission, review and notification status, the explanatory notes on DMF guidelines, the comparison with foreign regulations, FAQ, etc., so as to expedite the implementation of this system and support industries.

• KFDA will extend the DMF substances further and stepwise according to therapeutic classes, in line with the schedule of ensuring Bioequivalence qualifications, which has been also key objective to improve the quality assurance of pharmaceutical products.

• KFDA organizes and operates DMF T/F (since January 2004), and the issues for implementation after the extension of the DMF substances have been discussed in details and considered to be applied to the revision of the guideline as well.

[DMF Work Flow]



- **Considerations during Review**

- **Drug Safety Bureau**
  - Facilities for manufacturing and quality control
  - Data on Manufacturing process, packaging, container, cautions in handling, etc.
  - GMP certificate of each production or equivalent data

- **Drug Evaluation Division**
  - Data on Physicochemical properties and stability
  - Data on Manufacturing process, packaging, container, cautions in handling, etc.
  - Data on batch analysis for drug substances, analytical methods, the solvents used, etc.
  - Drug Substance Samples for the quality test.