[S1-1] [10/10/2003(Fri) 09:30-10:10/ Grand Ballroom 102]

The Process of JP Publication in relation with Drug Regulation in Japan and International Harmonization

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1. Role of pharmacopoeia in the regulation of drugs

Efficacy and safety of drugs are evaluated in the process of drug registration along with the basis of setting test method and acceptance criteria for assuring quality of the drugs.Quality of drugs plays a key role to guarantee the efficacy and safety of drugs approved in the evaluation process at the marketing stage after approval.

Most important role of pharmacopoeia is to give the basis of assuring the quality of drugs. Pharmacopoeia should have the content able 1) to show how quality of drugs should be and 2) to give the basis of pharmaceutical development, to cope with the progress in science & technology and the changes of international and domestic social situations.

2. Concepts for preparing the Japanese Pharmacopoeia (JP)

Fundamental concept for preparing JP is to assure the adequacy and constancy of drug quality in order to supply suitable drugs to the patients.Thus, it is not adequate to seek excessively high purity or content.The test methods and acceptance criteria should be set so as to be able to detect the changes or differences in the quality of drugs and to exclude drugs with inadequate quality. The following concepts for preparing 15th edition of JP were adopted at the Committee of Japanese Pharmacopoeia on November 8, 2001.

1) To make JP more substantial and useful by including all the drugs which are important from the viewpoint of health care and medical treatment.

2) To make it possible to take regulatory action more smoothly by revising JP partially as required.

3) To promote international harmonization.

4) To ensure transparency on the revision process of JP and to promote the utilization of JP.

5) To introduce test methods using newly-developed analytical technologies positively, and to promote the establishment of reference standards.

3. Organization for preparing JP

The Pharmaceutical and Food Safety Bureau of the Ministry of Health, Labour and Welfare (MHLW) is responsible for compiling and publishing JP under the Pharmaceutical Affairs Law. The Evaluation and Licensing Division of the Bureau serves as the secretariat for the revision of JP. However, only a few members of the Bureau are in charge of JP. The Committee on Japanese Pharmacopoeia (JP Committee) is organized in the Pharmaceutical Affairs and Food Sanitation Council (PAFSC), a consultative body of MHLW, to prepare JP. The JP Committee has 12 subcommittees (panels). Each panel is composed of experts of related fields selected from the members of national and local government institutes, universities and colleges, and representatives of pharmaceutical industries association. The term of panel members is two years.

Divisions related to drugs in the National Institute of Health Sciences (NIHS) give advises and supports for preparing JP on the scientific and technical aspects, for example, as the members of JP Committee. The Society of Japanese Pharmacopoeia (SJP) also supports the preparation of JP on the businesslike aspects, for example, by issuing the printings related to JP including JP Forum.

4. Composition of JP

JP has 2 parts (Part I and Part II). Part I includes General Notices, General Rules for Preparations, 69 General Tests, and 859 Official Monographs of frequently-used drug substance and its preparations in JP14. Part II includes General Rules for Crude Drugs, and includes 469 Official Monographs of crude drugs, excipients, etc. in JP14. Infrared and Ultraviolet-visible reference Spectra used for identification of drug substance are also included in JP. Since JP13, General Information section is added at the end of JP as the appendices, to show the information useful for assuring the quality of drugs, such as the concepts and methods applicable to GMP.

5. Revision process of JP

JP was revised every 5 years, and 2 supplements were issued in the meantime of the revisions. Current 14th edition of JP (JP14) was published on March 30, 2001, and 1st supplement of JP14 was published on December 27, 2002. "Guide for preparing the drafts for 15th edition of JP" was adopted at the Committee of Japanese Pharmacopoeia on November 8, 2001.

Usually, the JP secretariat asks an adequate license holder of the drug to prepare the draft monograph. On the other hand, test methods are usually drafted by the member of relevant panel or the expert outside the JP Committee. The relevant panel investigates the draft, and the questions raised by the panel are sent to the drafter through the JP secretariat. The panel also asks the relevant industries

association, pharmacist association, etc. to give the comments on the draft. Taking it into consideration with the answers (or revised draft) from the drafter and the comments from the relevant associations, the panel investigates the draft again.

When the panel finalizes the investigation, JP secretariat puts the draft into public consultation by publishing it in the JP Forum. The panel reconsiders the draft based on the opinions to the consultation, and final document prepared by the panel is published in JP or its supplement.

6. International harmonization by ICH and PDG

ICH has achieved the harmonization of almost 50 guidelines for registration of new drugs in the fields of efficacy, safety and quality in these 13 years. Such globalization of standards gives enormous impact on the development, manufacture and regulation of drugs in Japan. Success of ICH is due that 1) ICH has clear mechanism for decision making (regulatory authorities of 3 regions (FDA, EU and MHLW) participate positively in the ICH activities as well as pharmaceutical industries associations (PhRMA, EFPIA and JPMA)), 2) IFPMA supports ICH activities as the secretariat, and 3) ICH focused on prospective harmonization (primary target of ICH guidelines is new drugs).

The Pharmacopoeial Discussion Group (PDG) was organized to seek harmonization among USP, EP and JP in 1990. However, PDG activities was not so successful as ICH, because 1) it is somewhat difficult to make decision on the matter related to regulation, since regulatory authorities does not participate in PDG activities, 2) there are no secretariat for PDG, and 3) pharmacopoeial harmonization inevitably has the aspects of retrospective harmonization, since each pharmacopoeia contains many already-approved drugs and general test method used in the region for a long time. Because of the shortage in human resources, JP could not necessarily cope with the wide range of harmonization requested by USP and EP. Recently, as a trial to solve the problem, the Panel on PDG Harmonization was organized as a liaison group among panels related to pharmacopoeial harmonization.