Provisional Translation (as of March 22, 2011)[*]

Administrative Notice
June 9, 2010

To: Division of Pharmaceutical Affairs,
Prefectural Health Department (Bureau)

From: Evaluation and Licensing Division,
Pharmaceutical and Food Safety Bureau,
Ministry of Health, Labour and Welfare; and,

Compliance and Narcotics Division,
Pharmaceutical and Food Safety Bureau,
Ministry of Health, Labour and Welfare

Points to Consider for Reducing Total Review Time for New Drug Applications

The Mid-term Plan of the Pharmaceuticals and Medical Devices Agency (PFSB Authorization No. 0331002 of the Pharmaceutical and Food Safety Bureau, Ministry of Health, Labour and Welfare, dated March 31, 2009) sets forth the total time to be taken for reviews of new drug applications, which are to be reduced as indicated in the Attachment through the efforts of both the regulatory authorities and the applicant.

We have specified herein the guidance document for reducing total review time for new drug applications from the standpoint of shortening the time taken by the applicant (hereinafter "applicant's time"). All prefectural public health authorities are requested to fully recognize and thoroughly inform related companies and organizations under their jurisdiction of the information contained in this Administrative Notice.

1. Submission of documents to be attached to applications

With regard to documents to be attached to new drug applications, the use of the eCTD has been recommended for streamlining the review process. When an eCTD is not used, paper-based regulatory documents (original and duplicate copies) should be submitted. Copies of such

[*] This English version of the Japanese Administrative Notice is provided for reference purposes only. In the event of any inconsistency between the Japanese original and the English translation, the former shall prevail.

documents for reviewers should also be delivered without delay after filing a new drug application. Applicants should check with the relevant review office concerning the required number of document copies for reviewers.

2. Handling of data from long-term administration studies

The method of handling data from long-term administration studies has been set forth in the "Extent of Population Exposure to Assess Clinical Safety for Drugs Intended for Long-Term Treatment of Non-Life-Threatening Conditions" (PAB/ELD Notification No. 592 of the Evaluation and Licensing Division, Pharmaceutical Affairs Bureau, MHLW, dated May 24, 1995) and the "Handling of the Clinical Studies Conducted after Submission of New Drug Applications" (PMSB/ELD Notification No. 1061 of the Evaluation and Licensing Division, Pharmaceutical and Medical Safety Bureau, MHLW, dated December 1, 1998). In accordance with these Notifications, data from studies in which at least six months of treatment has been completed in all patients should be submitted when filing a new drug application. Furthermore, the final study report (it should include data of at least one year of treatment completed in all patients) and a draft revision of CTD should be submitted additionally as soon as possible, and should be filed no later than six months before the target total review time elapses.

It is preferable that a specific date of submission is agreed upon before filing a new drug application, by means of a clinical trial consultation or other communications with the Pharmaceuticals and Medical Devices Agency (PMDA). This is not applicable to orphan drugs and drugs intended for priority reviews; however, before filing the new drug application, the applicant should agree with PMDA by means of a specific clinical trial consultation or other communications, on the documents required at submission of each new drug application and the timing of submission for additional documents.

3. Handling of data from long-term stability studies

With regard to long-term stability studies, it is allowed to file a new drug application with data from an ongoing study on the premise that the said study data will be submitted afterward pursuant to the "Revision of the Guidelines on Stability Testing of New Drug Substances and Products" (PFSB/ELD Notification No. 0603001 dated June 3, 2003). The additional data should be submitted as a final report (it should include data necessary for determining the proposed expiration period) no later than six months before the target total review time elapses. Additional data obtained subsequently should be filed by the time when documents for the Expert Discussion are submitted.

It is preferable that a specific date of submission is agreed upon before filing a new drug application, by means of a clinical trial consultation or other communications with PMDA. This

is not applicable to orphan drugs and drugs intended for priority reviews; however, before filing a new drug application, the applicant should agree with PMDA, by means of a clinical trial consultation or other communications, on the documents required at submission of each new drug application and the timing of submission for additional documents.

4. Use of master file for drug substances, etc. (hereinafter referred to as "DMF")

When using DMFs, the applicant should adequately communicate with the DMF holders beforehand to verify the registration status of the DMFs. Also, the applicant should ensure that documents corresponding to the CTD Module 2 concerning the DMF will be submitted without delay after filing an application for the drug product in accordance with "Guidelines on Utilization of Master File for Drug Substances, etc." (PFSB/ELD Notification No. 0210004 dated February 10, 2005). In addition, the applicant should check the required number of copies with the review office.

5. Application for GMP compliance inspection

A GMP compliance inspection prior to approval is conducted when the review of the CMC section has almost been completed, and the description on manufacturing methods and other relevant matters in the application have been fixed. However, sometimes there is prolongation of the applicant's time due to delays in submission of the application for GMP compliance inspection or in preparations for inspection at the relevant manufacturing site(s). The applicant should submit the application for GMP compliance inspection at a suitable time, and make prior arrangements to accept the inspection of relevant manufacturing site(s) promptly when the inspection is considered to be feasible through communication with the review office.

6. Others

Applicants should make known to internal and external related parties the above-mentioned information on handling of data, submission of additional documents and other procedures. If, for no rational reason, the review time is prolonged by delays in submission and/or lack of data concerning documents for reviewers, additional documents or other relevant data, or application for GMP compliance inspection, such fact will be publicly stated in the review report.

(Attachment)

Target review time for products approved in each fiscal year excerpted from the Mid-term Plan of PMDA (Authorization No. 0331002 of PFSB, MHLW dated March 31, 2009).

Median review time for new drugs (standard review products)

Fiscal year	Total review time	Regulatory review time	Applicant's time
FY 2010	16 months	11 months	5 months
FY 2011-2013	12 months	9 months	3 months

Median review time for new drugs (priority review products)

Fiscal year	Total review time	Regulatory review time	Applicant's time
FY 2010	10 months	6 months	4 months
FY 2011-2013	9 months	6 months	3 months