Administrative Notice
April 15, 2013

To: Pharmaceutical Affairs Section, Prefectural Health Department (Bureau)

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

About Q&A on the Guidance for Preparation of Application Forms for Registration of Drug Master Files of Materials Relating to Manufacture of Cellular- and Tissue-Based Products and Data to be Attached

Documents on “Guidance for Preparation of Application Forms for Registration of Drug Master Files of Materials Relating to Manufacture of Cellular- and Tissue-Based Products and Data to be Attached” were issued as Administrative Notices dated March 8, 2013. As provided in the attachment, a new document on Q&A has been compiled. Please thoroughly inform the relevant business operators in your jurisdiction of this matter.

(Attachment)

Q&A on the Guidance for Preparation of Application Forms for Registration of Drug Master Files of Materials Relating to Manufacture of Cellular- and Tissue-Based Products and Data to be Attached

(Question 1) The Guidance for Preparation instructs that an application for registration of drug master files (hereinafter referred to as "MFs") of materials relating to manufacture of cellular- and tissue-based products (hereinafter referred to as "application form for registration") may have a dummy number in the "Manufacturing business license number or foreign manufacturer accreditation number and date" field if neither a license nor accreditation is required. How should this field be filled in?

(Answer)

Please fill in this field as provided below.

	License/accreditation number	Date of license/accreditation	Category of license/accreditation
Manufacturing site not requiring a manufacturing business license	99AZ555555	December 28, 2012	Non-Sterile drugs
Manufacturing site not requiring a foreign manufacturing business accreditation	AG99955555	December 28, 2012	Non-Sterile drugs

(Question 2) The Guidance for Preparation instructs that an application form for registration should include methods to inactivate/remove bacteria, fungi, viruses, and other adventitious agents in the manufacturing process. I understand that the same information is required for media, medium additives, and raw materials for cell processing. Is this understanding correct?

(Answer)

For cellular- and tissue-based products, their characteristics often preclude the inactivation/removal of bacteria, fungi, viruses, and other adventitious agents in the manufacturing process. Introduction of bacteria, fungi, viruses, and other adventitious agents from raw materials must be prevented.

For media, medium additives, and raw materials for cell processing that are used as raw materials of cellular- and tissue-based products and need to undergo treatment for inactivation/removal of bacteria, fungi, viruses, and other adventitious agents because of their biological origin status, the treatment for inactivation/removal in the manufacturing process should be registered in the MF.

For biological raw materials that have not undergone treatment for inactivation/removal of bacteria, fungi, viruses, and other adventitious agents in the manufacturing process, appropriate and adequate discussions with MF users should be made regarding how the safety of cellular- and tissue-based products (final products) manufactured using such raw materials is ensured in terms of contamination with bacteria, fungi, viruses, and other adventitious agents.

(Question 3) The Guidance for Preparation instructs that the specifications and testing methods (for registration of cells) should be "Testing methods established in the scientific knowledge in the public domain such as those in the Japanese Pharmacopoeia." What testing methods do these instructions refer to?

(Answer)

It refers to testing methods adopted as general tests in compendia such as the Minimum Requirements for Biological Products, Japanese Pharmaceutical Codex, Japanese Pharmaceutical Excipient in addition to the Japanese Pharmacopoeia.

Besides, testing methods adopted in documents for quality control of drugs or medical devices such as USP, EP, ISO, and JIS may be similarly handled as well in principle. However, for the testing methods that are included in these documents but not listed or adopted as official testing methods, for example, ones being under investigation, an explanation of their details may be requested during the review or research of cellular- and tissue-based products.

It should be noted that the above answer is limited to data attached to application forms for registration of materials relating to manufacture of cellular- and tissue-based products but does not alter handling of testing methods in applications for approval of drugs, etc.

(Question 4) I understand that attached data will be handled as information not disclosed to MF users. Is this understanding correct?

(Answer)

The understanding is correct. PMDA does not disclose any of the attached data to MF users. Which parts of the attached data the MF registrant will disclose to the MF user should be individually discussed between the two parties during MF registration or utilization.

However, information on safety included in an MF or attached data (e.g., conformance of biological raw materials to the Standards for Biological Raw Materials) is essential to utilization of the MF and thus should not be handled as matters not disclosed to MF users. Please keep this note in mind during registration. For details, see the answer to Question 2 in the "Questions and Answers (Q&A) on Drug Master Files (Part III)" (Administrative Notice dated December 28, 2012).