

Provisional Translation (as of March 2026).

This English document has been prepared for reference purpose only. In the event of inconsistency and discrepancy between the Japanese original and the English translation, the Japanese text shall prevail.

Administrative Notice
October 29, 2013

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

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

Questions and Answers (Q&A) on Drug Master Files (Part IV)

Documents on “Q&A on Drug Master Files” were issued as Administrative Notices dated July 28, 2005, December 20, 2005, and December 28, 2012. 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.

Q&A on the Master File (MF) System (Part IV)

(Question 1)

For an application for approval of a drug listed in the Japanese Pharmacopoeia (JP), the “Specifications and testing methods” field is allowed to dispense with the information that should be quoted from the JP. For application for MF registration of a drug listed in the JP, may the “Specifications and testing methods” field dispense with the information that should be quoted from the JP by including a statement such as “As provided under “XXX” in the Japanese Pharmacopoeia” or “As provided below, in addition to those under “XXX” in the Japanese Pharmacopoeia”?

(Answer)

For application for MF registration of a drug listed in the JP, the information that should be quoted from the JP may be replaced with the statement “As provided under “XXX” in the Japanese Pharmacopoeia” or “As provided below, in addition to those under “XXX” in the Japanese Pharmacopoeia.”

If the “Specifications and testing methods” field in an MF includes a JP-compendial testing method with partial modifications or specifications partially stricter than those in the JP, only the partially modified part may be described in the field as is done for an application for marketing approval.

In addition, for materials listed in the following standards, an MF may also be registered without the information consistent with the relevant standard as is done for an application for marketing approval.

- Minimum Requirements of Radiopharmaceuticals (Ministerial Announcement No. 83 of 2013 by the Ministry of Health, Labour and Welfare [MHLW])
- Insecticide Guidelines (1990) (PAB Notification No. 308 of 1990, of the Pharmaceutical Affairs Bureau, Ministry of Health and Welfare [MHW])
- Japanese Standards for Non-Pharmaceutical Crude Drugs 2012 (PFSB/ELD Notification No. 1030-1 of 2012, of the Evaluation and Licensing Division, Pharmaceutical and Food Safety Bureau, MHLW)
- Japanese Pharmaceutical Codex 2002 (PFSB Notification No. 0920001 of 2002, of the Pharmaceutical and Food Safety Bureau, MHLW)
- Japanese Standards of Quasi-Drug Ingredients 2006 (PFSB Notification No. 0331030 of 2006, of the Pharmaceutical and Food Safety Bureau, MHLW)
- Japanese Pharmaceutical Excipients 1998 (PMSB Notification No. 178 of 1998, of the Pharmaceutical and Medical Safety Bureau, MHW)
- Specifications and Standards for Food, Food Additives, Etc. (MHW Ministerial Announcement No. 370 of 1959, limited to specifications and standards for additives)

(Question 2)

Any change in the specifications and testing methods in an MF, if made, would require MF change registration, which usually entails an application for approval of partial changes in approved items (partial change application) for the drug product.

For example, some drug products using a drug substance registered in the MF database have marketing approval certificates in which the manufacturing method of the drug substance is quoted from the MF but the specifications and testing methods for the drug substance are different from those in the MF and specially established as the attached specifications or established in accordance with the compendia in Japan.

If the MF change registration involves only the specifications and testing methods but does not involve the manufacturing method (except for changes subject to minor change notification), the marketing approval certificate of the drug product utilizing the concerned MF would remain unaffected without practical changes, except the date of MF registration. In such a case, is the change of the date of MF registration in the concerned marketing approval certificate subject to minor change notification?

(Answer)

If changes in a registered MF of a drug substance involve only the specifications and testing methods for the MF drug substance but do not involve the manufacturing method (except for changes subject to minor change notification), and specifications and testing methods in the marketing approval certificate are different from those in the MF and separately established for the drug substance (for example, changes in specifications and testing methods in an MF accompanying changes in a foreign compendial but causing no changes in approved items for the drug product), the change only to the date of MF registration may be reported to the regulatory agency through a minor change notification. Of note, the marketing authorization holder must ensure that the post-change quality is comparable to the pre-change quality through adequate discussion with the MF registrant.

(Question 3)

If specifications and testing methods in an MF are as provided in the United States Pharmacopeia (USP) or European Pharmacopoeia (EP), may the concerned specifications and testing methods be replaced with the statement “As provided in the USP (or EP)”?

(Answer)

Only if all of the following conditions are met: (a) a product submitted for marketing approval uses a drug substance registered in the MF database; (b) an application for marketing approval includes separately established specifications and testing methods for the drug substance; and (c) specifications and testing methods in the concerned MF are as provided in the USP or EP, the space for specifications in the “Ingredients and their quantity or nature” field in the MF may be left blank with the statement “As provided under XXX in the USP (or EP).” Unless specifications and testing methods in the concerned MF are as provided in the USP or EP, omission of the specifications and testing methods from the MF is not allowed. However, if they are as provided in the JP or any of the compendia listed in (Answer) to Question 1 above, such omission is allowed.

If specifications and testing methods in an MF are as provided in a specific version of the USP or EP with modifications but not as provided in the current version, the relevant field should have a statement “As provided under XXX in the USP (or EP) Version YY.”

If specifications and testing methods in an MF include a USP- or EP-compendial testing method with modifications or specifications partially stricter than those in the USP or EP, the relevant field may be processed with the statement presented below.

- “As provided below, in addition to those under XXX in the USP (or EP)/XXX in the USP (or EP) Version YY.”
- “As provided under XXX in the USP (or EP)/XXX in the USP (or EP) Version YY, but for AAA, as provided below.”

(Question 4)

If the statement “As provided under XXX in the USP (or EP)” in the “Specifications and testing methods” field in a MF is changed to additionally designate the version (except cases where designation of the version results in practical changes to the existing specifications) or if the statement “As provided under XXX in the USP (or EP) Version YY” is changed to alter the version number (except cases where the change of the version number results in practical changes to the existing specifications), are such changes subject to minor change notification?

(Answer)

A minor change notification may be submitted for these changes.