Provisional Translation (as of June 2024)*

Administrative Notice
May 30, 2024

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

Medical Device Evaluation Division,
Pharmaceutical Safety Bureau,
Ministry of Health, Labour and Welfare
(Official seal omitted)

Compliance and Narcotics Division,
Pharmaceutical Safety Bureau,
Ministry of Health, Labour and Welfare
(Official seal omitted)

Questions and Answers (Q&A) on Release Testing of the Imported Regenerative Medical Products

Standard for quality control of regenerative medical products have been shown in the "Ministerial Ordinances on Good Gene, Cellular, and Tissue-based Products Manufacturing Practice (GCTP) for Regenerative Medical Products" (MHLW Ministerial Ordinances No. 93, 2014), which requires appropriate implementation of release testing.

Questions and Answers (Q&A) regarding release testing of the imported regenerative medical products have been compiled as attached. Please inform manufacturers and sellers placed under your administration to utilize this Q&A for their business operations.

*This English translation of the Japanese Administrative Notice is intended to be a reference material to provide convenience for users. In the event of inconsistency between the Japanese original and this English translation, the former shall prevail.

(Attachment)

Questions and Answers (Q&A) on Release Testing of the Imported Regenerative Medical Products

Q:

Regenerative medical product manufactured by the foreign manufacturer A will be imported to the domestic manufacturer B and shipped from the domestic manufacturer B. It is difficult to carry out the release testing of approved specifications at the domestic manufacturer B due to the individual properties and limited quantities of the product.

In such cases, is it acceptable that release testing by the domestic manufacturer B is not considered necessary if the foreign manufacturer A conducts release testing of approved specifications? If it is acceptable, is the domestic manufacturer B required to store the reference sample?

A:

Release testing of the imported product by the domestic manufacturer B is not always necessary if the foreign manufacturer A is specified, as approved matters, to conduct the release testing of approved specifications and all of the following requirements are met. Please contact Medical Device Evaluation Division, Pharmaceutical Safety Bureau, Ministry of Health, Labour and Welfare (PSB/MDED) if you are unsure whether the requirements are met.

It is not necessary to store the reference sample in the domestic manufacturer B if there is no possibility that the domestic manufacturer B will conduct any tests using the reference sample.

1. There are justifiable reasons that it is difficult to conduct release testing at the domestic manufacturer B (e.g., in cases where conducting release testing at the domestic manufacturer B makes it difficult to secure the doses of therapeutic products, which may cause disadvantage to the patients).
2. On request of the regulatory authority, marketing authorization holder should explain that there is no effect on the quality of the product due to transportation, packaging/labeling operations, storage conditions, etc. after release testing conducted by foreign manufacturer A.
3. The domestic manufacturer B (or marketing authorization holder) should conclude an agreement on quality control with foreign manufacturer A, including:
    1) the scope of responsibility for conducting investigations associated with test results and quality information
    2) the establishment of a management system to ensure traceability:
        - for cellular/tissue-based products, it should be ensured that the product identification number is correct by not simply checking the label, but by confirming traceability from the time of cell/tissue collection.

- for gene therapy products manufactured for individual patients, it should be ensured that the correspondence between the final product and the patient is correct.

4. The domestic manufacturer B should implement the following items for release:

   1) visual inspection to confirm that there are no problems with appearances/shapes.

   2) reviewing the records of manufacturing and release testing for each lot conducted by manufacturer A (including records of abnormalities and deviations). The preparation of the review reports of those records is considered as a substitute for release testing.