Administrative Notice
December 25, 2025

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

Medical Device Evaluation Division,
Pharmaceutical Safety Bureau,
Ministry of Health, Labour and Welfare

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

Questions and Answers (Q&A) on Timing of Product Replacement after Approval of Partial Changes in Approved (Certified) Items for In Vitro Diagnostics and Regenerative Medical Products

In association with issuance of the "Timing of Product Replacement after Approval of Partial Changes in Approved (Certified) Items for In Vitro Diagnostics and Regenerative Medical Products" (PSB/PED Notification No. 1225-1 and PSB/CND Notification No. 1225-1, dated December 25, 2025, jointly of the Medical Device Evaluation Division and Compliance and Narcotics Division, Pharmaceutical Safety Bureau, Ministry of Health, Labour and Welfare [MHLW]), related questions and answers have been compiled as provided in the appendix. Please understand the content and ensure that relevant companies under your jurisdiction are fully informed.

Please note that duplicate copies of this notification will be sent to the Pharmaceuticals and Medical Devices Agency, Federation of Pharmaceutical Manufacturers' Associations of Japan, Japan Association of Clinical Reagents Industries, Japan Federation of Medical Devices Associations, American Medical Devices and Diagnostics Manufacturers' Association in Japan, Medical Equipment & Diagnostics Committee of the European Business Council in Japan, Forum for Innovative Regenerative Medicine, Medical Technology Association of Japan, Japan Pharmaceutical Manufacturers Association, and Association of Registered Certification Bodies for Pharmaceuticals and Medical Devices.

This administrative notice supersedes the former "Questions and Answers (Q&A) on Timing of Product Replacement after Approval of Partial Changes in Approved (Certified) Items for In Vitro Diagnostics and Regenerative Medical Products" (Administrative Notice dated September 20, 2018, of the Medical Device Evaluation Division and Compliance and Narcotics Division, Pharmaceutical Safety and Environmental Health Bureau, MHLW).

[Appendix]

Questions and Answers (Q&A) on Timing of Product Replacement after Approval of Partial Changes in Approved (Certified) Items for In Vitro Diagnostics and Regenerative Medical Products

*Please note that in this Q&A document, abbreviations defined in the parent notification for product replacement are directly used without definition.

Q1
Are partial changes for in vitro diagnostics and regenerative medical products requiring revision of the package insert subject to this notification?

A1
Yes. Changes in the "Reactive ingredient(s)" or "Storage conditions and shelf life" field for in vitro diagnostics or in the "Shape, structure, ingredients, quantities, or nature" or "Storage and shelf life" field for regenerative medical products may require revision of the package insert. Where applicable, the marketing authorization holder should appropriately control the product replacement and inform medical institutions of necessary matters. If product replacement results in specific situations such as presence of both pre- and post-change products in clinical settings, needing both pre- and post-change package inserts to be publicly available, actions should be taken with reference to the "Question and Answers (Q&A) regarding 'Provision of Information on Precautions, etc. for Drugs, etc.'" (Administrative Notice, dated February 19, 2021, of the Pharmaceutical Safety Division, Pharmaceutical Safety and Environmental Health Bureau, MHLW).

Q2
Are the following repeated submissions acceptable? After initial partial changes in the manufacturing method, etc., another application for approval of partial changes or minor change notification involving the manufacturing method, etc. is submitted before the pre-change products relating to the initial partial changes run out.

A2
Repeated partial changes or minor changes without actual manufacturing practices are not desirable because they would complicate a relationship of products and procedures at the manufacturing site and the approval certificate, compromising the manufacturing control. If additional partial changes or minor changes in the manufacturing method, etc. are inevitably made before the pre-change products run out, procedures at the manufacturing site should be appropriately controlled, and manufacturing practices should be appropriately documented to clarify the manufacturing method, etc. in use for every product lot (every manufacturing number for products not manufactured on a batch basis).

Q3
Partial changes were made to 2 testing methods, but for stable supply, products with only 1 of the 2 post-change methods applied need to be released. Is such a release possible?

A3
In principle, release of the products manufactured according to a manufacturing method, etc. not approved as the integral process, such as the process with only a part of the partial changes applied, is not allowed. However, some inevitable releases, for example, one necessary for stable

supply, may be accepted if an impact on quality is clearly ruled out. Consultation with the Medical Device Evaluation Division should be conducted in advance.

Q4
Are partial changes related to changes in drug master files subject to this notification?

A4
Yes.

Q5
To make the products eligible for handling according to this notification, what information should be specifically included in an application form for approval?

A5
For each of the major items subject to change (applicable items for in vitro diagnostics), a statement should be given according to the examples provided below. After the products have run out, the above statements should be deleted at the time of next submission of an application for approval of partial changes or minor change notification.

However, the "Manufacturing site of the product to be marketed" field does not accept free-text entry owing to system limitations. If partial changes in this field relevant to the timing of product replacement are intended, the statement should be entered in the "Manufacturing method" field instead.

(1) Example of partial change application form for partial changes relevant to timing of product replacement for in vitro diagnostics

A. Example of the "Reactive ingredient(s)" field
[Reactive ingredient(s)]
Constitutive reagent A

**Antibody **μg/mL
Even after approval of the partial changes concerned, products meeting the pre-change approval (certification) certificate will be released until they run out.

B. Example of the "Manufacturing method" field
[Manufacturing method]
Name of manufacturing site and manufacturing process
XXX Plant Design
YYY Plant Filling and storage
Even after approval of the partial changes concerned, products meeting the pre-change approval (certification) certificate will be released until they run out.

C. Example of the "Storage conditions and shelf life" field
[Storage conditions and shelf life]
Storage conditions: **°C
Shelf life: ** years
Even after approval of the partial changes concerned, products meeting the pre-change approval (certification) certificate will be released until they run out.

(2) Example of partial change application form for partial changes relevant to timing of product replacement for regenerative medical products

A. Example of the “Shape, structure, ingredients, quantities, or nature” field:

[Shape, structure, ingredients, quantities, or nature]

Even after approval of the partial changes concerned, products meeting the pre-change approval (certification) certificate will be released until they run out.

B. Example of the “Manufacturing method”:

[Manufacturing method]

[Serial number] 999

[Name of manufacturing site]: Remarks

[Manufacturing method]

Even after approval of the partial changes concerned, products meeting the pre-change approval (certification) certificate will be released until they run out.

C. Example of the “Specifications and testing methods” field (including the “Attached specifications” field):

[Specifications and testing methods]

[Test name]: Remarks

[Specifications and testing methods]

Even after approval of the partial changes concerned, products meeting the pre-change approval (certification) certificate will be released until they run out.

D. Example of the “Storage and shelf life” field:

[Storage and shelf life]

Storage: ***

Container: *** container

Shelf life: ** years

Even after approval of the partial changes concerned, products meeting the pre-change approval (certification) certificate will be released until they run out.

After the products have run out, the above statements should be deleted at the time of the next submission of an application for approval of partial changes or minor change notification.

Example of a minor change notification form for “Deletion of statement for product replacement”

[Date of change]: MM DD, YYYY

[Reason for change]

Deletion of the statement for product replacement from the “XX” field of the partial change approval certificate dated MM DD, YYYY