Administrative Notice
October 3, 2025

To: Prefectural Health Departments (Bureaus)

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

Questions and Answers (Q&A) about Handling of Application for Confirmation of Change Protocol Related to Change of Strains for Influenza Vaccine or COVID-19 Vaccine

Handling of application for confirmation of change protocol for drugs, quasi-drugs, and cosmetics is specified in the “Handling of Application for Confirmation of Change Protocol for Drugs, etc.” (PSEHB/PED Notification No. 0616-14, dated June 16, 2021, of the Pharmaceutical Evaluation Division, Pharmaceutical Safety and Environmental Health Bureau, Ministry of Health, Labour and Welfare [MHLW]) and “Questions and Answers (Q&A) about Handling of Application for Confirmation of Change Protocol for Drugs, etc.” (Administrative Notice, dated July 30, 2021, of the Pharmaceutical Evaluation Division, Pharmaceutical Safety and Environmental Health Bureau, MHLW).

In association with issuance of the “Handling of Application for Confirmation of Change Protocol Related to Change of Strains for Influenza Vaccine or COVID-19 Vaccine” (PSB/PED Notification No. 1003-1, dated October 3, 2025, of the Pharmaceutical Evaluation Division, Pharmaceutical Safety Bureau, MHLW), a list of the questions and answers (Q&A) about the relevant notification is compiled as presented in the appendix. Please ensure that all the related companies under your jurisdiction are informed.

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

Appendix

Questions and Answers (Q&A) about Handling of Application for Confirmation of Change Protocol Related to Change of Strains for Influenza Vaccine or COVID-19 Vaccine

Abbreviations used

PACMP: The term refers to post approval change management protocol, which is a plan for partial changes in approved items of an approved product.

PACMP Q&A: The term refers to the “Questions and Answers (Q&A) about Handling of Application for Confirmation of Change Protocol for Drugs, etc.” (Administrative Notice, dated July 30, 2021, of the Pharmaceutical Evaluation Division, Pharmaceutical Safety and Environmental Health Bureau, MHLW).

Strain Change PACMP Notification: The term refers to the “Handling of Application for Confirmation of Change Protocol Related to Change of Strains for Influenza Vaccine or COVID-19 Vaccine” (PSB/PED Notification No. 1003-1, dated October 3, 2025, of the Pharmaceutical Evaluation Division, Pharmaceutical Safety Bureau, MHLW).

Partial Change Notification for Influenza Strain Changes: The term refers to the “Handling of Influenza Vaccines Manufactured Using Strains Other than Those Dispensed by the National Institute of Infectious Diseases (Notification)” (PSB/PED Notification No. 0131-1 and PSB/CND Notification No. 0131-1, dated January 31, 2024, of the Pharmaceutical Evaluation Division and Compliance and Narcotics Division, Pharmaceutical Safety Bureau, MHLW).

Partial Change Notification for Coronavirus Strain Changes: The term refers to the “Handling of Changes to COVID-19 Vaccine Strains (Notification)” (PSB/PED Notification No. 0523-1 and PSB/CND Notification No. 0523-3, dated May 23, 2024, of the Pharmaceutical Evaluation Division and Compliance and Narcotics Division, Pharmaceutical Safety Bureau, MHLW).

[1. General matters]

Q1: Is it acceptable to submit an application for confirmation of change protocol for strain changes of a product with the approval application (including applications for partial changes) currently under review before its approval?

A1:

Yes.

However, it should be noted that if review of the relevant approval application reaches a conclusion that no changes subject to the “Partial Change Notification for Influenza Strain Changes” or “Partial Change Notification for Coronavirus Strain Changes” should be allowed, confirmation of the change protocol will be declined.

Q2: We have the change protocol confirmed in the initial fiscal year and plan to repeat strain change for the subsequent seasons in accordance with the same change protocol. In this case, should we submit an application for confirmation of change protocol again?

A2:

No, you don’t have to. If, for the seasons subsequent to that with the change protocol confirmed, you make a strain change in accordance with the same change protocol, you may submit only a notification for the changes made in accordance with the change protocol.

Q3: According to QA3 of the PACMP Q&A, the median period from submission of an application for confirmation of change protocol (including submission for changes in the confirmed change protocol) to issuance of the confirmation certificate is intended to be up to 12 months wherever possible. For an application for confirmation of change protocol for a vaccine, which is subject to the Strain Change PACMP Notification, how long will it take?

A3:

The median period from submission of an application for confirmation of change protocol for a vaccine, which is subject to the Strain Change PACMP Notification, (including submission for changes in the confirmed change protocol) to issuance of the confirmation certificate is intended to be up to 6 months wherever possible.

[2. Scope of this notification]

Q4: Is it acceptable to utilize the PACMP system for strain changes for vaccines other than those relevant to the Partial Change Notification for Influenza Strain Changes or Partial Change Notification for Coronavirus Strain Changes?

A4:

Consultation with PMDA is highly recommended for individual cases.

[3. Matters to be described in the application for confirmation of change protocol for drugs, etc.]

Q5: If, in association with the strain change, a package insert, risk management plan (hereinafter referred to as “RMP”), and RMP materials are changed, is it acceptable to include draft revised versions of these materials in the change protocol?

A5:

Yes. The draft revised versions associated with the strain change (proposed texts) should be explained using a table for comparison between the old and new texts.

If draft revised versions of the package insert, RMP, and RMP materials have been included in the change protocol, the revised package insert, RMP, and RMP materials should be attached to the notification for changes made in accordance with the change protocol.

[4. Handling of changes in the change protocol]

Q6: According to Chapter 4 of the Strain Change PACMP Notification, if changes of the process, etc. (e.g., scale-up, addition of manufacturing sites) other than the strain change are approved as partial changes in items approved for marketing of drugs after completion of confirmation of the change protocol (after issuance of the confirmation certificate) and thus are intended to be reflected in the change protocol, submission of a minor change notification for confirmation items in the change protocol for drugs may suffice. In this case, how should we proceed with the change procedure?

A6:

The following procedure should be taken to proceed with the change procedure.

[1] After the partial change approval is obtained;

[2] The changes in [1] are reflected in the change protocol by a notification for changes in the change protocol;

[3] Data are collected in accordance with the change protocol (version with the changes in [1] revised in [2]); and

[4] The notification for changes made in accordance with the change protocol is submitted.

[5 Handling of changes made in accordance with change protocol]

Q7: Because the content in a notification for changes made in accordance with the change protocol becomes approved matters when 40 or 20 working days have passed since its acceptance, it is acceptable to include the text reflecting the content in the latest notification for changes made in accordance with the change protocol in the old text field of the table for comparison between the old and new texts in an approval application form, which is submitted with the notification for changes made in accordance with the change protocol for the subsequent seasons?

A7:

Yes.

[6. Others]

Q8: Because preparation of template DNA or virus seed for the candidate strains needs to be started in autumn and winter of the year before the strain change, is the following schedule acceptable? The preparation of template DNA or virus seed is started before confirmation of the application for confirmation of change protocol is completed, and manufacture of the active substance using the prepared template DNA or virus seed is started after the confirmation is completed.

A8:

Yes.

Q9: If no strain change has been made since issuance of the confirmation certificate of the application for confirmation of change protocol, is it allowed to omit the procedures for changes in the change protocol, etc.?

A9:

Yes. When a strain change is made in accordance with the confirmed change protocol in the next fiscal year or later, a notification for changes made in accordance with the change protocol should be submitted.

Q10: Should the change protocol clarify whether a compliance inspection for drugs, etc. is required?

A10:

No. If changes of the process, etc. associated with the strain change are ones that have a potential impact on manufacturing and quality control methods, they will be subject to GMP compliance inspection. The strain change, in this case, is not allowed to be made as a partial

change based on the Partial Change Notification for Influenza Strain Changes or Partial Change Notification for Coronavirus Strain Changes and thus is not subject to the Strain Change PACMP Notification. It should be noted that such case requires submission of an ordinary application for partial changes or application for confirmation of change protocol.

End of document