Provisional Translation (as of April 2026) *

Administrative Notice
October 3, 2025

To: (separately addressed)

Pharmaceuticals and Medical Devices Agency
Office of Vaccines and Blood Products

Mock-up of Application Form for Confirmation of Change Management Protocol, etc. Related to Change of Strains for Influenza Vaccine or COVID-19 Vaccine (Early Consideration)

We, the Pharmaceuticals and Medical Devices Agency (hereinafter referred to as "PMDA"), deeply appreciate your understanding of and cooperation in our review activities.

The "Handling of Application for Confirmation of Change Management 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, Ministry of Health, Labour and Welfare [MHLW]) and "Questions and Answers (Q&A) about Handling of Application for Confirmation of Change Management Protocol Related to Change of Strains for Influenza Vaccine or COVID-19 Vaccine" (Administrative Notice, dated October 3, 2025, of the Pharmaceutical Evaluation Division, Pharmaceutical Safety Bureau, MHLW) have instructed marketing authorization holders of influenza vaccines and COVID-19 vaccines how to change virus strains, which are to be used as antigens for the vaccines, utilizing the post-approval change management protocol (PACMP) system.

Now, based on the above notification, PMDA has prepared mock-ups of the Application Form for Confirmation of Change Management Protocol related to change of strains for influenza vaccine or COVID-19 vaccine, as provided in the appendix.

Please note that "Early Consideration" is a reference for promoting the practical application of new technologies and the development of innovative pharmaceuticals, even though scientific knowledge and information have not necessarily been sufficiently accumulated at this stage, and that it may change in the future due to newly obtained knowledge and scientific progress.

(addressed to)
Federation of Pharmaceutical Manufacturers' Associations of Japan
Japan Pharmaceutical Manufacturers Association
Pharmaceutical Research and Manufacturers of America
European Federation of Pharmaceutical Industries and Associations
Japan Association of Vaccine Industries
Japan Blood Products Association

Mock-up of Application Form for Confirmation of Change Management Protocol, etc. Related to Change of Strains for Influenza Vaccine or COVID-19 Vaccine (Early Consideration)

October 3, 2025
Pharmaceuticals and Medical Devices Agency
Office of Vaccines and Blood Products

Production strains/antigen strains used in the manufacture of seasonal influenza vaccines (manufactured using strains other than those dispensed by the National Institute of Infectious Diseases, Japan Institute for Health Security) and COVID-19 vaccines are recommended/selected around spring every year by the World Health Organization (WHO) or MHLW. To change the strains if this is deemed necessary, regulatory procedures should be promptly completed by the autumn.

For vaccines required to undergo changes of production strains/antigen strains repeatedly as described above, the currently issued "Handling of Application for Confirmation of Change Management 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) and "Questions and Answers (Q&A) about Handling of Application for Confirmation of Change Management Protocol Related to Change of Strains for Influenza Vaccine or COVID-19 Vaccine" (Administrative Notice, dated October 3, 2025, of the Pharmaceutical Evaluation Division, Pharmaceutical Safety Bureau, MHLW) have established handling procedures for utilizing the system for changing approved items on the basis of a protocol to change a part of approved items (or post-approval change management protocol, hereinafter referred to as "PACMP") from the viewpoint of enabling reasonable and highly predictable regulatory procedures.

This document is intended to promote understanding of utilization of PACMP for strain changes (hereinafter referred to as "strain change PACMP") in view of the above handling procedures and includes examples of the Application Form for Confirmation of Change Management Protocol, a notification form, and attached data in Attachments 1 to 4 as well as points to note for their preparation. This document, however, presents only examples, is not intended to be used as the sole basis for preparation of the application form, etc., and does not cover all the contents. Information to be entered and the data should be individually determined for each product.

Please note that this document was prepared based on knowledge and information available as of October 2025 and thus is subject to change as they change in the future. It should be also noted that this document applies only to influenza vaccines and COVID-19 vaccines.

Attachment 1 Application Form for Confirmation of Change Management Protocol and table for comparison between new and old texts
Attachment 2 Data to be attached to the Application Form for Confirmation of Change Management Protocol
Attachment 3 Change management protocol
Attachment 4 Notification Form for Changes Made According to Change Management Protocol

[Abbreviations]

PACMP: Post Approval Change Management Protocol or protocol to change a part of approved items for approved products

PACMP Notification: “Handling of Application for Confirmation of Change Management 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, MHLW)

PACMP Q&A Notice: “Questions and Answers (Q&A) on Handling of Application for Confirmation of Change Management 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: “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 Change: “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 Corona Strain Change: “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)

PMDA: Pharmaceuticals and Medical Devices Agency

Application for Confirmation of Change Management Protocol (Step 1): Application for confirmation under provisions in the first sentence of Article 14-7-2, Paragraph 1 of the Act

Application for Confirmation of Changes in Change Management Protocol: Application for confirmation under provisions in the second sentence of Article 14-7-2, Paragraph 1 of the Act

Notification for Changes in Change Management Protocol: Notification under provisions in Article 68-7, Paragraph 1 of the Amended Regulation

Notification for Changes Made According to Change Management Protocol (Step 2): Notification under provisions in Article 14-7-2, Paragraph 6 of the Act

[Application Form for Confirmation of Change Management Protocol and Table for Comparison between New and Old Texts]

Example of documents prepared for notification to be submitted according to confirmed change management protocol

(1) to (3) below show examples of texts in an application form, a notification form, and a table for comparison between new and old texts in the case where notifications are planned for submission according to a confirmed change management protocol in and after the season for which confirmation has been granted.

(1) Application for Confirmation of Change Management Protocol (Step 1) (season subject to confirmation, Year 1)
(2) Notification for Changes Made According to Change Management Protocol (Step 2) (season with confirmation granted, Year 1)
(3) Notification for Changes Made According to Change Management Protocol (Step 2) (subsequent season for which confirmation has been granted, Year 2)

The examples below reflect a case of strain changes in an influenza vaccine where the clade of type A subtype H1N1 (A/H1N1) is changed for the season with confirmation granted (Year 1) by the Notification for Changes Made According to Change Management Protocol (Step 2), and the clade of type B Victoria lineage (B/Victoria) is changed for the subsequent season for which confirmation has been granted (Year 2) by the Notification for Changes Made According to Change Management Protocol (Step 2).

(1) Application for Confirmation of Change Management Protocol (Step 1) (season subject to confirmation, Year 1)

Application Form for Confirmation of Change Management Protocol for Drugs

[Ingredients, quantities, or nature] (omitted) Strains of influenza virus (types A and B) used as the active substances are as follows: A/●/●/2025(H1N1) A/●/●/2025(H3N2) B/●/●/2025(B/Victoria)

Table for comparison between new and old texts

Pre-change	Post-change	Remarks
Strains of influenza virus (types A and B) used as the active substances are as follows: A/●/●/2025(H1N1) A/●/●/2025(H3N2) B/●/●/2025(B/Victoria)	Strains of influenza virus (types A and B) used as the active substances are as follows: A/●/●/2025(H1N1) A/●/●/2025(H3N2) B/●/●/2025(B/Victoria)	Production strains to be changed from the previous year are underlined (because production strains for this year are not determined at the time of application, the same strains are presented in both pre- and post-change fields)

(Comments)

- The Application Form for Confirmation of Change Management Protocol should include the contents of the approval certificate at the time of this application.
- The table for comparison between new and old texts may not have to follow the example above if a more appropriate arrangement is achievable based on parts potentially subject to changes associated with future strain changes where appropriate.

(2) Notification for Changes Made According to Change Management Protocol (Step 2) (season with confirmation granted, Year 1)

Notification Form for Changes Made According to Change Management Protocol

[Ingredients, quantities, or nature] (omitted) Strains of influenza virus (types A and B) used as the active substances are as follows: A/■/■/2026(H1N1) A/●/●/2025(H3N2) B/●/●/2025(B/Victoria)

Table for comparison between new and old texts

Pre-change	Post-change	Remarks
Strains of influenza virus (types A and B) used as the active substances are as follows: A/●/●/2025(H1N1) A/●/●/2025(H3N2) B/●/●/2025(B/Victoria)	Strains of influenza virus (types A and B) used as the active substances are as follows: A/■/■/2026(H1N1) A/●/●/2025(H3N2) B/●/●/2025(B/Victoria)	Clade of type A subtype H1N1 changed

Comments

・ In the table for comparison between new and old texts, the clade of type A subtype H1N1 to be changed in the season with confirmation granted is underlined, and the details are entered after the change.

(3) Notification for Changes Made According to Change Management Protocol (Step 2) (subsequent season for which confirmation has been granted, Year 2)

Notification Form for Changes Made According to Change Management Protocol

[Ingredients, quantities, or nature] (omitted) Strains of influenza virus (types A and B) used as the active substances are as follows: A/●/●/2026(H1N1) A/●/●/2025(H3N2) B/●/●/2027(B/Victoria)

Table for comparison between new and old texts

Pre-change	Post-change	Remarks
Strains of influenza virus (types A and B) used as the active substances are as follows: A/●/●/2026(H1N1) A/●/●/2025(H3N2) B/●/●/2025(B/Victoria)	Strains of influenza virus (types A and B) used as the active substances are as follows: A/■/■/2026(H1N1) A/●/●/2025(H3N2) B/▼/▼/2027(B/Victoria)	Type B Victoria lineage changed

(Comments)

- In the table for comparison between new and old texts, the clade of type A subtype H1N1 changed in the season with confirmation granted (post-change clade of type A subtype H1N1) is reflected in the "Pre-change" field. In the table for comparison between new and old texts, the clade of type B Victoria lineage to be changed in the subsequent season for which confirmation has been granted (Year 2) is underlined, and details are entered after the change.
- The "Pre-change" field in the "Notification Form for Changes Made According to Change Management Protocol" after the season with confirmation granted (and later Year 2) should reflect the condition after the notification at Step 2 of the previous season, which is different from the corresponding part in the Application for Confirmation of Change Management Protocol for the season with confirmation granted (Year 1), but no procedure for changing the change management protocol to reflect the difference is required.

[Data Attached to Application Form for Confirmation of Change Management Protocol]

1) Draft post-change approval certificate reflecting the change management protocol and table for comparison between relevant texts before and after the changes (including a draft table for comparison between new and old approval certificates)
2) Change management protocol
   - Explanation for proposed changes
   - Plan for evaluation necessary for preparation of the data listed in (4) in 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) or (6) in the "Handling of Changes to COVID-19 Vaccine Strains" (PSB/PED Notification No. 0523-1 and PSB/CND Notification No. 0523-3, dated May 23, 2024)
   - Other data supporting the change management protocol (e.g., draft revised versions of the package insert, risk management plan [hereinafter referred to as "RMP"], and RMP materials)
3) Prior approvals after the first approval if approvals for partial changes in approved items under provisions in Article 14, Paragraph 15 of the Act have been granted or minor change notifications under provisions in Article 14, Paragraph 16 of the Act have been submitted since that time. Duplicate copies of approval certificates for the products concerned and duplicate copies of minor change notifications submitted during a period from the approval for the products concerned or the last approval of partial changes in approved items to the application for confirmation of a change management protocol

(Comments)

- Data should be attached with reference to Section 3.2 (2) of the PACMP Notification and Section 3 of the Strain Change PACMP Notification.
- For draft revised versions of the package insert, risk management plan (RMP), and RMP materials, proposed changes (proposed texts) at the time of revision in response to a strain change should be explained in the table for comparison between new and old texts, etc.

[Change Management Protocol]
Example of Change Management Protocol

Table of contents

1. Introduction

This document pertains to a change management protocol (strain change PACMP) defined in Section 2 of the PACMP Notification and shows an overview of the change management protocol for changes subject 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, hereinafter referred to as the "Partial Change Notification for Influenza Strain Change") and "Handling of Changes to COVID-19 Vaccine Strains" (PSB/PED Notification No. 0523-1 and PSB/CND Notification No. 0523-3, dated May 23, 2024, hereinafter referred to as the "Partial Change Notification for Corona Strain Change") .

The active substances are manufactured by modifying the approved virus seed (template DNA).

The objective of this strain change PACMP is to demonstrate that the same manufacturing method as that for the pre-change product produces the post-change product comparable to the pre-change one except for a difference in amino acid (base) sequence caused by the strain change.

2. Outline of changes planned

2.1. Manufacturing method

Virus seed (template DNA) is changed (added). The other manufacturing method remains unchanged.

(Comments)

• For parts of the manufacturing method (e.g., raw materials) changed, their details and reasons are provided. For the parts of the manufacturing method unchanged, the status (being the same) is explained.

2.2. Specifications and testing methods

Primers and reference sequences used for identification are changed. The primary antibody and reference materials used for the titer assay are changed. The other specifications and testing methods remain unchanged.

(Comments)

- For parts of the specifications and testing methods changed, their details and reasons are provided. For the parts of the specifications and testing methods unchanged, the status (being the same) is explained.

2.3. Table for comparison between relevant texts before and after the changes

A table for comparison between new and old texts (draft) in the Application Form for Confirmation of Change Management Protocol is provided in an attachment.

(Comments)

- In this mock-up, the table for comparison between new and old texts (draft) is omitted.

3. Evaluation plan for strain change

A list of studies or investigations to evaluate potential impacts of the strain change on quality as well as their testing methods and acceptance criteria, prepared based on risk assessment, are provided, and compliance with the approved control strategy or a plan for discussion about potential changes in control strategy required in association with the intended changes is provided.

(Comments)

- More specifically, a plan for evaluation necessary for preparation of the data listed in (4) in the Partial Change Notification for Influenza Strain Change or (6) in the Partial Change Notification for Corona Strain Change should be provided. Based on results from the above evaluation, compliance with the approved control strategy or a plan for discussion about potential changes in pre-strain-change control strategy should be provided.
- If the evaluation plan has been developed utilizing knowledge from a risk assessment at the time of a past strain change, no summary of the risk assessment is required. If the evaluation plan has been developed based on results from a risk assessment separately performed for every strain change, a summary of the risk assessment is provided in table form (list of brief descriptions about changes, impact evaluation, and risk reduction activities).

3.1 Evaluation of quality attributes

The strain change is justified by characterization and batch analyses using at least 3 lots each of the active substance and vaccine product manufactured in the post-strain-change process at a commercial scale. Results in the characterization and batch analyses are assessed using acceptance criteria established based on existing knowledge about strain changes.

(Comments)

- The number of lots is determined for each product according to an extent of the existing knowledge.
- If a strain change requires evaluation of performance of the manufacturing process, its plan is provided as done for characterization and batch analyses.

3.1.1. Characterization

Virus seed (template DNA)

Test item	Testing method	Acceptance criteria
Assay	xxx method	xxx
Description	xxx method	xxx
Identification	xxx method	xxx
Characteristic value	xxx method	xxx
Purity	xxx method	xxx
Product-related impurities	xxx method	xxx
Process-related impurities	xxx method	xxx
Contaminants	xxx method	xxx

(Comments)

- This table is just presented as an example and thus not intended to guide coverage of test items or recommend specific analytical procedures. Test items should be determined according to attributes of the product, and analytical procedures suitable for the objective should be selected.
- The test items, testing methods (analytical procedures), and acceptance criteria are established based on existing knowledge obtained from pre-strain-change products. The test items and testing methods (analytical procedures) remain unchanged from those for the pre-strain-change product in principle. The acceptance criteria are established to confirm that the strain change in virus seed (template DNA) leads to expected changes in quality attributes (e.g., base sequence). Acceptance criteria for other quality attributes expected to remain unchanged are established based on manufacturing results of pre-change products in principle.

Active substances

Test item	Testing method	Acceptance criteria
Structural analysis/confirmation	xxx method	xxx
Physicochemical properties	xxx method	xxx
Biological activities	xxx method	xxx
Product-related impurities	xxx method	xxx
Process-related impurities	xxx method	xxx
Contaminants	xxx method	xxx

(Comments)

- This table is just presented as an example and thus not intended to guide coverage of test items or recommend specific analytical procedures. Test items should be determined according to attributes of the product, and analytical procedures suitable for the objective should be selected.
- The test items, testing methods (analytical procedures), and acceptance criteria are established based on existing knowledge obtained from pre-strain-change products. The test items and testing methods (analytical procedures) remain unchanged from those for the pre-strain-change product in principle. The acceptance criteria are established to confirm that the strain change leads to expected changes in quality attributes (e.g., base sequence) of the active substance. Acceptance criteria for other quality attributes expected to remain unchanged are established based on manufacturing results of pre-change active substances in principle.

Vaccine product

Test item	Testing method	Acceptance criteria
Structural analysis/confirmation	xxx method	xxx
Physicochemical properties	xxx method	xxx
Biological activities	xxx method	xxx
Immunogenicity	xxx method	xxx

(Comments)

- This table is just presented as an example and thus not intended to guide coverage of test items or recommend specific analytical procedures. Test items should be determined according to attributes of the product, and analytical procedures suitable for the objective should be selected.
- The test items, testing methods (analytical procedures), and acceptance criteria are established based on existing knowledge obtained from pre-strain-change products. The test items and testing methods (analytical procedures) remain unchanged from those for the pre-strain-change product in principle. The acceptance criteria are established to confirm that the strain change leads to expected changes in quality attributes (e.g., base sequence) of the vaccine product. Acceptance criteria for other quality attributes expected to remain unchanged are established based on manufacturing results of pre-change vaccine products in principle.
- A study plan for "Data on immunological characteristics of antigen strains" under (6) in the Partial Change Notification for Corona Strain Change is included in a plan for characterization of the vaccine product.

3.1.2. Specifications and testing methods

3.1.2.1 Validation of Analytical Procedures

Validation of analytical procedures for identification and titer assay is performed using acceptance criteria established based on existing knowledge on strain changes.

Identification

Validation characteristic	Acceptance criteria
Specificity	xxx

Titer assay

Validation characteristic	Acceptance criteria
Specificity	xxx
Range	xxx
Accuracy	xxx
Precision Repeatability Intermediate precision	 xxx xxx

(Comments)

- If a strain change requires changes in operating procedures, reagents, reference materials, etc. of a testing method, a plan for validation of analytical procedures for the post-change test is presented. The example shows the case where identification test and titer assay are changed.
- Unless changes in testing methods associated with the strain change are planned, data from validation of analytical procedures are exempted from submission.

3.1.2.2 Batch analyses

Active substances

Test item	Testing method	Acceptance criteria
Assay	xxx method	xxx
Description	xxx method	xxx
Identification	xxx method	xxx
Characteristic value	xxx method	xxx
Purity	xxx method	xxx
Product-related impurities	xxx method	xxx
Process-related impurities	xxx method	xxx
Contaminants	xxx method	xxx

(Comments)

- This table is just presented as an example and thus not intended to guide coverage of test items or recommend specific analytical procedures. Test items should be determined according to attributes of the product, and analytical procedures suitable for the objective should be selected.
- The test items, testing methods (analytical procedures), and acceptance criteria are established based on existing knowledge obtained from pre-strain-change products. The test items and testing methods (analytical procedures) remain unchanged from those for the pre-strain-change product in principle. The acceptance criteria are established to confirm that the strain change leads to expected changes in quality attributes (e.g., base sequence) of the active substance. Acceptance criteria for other quality attributes expected to remain unchanged are established based on manufacturing results of pre-change active substances in principle.

Vaccine product

Test item	Testing method	Acceptance criteria
Assay	xxx method	xxx
Description	xxx method	xxx
Identification	xxx method	xxx
Characteristic value	xxx method	xxx
Purity	xxx method	xxx
Product-related impurities	xxx method	xxx
Process-related impurities	xxx method	xxx
Contaminants	xxx method	xxx

(Comments)

- This table is just presented as an example and thus not intended to guide coverage of test items or recommend specific analytical procedures. Test items should be determined according to attributes of the product, and analytical procedures suitable for the objective should be selected.
- The test items, testing methods (analytical procedures), and acceptance criteria are established based on existing knowledge obtained from pre-strain-change products. The test items and testing methods (analytical procedures) remain unchanged from those for the pre-strain-change product in principle. The acceptance criteria are established to confirm that the strain change leads to expected changes in quality attributes (e.g., base sequence) of the vaccine product. Acceptance criteria for other quality attributes expected to remain unchanged are established based on manufacturing results of pre-change vaccine products in principle.

3.1.2.3 Reference materials

Reference materials

Item	Testing method	Acceptance criteria
Assay	xxx method	xxx
Description	xxx method	xxx
Identification	xxx method	xxx
Characteristic value	xxx method	xxx
Purity	xxx method	xxx
Product-related impurities	xxx method	xxx
Process-related impurities	xxx method	xxx
Contaminants	xxx method	xxx

3.2. Stability

Stability protocol of the active substances (Supporting data held by the marketing authorization holder)

Study	Condition	Sampling points	Number of lots tested
Long-term storage	-20°C	Months 1, 3, 6, 9, 12, 15, and 18	1 lot
Accelerated	2 to 8°C	Months 1, 3, and 6	1 lot

Test items of active substances and acceptance criteria

Test item	Testing method	Acceptance criteria
Assay	xxx method	xxx
Description	xxx method	xxx
Identification	xxx method	xxx
Characteristic value	xxx method	xxx
Purity	xxx method	xxx
Product-related impurities	xxx method	xxx
Process-related impurities	xxx method	xxx
Contaminants	xxx method	xxx

(Comments)

- This table is just presented as an example and thus not intended to guide coverage of test items or recommend specific analytical procedures. Test items should be determined according to attributes of the product, and analytical procedures suitable for the objective should be selected. The test items, testing methods (analytical procedures), and acceptance criteria are established based on existing knowledge obtained from pre-strain-change products. To evaluate an impact of the strain change on stability, the same plan as that for pre-strain-change products is developed.
- If the plan has some sampling points where test items are reduced, a list is provided to clarify what test items are performed at which sampling points.

Protocol for long-term storage study of the vaccine product (internal assurance)

Study	Condition	Sampling points	Number of lots tested
Long-term storage	-20°C	Months 1, 3, 6, 9, 12, 15, and 18	1 lot
Accelerated	2 to 8°C	Months 1, 3, and 6	1 lot

Test items of vaccine product and acceptance criteria

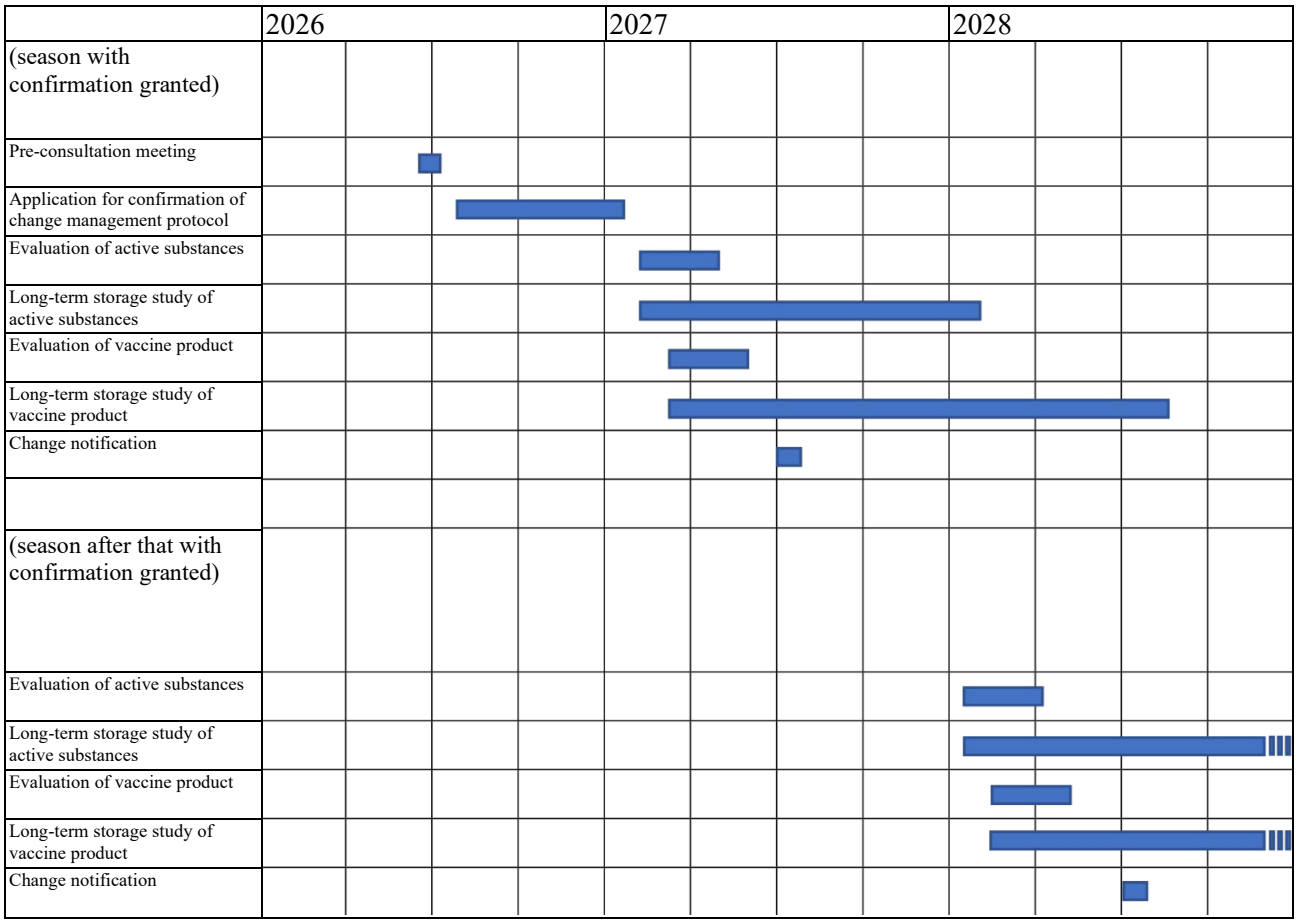
Test item	Testing method	Acceptance criteria
Assay	xxx method	xxx
Description	xxx method	xxx
Identification	xxx method	xxx
Characteristic value	xxx method	xxx
Purity	xxx method	xxx
Product-related impurities	xxx method	xxx
Process-related impurities	xxx method	xxx
Contaminants	xxx method	xxx

(Comments)

- This table is just presented as an example and thus not intended to guide coverage of test items or recommend specific analytical procedures. Test items should be determined according to attributes of the product, and analytical procedures suitable for the objective should be selected.
- The test items, testing methods (analytical procedures), and acceptance criteria are established based on existing knowledge obtained from pre-strain-change products. To evaluate an impact of the strain change on stability, the same plan as that for pre-strain-change products is developed.
- If the plan has some sampling points where test items are reduced, a list is provided to clarify what test items are performed at which sampling points.
- If an accelerated study is conducted, the study protocol as well as test items and acceptance criteria are provided in table form as done for the long-term storage study.

4. Data acquisition schedule

Table X shows an overview of the plan for manufacture, studies, and submission of notifications for a strain change to be performed every year.



Comments

- A representative schedule by year is provided in Gantt chart form. The following regulatory procedures, which may have difficulty fitting in the representative schedule, can be omitted from the concerned schedule: future partial change approval applications, minor change notifications, applications for confirmation of changes in confirmed items in the change management protocol, and minor change notifications for confirmed items in the change management protocol.
- If manufacturing and regulatory activities are performed on a schedule that differs from the representative schedule; or where data attached to the Notification for Changes Made According to Change Management Protocol (Step 2) include partial change approval applications, minor change notifications, applications for confirmation of changes in confirmed items in the change management protocol, or minor change notifications for confirmed items in the change management protocol, sharing the schedule with PMDA in a timely manner is encouraged to facilitate PMDA's review on the data attached to the notification form. For timing, the schedule should be shared immediately after the marketing authorization holder decides to change the strain through the Notification for Changes Made According to Change Management Protocol, taking into account production strains recommended and selected by the Ministry of Health, Labour and Welfare.

[Notification Form for Changes Made According to Change Management Protocol]

<Notification form>

Changes made according to the change management protocol are reflected in the "Last partial changes, minor changes" field.

<List of attached data>

1) Study results demonstrated to meet predetermined acceptance criteria and overview
2) - (not applicable)
3) Relevant texts in a draft changed approval certificate reflecting the change management protocol and table for comparison between them before and after the changes (including a draft table for comparison between new and old approval certificates)
4) Duplicate copies of prior confirmation certificates
5) Data on notifications submitted under provisions in Article 68-7, Paragraph 1 of the Regulation where applicable
6) Current change management protocol
7) Duplicate copies of approval certificates (including those of prior approval certificates for partial changes in approved items where applicable)
8) Duplicate copies of minor change notifications submitted during a period from approval for the products concerned, previous partial change approval, or previous confirmation of the change management protocol to submission of notification for changes made according to the change management protocol (Article 14, Paragraph 16 of the Act)
9) Written statement that the data have been collected and prepared under provisions in Article 43 of the Regulation.
10) Draft revised versions of package insert, RMP, and RMP materials

Comments

- Attached data are prepared in accordance with Section 5.1 (1) of the PACMP Notification.
- Section 5.1 (1) of the PACMP Notification "2) Duplicate copies of confirmation result notifications for compliance status of drugs, etc. if the confirmation of compliance status is required" is not applicable, because changes subject to a Strain Change PACMP Notification are limited to those not requiring confirmation of compliance status of drugs, etc.
- For Section 5.1 (1) of the Operational Notification "6) Current change management protocol," the change management protocol reflecting the submitted "Application for Confirmation of Changes in Confirmed Items in Change Management Protocol" or "Minor Change Notification for Confirmed Items in Change Management Protocol" where applicable.
- Draft revised versions of the package insert, RMP, and RMP materials are attached if their prior versions have been included in the change management protocol at the time of Application for Confirmation of Change Management Protocol (Step 1).

[Data Attached to Notification Form for Changes Made According to Change Management Protocol]
Example of "1) Study results demonstrated to meet predetermined acceptance criteria and overview"

Table of contents

1. Introduction

A summary of the strain change in the year with Notification for Changes Made According to Change Management Protocol (Step 2) is provided.

2. Information on production lots

Virus seed (template DNA)

Lot number	T2601
Date of manufacture	January 2026
Lot size	xx L
Manufacturing scale	Commercial scale

Active substances

Lot number	DS2601	DS2602	DS2603
Date of manufacture	March 2026	March 2026	April 2026
Lot size	xx g	xx g	xx g
Manufacturing scale	Commercial scale	Commercial scale	Commercial scale

Vaccine product

Lot number	DP2601	DP2602	DP2603
Date of manufacture	April 2026	April 2026	May 2026
Lot size	xxx,xxx vials	xxx,xxx vials	xxx,xxx vials
Manufacturing scale	Commercial scale	Commercial scale	Commercial scale

Reference materials

Lot number	SD2601
Date of manufacture	March 2026
Lot size	xx L
Manufacturing scale	Commercial scale

3. Results on production lots obtained according to the change management protocol

Results from sequencing of virus seed (template DNA), characterization, validation of analytical procedures, and batch analyses obtained according to the change management protocol are provided.

Comments

• A list of quality attributes, testing methods and acceptance criteria as well as measured values for each lot, as agreed in the Application for Confirmation of Change Management Protocol (Step 1), is provided.

3.1. Results from characterization

Virus seed (template DNA)

Quality attribute	Testing method	Acceptance criteria	T2601
Assay	xxx method	xxx	xxx
Description	xxx method	xxx	xxx
Identification	xxx method	xxx	xxx
Characteristic value	xxx method	xxx	xxx
Purity	xxx method	xxx	xxx
Product-related impurities	xxx method	xxx	xxx
Process-related impurities	xxx method	xxx	xxx
Contaminants	xxx method	xxx	xxx

Active substances

Quality attribute	Testing method	Acceptance criteria	DS2601	DS2602	DS2603
Structural analysis/confirmation	xxx method	xxx	xxx	xxx	xxx
Physicochemical properties	xxx method	xxx	xxx	xxx	xxx
Biological activities	xxx method	xxx	xxx	xxx	xxx
Product-related impurities	xxx method	xxx	xxx	xxx	xxx
Process-related impurities	xxx method	xxx	xxx	xxx	xxx
Contaminants	xxx method	xxx	xxx	xxx	xxx

Vaccine product

Quality attribute	Testing method	Acceptance criteria	DP2601	DP2602	DP2603
Structural analysis/confirmation	xxx method	xxx	xxx	xxx	xxx
Physicochemical properties	xxx method	xxx	xxx	xxx	xxx
Biological activities	xxx method	xxx	xxx	xxx	xxx
Immunogenicity	xxx method	xxx	xxx		

3.2 Results from validation of analytical procedures

Identification

Validation characteristic	Acceptance criteria	Result
Specificity	xxx	xxx

Titer assay

Validation characteristic	Acceptance criteria	Result
Specificity	xxx	xxx
Range	xxx	xxx
Accuracy	xxx	xxx
Precision Repeatability Intermediate precision	xxx	xxx

3.3. Results from batch analyses

Active substances

Item	Testing method	Acceptance criteria	DS2601	DS2602	DS2603
Assay	xxx method	xxx	xxx	xxx	xxx
Description	xxx method	xxx	xxx	xxx	xxx
Identification	xxx method	xxx	xxx	xxx	xxx
Characteristic value	xxx method	xxx	xxx	xxx	xxx
Purity	xxx method	xxx	xxx	xxx	xxx
Product-related impurities	xxx method	xxx	xxx	xxx	xxx
Process-related impurities	xxx method	xxx	xxx	xxx	xxx
Contaminants	xxx method	xxx	xxx	xxx	xxx

Vaccine product

Item	Testing method	Acceptance criteria	DP2601	DP2602	DP2603
Assay	xxx method	xxx	xxx	xxx	xxx
Description	xxx method	xxx	xxx	xxx	xxx
Identification	xxx method	xxx	xxx	xxx	xxx
Characteristic value	xxx method	xxx	xxx	xxx	xxx
Purity	xxx method	xxx	xxx	xxx	xxx
Product-related impurities	xxx method	xxx	xxx	xxx	xxx
Process-related impurities	xxx method	xxx	xxx	xxx	xxx
Contaminants	xxx method	xxx	xxx	xxx	xxx

3.4 Results from control testing of reference materials

Reference materials

Item	Testing method	Acceptance criteria	SD2601
Assay	xxx method	xxx	
Description	xxx method	xxx	
Identification	xxx method	xxx	
Characteristic value	xxx method	xxx	
Purity	xxx method	xxx	
Product-related impurities	xxx method	xxx	
Process-related impurities	xxx method	xxx	
Contaminants	xxx method	xxx	

4. Protocol for long-term storage study

Active substances

Sampling point (Month)	0	1	3	6	9	12	18
DS2601	3/2026	4/2026	6/2026	9/2026	12/2026	3/2027	6/2027
DS2601	3/2026	4/2026	6/2026	9/2026	12/2026	3/2027	6/2027
DS2602	4/2026	5/2026	7/2026	10/2026	1/2027	4/2027	7/2027

Vaccine product

Sampling point (Month)	0	1	3	6	9	12	18
DP2601	4/2026	5/2026	7/2026	10/2026	1/2027	4/2027	7/2027
DP2601	4/2026	5/2026	7/2026	10/2026	1/2027	4/2027	7/2027
DP2602	5/2026	6/2026	8/2026	11/2026	2/2027	5/2027	8/2027

Comments

- Based on the date of manufacture of each lot, a schedule of future test result acquisition is specifically provided.

5. Conclusion

All the test results conform to the acceptance criteria agreed in advance, and the control strategy for the pre-strain-change product remains applicable to the post-strain-change product as well. The strain change has been validated.

The long-term storage study will be continued to confirm that the strain change has no impact on stability.