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To: Directors of Prefectural Health Departments (Bureaus)

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

Handling of Changes to COVID-19 Vaccine Strains
(Notification)

Handling of cases where strains used as antigens of COVID-19 vaccine (hereinafter referred to as “antigen strains”) need to be changed at a marketing authorization holder is organized as provided below. Please understand the content and ensure that all the companies under your jurisdiction are informed.

(1) For a change of antigen strains for COVID-19 vaccine, approval of partial changes in items approved under Article 14, Paragraph 1 of the Act on Securing Quality, Efficacy and Safety of Products Including Pharmaceuticals and Medical Devices (Act No. 145 of 1960, hereinafter referred to as “PMD Act”) pursuant to Paragraph 15 of the same article (hereinafter referred to as “partial change approval”) should be obtained.

(2) In general, to change the antigen strains for COVID-19 vaccine, quality attributes of vaccines before and after the change of antigen strains should be analyzed and evaluated. In addition, the post-change vaccine should be demonstrated to have immunogenicity against the new target antigen strains and safety largely comparable to that of the pre-change vaccine by clinical study

results.

(3) Of vaccines approved in Japan for which a change of antigen strains has been qualified by analyses and evaluation as well as clinical study results in the preceding paragraph, vaccines that are highly likely to have quality and safety unaffected by the change of antigen strains, and immunogenicity potentially predicted in non-clinical studies should be subject to actions described in (4) to (12) below.

(4) To ensure that COVID-19 vaccines using the latest antigen strains are supplied before the start of regular vaccination campaigns scheduled in autumn and winter, the partial change approval should be obtained promptly. An application to obtain the partial change approval pursuant to Article 14, Paragraph 15 of the PMD Act (hereinafter referred to as “partial change application”) should be submitted by the end of June at the latest. To contribute to expedited reviews, the partial change application for a change of antigen strains should not include any changes in items approved for marketing other than those associated with the change of antigen strains. The expedited reviews will not be applied to the partial change applications that involve a process change for the change of antigen strains (except minor changes) and need to undergo a GMP compliance inspection specified in Article 14, Paragraph 7 of the PMD Act.

(5) A partial change application falls under any of the categories, (10), (10-2), (10-3), and (10-4). The category should be selected in view of whether the product is within a reexamination period, whether the change corresponds to a process change, etc.

(6) For a partial change application, the applicant should submit some of the following data as appropriate at the time of application in consultation with the Pharmaceuticals and Medical Devices Agency (hereinafter referred to as “PMDA”). Even before the partial change application, any data ready for submission should be submitted. Or if submission of the data at the time of a partial change application seems difficult, the applicant should consult with PMDA about timing of the submission in advance. Submission of the data after the partial change application may be allowed in some cases.

- Data on immunological properties of the antigen strains (e.g., immunogenicity data in non-clinical studies of the vaccine)
- Data on product quality after the change of antigen strains (e.g., results of control tests of template DNA, cell bank, and virus seed used for production of the vaccine, results of characterization during manufacture of the active

substance and vaccine product and batch analyses of the active substance and vaccine product [results of specification tests, etc. of lots reflecting commercial production], and plans to obtain stability data)

- Other data required at the discussion with MHLW and PMDA

(7) In the following case, administrative processing of the partial change application will generally take 2 months until its approval: the antigen strains used in COVID-19 vaccine are within a scope of strains selected by MHLW; and the partial change application for the concerned antigen strains is submitted to ensure that the vaccine is supplied to the regular vaccination campaign of COVID-19 vaccines in Japan. However, this period may vary depending on when the data listed in (6) are submitted.

(8) Partial change applications for vaccines applicable to (3) will not need to undergo GMP compliance inspection.

(9) If an individual discussion about timing of application, data to be submitted, etc. is necessary for the partial change application, the applicant should consult with MHLW and PMDA in advance.

(10) If national assay involves an on-site test, of the test reagents and report documents on their preliminary test results, reagents to be supplied by the applicant should be submitted by the due date designated by the National Institute of Infectious Diseases (hereinafter referred to as “NIID”). The test reagents should be submitted well in advance before application for lot assay.

(11) If formats of Summary Lot Protocol need to be prepared or changed, the application should be submitted to NIID by the due date designated by NIID.

(12) For the schedule of application for lot assay for the national assay, a vaccine application plan should be submitted by the due date designated by NIID.