Provisional Translation (as of June 2022)*

PSEHB/PED Notification No. 0401-7
April 1, 2022

To: Prefectural Health Department (Bureau)
To: Regional Bureau of Health and Welfare

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

New Drug Applications Using the Gateway System

Regarding new drug applications, handling of methods on submitting an application form and part of documents to be appended to the application form (hereinafter referred to as "appended documents") via an electronic study data system (hereinafter referred to as "gateway system") in place of flexible disks (hereinafter referred to as "gateway application") has been notified in the "Notification on Practical Operations of Electronic Study Data Submissions" (PFSB/ELD Notification No. 0427-1, by the Director of Evaluation and Licensing Division, Pharmaceutical and Food Safety Bureau, Ministry of Health, Labour and Welfare, dated April 27, 2015; hereinafter referred to as "notification on practical operations").

In relation to the consolidation of the notification on practical operations as the "Notification on Handling of Submission of Electronic Study Data for New Drug Applications" (PSEHB/PED Notification No. 0401-10, by the Director of Pharmaceutical Evaluation Division, Pharmaceutical Safety and Environmental Health Bureau, Ministry of Health, Labour and Welfare, dated April 1, 2022; hereinafter referred to as "notification on electronic study data"), we have decided to particularly organize and summarize the matters related to the gateway application into this notification; therefore, we ask you to be informed of this notification and inform manufacturers and sellers placed under your administration.

Please also be informed that the copy of this notification is also released to the heads of concerned organizations indicated in the appended list.

Notice

1 New drug applications subject to gateway application

New drug applications, which are categorized into from (1) to (7), (9) and (9-2) listed in the appendix 2-(1) of the notification entitled "Approval Application of Pharmaceuticals" (PFSB Notification No. 1121-2, by the Director of Pharmaceutical and Food Safety Bureau, Ministry

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

of Health, Labour and Welfare, dated November 21, 2014; hereinafter referred to as "notification by the director"), are subject to the gateway application, in principle, in accordance with this notification.

In cases in which the appended documents do not include any electronic files as defined in the notification on electronic study data (hereinafter referred to as "electronic study data"), the new drug application that is categorized into from (1) to (7), (9) and (9-2) listed in the appendix 2-(1) of the notification by the director may be made in accordance with the "Handling of Flexible Disk Applications" (PSEHB/PED Notification No. 216-1 and PSEHB/MDED Notification No. 0216-1, by the Director of Pharmaceutical Evaluation Division and the Director of Medical Device Evaluation Division, Pharmaceutical Safety and Environmental Health Bureau, Ministry of Health, Labour and Welfare, dated February 16, 2022; hereinafter referred to as "notification on FD applications"), instead of making the gateway application.

2 Submission of an application form and appended documents subject to the gateway application

(1) Documents to be submitted using the gateway system

Among the application form and appended documents submitted in the gateway application, electronic files that record items listed in each column for applicable documents as specified in the notification on FD applications (hereinafter referred to as "FD data"), electronic files of CTD [referring to CTD defined in the "On Organization of Application Dossier Appended to New Drug Application (NDA) for Approval" (PMSB/ELD Notification No. 899, by the Director of Evaluation and Licensing Division, Pharmaceutical and Medical Safety Bureau, Ministry of Health, Labour and Welfare, dated June 21, 2001); the same applies hereinafter] documents digitalized in accordance with the "Approval Application with Electronic Common Technical Document (eCTD)" (PSEHB/PED Notification No. 0705-1, by the Director of Pharmaceutical Evaluation Division, Pharmaceutical Safety and Environmental Health Bureau, Ministry of Health, Labour and Welfare, dated July 5, 2017) (hereinafter referred to as "eCTD"), and electronic study data need to be submitted using the gateway system. Regarding appended documents, CTD documents should be submitted as the eCTD for applications that require submission of CTD documents and electronic study data. Even for applications that do not require submission of electronic study data, CTD documents should preferably be submitted as the eCTD if the gateway application is made.

Other appended documents and responses to inquiries, with the exception of documents shown in (2), may be submitted in electronic files, instead of in paper form, using the gateway system.

Refer to the appendix for the necessity of submission of CTD documents, the eCTD or electronic study data and for the usability of the gateway system in accordance with this notification.

(2) Documents to be submitted in paper form

In the gateway application, the application form and appended documents that correspond to the following should be submitted in paper form.

- Documents listed in Article 284-1 of the Ministerial Ordinance for Enforcement of the Act on Securing Quality, Efficacy, and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products and Cosmetics (hereinafter referred to as "Ministerial Ordinance") (including revenue stamps attached)
- "Documentation of FD contents" specified in the notification on FD applications
- Review/Inspection Application Form [specified in Ministerial Ordinance Form No. 27 and including a copy of a document attached on the back that certifies that the processing fee has been paid to the account of the Pharmaceuticals and Medical Devices Agency (hereinafter referred to as "PMDA")]
- A copy of license for marketing authorization holder

3 Submission using the gateway system

(1) Advance notice of application

In case of the gateway application, the applicant should make an advance notice of the application (hereinafter referred to as "application notice") during the period from 5 weeks to 1 week before the scheduled date for the application, in principle, by entering required information into the gateway system. After an application notice has been made, the PMDA should contact the applicant to schedule a date for the application and discuss other administrative matters.

In addition, a documentation of the application notice (hereinafter referred to as "application notice receipt form") should be printed out in paper form.

(2) Submission of electronic files using the gateway system

After making an application notice, the applicant should send FD data, the eCTD, electronic study data, and other electronic files using the gateway system after appending necessary information. In this case, the gateway system will perform virus check and validation, and only electronic files that are deemed acceptable will be accepted.

Of note, at the time the new drug application is received at the PMDA window as specified in (4), the virus check of all electronic files sent by the applicant should have been completed and the results of the validation of FD data should have been shown to be acceptable. Therefore, the applicant should take into account the processing time for the virus check, etc. and perform necessary operations on and before the scheduled date for the application.

For specific procedures and operations on the gateway system, refer to the "Technical Conformance Guide on Electronic Study Data Submissions" (PMDA/CPE Notification No.

0401003 and PMDA/CRS Notification No. 0401001, by the Director of Center for Product Evaluation and the Director of Center for Regulatory Science, Pharmaceuticals and Medical Devices Agency, dated April 1, 2022), the website of the gateway system (see 5 (1)), the PMDA's website (https://www.pmda.go.jp/), and the operation manual for the gateway system.

(3) Method of submission of electronic files that cannot be submitted using the gateway system

If there are any electronic files that cannot be submitted using the gateway system due to inevitable reasons after making the application notice specified in (1), the files should be recorded in a recording medium and the medium, with the application notice receipt form, should be brought to the PMDA window by a day before the scheduled date for the application or sent to the PMDA window for arrival by a day before the scheduled date for the application. In this case, except for when referencing electronic study data from the XML message of the eCTD, additional information on the content of electronic study data should be submitted in a tab-separated values (TSV) file. For preparation methods for TSV files, refer to the PMDA's website. The acceptable recording media, in principle, are DVD-R/RW or BD-R/RE (including multi-layer discs, respectively). Consult the PMDA beforehand if you wish to submit in any other medium. If the application notice specified in (1) has been made, the subsequent electronic files of documents related to the new drug application can be submitted using the gateway system.

If the application notice specified in (1) cannot be made due to inevitable reasons, the applicant cannot use the gateway system for the application. Therefore, the new drug application should be made in accordance with the notification on FD applications.

(4) Procedures for a new drug application after sending electronic files

After the submission of electronic files is completed, the applicant should submit the documents in paper form to the PMDA window with the application notice receipt form.

The receipt of the new drug application is completed when it is deemed acceptable after the PMDA confirms that the electronic files (excluding electronic study data and the eCTD) and the documents in paper form are complete and that the prespecified processing fee has been paid and performs other formal reviews. The results of the validation of electronic files other than FD data will not be used to determine whether or not to receive the new drug application.

After the completion of the receipt, a receipt form that indicates the receipt number and other information identifying the new drug application will be issued by the PMDA to the applicant.

4 Handling of the date of application in the gateway application

(1) Date of application

The date of submission (date of bringing or sending) to the PMDA window stated in 3 (4) will be considered the date of application and should be indicated on the new drug application form.

(2) Date of receipt

The date of completion of the receipt by the PMDA stated in 3 (4) will be considered the date of receipt.

5 Others

(1) Gateway system

The gateway system is available at the following website, 24 hours a day 365 days a year, excluding downtime due to maintenance, etc. Make sure information on electronic certificate required for using the gateway system and other technical information that are published on the same website.

(address of the website: https://esg.pmda.go.jp/Ssk/comn001p01.init)

(2) Future gateway application

In the future, if the gateway application can be used for new drug applications categorized into (8), (8-2), and from (10) to (10-4) listed in the appendix 2-(1) of the notification by the director and other new drug applications, it will be directed in accordance with this notification.

(3) Future online application

In the future, documents in paper form specified in Article 284 of the PMD Regulations will also be able to be submitted in electronic files (this method of submission is hereinafter referred to as “online application”). The specific time and method will be notified separately, and this separate notification should be followed when making an online application, regardless of stipulations in this notification. In addition, after the start of the online application, new drug applications should be made using the online application, not the gateway application, as long as possible.

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(Appendix)

Category in the appendix 2-(1) of the notification entitled "Approval Application of Pharmaceuticals"	Submission of CTD (*1)	Submission of eCTD	Submission of electronic study data	Usability of the gateway system
(1) Drugs with a new active ingredient	○	○	○	○
(2) New combination drugs	○	○	○	○
(3) Drugs with a new route of administration	○	○	○	○
(4) Drugs with a new indication	○	○	○	○
(5) Drugs in a new dosage form	○	○	○	○
(6) Drugs with a new dosage	○	○	○	○
(7) Biosimilars	○	○	○	○
(8) Drugs in additional dosage form (within re-examination period)	○	△	×	unavailable
(8-2) Drugs in additional dosage form (exceeded re-examination period)	○ (*2)	△	×	unavailable
(9) Combination prescription drugs with similar formulations (within re-examination period)	○	○	○	○
(9-2) Combination prescription drugs with similar formulations (exceeded re-examination period)	△	△ (*3)	○	○
(10) Other drugs (within re-examination period)	○	△	×	unavailable
(10-2) Other drugs (in the case of (10) and manufacturing change of biological products, etc.)	○	△	×	unavailable
(10-3) Other drugs (exceeded re-examination period)	○ (*2)	△	×	unavailable
(10-4) Other drugs (in the case of (10-3) and manufacturing change of biological products, etc.)	○	△	×	unavailable

○: mandatory, △: optional, ×: unnecessary

*1: Specified by "Handling of Application Dossier Appended to New Drug Application (NDA)" (PSEHB/ELD Notification No. 0311-3, by the Director of Evaluation and Licensing Division, Pharmaceutical Safety and Environmental Health Bureau, Ministry of Health, Labour and Welfare, dated March 11, 2016), "Points to be Considered for Drug Approval Application" (PFSB/ELD Notification No. 1121-12, by the Director of Evaluation and Licensing Division, Pharmaceutical and Food Safety Bureau, Ministry of Health, Labour and Welfare, dated November 21, 2014), and "On Organization of Application Dossier Appended to New Drug Application (NDA) for Approval" (PMSB/ELD Notification No. 899, by the Director of Evaluation and Licensing Division, Pharmaceutical and Medical Safety Bureau, Ministry of Health, Labour and Welfare, dated June 21, 2001)

*2: Among (8-2) and (10-3), the following cases are "△: optional."
[1] Biological products, [2] Radiopharmaceuticals, [3] Products manufactured using recombinant technology,
[4] Products that have been specified by the Minister of Health, Labour and Welfare, as those requiring special attention to manufacturing control or quality control, according to the provision E of Article 80-2-7 of the Cabinet Order for Enforcement of the Act on Securing Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics [PMD Act] (Order No. 11, 1961)
(a) Products manufactured using human-derived or animal-derived cells, (b) cell- and tissue-based products, (c) specified biological products
[5] Products whose drug substance is a biological ingredient, herbal products or extracts of animal or plant origin, [6] in vitro diagnostics,
[7] Products listed in Article 96 of Ministerial Ordinance for Enforcement of PMD Act (MHLW Ordinance No. 1, 1961) (products which are not required conformity to the standards of the "Ministerial Ordinance on Standards for Manufacturing Control and Quality Control for Drugs and Quasi-drugs" (MHLW Ordinance No. 179, 2004)
At the time of an application for partial changes, only CTD documents with applicable changes related to the application should be submitted or a summary of the influence of the applicable changes on the quality discussed from the scientific viewpoint with supporting data should be submitted.

*3: For (9-2), as in the past, submission of the eCTD is not always required for the time being. Even if the eCTD is not submitted, only electronic study data should be submitted using the gateway system in accordance with 3 of this notification.

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[Appended List]

Chief Executive of the Pharmaceuticals and Medical Devices Agency

President of the Federation of Pharmaceutical Manufacturers' Associations of JAPAN

President of the Japan Pharmaceutical Manufacturers Association (JPMA)

Chair of the Technical Committee of the European Federation of Pharmaceutical Industries and Associations, Japan

Chair of the Japan Based Executive Committee of the Pharmaceutical Research and Manufacturers of America

Chairman of the Japan CRO Association