FAQs on Electronic Study Data Submission

1. Questions on new drug review and consultation

Q1-1: Deleted

Q1-1-1: Deleted

Q1-2: In the gateway application, is it appropriate to specify a date when the new drug application is to be made in the cover and the "Date of submission" column in the application form (including FD application data) and in the "Date of application" column in the eCTD cover letter and specify a date when the electronic file is to be submitted in the gateway system in the "Date of submission" column in the eCTD cover letter?

A: Yes. The concept of the date to be specified in the "Date of application" column and the "Date of submission" column is as before. When submitting FD application data for replacement or the revised version of eCTD using the gateway system, please specify a date when sending of the data is to be started.

Q1-3: Please explain briefly the flow of new drug applications using the gateway system, what the applicant should do when using the gateway system, and when the applicant should do them.

A: The flow of new drug applications using the gateway system is as shown below.
A possible or recommended time period for the applicable activity is specified in [ ].

a) Prepare an electronic certificate of individuals, and register them as a user of the gateway system. [Figure 1-3 (0)]
[Recommend approximately 1 month before the scheduled date of application]
b) Give notice of a summary of the new drug application, planned submissions, and the scheduled date of application to the PMDA from the gateway system. The submission notice enables the applicant to receive an eCTD receipt number. [Figure 1-3 (1)]
[From 5 weeks to 1 week before the scheduled date of application]
* Please note that you cannot give notice of the application less than 1 week before the scheduled date of application.
c) Submit the electronic file to the PMDA from the gateway system. Necessary information on electronic study data should be registered by entering on the screen or by loading separately created TSV files. [Figures 1-3 (1) to (3)]
[Time period from giving notice of the date of application as shown in b) to the application submission in d)]
d) The applicant can submit the new drug application when a virus check of all electronic files planned to be submitted is completed and the results of validation of FD application data are shown to be acceptable. The applicant shall print out the application notice receipt form and submit it to the PMDA window with the application form. [Figure 1-3 (4)]

Figure 1-3：The flow of new drug applications using the gateway system
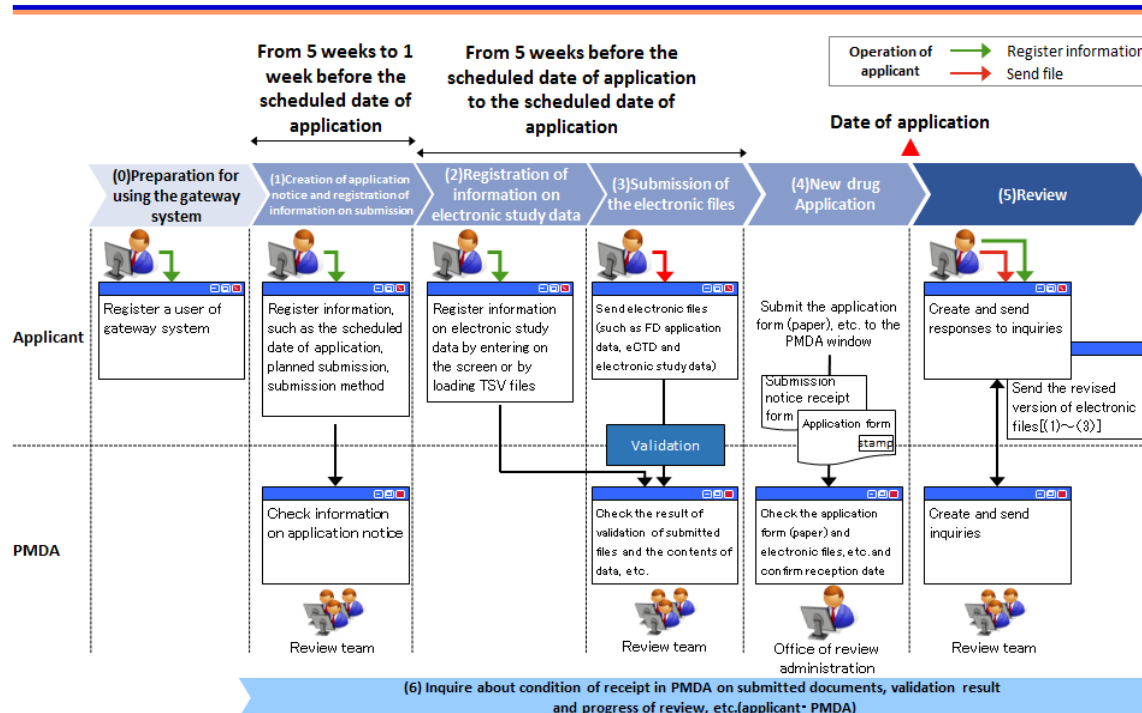
Q1-4: Deleted

Q1-5: Regarding clinical trial consultations, consultations related to submission of electronic study data, and Pre-NDA meetings, please advise us about the contents and points to consider of each consultation.

A: The contents and points to consider of each consultation are shown in the table below. If an applicant wonders which consultation should be used for their questions, please confirm them at the pre-meeting as needed.

Category of consultations	Contents and points to consider
Clinical trial consultations	In this consultation, an applicant and the PMDA identify which electronic study data and/or analysis data are subject to be submitted among the clinical data package necessary for the new drug applications. If the applicant submits electronic study data of all studies and analyses within clinical data package, it is sufficient to state it at a pre-meeting etc.

Consultation on exemption of submission of electronic study data	In this consultation, an applicant and the PMDA discuss the following contents etc., regarding each electronic study data identified to be subject to be submitted in the clinical trial consultation. · whether submission of a part of or whole of electronic study data could be exempted, based on the circumstances of holding data, when it is difficult to prepare electronic study data, according to Question 2 in the Q&A regarding the notification on electronic study data · adequacy of the reason why electronic study data would be submitted in a format other than the CDISC standards and sufficiency of the contents of electronic submission (information of electronic study data and analyses), when electronic study data in a format other than the CDISC standards is submitted, according to Question 15 in the Q&A regarding the notification on electronic study data
Consultation on preparation of submission of electronic study data	In this consultation, an applicant and the PMDA discuss the following contents etc., regarding electronic study data and/or analysis data planned to be submitted. · method of storing data, handling of variables, submission method of electronic study data, and strategy of storing data which cause the violations of CDISC conformity · special circumstances, such as the situation in which submission timing of electronic study data is compelled to be different from submission timing of study results
Consultation on data format of submission of electronic study data	In this consultation, which is conducted when a pre-NDA meeting is not expected before electronic study data submission, the PMDA confirms an explanation of a violation of the validation rule corresponding to "Error" that is detected based on the results of a validation performed in advance and the reasons why it cannot be corrected, as needed.
Pre-NDA meeting	In this consultation, the PMDA does a final confirmation of the contents of application documents and scheduled timing of submission.

Q1-6: Deleted

Q1-6-1: Deleted

Q1-6-2: Deleted

Q1-6-3: Deleted

Q1-7: When can an applicant submit electronic files using the gateway system for a new drug application? In addition, is it permissible to submit electronic files using the gateway system not on

the scheduled date of submission specified in the submission notice?

A: Applicants can send electronic files from the day when the application notice is created in the gateway system to the scheduled date of submission of the application form (the scheduled date of application) specified in the application notice. It is permissible to send electronic files not on the scheduled date of submission if they are sent before the scheduled date of application. If the files are sent beyond the scheduled date of submission, please correct the submission notice. Electronic files cannot be sent beyond the scheduled date of application. Please make sure to send them by the scheduled date of application.

Of note, at the time the new drug application is received at the PMDA window, a virus check of all electronic files sent by the applicant should have been completed and the results of validation of FD application data should have been shown to be acceptable. A certain amount of time is necessary to complete the virus check of electronic files, etc., and the process may require time in case of heavy access. Therefore, applicants are requested to plan extra time for electronic submission.

Q1-8: A "pre-NDA meeting number" is required in the gateway system. What should be referenced when entering this?

A: Please enter a receipt number of the pre-NDA meeting. PMDA staff will notify the receipt number of the pre-NDA meeting when contacting an applicant to schedule the date of meeting.

Q1-9: Is there any change in the method of creating files of inquiries and responses to inquiries by using the gateway system?

A: There is no change in the method of creating these files. For the file size of responses to inquiries, please refer to the operation manual for the gateway system.

Q1-10: Deleted

Q1-11: If an application for such as additional indication is made for a drug with a new active ingredient that is under review (hereinafter referred to as "additional indication application during a new application"), it will be made as a separate application for a drug with a new active ingredient. The additional indication application during a new application will be cancelled after the applicable new drug is approved as a drug with a new active ingredient, and a partial change approval application will be made anew. In this case, is it necessary to submit all the electronic study data again that have been submitted for the additional indication application during a new application?

A: Yes. However, it is not necessary to submit electronic study data that overlap with those already submitted at the time of approval of the new drug as a drug with a new active ingredient. Of note, at the time the partial change approval application is made, if reception has been closed for a version of the standards or a version of the validation rule that was available at the time the application for a drug with a new active ingredient was made, data that were submitted for the application for a drug with a new active ingredient and are required to be submitted again for the additional indication application basically require no additional actions, unless there is a change to the submitted data.

Q1-12: Deleted

Q1-13: Deleted

Q1-14: Deleted

Q1-14-1: Deleted

Q1-14-2: Deleted

Q1-15: When seeking advice on the scope of electronic study data to be submitted at the clinical trial consultation, what kind of consultation document should an applicant submit?

A: In addition to the documents used for the consultation on the application data package, applicants are required to give an explanation of the appropriateness of the scope of electronic study data to be submitted based on the notification on electronic study data.

Q1-16: When an applicant performs validation with software that the vender claims is compatible with the software used by the PMDA, and then corrects data or explains the results, are there any particular points to consider?

A: If an applicant uses the software that the vender claims is compatible with the software used by the PMDA in an advance validation of electronic study data and the PMDA confirms that data have been corrected based on the applicable results for a violation of the validation rule corresponding to "Reject", the PMDA, after receiving electronic study data, will accept the approval application and begin the review if there are no inadequacies in the FD application data, eCTD, or other documents, in principle. However, if violations of the validation rule corresponding "Reject" are newly detected by validation at the PMDA, the PMDA will require correction of data. For a violation of the validation rule corresponding to "Error" detected by the validation performed by the applicant in advance, it should be described the reasons why it happened and why it cannot be corrected in the reviewer's guide.

Q1-17: If a detected violation is attributed to a bug of the validation software, is it necessary to correct the data?

A: When there is no obvious violation based on a check of actual datasets, even though a violation is detected by the validation software, the applicant may give the rationale that the violation is caused by a bug in the validation software. Explain the rationale on the reviewer's guide. When the validation software vender publishes the bug, the applicant may point to it as the explanation.

Q1-18: After submission of electronic study data, how will the PMDA perform a validation and a virus check in the system and how can an applicant confirm the results of the validation? If correction of electronic study data is required, how will it be notified to an applicant?

A: After receiving electronic study data, the PMDA will perform a virus check and signature verification, and if there are no inadequacies, perform a validation. In addition, based on a validation report that has been output and the reviewer's guide, etc., PMDA staff will determine whether the data are acceptable or not and input the result in the gateway system.

After completion of the signature verification, the PMDA will perform a validation. While determination of the data acceptability is ongoing, the status displayed by the system is "validation ongoing", and when the result of determination of the data acceptability is input in the system, the status will be changed to "validation completed". Determination of the data acceptability is expected to take 5 business days usually after submission of electronic study data.

Applicants can check the result of the virus check and the results of the validation at the PMDA when the virus check is completed and when PMDA staff input the result of determination of the data acceptability in the system, respectively. For the detailed method of checking these results, please refer to the operation manual for the gateway system.

If the validation at the PMDA detects a violation of the validation rule corresponding to "Reject", electronic study data that require action and the validation rule will be notified to applicants in writing if the application has not been made yet or as an inquiry if the application has already been made. If there is no explanation in the reviewer's guide for a violation of the validation rule corresponding to "Error" detected by the validation performed by the applicant in advance, the explanation will be required by an inquiry after the application is made.

Q1-19: Deleted

Q1-20: Can an applicant receive feedback on how the PMDA used electronic study data submitted for a new drug application for a certain product during review?

A: Appendix 7 of the "Confirmation of the Progress Status of New Drug Review" (PMDA Notification No. 1227001, by the Chief Executive of Pharmaceuticals and Medical Devices Agency, dated December 27, 2010) states that an exchange of opinions on issues related to the applicable application or review and future issues shall be conducted as a trial at an appropriate time after completion of the review, if either the applicant or the PMDA requests it and both of them deem it necessary. The PMDA also provides feedback on electronic study data during this exchange of opinions. So, please make a request to the responsible review office as needed.

Q1-21: Is it necessary to submit a copy of a record of a consultation on submission of electronic study data on a new drug as a document appended to the application form?

A: Yes. If a consultation on submission of electronic study data on a new drug has been conducted, please submit a copy of the following according to the type of the consultation conducted as "(2) Records of Clinical Trial Consultations (Copies)" in "13. Others" in Module 1 of CTD: "Summary

of Results of a Consultation on Data Format of Submission of Electronic Study Data" for a consultation on data format of submission of electronic study data (charged), "Summary of Results of a Consultation on Preparation of Submission of Electronic Study Data" for a consultation on preparation of submission of electronic study data, and a consultation record for a consultation on exemption of submission of electronic study data.

Q1-22: Is it necessary to include Rule ID in the results of validation in the reviewer's guide?

A: Yes. Please include the Rule ID of the published "PMDA Study Data Validation Rules" in validation results in the reviewer's guide.

Q1-23: Is there anything special to consider when the applicant provides the necessary explanation for the violations of "Error" that cannot be corrected in reviewer's guide?

A: Regarding violations of "Error" that cannot be corrected, since PMDA evaluates the amount of influence on analyses conducted in the review process based on the explanation provided by the reviewer's guide, please explain how the data is stored actually about the violation, etc. When the applicant explains "it does not affect analyses conducted by the applicant", please explain the reason that led to the conclusion.
Regarding violations of "Error" that cannot be corrected, please explain the reason why it cannot be corrected.

Q1-24: What kind of validation does PMDA conduct regarding the validation of electronic study data for the conformity to the CDISC standards?

A: The PMDA conducts validation for the consistency between SDTM datasets and ADaM datasets as well as validations of each SDTM or ADaM dataset. Moreover, the PMDA conducts validation for the consistency between define.xml and each SDTM/ADaM dataset as well as validation for the structure of XML in define.xml. Please note that same validations must be performed, when the applicant evaluates the conformity in advance.

Q1-25: What are points to consider when entering the analysis type that is required to be entered on the "Study Data Submission" window of the gateway system?

A: Since information entered in the analysis type is used to identify files on clinical pharmacology when creating the "Explanation of electronic study data package on clinical pharmacology" described in Section 4.2.1 of the technical conformance guide, the analysis type should be appropriately entered to include the appropriate contents in the "Explanation of electronic study data package on clinical pharmacology".
For studies or analyses that do not include electronic study data on a clinical pharmacology analysis, please select Non-CP for all files.
When electronic study data on a clinical pharmacology analysis are included, the relationship between the type of documents subject to electronic submission and the analysis type is as shown in Table 1-25 below, which is based on the category in the notification on electronic study data.

Therefore, please select the same analysis type for all files for each study or analysis based on the idea below. However, if a standard pharmacokinetic analysis and a population analysis are included in one study report, select POP for the files of the population analysis and STS for all other files. In addition, in case of a confirmatory study that also conducted a population analysis for which an independent report does not exist, select POP for files related to the population analysis and Non-CP for all other files for this study.

Table 1-25 Relationship between the type of documents subject to electronic submission and the analysis type when electronic study data on a clinical pharmacology analysis are included.

Section in notification on electronic study data	Content		Individual clinical study data	Analysis dataset	
				Concerning efficacy and safety analysis	Concerning PK or PK/PD analysis
2 (1) b (a)	Data on results from all phase II and phase III studies (including long-term studies) that are generally regarded to be a major evidence for evaluation of efficacy, safety, and dose and administration		SDTM	**Select the Analysis Type corresponding a clinical pharmacology analysis** ADaM	
2 (1) b (b)	Data on result from phase I studies and clinical pharmacology studies listed right	Phase I studies of oncology drugs	SDTM	ADaM	
		Phase I studies that have been conducted in both Japanese and non-Japanese subjects (e.g.; in case of a strategy of global clinical trials and bridging studies)	SDTM	In principle, ADaM*², but other formats may be acceptable in certain cases	
		QT/QTc studies based on the ICH E14 guideline			
2 (1) b (c)	Other Phase I studies and clinical pharmacology studies, which were deemed necessary by PMDA	Clinical studies where standard pharmacokinetic analysis was performed	SDTM*¹	ADaM*²	ADaM is preferable, but other formats are acceptable
		Population analyses			
		Physiologically based pharmacokinetic model analyses			
2 (1) b (c)	References which were deemed necessary by PMDA		SDTM	ADaM	
2 (1) b (c)	Integrated summary of safety and efficacy (ISS/ISE)		SDTM	ADaM	

Overlaid text on table:
- **Select STS (Select STS for all files, including SDTM datasets, ADaM datasets and analysis programs)**
- **Select POP** formats other than CDISC standard would be sufficient
- **Select PBPK**
- **Select the Analysis Type corresponding a clinical pharmacology analysis**

When submitting a file on a clinical pharmacology analysis that is not STS, POP, or PBPK, please select Other.
For files for which STS, POP, PBPK, or Other is selected in the analysis type, please complete the Description. However, of files for which STS or Other is selected, electronic study data that conform to the CDISC standards and related documents (refer to Section 4.1 of the technical conformance

guide) may be described as "-" in the Description.

Q1-26: Deleted

Q1-27: Deleted

Q1-28: Deleted

Q1-29: If data can be submitted in formats as shown in "Table: Types and submission formats of documents subject to electronic submission" in Question 10 in the Q&A regarding the notification on electronic study data, is it not necessary to conduct a consultation on exemption of submission of electronic study data?

A: A consultation on exemption of submission of electronic study data is conducted when submission of a part of or whole of electronic study data is difficult according to Question 2 or Question 15 in the Q&A regarding the notification on electronic study data. If data can be submitted according to Question 10, a consultation on exemption of submission of electronic study data is not necessary.

Q1-30: In Section 4 (2) b (e) of the notification on electronic study data, it is stated that if it is difficult to convert some of the clinical study data in a format other than SDTM into the SDTM format on submission of the application, such as when there are data that cannot be converted in accordance with the controlled terminology recommended because of the setting at the time of data acquisition, discuss with the PMDA prior to the application using consultations. In this case, which consultation should be used?

A: Please consult at a consultation on preparation of submission of electronic study data.

Q1-31: In Question 18 in the Q&A regarding the notification on electronic study data, there are statements as shown below regarding submission of electronic study data on phase I study and clinical pharmacology study results and clinical pharmacology analyses. Which consultation should be used for each of these cases?
(1) Of studies listed in Section 2 (1) b (b) of the notification on electronic study data, (1) of Question18 in the Q&A guide states that analysis dataset of efficacy and safety from phase I studies performed in both Japanese and non-Japanese subjects "may not necessarily need to be submitted. Therefore, if submission of the analysis datasets of efficacy and safety is difficult, consult with the PMDA in advance on whether or not the datasets need to be submitted using consultations".
(2) Of studies listed in Section 2 (1) b (b) of the notification on electronic study data, with respect to the analysis dataset on pharmacokinetics or pharmacokinetics/pharmacodynamics from phase I studies performed in both Japanese and non-Japanese subjects, (1) of Question18 in the Q&A guide states that, "formats other than ADaM may be acceptable in some cases. Thus, if it

        is difficult to submit the analysis datasets on pharmacokinetics or pharmacokinetics/pharmacodynamics in the ADaM format, consult with the PMDA in advance in the same manner as explained above".

(3) Of the studies listed in Section 2 (1) b (c), with respect to clinical studies where standard pharmacokinetic analysis was performed, (2) of Question 18 in the Q&A guide states that, "the analysis datasets on efficacy and safety may not necessarily need to be submitted for clinical studies where standard pharmacokinetic analysis was performed. Therefore, if it is difficult to submit such analysis datasets, consult with the PMDA in advance on whether or not such datasets need to be submitted using consultations".

(4) In case for which standard pharmacokinetic analysis was performed using a dataset that integrated the data from multiple clinical studies, (3) of Question 18 in the Q&A guide states that, "submission of electronic study data will be required for individual studies subject to electronic submission, in addition to the analysis datasets that were used for integrated analyses. If it is difficult to submit electronic study data, consult with the PMDA in advance using consultations".

A:
(1) Please consult at a clinical trial consultation.
(2) Please consult at a consultation on preparation of submission of electronic study data.
(3) Please consult at a clinical trial consultation.
(4) Please consult at a consultation on preparation of submission of electronic study data.

Q1-32: In reference to Question 19 in the Q&A regarding the notification on electronic study data, it is stated, "Electronic study data of population analyses based on data from clinical studies performed in the later phases of development may be submitted after the application in some cases. If submission of some electronic study data is difficult at the time of an application, the acceptability of the electronic study data submission that will be made after the application and the specific timing of the submission should be agreed with the PMDA in advance using consultations". In this case, which consultation should be used?

A: If submission of electronic study data of population analyses is difficult at the time of application, please consult with the PMDA at a consultation on preparation of submission of electronic study data, along with matters unique to electronic study data.

Q1-33: In Question 16 in the Q&A regarding the notification on electronic study data, with regard to points to consider when data created in a format other than the CDISC standards are converted to the CDISC standards-compliant data and submitted, it is stated, "if there are unavoidable circumstances, submission after the application may be acceptable only for clinical studies that fall under 2 (1) b (c) of the notification on electronic study data and that the start date (the day when the first subject was enrolled) is before June 20, 2014. In such cases, the applicant should consult with the PMDA in advance". In this case, which consultation should be used?

A: Please consult at a consultation on preparation of submission of electronic study data.

Q1-34: Regarding data standards at the time of submission of electronic study data, it is stated in 4

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(1) of the notification on electronic study data, "Clinical study data subject for submission should be in a format conforming to the CDISC standards. However, it is not applied to studies of orphan drugs, etc. that had started before April 1, 2020". Please advise us about the handling of data on integrated analyses of orphan drugs.

A: Data on integrated analyses may also be submitted in a format other than the CDISC standards if the analysis report was prepared before April 1, 2020.

Q1-35: When registry data are utilized in documents of clinical data for a new drug application, what are the contents of electronic study data to be submitted?

A: Even if registry data are utilized in document of clinical data, it is still important, as with the case of clinical studies, to submit data that provide the major evidence for the efficacy, safety, and dosage and administration for a new drug application in a format conforming to the CDISC standards basically.
On the other hand, the scope, contents and format of registry data to be submitted may require individual judgment, depending on the contents and purpose of registry data. Therefore, please consult with the PMDA in advance at an applicable consultation.
Regarding the submission format of data, if registry data are used at least for an evaluation of efficacy as an external control in a clinical study* and an analysis that uses registry data corresponds to analyses subject to submission of analysis datasets as described in Section 4.1.1.3 of the technical conformance guide, please submit datasets used for the analysis in the ADaM format as part of the analysis datasets of the clinical study. If submission in the ADaM format is difficult because of the method of analysis or other technical reasons, please consult with the PMDA at a consultation on preparation of submission of electronic study data.

* Reference: Basic principles on Utilization of Registry for Applications (PSEHB/PED Notification No. 0323-1, PSEHB/MDED Notification No. 0323-1, dated Mar. 23, 2021）

2. Questions on the relationship between electronic submission data and eCTD

Q2-1: If the eCTD is submitted from the gateway system, how should the type of electronic medium section and the number of pages submitted section be described in the eCTD cover letter?

A: If eCTD v3.2.2 is submitted from the gateway system, "Type of electronic medium" should be described as "Gateway system" and "Number of pages submitted" as "-" (hyphen) in the cover letter. If eCTD v4.0 or later is submitted from the gateway system, submission of the cover letter is not required, but necessary information, such as checksum value of XML instance, must be entered in the gateway system.

Q2-2: Is it acceptable that the submission date of electronic study data is different from the submission date of eCTD? If acceptable, are there any rules for the order of submission?

A: It is acceptable that the submission date of electronic study data is different from the submission date of eCTD. There are no rules for the order of submission when the applicant uses eCTD v3.2.2.

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When the applicant uses eCTD v4.0 and submits (1) eCTD including only electronic study data and (2) eCTD with CTD documents and without electronic study data separately, (1) must be submitted before the submission of (2). Please refer to Appendix 1, "ICH Electronic Common Technical Document (eCTD) v4.0 Implementation Guide in Japan" of "Approval Application with Electronic Common Technical Document (eCTD)" (PSEHB/PED Notification No. 0705-1, dated July 5, 2017) in detail.

Q2-3: Deleted

Q2-4: If electronic study data are not referenced from the XML message of the eCTD and there is a change to electronic study data (addition, replacement, deletion), is it necessary to revise the eCTD for each change?

A: Whether or not there is a change to electronic study data and it is not limited to before a meeting of committee on drugs, the revised eCTD must be submitted as previously if deemed necessary by the PMDA. Even if there is a change to the electronic study data, revision for each change may not be required and multiple changes may be collectively reflected in one revision in some cases in light of the type of the change and the efficiency of application/review operations. Please consult with the responsible review team for timing of submission of the revised eCTD.

Q2-5: Deleted

Q2-6: In Section 5.5 (2) of the technical conformance guide, "Electronic study data submitted during the revision of the eCTD," it is stated, "Only submit the difference with the previously submitted datasets." It may be difficult to only submit the difference if, for example, electronic study data of clinical study results up to Week 24 are submitted for a new drug application and electronic study data of the same clinical study up to Week 52 are submitted during review. In such cases, how should the difference between the electronic study data be submitted?

A: During the revision of the eCTD, only the difference with the previously submitted datasets should be submitted. The "difference" here means a difference in terms of studies or files. Therefore, a dataset to which a variable or record is added during review must be submitted as the latest dataset, including the previously submitted variables and records.

Q2-7: Deleted

Q2-8: Deleted

Q2-9: Deleted

Q2-9-1: Deleted

3. Questions on gateway system

Q3-1: Deleted

Q3-2: Deleted

Q3-3: In case of an operational error in the gateway system, who can be contacted?

A: Please check the e-mail address of the contact provided in the inquiry form that is posted on the top page of the gateway system. After login to the gateway system, it is also possible to make an inquiry using the inquiry function of the system according to the operation manual. Please note that a response to your inquiry may take time, depending on the opening hours of the help desk.

Q3-4: In the gateway application, what kind of electronic files can be submitted from the gateway system?

A: An example of electronic files that can be submitted from the gateway system is shown in Table 3-4.

Table 3-4 Example of electronic files that can be submitted from the gateway system

Two of the FD application data:
    Marketing approval application form*
    Partial change approval application form[*]

eCTD
Electronic study data**
List of committee members/expert advisors involved in application document preparation
List of competing products/competitors
List of committee members/expert advisors involved in competing products
Excipient conversion factor CSV
Responses to inquiries
Documents submitted to the PMDA for First and Second Committee on Drugs

* Submission in writing is required aside from electronic submission (the same applied to replacement during review).
** See Attachment 1 of the technical conformance guide.

Q3-4-1: In reference to Q3-4, please show the necessity of submission in writing and timing of submission for each of the electronic files in Table 3-4.

A: Documents that are required by notifications, etc. to be submitted in writing need to be submitted in writing as previously. Regarding the timing of submission of documents that are required by notifications, etc. to be submitted at the time of making a new drug application, the electronic files

of the documents may be submitted using the gateway system before a new drug application is made.

Q3-5: Deleted

Q3-6: Deleted

Q3-7: Regarding the folder structure when electronic study data are stored, [*study id* / iss / ise] is described in Section 3.5 of the technical conformance guide. What does it mean?

A: [*study id* / iss / ise] means an ID that the applicant designates for each clinical study. Although applicants can freely decide the ID if it is the study number or the type of analysis that allows the unique identification of each study, please make sure to use the same name as the folder name for the clinical study report in eCTD M5 if the eCTD is submitted and if electronic study data are not referenced from the XML message of the eCTD.

Q3-7-1: What are points to consider about the folder structure when electronic study data are stored and about information to be stored?

A: Basically, information to be stored in a folder that stores the clinical study report in eCTD M5 and information to be stored in a folder that stores electronic study data should correspond to each other on a one-to-one basis.
Shown below are examples of cases that require special attention to make the folder structure and information to be stored in the respective folders correspond to each other on a one-to-one basis:
· If one clinical study report is prepared for a clinical study but more than one set of clinical study datasets (occasionally with analysis datasets) are submitted for electronic study data on this clinical study (e.g., clinical study datasets are created for each evaluation time point), create folders corresponding to each set and then store the respective electronic study data in these folders. Also, create folders to store the clinical study report to correspond to the folders storing each electronic study data and then store the same clinical study report in the respective folders. Or store the clinical study report in one folder and store in the other folder a document (PDF file) that states that the folder storing the clinical study report be referred to.
· If multiple reports with a different study ID share the same electronic study data within the same application, create folders that correspond to each report and store the respective reports in these folders. Also, create folders to store the electronic study data to correspond to the folders storing each report and then store the same electronic study data in the respective folders. Or store the electronic study data in one folder and store in the "misc" folder under the other folder only a document (PDF file) that states that the folder storing the electronic study data be referred to.

Q3-8: When sending electronic files, is it necessary to encode these electronic files?

A: Applicants do not need to encode electronic files because the path for transmission of electronic files is automatically encoded by the gateway system.

Q3-9: Deleted

Q3-10: Is it possible to replace the submitted electronic study data if there is an error in the data? If possible, is it permissible to replace only the part with the error?

A: If applicants replace the electronic study data for their own reasons, the PMDA needs to unlock the data to allow for data replacement by applicants. In such cases, please contact the responsible staff of the review office.

The scope of submission of the replaced electronic study data depends on the timing of submission and the status of validation. Please refer to Table 3-10 below before submission of the replaced data.

Table 3-10 Scope of submission of replaced electronic study data

		Timing of replacing data	
		Before application	After application
Status of the submitted electronic study data	Accepted	Whole of electronic study data	Only an electronic file with error (submit as revision)
	Not accepted	Whole of electronic study data	Whole of electronic study data

Q3-11: In the entry window for the application notice in the gateway system, there are boxes to specify the status of submission of GLP- and GCP-related documents. What kind of documents are supposed to be entered in these boxes?

A: The application notice creation window is supposed to be completed according to descriptions in a facsimile sent to the Office of Review Administration before making a new drug application. Therefore, please enter the status of submission of inspection-related documents at the time of application. As notified previously, applicants are not expected to submit electronic files of GLP and GCP-related inspection documents using the gateway system.

Q3-12: Is there an upper limit for the size of electronic files that can be submitted via the gateway system?

A: For the upper limit for the file size, please refer to the operation manual for the gateway system.

Q3-13: Please advise us about actions to take when a file exceeds the upper limit for the size of electronic files that can be submitted.

A: Examples of actions to take when the size of a file exceeds the upper limit are shown below:
・ Compress the file:
    Example: Compress the "Other" file (Note: "Other" is one of the file types submitted via the gateway) into ZIP file format and submit it. In this case, the file must not be encoded.
・ Use the other path for submission:

Example: Submit as the "Other" file if the size of a file attached to the response to inquiries exceeds the upper limit.
・ Split a file into pages to create multiple files:
Example: If the size of a PDF file of the eCTD exceeds the upper limit, split the file in the middle of the document to create multiple files with a size below the upper limit.

If the actions mentioned above are not feasible for PDF files included in electronic study data, eCTD, excipient conversion factor CSV, "Other" file, and files submitted as responses to inquiries, please split the files and send the respective files. In this case, please notify the PMDA of the method to restore (combine) the files without delay.

Q3-14: Deleted

Q3-15: Can the gateway system be out of service due to maintenance, etc.? How will the system being down become known?

A: System maintenance will be performed as appropriate to maintain the health of the system. Since it is scheduled in advance, it will be notified on the top page of the gateway system approximately 4 weeks before the scheduled date.
If a system down that involves the top page occurs and the method of notification mentioned above is not available, information will be provided on the PMDA's website (https://www.pmda.go.jp/).

Q3-16: Deleted

Q3-17: Deleted

Q3-18: In the gateway application, after FD application data of the application form have been submitted using the gateway system and the virus check and validation have been completed, are there any cases where the PMDA requires correction of the application form including the FD application data when the application form is submitted to the PMDA window?

A: Yes. In this case, please submit the FD application data revised according to the operation manual for the gateway system using the gateway system. Then, please submit the application form revised accordingly to the PMDA window.

Q3-19: Deleted

Q3-20: When additionally submitting datasets of electronic study data after the application, how can they be submitted and what are points to consider?

A: Possible methods and means to additionally submit datasets of electronic study data after the

application are as follows:

<Methods of additional submission>

・ Additionally submit new datasets.

・ Add information to (or update information in) datasets already submitted and replace the dataset.

<Means of additional submission>

・ Revise the CTD/eCTD.

When additionally submitting electronic study data after the application, regardless of the methods/means, datasets should be stored in the folder structure presented in Section 3.5 of the technical conformance guide in the same way as they were submitted previously, and datasets with additions or changes should be submitted via the gateway system as specified in the operation manual for the gateway system. Aside from the specific SDTM domains or ADaM datasets with changes, if there are any other documents with additions/changes associated with the addition/change of datasets (e.g., documents appended to the datasets for submission and analysis program), please also submit them.

Of note, the PMDA separates upper folders every time it receives data. Therefore, even if the additionally submitted data are stored and submitted in a folder with the same name as the folder that has already been submitted, the electronic study data that have already been submitted will not be overwritten by the additionally submitted data, and these data will be under version control.

Although the PMDA does not always require additional submission of electronic study data during review for clinical studies that are ongoing after the application, additional submission may be preferable for review in some cases. Therefore, please consult with the review team on the necessity and timing of additional submission.

Q3-21: Deleted

Q3-22: Deleted

Q3-23: Is it possible to submit electronic study data of multiple clinical studies all at once with one operation?

A: Yes, it is possible to submit data of multiple clinical studies all at once with one operation.

Q3-24: For a new drug application, we are planning to submit to the PMDA window the electronic files that are supposed to be submitted using the gateway system due to inevitable reasons. What are points to consider in that case?

A: If an applicant tries to send electronic files using the gateway system but changes its plan and submits the files to the PMDA window due to inevitable reasons, the following points should be considered.

(At advance submission)

・ Send an application notice using the gateway system.

・ Select "Gateway" in the "Method of submission" column in the submission notice information.

・ Notify the help desk of the responsible review office, name of the product, submission to the PMDA window instead of submission using the gateway system, and the preferred date of

submission of the recording medium to the window (by 1 business day before the scheduled date of application at the latest) and gain approval for submission to the PMDA window by 2 business days before the scheduled date of application. If two or more recording media are submitted, please also notify this. Even after declaration of the request for submission to the PMDA window, please attempt gateway submission as long as possible until the date of submission to the PMDA window. If the date of submission to the PMDA window is 1 business day before the scheduled date of application, please submit during the morning, if possible, to allow for time for reception processing.

· In case of submission to the PMDA window, please prepare the recording medium that stores application documents initially supposed to be submitted using the gateway system and the application notice receipt form (paper) and bring or mail them to the Administration Division I of the Office of Review Administration. Please specify the gateway receipt number, name of the applicant, brand name, and scheduled date of application on the surface of the recording medium and specify in red, "GW registration", in the application notice receipt form (paper). Please note that the PMDA cannot accept the recording medium if the product cannot be identified because of a loss of the receipt form or other reasons in order to avoid a risk of mix-up. For submission of recording medium to the PMDA window, applicants do not need to send a prior notification to the Administration Division I of the Office of Review Administration.

· If multiple types of FD application data, eCTD, electronic study data, and other documents are submitted, please use separate recording medium for each type. Please do not submit to the PMDA window the types of documents that could be submitted using the gateway system and submit to the PMDA window only the types of documents that could not be submitted. If multiple types of electronic files other than electronic study data are submitted to the PMDA window, please submit them all at once.

· If new drug applications are made for multiple products concurrently, please present information (correspondence table) that uniquely link the file name of FD application data to the name of the product.

· When submitting eCTD stored in a DVD, it can be split into multiple discs for storage. However, please store it in one disc, such as a multi-layer disc, as long as possible. It is not necessary to acquire the eCTD receipt number again. Please use the number acquired at the time of giving the application notice.

· If electronic study data are divided and submitted in the form of more than one recording medium, it is difficult for the PMDA to reproduce the original folder structure or to check if reproduction is successful. Therefore, please submit the data in a single medium by using BD (including multilayer disc), etc., in principle. If the data cannot be recorded in a single medium, even when using a two-layer DVD-R, multilayer BD-R/RE, etc., please consult with the PMDA.

· Unless electronic study data are referenced from the XML message of the eCTD, submission of a tab-separated values (TSV) file that shows the contents of the clinical study data (electronic study data) to be submitted is mandatory at the time of submission of electronic study data. Therefore, please create a TSV file that shows the contents of the clinical study data to be submitted and submit the file after storing it using the same path as for an m5 folder. Preparation methods for TSV files will be posted separately on the PMDA's website (https://www.pmda.go.jp/), which should be used as a reference, and TSV files should be named according to the naming rules for dataset files specified in Section 3.5 of the technical conformance guide.

· In principle, the submitted recording medium will be disposed by the PMDA. If applicants wish to have it returned, please indicate the preference in the application notice receipt form.

(Scheduled date of application)

- The PMDA will perform an advance virus check of all electronic files that should be submitted for a new drug application to see if there are no problems with the files, such as an infection, and if the results of validation of FD application data are shown to be acceptable, the PMDA will notify the applicant of its completion. After this notification, please bring or mail application documents that should be submitted in writing to the Administration Division I of the Office of Review Administration.

Q3-24-1: In reference to Q3-24, in Section 2 (1) a of the notification on electronic study data, it states, "The submission of electronic study data may not be required for drugs that will be urgently used to prevent the occurrence or spread of health hazards". Please advise us the method for submitting electronic files without using the gateway system when submitting those files voluntarily.

A: Please prepare the recording medium that stores electronic files and the application notice receipt form (paper) and bring or mail them to the Administration Division I of the Office of Review Administration. For submission of recording medium to the PMDA window, applicants do not need to send a prior notification to the Administration Division I of the Office of Review Administration. Please specify the gateway receipt number, name of the applicant, brand name, and scheduled date of application on the surface of the recording medium and specify in red, "GW registration", in the application notice receipt form. Please note that the PMDA cannot accept the recording medium if the product cannot be identified because of a loss of the receipt form or other reasons in order to avoid a risk of mix-up. In principle, the submitted recording medium will be disposed by the PMDA. If applicants wish to have it returned, please indicate the preference in the application notice receipt form.

Q3-25: If an applicant makes a new drug application before the scheduled date of submission of the application form specified in the application notice, is it necessary to correct the application notice?

A: If applicants wish to change the scheduled date and time of submission of the application form, please contact the Administration Division I of the Office of Review Administration to adjust the schedule and then correct the information registered in the application notice. If any of the electronic files for which the submission notice was given has been submitted using the gateway system, the PMDA needs to take action to correct the scheduled date and time. Therefore, please notify this at the time of the contact mentioned above.

Q3-26: Deleted

Q3-27: Deleted

Q3-28: In the gateway application, when outputting FD application data for submission using the FD application software, an applicant can select the following two output formats. What is the method of output when submitting the data using the gateway system?

- File output for CD-R writing

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- Output for online application

A: For FD application data to be submitted using the gateway system, please use data output using the "file output for CD-R writing".

Q3-29: Are there any cases where the PMDA does not accept the application because of an inadequate TSV file when submitting electronic files to the PMDA window?

A: Yes, there are cases where the PMDA does not accept the application because of an inadequate TSV file. When electronic study data are submitted to the PMDA window, the PMDA performs the following operations using the gateway system: (1) load of the TSV file, (2) verification and saving of the TSV file (including consistency with the folder structure of the electronic study data submitted concurrently), and, if no problems are identified, (3) registration of the electronic study data. If the "inadequate TSV file" in question is detected at the time of the load of the TSV file or by the verification function, an error occurs during these operations and the operation of registration of the electronic study data cannot be completed, making it impossible to complete the virus check. Accordingly, the PMDA cannot accept the application.

Q3-30: What is the difference between "OK" and "Acceptable," which are the results of the validation of electronic study data?

A: If no violations of the validation rule are detected as a result of validation, "OK" will appear. On the other hand, if a violation of the validation rule is detected as a result of validation but it is deemed permissible to accept the electronic study data based on explanations given in advance, "Acceptable" will appear.

Q3-31: If the virus check and signature verification have been completed on the gateway system for all electronic files submitted using the gateway system and if appropriate documents have been submitted to the PMDA window, will the PMDA accept the application even if the results of the validation are not available yet?

A: For FD application data, the validation needs to have been completed by the time of receipt of the application and the result of validation needs to be "OK". On the other hand, for eCTD and electronic study data, the results of the validation will not be used to determine whether or not to receive the application.

Q3-32: Deleted

Q3-33: In reference to Question 7 in the Q&A regarding notification on electronic study data, please advise about the format of the electronic study data and the submission method when electronic study data are submitted in advance of approval application or re-examination application for a new drug.

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A: Please take note of the following points when submitting (optional) electronic study data at the consultation, before the new drug applications for anti-HIV, at the request for removal of approval conditions, etc.

(Datasets)
- Please consult with the office in charge of review in advance about the studies and analyses subject to submission of electronic study data.
- Submission of a tab-separated values (TSV) file that shows the contents of the clinical study data to be submitted is mandatory at the time of submission of electronic study data. Therefore, please create a TSV file that shows the contents of the clinical study data to be submitted and submit the file after storing it using the same path as for an m5 folder. Preparation methods for TSV files will be posted separately on the PMDA's website (https://www.pmda.go.jp/), which should be used as a reference, and TSV files should be named according to the naming rules for dataset files specified in Section 3.5 of the technical conformance guide.
- Please follow the method specified in Section 3.5 of the technical conformance guide for the folder structure. The name of the folder that contains the clinical study report should be the same as the name of the folder that contains the study data [*study id* / iss / ise]. Please make sure that information contained in the folder for the clinical study report corresponds one-to-one to that contained in the folder for the study data.
- In principle, please submit the electronic study data in a single zip file that maintains the folder structure. However, if the file size of the zip file exceeds the upper limit indicated in the operation manual for the gateway system or the upper limit of a recording medium, please split the file into several zip files, e.g., for each study, and submit them. If a dataset needs to be split, please contact the help desk.

(Submission destination and submission method)
- Please submit it to the same destination as the other review and consultation materials.
- In principle, please submit electronic study data using the gateway system or a recording medium to the Office of Review Management during the period from the date of submission of the consultation application to the date which the consultation materials are scheduled to be submitted. If electronic study data are submitted on a date different from the date of the consultation materials submission, please contact the Office of Review Management by e-mail (shinyaku-uketsuke[at]pmda.go.jp (please replace [at] with @)) to provide the scheduled submission date in advance. When electronic study data are submitted on the date of the consultation materials submission, the advance contact is not required.
- When electronic study data are submitted using the gateway system, please describe in the "submission name" (or in the correspondence field) of the gateway system that electronic study data are to be submitted.
- When electronic study data are submitted using a recording medium, please submit the data in a single medium by using BD (including multilayer disc), etc., in principle. Also, please describe on the face of the recording medium or on the cover letter of consultation materials that electronic study data are to be submitted, and please describe the consultation category, consultant applicant, reception number, brand name, and non-proprietary name on the face of the recording medium. In principle, the submitted recording medium will be disposed by the PMDA. If applicants wish to have it returned, please indicate the preference in the application form, etc.

Q3-34: Deleted

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4. Questions on CDISC-conformant electronic study data

Q4-1: What is the base date for the "Date Support Begins (YYYY-MM-DD)" and the "Date Support Ends (YYYY-MM-DD)" in the PMDA Data Standards Catalog?

A: The base date is the submission date recorded by the applicant on the FD application data of the new drug application form.

Q4-2: In the case where electronic study data is added or replaced during review, is it necessary to follow the standards with the same version number as those at the time of original submission?
If the "Date Support Ends" of the version used at the time of the original submission has already passed, what procedures should be followed?

A: Basically, it is necessary to use the same version as that used at the time of the original submission. To submit additional data to the previously submitted dataset, it is necessary to use the same version as that used for the original dataset.
In addition, on the following occasions where the (initial) application is submitted during the overlapping period of versions, the applicant can use the newer version that is included in the "PMDA Study Data Validation Rules" used at the time of application:

· Submission of a completely new set of study data
· Submission of an entire set of previously submitted data along with additional data where both are created using the newer version of the standard

Figure 4-2: Version of the standards
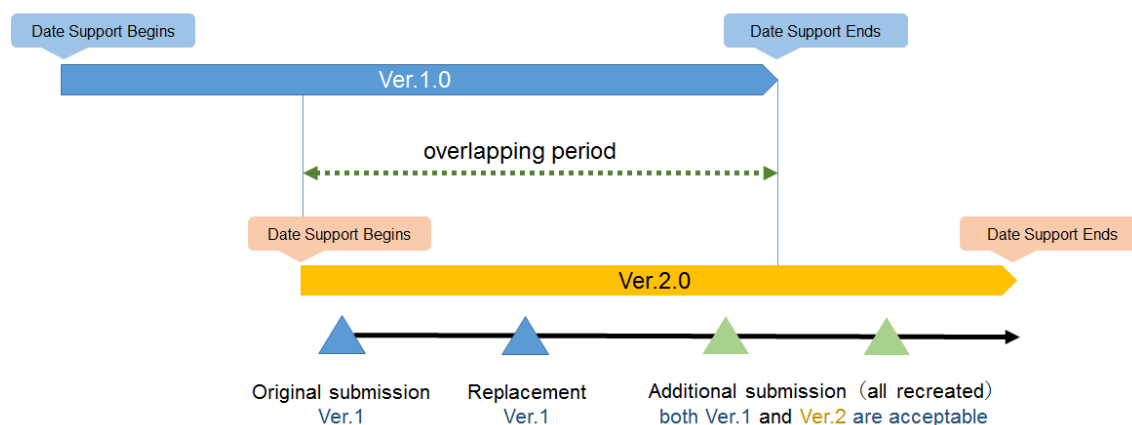
Q4-3: Which files or contents will be included in the scope of CDISC-conformant validation performed by the PMDA?

A: The PMDA performs validation on SDTM datasets, ADaM datasets, dataset definition documents, controlled terminologies and dictionaries. When the data written in Japanese ("Japanese data" in Section 4.1.5 of the technical conformance guide) is submitted, no validation is performed on Japanese data and the validation is performed on the corresponding alphanumeric dataset.

Q4-4: Please demonstrate the contents of electronic study data on integrated analyses (ISS/ISE) that should be submitted.

A: At the submission of electronic study data for ISS/ISE, definition documents and analysis programs (or program specifications) are required in addition to integrated analysis datasets. Although the reviewer's guide should also be submitted in principle, it may be acceptable not to submit it depends on the format or structure of electronic study data for ISS/ISE. To confirm the details of such datasets, including file types to be submitted, etc., use a consultation on preparation of submission of electronic study data.

Q4-5: Deleted

Q4-6: If the protocol, etc., is prepared in Japanese, is it necessary to translate the information on the design of the clinical study into English, and store it in the SDTM Trial Design Model domain? Please indicate parameters and codes that the PMDA requests at a minimum for the TS domain of SDTM.

A: It is not likely that much information will be lost when Japanese data are translated into English for storing in the Trial Design Model. Therefore, when the protocol, etc., is prepared in Japanese, each piece of information must be stored in English after translation.

If SDTM datasets are prepared in accordance with SDTM IG v3.1.3 or later versions, it is necessary to include parameters classified into "Required" or "Conditionally Required" in the TS domain. If SDTM datasets are prepared in accordance with SDTM IG v3.1.2, include parameters that can be stored based on Section 7.6.2-4 of the SDTM IG. For parameters using controlled terminologies and ISO codes, store appropriate code values. For Registry Identifier, store registration numbers issued by CLINICALTRIALS.GOV, EUDRAC, JAPIC, jRCT etc. For parameters using UNII, NDF-RT, MED-RT, DUNS, or SNOMED CT, it is acceptable to store only code values available to the applicant. Table 4-6 shows the relationship between codes and parameters that use the codes other than controlled terminologies or ISO codes.

Table 4-6 Codes Corresponding to TS Domain Parameters and WEB Sites

TSPARMCD	TSPARAM	Code	Website
CURTRT	Current Therapy or Treatment	UNII	FDA's Global Substance Registration System https://precision.fda.gov/uniisearch
TRT	Investigational Therapy or Treatment	UNII	FDA's Global Substance Registration System https://precision.fda.gov/uniisearch
PCLAS	Pharmacological Class of Investigational Therapy	NDF-RT/MED-RT	NCI Term Browser https://nciterms.nci.nih.gov/ncitbrowser/pages/multiple_search.jsf;
REGID	Registry Identifier	CLINICALTRIALS.GOV	ClinicalTrials.gov https://clinicaltrials.gov/

		EUDRAC	EU Clinical Trials Register https://www.clinicaltrialsregister.eu/ctr-search/search
		JAPIC	JAPIC Clinical Trials Information https://www.clinicaltrials.jp/cti-user/common/Top.jsp
		jRCT	Japan Registry of Clinical Trials https://jrct.niph.go.jp/
SPONSOR	Clinical Study Sponsor	DUNS	TOKYO SHOKO RESEARCH https://duns-number-jp.tsr-net.co.jp/search/jpn/login.asp

Q4-7: In Section 4 (2) d of the notification on electronic study data, it states, that encoded information must also be included for data that can be encoded using "the WHODrug Global for drugs". Please explain the background of the need to use WHODrug Global, and give an example of how to store WHODrug Global data under the CM domain of SDTM.

A: In order to promote international standardization of clinical study data, and to allow cross-product analyses in the future, use of WHODrug Global is required for electronic study data submission. It is possible to use applicant-defined codes if no WHODrug Global equivalent codes are identified; in this case, it will be necessary to specify in the reviewer's guide which applicant defined codes have been assigned to which variables.
Table 4-7 presents examples of how to assign WHODrug Global codes to the CM domain of SDTM. It is also necessary to store WHODrug Global ATC codes wherever possible.
In cases where it is impossible to identify the single ATC code in WHODrug Global due to not collecting indication for use of the concomitant drug, please store not only single ATC code but also all ATC codes that correspond to the drug using the "Supplemental Qualifier special-purpose dataset".

Table 4-7 Relationship between CM Domain and WHODrug Global

Variable Name	Variable Label	WHODrug Global
CMDECOD	Standardized Medication Name	Generic name
CMCLAS	Medication Class	ATC text
CMCLASCD	Medication Class Code	ATC code

Q4-8: In Section 4 (2) d of the notification on electronic study data, it states, "if data were collected in units that are conventionally used in guidelines for diagnosis, treatment, and therapeutic evaluation for various diseases where conversion of the data to those in SI units is possible, separately store the converted data in SI units in the SDTM dataset as data in the standard units and submit them". Please indicate the scope of variables that need to be converted to SI units. Also, if data are collected in units other than SI units, how can the original data and the converted data be stored within the SDTM dataset?

A: The use of SI units is required for all variables and parameters of test results to be stored in the

Findings class domain of the SDTM dataset, as long as SI units are applicable. However, it is acceptable to store only the data in mmHg in the SDTM dataset without storing the converted data in SI unit for test results (e.g. blood pressure) collected in mmHg as conventional unit.

When the original data and the converted data in SI units are stored together in the SDTM dataset, store the converted data into "--STRESC" (or "--STRESN" if necessary) and the original data into "--ORRES". Also, in the reviewer's guide or dataset definition document, describe how each datum (original and converted) is stored, as well as the conversion equation.

In the case of multicenter or multiregional studies, etc., where different measurement units are used for capturing data by center or region, data in multiple units could be obtained for a single parameter (laboratory test). In such cases, it is possible to store data in uniform units other than SI units into "SUPP--" if necessary.

<Example of how to store data in conventional units and SI units into SDTM>
When values in domestically conventional units and internationally conventional units both exist:
Store values in domestically conventional units under "--ORRES" and values in internationally conventional units under "SUPP--." Store SI values under "--STRESC" (or "--STRESN" if necessary).

Q4-9: Some values need to be displayed in Japanese on analysis results, and such values need to be stored in datasets in Japanese. In such cases, should only datasets with alphanumeric values be separately prepared for electronic study data submission?

A: Basically, it is only necessary to submit datasets with alphanumeric values for electronic study data submission. For variables that can be properly translated (from those displayed in Japanese analysis results into English) without loss of information, it is acceptable to store the translated variables in datasets, and to submit only the datasets with alphanumeric values. In such cases, it is possible, in addition to the datasets with alphanumeric values, to submit together the original datasets with Japanese characters that were used for displaying analysis results instead of alphanumeric values, from the viewpoint of traceability between the original and translated datasets or to present reference materials. If certain information is likely to be lost when Japanese data is translated into English, follow Section 4.1.5 of the technical conformance guide for submission. In the case of datasets translated at the time of their creation, this should be described in the reviewer's guide.

Q4-10: If datasets include languages other than English or Japanese, what procedures should be followed?

A: Basically, the requirement is that submitted datasets be entirely translated into English. However, the need to translate specific variables into English may depend on the level of importance of the relevant variables; thus, use the "consultation on preparation of submission of electronic study data" for each case if needed. In the event that datasets are translated, this should be described in the reviewer's guide.

Q4-11: When translation is performed (e.g., from Japanese to English), is it necessary to certify the correctness of the translation?

A: No written form is required, but the applicant is responsible for ensuring the accuracy of the translation.

Q4-12: Deleted

Q4-13: Please indicate examples of the contents to be described in the "specifications that show the analysis algorithm".

A: In the "specifications that show the analysis algorithm", please specify datasets and variables to be analyzed, and details of analytical methods.

Q4-13-1: Is it possible to submit "specifications that show the analysis algorithm" in English?

A: Yes.

Q4-13-2: If analysis software is used that requires no explicit program creation, is it permissible to submit an operational log instead of a program? Or will "the submission of specifications that show the analysis algorithm" be separately requested?

A: Submission of an operational log will be sufficient instead of the program, if the log clarifies the analysis algorithm. In the event that the operational log is unlikely to clarify the analysis algorithm, as in the case where "submission of the program itself is difficult", then "the submission of specifications that show the analysis algorithm" will also be needed.

Q4-14: Deleted

Q4-15: When submitting electronic study data of an integrated analysis (ISS/ISE), in which folder should they be stored?

A: Basically, we expect that data from multiple studies subject to an integrated analysis will be combined into a single dataset, and that one analysis dataset will be submitted for each analysis. When datasets from multiple studies are consolidated by a program for analysis, it is possible to submit the datasets of each study and the program containing the process of consolidation. Regardless of whether or not datasets are integrated, store datasets for the integrated analysis within the "iss / ise" folder.

Q4-16: When submission of the analysis program is difficult, submission of the "specifications that show the analysis algorithm" may be considered. In which folder should they be stored?

A: Store the analysis specifications in the "programs" folder. This should be explained in the reviewer's guide.

Q4-17: Deleted

Q4-18: Deleted

Q4-19: In Section 4.1.1.4 of the technical conformance guide, it states, "the character sets or the encoding scheme used to create the dataset should be described in the reviewer's guide"; please give specific examples of the character sets and encoding scheme that must be described.

A: Information on the character sets and the encoding scheme is needed to identify the characters intended by the dataset creator.

Examples of character set information to be described in the reviewer's guide:
[Character set] JISX0208   [Encoding scheme] Shift-JIS
[Character set] JISX0208   [Encoding scheme] EUC-JP
[Character set] UNICODE   [Encoding scheme] UTF-8

Q4-19-1: In connection with Q4-19 above, how can information be obtained on the encoding scheme used?

A: In principle, encoding-scheme-related information can be obtained from the property of the dataset. In the case of an unconventional encoding scheme used for relevant character sets, provision of detailed data may be additionally requested.

Q4-19-2: Deleted

Q4-20: If the application is to be made based on the results of an interim analysis, is it permissible to include data obtained after the cutoff of the interim analysis up to the time of application with data submitted for the application?

A: If the application is to be made based on the results of an interim analysis, it is required that data up to the cutoff of the interim analysis be included in electronic study data submission; it is also acceptable, however, to include data after the cutoff. For instance, if the application is made after a certain period of time from the interim analysis, it may be useful to include data after the interim analysis. If the application is made including data after the interim analysis, clearly distinguish data before and after the cutoff, and the handling of the relevant data must be explained in the reviewer's guide.

Q4-21: Is there anything special to consider when the SDTM IG v3.1.2 Amendment 1 is used for

the creation of the SDTM datasets?

A: The PMDA does not perform the validation based on SDTM IG v3.1.2 Amendment 1. Applicants should perform validation of electronic study data based on the version other than SDTM IG v3.1.2 Amendment 1 and take the necessary action. Moreover, applicants should specify the version of SDTM IG used for validation on the dataset definition document. Basically, it is recommended that applicants perform validation based on SDTM IG v3.1.3 in that situation.

Q4-22: Is it possible to store and submit the datasets not conforming to CDISC or files other than datasets in the folder that is defined to store SDTM datasets or ADaM datasets?

A: Within the folder storing SDTM datasets or ADaM datasets, it is possible to store and submit datasets in the SAS XPORT format conforming to the CDISC standards, together with the accompanying definition documents in the XML format, style sheets, and PDF documents. Do not store and submit csv files, XML files other than definition documents, or SAS XPORT datasets not conforming to the CDISC standards.

Q4-22-1: When submitting files that cannot be stored and submitted in folders storing SDTM datasets or ADaM datasets according to in Q4-22, in which folder should these files be stored? What are points to consider when submitting such files?

A: Applicants can store and submit these files in the "misc" folder, the "legacy" folder, etc. according to their usage.
For example, reference data used to create ADaM datasets (reference tables such as Lookup tables, Metadata, etc.) can be stored and submitted in the "misc" folder. If a program used to create the ADaM datasets are submitted and these files are used in the program, the files can be stored in the "programs" folder as program-related files.
Data used to impute missing data (e.g., by multiple imputation) can also be stored and submitted in the "misc" folder. In this case, please explain the handling of missing data in the dataset definition document and in the reviewer's guide.
To explain traceability when datasets in a format other than the CDISC standards are converted into a CDISC-conformant format for submission, applicants can store and submit the datasets before conversion into a CDISC-conformant format, the explanation of traceability, and the accompanying files in the "legacy" folder.

Q4-23: In Section 4 (2) d of the notification on electronic study data, it states, "The values are to be in SI units, in principle". Please indicate the SI units that the PMDA considers acceptable, and any other points that should be considered when storing data in SI units.

A: Currently, the PMDA considers the use of SI units, non-SI units that are accepted for use with SI units, and SI prefixes listed in published BIPM (Bureau International des Poids et Mesures) brochure as acceptable use of the SI units. Prefixes should be used to keep numbers in the range of 0.1–1000.

Q4-24: For a clinical study with interim analyses, when is it necessary to submit the interim analysis

data in addition to the final analysis data? Please indicate the format and method for submission, and the points to consider when the interim analysis data and the final analysis data are to be submitted together at the time of application.

A: In a clinical study subject to electronic study data submission, if a decision is made regarding discontinuation/continuation of the study, the need for an important study design amendment or the contents of the amendment, etc., based on the interim analysis results, applicants may be asked to submit the analysis datasets used for the interim analysis in addition to the final analysis data (or data at the final cutoff used for the application) at the time of application. If analysis datasets and analysis programs used for the interim analysis are to be submitted, store them with the dataset definition document in the "misc" folder. It must be mentioned in the reviewer's guide that the analysis datasets used for the interim analysis are to be submitted. If no SDTM dataset is created exclusively for the interim analysis, submission of SDTM dataset for the interim analysis will not be necessary. Please use the clinical consultation to verify the necessity of data submission of the interim analysis and the scope of submission.

Q4-25: In Section 3 (3) of the notification on electronic study data, it states, "if the application is to be made during a long-term study or based on the results of an interim analysis, the data from this clinical study submitted after the application should include the data previously submitted at the time of the application as well as the additional data". If data from long-term continuous studies with different study numbers are compiled (e.g., in a case where subjects who completed the phase III study, Study No. 001, were enrolled in the continuous treatment study, Study No. 002, and the data from Study No. 001 and Study No. 002 are compiled. [Note that submission of data from the phase III study was already made at the time of application]), how will the folder name be specified for additional data submission?

A: Under the circumstances described above (to submit additional electronic study data after the application), store the additional data (Study No. 001 and 002 combined) in the folder for Study No. 002 submission. For the methods and procedures of submission of CDISC-conformant datasets after the application, refer to the Answer to Q3-20.
For combined data from multiple studies, it will be necessary to specify in the dataset which study each data comes from. The reviewer's guide must include points to consider, such as the fact that there is an additional submission of compiled data from multiple studies, the method for compiling data, and the presence/absence in the additional data of new subjects from the continuous treatment study. For details regarding methods for data compilation and submission, please utilize a consultation on preparation of submission of electronic study data as needed.

Q4-26: Deleted

Q4-27: Are there any issues to consider when multiple versions of CDISC standards, CDISC Controlled terminology, or external dictionaries are used in the same study or analysis?

A: In Section 4 (2) e of the notification on electronic study data, it states that, "a single version of the standards must be used within a clinical study or an analysis. If different versions are used for

any parts of the same clinical study or the same analysis, it should be explained in the reviewer's guide, with the reasons for the use of the different versions indicated". At the PMDA, validation of electronic study data will be conducted in the gateway system based on the single CDISC standards version and single MedDRA version stated in the define.xml as well as single CDISC Controlled terminology version entered in the gateway system. Applicants should also perform validation of electronic study data based on versions of SDTM IG, ADaM IG, MedDRA in the define.xml and single CDISC Controlled terminology version planned to be entered in the gateway system, and correct electronic study data or explain errors based on the results.

Q4-28: Are there any points to consider when the CDISC Controlled Terminology version used to create the dataset and that used at validation are different?

A: Necessary actions are as follows,
·   In the "Terminology" column of gateway system, enter the CDISC Controlled Terminology version used for validation by an applicant.
·   In the reviewer's guide, explain the fact that the CDISC Controlled Terminology version used to create datasets and that used for the validation are different, and specify each version.

Q4-29: The applicant plans to code drugs with Japanese IDF codes, convert to WHODrug Global data using Cross Reference Tool Japan (CRT Japan), and then store in SDTM. Is it possible to submit data with blanks in the variables except for drug information converted by CRT Japan?

A: If an applicant stores information such as drug names that cannot be converted by CRT Japan to the dataset, it is possible to submit only data that is converted by CRT Japan in the SDTM dataset.

Q4-30: An applicant collects the adverse event terms in Japanese during the clinical study, creates the AE domain in both Japanese and English, and creates figures or tables based on the English dataset. In this case, is it possible to submit only the English dataset? In the meantime, what should the applicant do if the figures or tables are created based on the Japanese dataset?

A: In both cases, it is possible to submit only the English dataset if all information on the Japanese dataset is included in the English dataset. It is also possible to submit the Japanese dataset along with the English dataset.

Q4-31: When submitting the additional data of the studies that were ongoing at the time of application during review, should CSR in eCTD M5 and electronic study data be submitted as new or replace? In addition, is there anything special to consider for the storing methods?

A: Basically, when submitting the additional data of the studies, both storing CSR in eCTD M5 and electronic study data in newly created folders[*study id* / iss / ise] as new data and replacing CSR and electronic study data previously submitted with CSR and electronic study data newly submitted in existing folders[*study id* / iss / ise] are acceptable. However, preferable method may depend on study design, and the method of preparing CSR and creating datasets. Therefore, please consult with the PMDA at a consultation on preparation of submission of electronic study data in each case if

necessary.

Q4-32: In reference to Section 4 (1) of the notification on electronic study data, "However, it is not applied to studies of orphan drugs, etc. that had started before April 1, 2020." and Question 15 in the Q&A regarding notification on electronic study data, please advise us about the contents and methods of submission if electronic study data of clinical studies that are not formatted in accordance with the CDISC standards have to be submitted. It is also stated that if electronic study data that are not formatted in accordance with the CDISC standards have to be submitted, a prior consultation with the PMDA should be carried out about the relevant studies and submission contents. In cases where an applicant consults with the PMDA about the contents of electronic study data to be submitted that are not formatted in accordance with the CDISC standards, which consultation should be used and what should be explained at the consultation?

A: When electronic study data of clinical studies that are not formatted in accordance with the CDISC standards are submitted, at least the clinical study data containing data collected by CRF, etc. (information that would correspond to the SDTM dataset if it were CDISC-conformant), the analysis datasets and analysis programs used for obtaining the results described in the CTD and the electronic study data corresponding to the dataset definition documents should be submitted. Therefore, please use a consultation on exemption of submission of electronic study data and make sure to explain the contents at the consultation with the "Explanation of Electronic Study Data (Form B)", when the applicant consults about the contents of electronic study data to be submitted that are not formatted in accordance with the CDISC standards in advance. In addition, please explain whether there is information corresponding to the Annotated CRF and the reviewer's guide and whether the information can be submitted. Please store electronic study data of clinical studies that are not CDISC-conformant in the legacy folder of the folder structure shown in Section 3.5 of the technical conformance guide. When storing analysis datasets on PK analysis or PK/PD analysis, it is possible to create and store them in a "cp" folder, referring to Section 3.5 of the technical conformance guide.
Please also describe the standard pharmacokinetic analysis of clinical studies that are not CDISC-conformant in "5.2 Standard pharmacokinetic and/or pharmacodynamic analysis of clinical pharmacology" in the "Explanation of Electronic Study Data (Form B)".

Q4-32-1: In Section 4 (1) of the notification on electronic study data, it is stated that "Regarding studies categorized in 2 (1) b (b) and (c) with the exception of Phase I studies of oncology drugs, the submission of electronic study data in a format other than the CDISC standards is sufficient for studies that had started before April 1, 2020." Regarding such clinical studies, please advise us about the contents and methods of submission if electronic study data of clinical studies that are not formatted in accordance with the CDISC standards have to be submitted.

A: When electronic study data of clinical studies that are not formatted in accordance with the CDISC standards are submitted, at least the clinical study data containing data collected by CRF, etc. (information that would correspond to the SDTM dataset if it were CDISC-conformant), the analysis datasets and analysis programs used for obtaining the results described in the CTD and the electronic study data corresponding to the dataset definition documents should be submitted. In addition, if the applicant has information corresponding to the Annotated CRF and the reviewer's guide, please submit them as well. Please store electronic study data of clinical studies that are not

CDISC-conformant in the legacy folder of the folder structure shown in Section 3.5 of the technical conformance guide. When storing analysis datasets on PK analysis or PK/PD analysis, it is possible to create and store them in a "cp" folder, referring to Section 3.5 of the technical conformance guide.

Q4-33: Prior to the application for re-examination, an applicant submitted electronic study data on post-marketing clinical studies that are required to be submitted at re-examination, but the version used to create the data is not included in the list of versions acceptable at the PMDA at the time of the re-examination application. Does the applicant need to correct the data again and then re-submit the data? In addition, if the reception of the validation rule used at the time of submission is closed at the time of the re-examination application and an applicant cannot select the rule, what are necessary actions?

A: In such cases, no additional actions are required basically if there are no changes to the submitted data.

Q4-34: In Section 2 (1) b of the notification on electronic study data, it states that "For an application for partial changes, it is not necessary to resubmit electronic study data that have already been electronically submitted at the time the approval was obtained". When the same electronic study data as the data/analysis that have already been submitted to the PMDA in the past, are used for a new application in the situation where the prior application has not been approved yet, is it necessary to submit the same data for the new application? In the cases where it is necessary to submit the same data for the new application, if the version used to create the data for the prior application is not included in the PMDA Data Standards Catalog at the time of the new application, do we need to correct the data again and then re-submit the data even if the data for the new application are the same one as the data that have already been submitted?

A: If the applicant uses the same electronic study data as the data that have already been submitted to the PMDA for the prior application and the prior application has already been approved, according to Section 2 (1) b of the notification on electronic study data, it is not necessary to submit the same data for the new application. However, like the case of this question, in the cases where it is assumed that the scheduled application date of the new application is earlier than the approval date of the prior application, it is necessary to submit the same data for the new application, even if the data are same as the data that have already been submitted. Therefore, please perform the validation in advance prior to the new application and take the necessary action. If the version used to create the data for the prior application is not included in the PMDA Data Standards Catalog at the time of the new application, the applicant needs to correct the data and then re-submit the data.

Q4-35: When electronic study data that are not formatted in accordance with the CDISC standards are submitted, does the applicant need to use the WHODrug Global when coding drugs?

A: The applicant does not need to use the WHODrug Global.

Q4-36: When an applicant creates electronic study data at multiple time points (cut-off points) for a clinical study subject to electronic submission and submits the electronic study data at multiple time

points for application (e.g., submitting electronic study data at 2 time points, the interim analysis and the final analysis), in which folder should each of the electronic study data be stored?

A: If applicants submit electronic study data at multiple time points, it is permissible to store all electronic study data at the primary cut-off point that supports the application in the "m5\datasets\[*study id* / iss / ise]\[analysis / tabulations]" folder and store electronic study data at the other cut-off points in the "misc" folder. For selection of the primary data cut-off point and the necessity and scope of submission of electronic study data at the other data cut-off points, please consult with the PMDA at the clinical trial consultation.

Please note that electronic study data at the primary cut-off point need to contain all data that should be submitted. For example, if electronic study data are created at 2 time points, the interim analysis and at the final analysis (the primary cut-off point), and datasets with no updates after the interim analysis are not included in the electronic study data at the final analysis, the datasets with no updates after the interim analysis need to be added to the electronic study data at the final analysis for submission.

5. Questions on electronic study data on clinical pharmacology

Q5-1: Deleted

Q5-2: Please provide a more precise definition and explanation of "clinical studies where standard pharmacokinetic analysis was performed".

A: These are clinical studies where the pharmacokinetics of a drug was evaluated using the method defined as a standard pharmacokinetic study in the "Clinical Pharmacokinetic Studies of Pharmaceuticals" (PMSB/ELD Notification No.796, dated June 1, 2001)

Q5-3: In Question 10 of the Q&A regarding notification on electronic study data, what are "individual clinical study data" in "clinical studies where standard pharmacokinetic analysis was performed"?

A: They involve not only SDTM datasets (e.g., PC domain or PP domain) related to pharmacokinetic or pharmacokinetic/pharmacodynamic analyses but also all SDTM datasets of the clinical studies subject to submission.

Q5-4: In the case of a population analysis being subject to submission, which data used to create the population analysis datasets - e.g., SDTM datasets, analysis datasets on standard pharmacokinetic analysis, and efficacy and safety analysis datasets of the clinical studies - are subject to submission?

A: For a population analysis, only electronic study data related to the population analysis (such as analysis datasets for the population analysis) are subject to submission. In the case where each clinical study used for creation of population analysis datasets is inconsistent with studies that must be electronically submitted, as listed in Section 2 (1) b of the notification on electronic study data, it is unnecessary to submit the SDTM datasets, analysis datasets on standard pharmacokinetic

analysis, and efficacy and safety analysis datasets of the clinical studies from which data was drawn.

Q5-5: In Section 4 (3) of the notification on electronic study data, it states "Regarding data that were excluded from the analysis for reasons other than those specified in the analysis plan (e.g., excluded data because they were determined to be outliers at the time of analysis), steps should be taken to clarify how the data were handled during the analyses, such as by flagging to identify them". Is it possible to explain the handling of excluded data during the analysis by submitting the following two types of datasets: the final datasets (from which outliers, etc., were excluded) and whole datasets (including outliers, etc., with flagging to identify them)?

A: Yes, it is possible. The above statement in Section 4 (3) of the notification means that it is necessary to submit datasets in a manner that clarifies which data was excluded from analyses; thus, submission can be made in other ways as long as it fulfills this aim.

Q5-6: Deleted

Q5-7: Deleted

Q5-8: Deleted

Q5-9: Deleted

Q5-10: Deleted

Q5-11: Deleted

Q5-12: Deleted

Q5-13: Deleted

Q5-14: Deleted

Q5-15: Deleted

Q5-16: Deleted

Q5-17: Please demonstrate what kind of variables should be included in pharmacokinetics or pharmacokinetics/pharmacodynamics analysis datasets.

A: Please include the variables necessary for being 'analysis ready' datasets. For example, information on doses for an individual subject, information on actual elapsed time from the start of administration to sampling time, derived values needed for the analysis such as AUC used as a PK index, the change in a PD marker from baseline, and flags to extract records for analysis should be included in the dataset. When analysis datasets in ADaM format are submitted, the variables that are required in the ADaM IG need to be included.

Q5-18: Regarding in Section 4 (3) b (b) of the notification on electronic study data, is it necessary to submit program or output files for covariate models or model evaluation so that it is possible to trace the series of processes used in establishing the final model?

A: As the basic model and final model represent the basic scope of submissions, it is not necessary to submit program or output files for covariate models or model evaluation. However, if the process of covariate models or model evaluation is complicated, and the applicant considers that such files would aid understanding of the analysis method, it is possible to submit these files.

Q5-19: Regarding in Section 4 (3) b (b) of the notification on electronic study data, the output files with major results should be submitted. Is it necessary to submit the output files even if the major results are described in the analysis report?

A: If major results are described in the analysis report, it is not necessary to submit the output files.

Q5-20: Deleted

Q5-20-1: Deleted

Q5-20-2: Deleted

Q5-21: Analysis results can be slightly different depending on the analysis software version. When confirming the results of analysis during the review, will reviewers always use the same software version the applicant used to prepare the results? Is it necessary for applicant to complete the analysis with the latest version of the software?

A: It is preferable for the PMDA to analyze in the same environment as the applicant, but it is not realistic for to assume this will always be the case. Therefore, in some cases, the PMDA analysis will be conducted using a different software or version, with the understanding that analysis results would be slightly different depending on the environment. The applicant does not necessarily need to use the latest version of the software.

Q5-22: Have there been cases where the PMDA has sent inquiries after a new drug application because the reviewer had questions about the contents of submitted data or when the program doesn't run in the PMDA's environment?

A: Basically, the PMDA will not send inquiries regarding the contents of programs or data. Please record details such as definition files, analysis specifications, and program procedures in each briefing document.

Q5-23: When a program requires modifications in order to run at the PMDA, does the applicant need to modify and resubmit the program?

A: No, that will not be necessary.

Q5-24: Have there been cases where the PMDA requires applicants to submit variables not used in the population analysis (including simulations)?

A: In general, the PMDA won't require the creation and submission of a dataset with new variables after application. On the other hand, at the clinical consultation, the PMDA can propose the creation of a dataset with new variables (e.g., weight, age, when considering dose setting in children).

Q5-25: Deleted

Q5-26: When PK analyses are conducted at multiple time points in a single study, in which folder should ADaM datasets for each time point be stored?

A: If timing of analysis for efficacy and safety is different from that of analyses for PK (e.g., [1] multiple PK analyses are conducted during the study period where a single analysis for efficacy and safety is conducted, or [2] the timing of PK data collection is different from that of efficacy and safety), use different file names for the ADaM dataset based on analysis timing, and store them in [*study id* / iss / ise]\analysis\adam\datasets folder. When the method above is difficult to apply, or when there are multiple time points to analyze as a whole study (i.e., when interim analysis is conducted and submitted with the final analysis), store the most important ADaM dataset for evaluation in [*study id* / iss / ise]\analysis\adam\datasets folder, and store other datasets in the "misc" folder. If an applicant needs to discuss which time point should be considered the most important for evaluation, or whether analyses at each time point should be submitted, please use clinical trial consultations. If the applicant needs to discuss how to store data, please use a consultation on preparation of submission of electronic study data.

Q5-27: For phase I, clinical pharmacology studies and clinical pharmacological analysis, is there any particular format for the dataset definition document to be submitted along with the analysis dataset that are not based on CDISC standards? Is it possible to submit the definition document in

English?

A: There is no particular format, and it is possible to submit the definition document created by the applicant without any changes. It is also possible to submit the definition document in English.

Q5-28: In Section 4.2.2.1 of the technical conformance guide, it is stated that if detailed information regarding analysis specifications is included in the analysis dataset, it is sufficient to state it clearly. Is there a proper document in which such information can be stated?

A: Please include the information in the document submitted for new drug applications, such as analysis specifications. Of note, if the information is included in documents such as analysis plan to be submitted, explain the circumstances in the analysis specifications.

Q5-29: Is it possible to submit attachment 5 of the technical conformance guide in English?

A: Yes, it is possible.

Q5-30: Please demonstrate the examples of clinical pharmacology analysis of which Analysis Results Metadata is subjected to submission, when an applicant submits electronic study data on clinical studies where a standard pharmacokinetics analysis was performed.

A: For clinical studies where standard pharmacokinetic analysis was performed, analyses to calculate pharmacokinetic or pharmacodynamic parameters by a non-compartment analysis are not subject to submission of the Analysis Results Metadata. On the other hand, submission of the Analysis Results Metadata is recommended for analyses used for statistical evaluation of pharmacokinetic or pharmacodynamic parameters, which are subject to submission of analysis datasets. However, submission of the Analysis Results Metadata is not required if analysis datasets are submitted in a format other than ADaM.

Q5-31: In Question 18 of the Q&A regarding notification on electronic study data, it states that regarding phase I studies performed in both Japanese and non-Japanese subjects and studies listed in Section 2 (1) b (c) of the notification on electronic study data, analysis dataset of efficacy and safety from those studies may not necessarily need to be submitted. Regarding safety assessment of these studies, if adverse events and laboratory test values are counted or summarized simply using clinical study data (e.g., SDTM datasets), and analysis datasets are not created regardless of the format (e.g., ADaM), is it necessary to create analysis datasets and submit them?

A: Regarding safety assessment of these studies, if adverse events and laboratory test values are counted or summarized simply using clinical study data (e.g., SDTM datasets), and analysis datasets are not created, it is not necessary to create analysis datasets and submit them.

Q5-32: In reference to Section 4.2.2.1 of the technical conformance guide, is it permissible to submit the Core Output file of Text Output of Phoenix Projects (*.phxproj) or Phoenix Projects (*.phxproj)

containing the applicable file as information to be submitted in accordance with the analysis specifications on pharmacokinetics or pharmacokinetics/pharmacodynamics?

A: Yes, it is permissible.

Q5-33: If physiologically based pharmacokinetic model analysis is performed for a drug (Drug A) which differs from a submitted drug in a PBPK model analysis report aimed to investigate drug interaction, is it necessary to submit the files for PBPK model analysis of Drug A as well as the files of a submitted drug?

A: Yes, it is necessary to submit the files of Drug A.

Q5-34: In Question 17 (2) (b) of the Q&A regarding notification on electronic study data, population analysis that the applicant considers as evidence for setting dosage and administration for confirmatory studies is explained as subject to submission of electronic study data. Regarding population analysis using evidence for setting dosage and administration for confirmatory studies, if the analysis dataset and/or model are updated using the data from the confirmatory study after the confirmatory study is conducted and the updated analysis is utilized as evidence for setting dosage and administration, is it permissible to submit only electronic data on the updated analysis and not the electronic data on the pre-update analysis?

A: Yes, it is permissible.

Notifications
- **Notification on Electronic Study Data**

Revision of Notification on Handling of Submission of Electronic Study Data for New Drug Applications (PSB/PED Notification No. 0408-3, by the Director of Pharmaceutical Evaluation Division, Pharmaceutical Safety Bureau, Ministry of Health, Labour and Welfare, dated April 8, 2024)
- **Q&A Regarding Notification on Electronic Study Data**

Question and Answer Guide Regarding "Notification on Handling of Submission of Electronic Study Data for New Drug Applications" (Administrative Notice of the Pharmaceutical Evaluation Division, Pharmaceutical Safety Bureau, Ministry of Health, Labour and Welfare, dated April 8, 2024)
- **Notification on Gateway Application**

New Drug Applications Using the Gateway System (PSEHB/PED Notification No. 0401-7, by the Director of the Pharmaceutical Evaluation Division, Pharmaceutical Safety and Environmental Health Bureau, Ministry of Health, Labour and Welfare, dated April 1, 2024)
- **Technical Conformance Guide**

Revision of Technical Conformance Guide on Electronic Study Data Submissions (PMDA/CPE Notification No. 1345 and PMDA/CRS Notification No. 21, by the Director of Center for Product Evaluation and the Director of Center for Regulatory Science, Pharmaceuticals and Medical Devices Agency, dated April 8, 2024)

* 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.