

Administrative Notice

January 24, 2019

To: Prefectural Health Department (Bureau)

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

Question and Answer Guide Regarding  
“Notification on Practical Operations of Electronic Study Data Submissions”

The practical matters on electronic submission of study data for new drug applications have been notified in the “Notification on Practical Operations of Electronic Study Data Submissions” (PFSB/ELD Notification No. 0427-1, by the Director of the Evaluation and Licensing Division, Pharmaceutical and Food Safety Bureau, Ministry of Health, Labour and Welfare, dated April 27, 2015; hereinafter referred to as “notification on practical operations”). A question and answer guide for these matters has been notified in the “Question and Answer Guide Regarding [Notification on Practical Operations of Electronic Study Data Submissions]” (Administrative Notice of the Evaluation and Licensing Division, Pharmaceutical and Food Safety Bureau, Ministry of Health, Labour and Welfare, dated May 17, 2018).

Based on the experience of electronic submission of study data for new drug applications, we have decided a new question and answer guide, including the revision of Q2, Q10, Q11, and Q12, and the addition of Q10-2 and Q19 to the previous Administrative Notice, as shown in the appendix; therefore, we ask you to inform manufacturers and sellers placed under your administration to utilize for their business operations.

In accordance with the release of this Administrative Notice, the previous Administrative Notice is abolished.

\* 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.

Appendix

Question and Answer Guide Regarding  
“Notification on Practical Operations of Electronic Study Data Submissions”

Question 1:

In 1. (3) of the “notification on practical operations”, it is stated that even when the data has already been submitted electronically, “if additional analyses have been performed, the submission of relevant analysis datasets and programs may be requested.” What should I do if I used an existing analysis dataset without making any changes?

Answer:

Even when you have used an existing analysis dataset without any change, in principle, you must submit both the analysis dataset and the program.

Question 2

In 1. (4) of the “notification on practical operations”, it is stated that “regarding products for which new drug applications are made while appended with electronic data after April 1, 2020, and for which conduct of a post-marketing study is requested during the review process, in principle, electronic submission of the post-marketing study data is required on the application for re-examination”. Can electronic submission be requested for data from studies other than post-marketing clinical studies whose implementation was requested as conditions for approval?

Answer:

Regardless of whether it was set as conditions for approval, electronic submission will be requested on the application for re-examination for data from post-marketing clinical studies whose implementation was requested by Pharmaceuticals and Medical Devices Agency (hereinafter referred to as “PMDA”) in the review process.

\* 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.

**Provisional Translation (as of April 2019) \***

**Question 3:**

Where do I obtain the electronic certificate for using the portal site? Also, should an electronic certificate be created per organization?

**Answer:**

For the portal site, use the Medicertified electronic certificate issued by the Medical Information System Development Center.

One electronic certificate per user name will be required for the portal site. Because this electronic certificate is issued per natural person, the applicant must prepare the required number of electronic certificate for its staff.

For the method of obtaining the electronic certificate and the number of days it takes to obtain it, refer to the Medical Information System Development Center's website.

**Question 4:**

In the case where I was not able to submit some electronic files via the portal site for some reason, after making an advance notice of the application on the portal site, can I submit those electronic files to the PMDA window?

**Answer:**

If it is unavoidable circumstance, you can submit those electronic files to the PMDA window. However, you should submit only the electronic files which were not able to be submitted via the portal site to the PMDA window no less than one business day before the scheduled date of the new drug application.

**Question 4-2:**

In the case where no advance notice of the application was made on the portal site and the electronic files were submitted to the PMDA window without using the gateway system at the time of the application, can I make subsequent submissions of the electronic files concerning this application via the portal site?

**Answer:**

No. All subsequent submissions of the electronic files concerning this application must be made to the PMDA window.

\* 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.

**Provisional Translation (as of April 2019) \***

**Question 5:**

When electronic files are submitted via the portal site, can I submit the new drug application on the same day as “the date on which each electronic file has reached PMDA” specified in 2. (3) of the “notification on practical operations”?

**Answer:**

Yes. However, because the application cannot be received if the virus check of the electronic files is not complete at the time the new drug application is received at the PMDA window, the applicant should take into account the processing time for the virus check, etc.

**Question 6:**

What should I do if an error occurs while transferring the files?

**Answer:**

If an error occurs, an error dialog will appear on the portal site. The error dialog will display information about the error with an email link to the portal manager.

When an error report is received, the portal manager will confirm whether there are any files that have not been transferred and will contact the applicant if any files need to be transferred again and how to transfer such files. Thus, the applicant should take necessary measures.

**Question 7:**

It is stated that with the requirement to electronically submit study data, the attachments to the new drug application of a product subject to electronic submission, in principle, should be submitted in accordance with the eCTD. How will the scope of the eCTD differ from that of the conventional CTD?

**Answer:**

As stated in 2. (1) of “Basic Principles on Electronic Submission of Study Data for New Drug Applications” (PFSB/ELD Notification No. 0620-6 of the Evaluation and Licensing Division, Pharmaceutical and Food Safety Bureau, Ministry of Health, Labour and Welfare, dated June 20, 2014; hereinafter referred to as “notification of basic principles”), products subject to electronic submission are new drugs, which are

\* 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.

**Provisional Translation (as of April 2019) \***

categorized into (1) to (7), (9) and (9-2) listed in the appendix 2-(1) of the notification entitled “Approval Application of Pharmaceuticals” (PFSB Notification No. 1121-2 of the Pharmaceutical and Food Safety Bureau, Ministry of Health, Labour and Welfare, dated November 21, 2014). However, application by the CTD has not previously been a necessity for new drugs categorized into (9-2) listed in the appendix 2-(1).

Therefore, for the time being, submission of the eCTD will not be required for new drugs categorized into (9-2) listed in the appendix 2-(1).

**Question 8:**

If the application is withdrawn after having made a new drug application, how will the electronic data be handled?

**Answer:**

As stated in the “notification of basic principles”, the purpose of introducing the electronic submission of study data for new drug applications is to promote the establishment of a more practical and efficient evaluation and assessment process by accumulating study data of various products and enabling the cross-sectional analysis of these products.

Therefore, although the submitted study data and programs are regarded as a part of the appended documents for a new drug application, the study data and programs may be used by PMDA for the cross-product analyses unlike previously after discussion with the applicant, even when the application has been withdrawn.

Of the conventional appended documents that will now be submitted as an eCTD, protocols and other documents needed for analyses are expected to be used together for cross-product analysis, etc. However, other appended documents will be appropriately destroyed by PMDA upon withdrawal of the application.

**Question 9:**

If the SDTM and ADaM datasets have been created from a database that was summarized in formats other than the CDISC standards, can I submit the dataset that was summarized in formats other than the CDISC standards together to explain the

\* 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.

**Provisional Translation (as of April 2019) \***

relationship between the database that was used to create the datasets and the SDTM and ADaM datasets?

Answer:

If the dataset created in formats not conforming to the CDISC standards was converted into the CDISC standard format and the applicant has determined that submitting the original dataset will make it easier to explain the traceability of the CDISC-conformant dataset, such datasets may be submitted together with the Annotated CRF. However, in principle, the review will be performed using submitted data that has been converted into the CDISC standard format, and datasets that were created in formats other than the CDISC standard will only be used to understand the datasets in the CDISC standard format.

Question 10:

As stated in 1. (1) of the “notification on practical operations”, regarding phase I and clinical pharmacology study results and clinical pharmacology analyses (including population analyses and simulations) in addition to the materials mentioned in 2. (2) b of the “notification of basic principles”, it is necessary to submit electronic data of materials that are considered to provide major evidence for dosage and administration based on the evaluation of pharmacokinetics or pharmacodynamics. What kind of data are subject to electronic submission?

Answer:

Generally, if the evaluation of pharmacokinetics or pharmacodynamics is used as the evidence for setting the proposed dosage and administration or the dosage and administration in a confirmatory study, the evidence for a caution in the package insert of the ethical drug by the applicant, or the applicant’s judgment on the need for dose adjustment in specific patients, electronic data on the study and analysis are subject to submission, as in the following documents.

(1) Clinical studies where standard pharmacokinetic analysis was performed

- (1) For example, phase I and phase II studies of antibacterial drugs, where the results of pharmacokinetics or pharmacokinetics/pharmacodynamics provide a major evidence for the dosage and administration

\* 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.

**Provisional Translation (as of April 2019) \***

- (2) Clinical pharmacology studies that provide a major evidence for dosage and administration or dose adjustment in pediatric, elderly, and hepatic or renal disorder patients
  - (3) Clinical pharmacology studies that provide a major evidence for dose adjustment because of drug interactions
  - (4) Studies investigating the effect of food, which provide a major evidence for dosage and administration, for example, when restrictions on diet are established for dosage and administration based on the study results
  - (5) Clinical pharmacology studies that provide major evidence for dosage and administration or dose adjustment in relation to sex, body weight (obesity, etc.), severity of disease, genetic factors such as genetic polymorphism, alcohol, and smoking.
  - (6) Relative bioavailability studies that investigated the influence on the pharmacokinetics by administration site using subcutaneous injection preparation, patch, etc.
  - (7) Bioequivalence studies that provide a major evidence for efficacy, safety, and dosage and administration. For example, bioequivalence studies of both drug products, where the formulation used in confirmatory studies is different from the drug product to application or bioequivalence studies comparing the coadministration of a single drug product and administration of a combination drug product, where coadministration of a single drug product was used in confirmatory studies for a combination drug product
  - (8) Pharmacokinetic or pharmacokinetic/pharmacodynamic studies that investigated the comparability of reference products that provides a major evidence for the efficacy, safety, and dosage and administration of follow-on biologics (biosimilars)
- (2) Population analysis (including simulations)
- (1) Population analysis that investigated the similarity in pharmacokinetics or pharmacokinetics/pharmacodynamics between Japanese and non-Japanese subjects in the development using global clinical trials and bridging studies
  - (2) Population analysis that the applicant considers as evidence for setting dosage and administration for confirmatory studies
  - (3) Population analysis including data from phase III studies

\* 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.

**Provisional Translation (as of April 2019) \***

- (4) Population analysis that provides major evidence for dosage and administration or dose adjustment for drug interactions, pediatric and elderly patients as well as patients with hepatic or renal impairment, etc.
- (3) Physiologically based pharmacokinetic model analysis (including simulations)
  - (1) Physiologically based pharmacokinetic model analysis that provides major evidence for dose adjustment because of drug interactions and for dosage and administration or dose adjustment in pediatric and elderly patients as well as patients with hepatic or renal impairment, etc.
  - (2) Physiologically based pharmacokinetic model analysis used as the evidence for not conducting clinical drug interaction studies

For studies investigating the effect of endogenous or exogenous factors on pharmacokinetics and pharmacodynamics, if the applicant considers that it is necessary to issue a caution on pharmacokinetics or pharmacodynamics in the package insert, the electronic data of the studies are subject to submission. Independent of whether a caution is issued or not, if the 90% confidence interval of the geometric mean ratio of pharmacokinetic parameters does not fall entirely within the range of 0.8 to 1.25 (assuming a lognormal distribution of the pharmacokinetic parameter) in studies investigating the influence on pharmacokinetics, the electronic data of the studies are subject to submission.

For studies aimed at investigation of absolute bioavailability and mass balance studies, the electronic data are not subject to submission, in principle.

**Question 10-2:**

Regarding the materials mentioned in 2. (2) b of the “notification of basic principles”, please explain the following points.

- (1) Since electronic study data should be submitted for phase I studies of oncology drugs, should electronic study data therefore be submitted for all phase I studies of oncology drugs?
- (2) QT/QTc studies based on the ICH E14 guideline are subject to submission. If clinical pharmacology analyses (concentration-response analysis, etc.) was

\* 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.

**Provisional Translation (as of April 2019) \***

performed as an alternative for QT/QTc studies, is this analysis subject to submission?

Answer:

- (1) Generally, phase I studies that provide the evidence for setting of the dosage and administration in phase III studies are applicable.
- (2) Clinical pharmacology analyses (drug concentration-response analysis, etc.) performed as an alternative to QT/QTc studies are subject to submission.

Question 11:

Please explain the following points concerning the electronic submission of study data from phase I and clinical pharmacology studies and clinical pharmacological analysis

- (1) With respect to the studies listed in 2. 2) b of the “notification of basic principle”, the technical notification states that ADaM datasets used for main analyses should be submitted. If the main purpose of a clinical study, such as phase I studies performed in both Japanese and non-Japanese subjects (e.g.; in case of a strategy of global clinical trials and bridging studies), was the evaluation of pharmacokinetics, do I need to submit the analysis datasets on efficacy and safety? Also, with respect to analysis datasets on pharmacokinetics or pharmacokinetics/pharmacodynamics of phase I studies performed in both Japanese and non-Japanese subjects, is it acceptable to submit the analysis datasets in a format other than ADaM, as with clinical studies where standard pharmacokinetic analysis was performed (among the documents listed in 2. 2) c of the “notification of basic principles”)?
- (2) Of the studies listed in 2. 2) c of the “notification of basic principles”, the “notification on practical operations” states that with respect to clinical studies where standard pharmacokinetic analysis was performed, in principle, analysis datasets on efficacy and safety must be submitted in addition to the analysis datasets on pharmacokinetics or pharmacokinetics/pharmacodynamics. If the main purpose of the clinical studies where standard pharmacokinetic analysis was performed was to evaluate the pharmacokinetics or pharmacokinetics/pharmacodynamics, is it necessary to submit the analysis datasets on efficacy and safety?

\* 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.

(3) If standard pharmacokinetic analysis was performed using a dataset that integrated the data from multiple clinical studies, what type of study data should I submit electronically?

Answer:

- (1) 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 dataset of efficacy and safety in the ADaM format is difficult, consult with the PMDA beforehand on whether or not the dataset needs to be submitted using consultations. With respect to the analysis dataset on pharmacokinetics or pharmacokinetics/pharmacodynamics from this study, formats other than ADaM may be acceptable in some cases. Thus, if it is difficult to submit the analysis dataset on pharmacokinetics or pharmacokinetics/pharmacodynamics in the ADaM format, consult with the PMDA beforehand in the same manner as explained above.
- (2) Of the studies listed in 2. 2) c of the “notification of basic principles”, the analysis dataset 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 an analysis dataset in the ADaM format, consult with the PMDA beforehand on whether or not such a dataset needs to be submitted using consultations.
- (3) In principle, submission of datasets in the SDTM format will be required for individual studies, in addition to the analysis datasets that were used for integrated analyses. If it is difficult to submit the dataset in the SDTM format, consult with the PMDA beforehand using consultations.

Question 12

I would like to confirm the relationship between the data that are subject to electronic submission and the required format of the datasets.

Answer:

The relationship between the data and the format of the datasets are shown below based on the section they are mentioned in the notification of basic principles.

\* 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.

**Provisional Translation (as of April 2019) \***

Table Types and submission formats of documents subject to electronic submission

Section in notification of basic principles	Content	Individual clinical study data	Analysis dataset		
			Concerning efficacy and safety analysis	Concerning PK or PK/PD analysis	
2. 2) a	Data on results from all phase II and phase III studies (including long-term studies) that are generally regarded to be the major evidence for evaluation of efficacy, safety, and dose and administration	SDTM	ADaM		
2. 2) b Note	Study data from phase I studies and clinical pharmacology studies listed right	SDTM	ADaM	ADaM	
				In principle, ADaM, but other formats may be acceptable in certain cases	
				ADaM	
2. 2) c	Other Phase I and clinical pharmacology studies, which were deemed necessary by PMDA	SDTM	ADaM	ADaM is preferable, but other formats are acceptable	
				formats other than CDISC standard would be sufficient	
				formats other than CDISC standard would be sufficient	
2. 2) c	References which were deemed necessary by PMDA	SDTM*	ADaM*		
2. 2) c	Integrated summary of safety and efficacy (ISS/ISE)	SDTM**	ADaM		

PK: pharmacokinetics, PD: pharmacodynamics

Note: Results of phase I and clinical pharmacology study results and clinical pharmacological analyses

\*: If necessary, consult beforehand

\*\* : In principle, submission of the analysis dataset by ADaM is required, but if the SDTM dataset had been used for analysis, submission of SDTM study data is acceptable

**Question 13:**

In some cases, the study data of population analysis based on data from clinical studies performed in the later phases of development may be difficult to submit at the same time as other study data. Is it possible to submit such study data after making the new drug application?

**Answer:**

Study data of population analyses based on data from clinical studies performed in the later phases of development may be submitted after the new drug application in some cases. If submission of some study data is difficult at the time of a new drug application, consult with the PMDA on the timing of submitting such data using consultations.

\* 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.

**Provisional Translation (as of April 2019) \***

**Question 14:**

It is stated that during the transitional period, the electronic submission of certain data will be accepted. Will certain datasets from a single study be also accepted?

**Answer:**

The smallest acceptable unit of study data is by the study. During the transitional period, it is possible to submit the study data from some of the studies for which electronic submission is requested. However, submission of a part of such study data from one study (for example, only the SDTM) will not be accepted.

**Question 15:**

It is stated that the SDTM datasets should be prepared in English. Is there any change in the measure that “all adverse event terms should be preferably written in Japanese” as stated in “Format for Preparing the Common Technical Document for Submission of New Drug Applications to Reduce Total Review Time” (PFSB/ELD Administrative Notice dated January 17, 2011)?

**Answer:**

For the time being, for CTDs, the measure that “all adverse event terms should be preferably written in Japanese” will continue to apply.

**Question 16:**

In the “notification on practical operations”, the attachments to the new drug application of subject products must, in principle, be via the eCTD. Moreover, in the same notification, FD application data, eCTD, and electronic data should be submitted via the gateway system. Regarding the submission of eCTD and study data, and utilization of the gateway system, please show the relationship with category listed in the appendix 2-(1) of the notification entitled “Approval Application of Pharmaceuticals” (PFSB Notification No. 1121-2 of the Pharmaceutical and Food Safety Bureau, Ministry of Health, Labour and Welfare, dated November 21, 2014)

**Answer:**

The relationship between the application category and the submission of CTD, eCTD and study data, and utilization of the gateway system is as shown in the table below.

\* 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.

**Provisional Translation (as of April 2019) \***

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

○: mandatory, △: optional, ×: unnecessary

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

\*2: Among (8-2) and (10-3), the following cases are “△: optional”.

① Biological products, ② Radiopharmaceuticals, ③ Products manufactured using recombinant technology, ④ Products that have been specified by the Minister of Health, Labour and Welfare, as those requiring special attention to manufacturing control or quality control, according to the provisions of Article 80-2-7 of the Order of Enforcement of the Act on Securing Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics [PMD Act] (Order No.11, 1961)

(a) Products manufactured using human-derived or animal-derived cells

(b) cell- and tissue-based products

(c) specified biological products

⑤ Products whose drug substance is biological ingredient, herbal products or extracts of animal or plant origin, ⑥ *in vitro* diagnostics, ⑦ products listed in Article 96 of Ministerial Ordinance for Enforcement of PMD Act (MHLW Ordinance No.1, 1961) (products which are not required conformity to the standards of the “Ministerial Ordinance on Standards for Manufacturing Control and Quality Control for Drugs and Quasi-drugs”(MHLW Ordinance No.179, 2004)

\*3: Regarding (9-2), submit in accordance with the method specified in section 3 of the “Technical Conformance Guide on Electronic Study Data Submissions” (Notification No. 0427001, dated April 27, 2015), in the case where the documents to be attached to the new drug application form is not created as eCTD format and only study data is submitted via gateway system.

\* 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.

**Question 17:**

In the “notification of basic principles”, applications of new drugs which are categorized into (1) to (7), (9) and (9-2) listed in the appendix 2-(1) of the notification entitled “Approval Application of Pharmaceuticals” , are subject to electronic submission. In the case where there is no subject data that should be electronically submitted in the application, do I have to submit the attachments to the new drug application of subject products in eCTD format? Moreover, do I have to use the gateway system?

**Answer:**

In such case, you do not have to submit them in the format of eCTD and do not have to use the gateway system.

**Question 18:**

In the case where there is no subject data that should be electronically submitted in the application, can I use the gateway system to submit FD application data or eCTD?

**Answer:**

The gateway system is constructed mainly for the purpose of submitting electronic data. However, from the viewpoint of streamlining the procedures for applications, you can use the gateway system even in an application, which there is no subject data that should be electronically submitted, as long as the application is a new drug categorized into (1) to (7), (9) and (9-2) listed in the appendix 2-(1) of the notification entitled “Approval Application of Pharmaceuticals”

**Question 19:**

Regarding products for which the evaluation of study results is practically carried out before new drug applications (products subject to the Sakigake designation system, anti-HIV drugs, etc.) or products for which the evaluation of results from post-marketing clinical studies is carried out before application for re-examination (at a consultation about package insert revisions, a request for removal of approval conditions, etc.), we would like to make sure points to consider, such as the contents

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

of electronic data submission and submission methods, at the time of the evaluation of study results.

Answer:

- (1) Basically, electronic data of studies and analyses subject to evaluation should be submitted.
- (2) Currently, it is difficult to use the gateway system to submit electronic study data when approval application is not involved, therefore the electronic study data should be submitted by using a recording medium at the time of the evaluation of study results.
- (3) The electronic data submission via a recording medium should be carried out during the period from 5 weeks before the date on which the study results are scheduled to be submitted to the date of the study result submission.
- (4) Even if electronic data are submitted when study results were practically evaluated, they remain part of the document to be attached to the new drug application form or re-examination application form. Accordingly, the electronic data should be resubmitted via the gateway system at the time of new drug application or re-examination application.
- (5) Prior to the submission of electronic data, conformance of the data with the CDISC standards should be confirmed. If violation deemed to be important by the PMDA as shown in the Technical Conformance Guide is identified but cannot be corrected, consult with the PMDA by utilizing consultations prior to submission of electronic data.
- (6) In addition, the following points should be considered for each product.
  - (1) Products subject to the Sakigake designation system

When submitting individual study/analysis results, electronic data corresponding to the results should be submitted for prior assessment. It is acceptable to submit only electronic data of studies or analyses that can be submitted at this point of time.
  - (2) Anti-HIV drugs, products subject to prior assessment consultation, products subject to package insert revision consultation, or products for which removal of approval condition is requested

For prior assessment, electronic data should be submitted at once for studies and analyses that are subject to submit as mentioned in the “notification of basic principles”.

\* 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.