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Process optimization for efficient and smooth e-data submissions to both FDA and PMDA

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ABSTRACT

The data submission of NDA to FDA has already been mandatory, application to PMDA will be also mandatory after April 2020. We need to consider and to construct the process for e-data submission to FDA/PMDA simultaneously with a single data package.

SHIONOGI has headquarters in Japan, recently, we established group of companies in US and Europe to promote drug development globally. As a result, we will be doing e-data submission to not only either FDA or PMDA but also both authorities simultaneously.

Currently, we are preparing SDTM, ADaM datasets and the other related submission deliverables (e.g., define.xml, SDRG and ADRG) according to CDISC standards in all our clinical trials. We established global programming process to ensure compliance to CDISC standards and regulatory submissions.

As we all know that, some rules for e-data submission are different between FDA and PMDA. Therefore, we prepare separate data package for the submission to FDA and PMDA. However, we think that the process is very inefficient. As a global company, we try to optimize the process to enable us to prepare only one package that meets the most common rules for both authorities from the viewpoint of the greatest common divisor or least common multiple.

In that background, we would like to share our recent experience in establishing the global process for smooth e-data submissions to both authorities and the results. In addition, we suggest efficient way to communicate between Japan and US team members that required in the project.

INTRODUCTION

FDA has started to accept CDISC standards as the package of electronic study data (e-data) from 2004. In PMDA, “Office of Advanced Evaluation with Electronic Data” was established in 2013 and they have started to consider the review and/or consultation utilizing clinical data. PMDA has also started accepting e-data from October 1, 2016 with 3.5-year transitional period. The data submission of NDA to FDA has already been mandatory, application to PMDA will be also mandatory after April 2020.

In the past we have prepared separate data package to FDA and PMDA submissions. However, as a global company, we need to optimize the process to enable us to prepare only one package that meets the most common rules for both authorities. For achieving the goal, our colleagues of Japan and US. have been collaborating to consider the optimization.

In this paper, we introduce standardization history, timing, contents of standardization for CDISC compliance and e-data submission to authorities at Shionogi. This will be helpful information for companies that have not yet prepared for e-data submission or are just started. We also describe the main differences of some rules for e-data submission between FDA and PMDA. Based on that, we would like to share our recent experience in establishing the global process for smooth e-data submissions to both authorities and the results. We propose one of the ways to prepare only one package that meets the most common rules for both authorities from the viewpoint of the greatest common divisor or least common multiple. Finally, we suggest efficient way to communicate between Japan and US team members that required in the project.

This was prepared or accomplished by in our personal capacity. The opinions expressed in this paper are the authors' own and do not reflect the view of the Shionogi & Co., Ltd. and Shionogi Inc.

THE HISTORY OF STANDARDIZATION FOR PROGRAMMING ACTIVITIES IN SHIONOGI

At Shionogi, drug development has become more globalized from 2005. However, we had not been established consistent standards with End (Clinical Database) to End (Tables, Listings and Figures (TLFs)). It was important for us to upgrade from local standards to global standards, compliance to CDISC and to support FDA submission requirements.

The standardization was done in two Phases in 2010 and 2016. In both phases, Biostatistics department led and drove global standardization with cooperation from related departments Working Groups (WGs) comprised of our colleagues from Japan and US.

THE FISRT PHASE OF STANDARDIZATION

In the first phase of standardization, we considered some programming deliverables according to CDISC standards and the process for preparing these deliverables. Simultaneously, we also discussed a data repository for storing programming process records including each deliverable appropriately. It is because human resource mobility is increased with globalization.

We were divided into the following three WGs to consider in the first phase of standardization.

1. Establishment of integrated clinical databases system
2. SDTM standardization
3. ADaM standardization

In the first phase of standardization, we were more motivated to build data repository and analysis programming processes than to prepare for e-data submission to the authorities. At that time, we selected SAS Drug Development (SDD) as a global data repository. About folder structure, we referred to the Study Data Technical Conformance Guide published by FDA (Koretaka et al., 2014). We have created new role "Lead Programmer" to manage throughout the diversifying programming activities and to ensure consistency in programming deliverables. In addition, we enhanced the Quality Control (QC) process to keep the quality of the deliverables. These changes have enabled validation activities that are not dependent on personnel. On the other hand, we did not prepare SDTM and ADaM (especially ADaM) to be fully compliant with CDISC standards, considering the industry trends at that time and impact on our programming activities. We chose to do step-by-step standardization rather than change everything at once.

THE SECOND PHASE OF STANDARDIZATION

In the second phase of standardization, we created or updated procedures and templates of programming activities for preparing the deliverables fully compliant with CDISC standards. In addition, prepared fully compliant submission package to FDA and/or PMDA.

Moreover, due to increasing opportunities to work together with Japan and US programming teams because we have more global products recently. Based on that background, we also set a goal that the quality of deliverables was ensured regardless of Japan/ US locations from the viewpoint of e-data submission.

1. Preparation of the deliverables that can be submitted to authorities (Define.xml, SDTM/ ADaM specification, Reviewer's Guide)

   Define.xml:
   At first, we decided to use Pinnacle21 for preparing Define.xml according to CDISC Define-XML Specification Version2.0.

   Templates of SDTM/ ADaM specifications:
   We prepared templates of SDTM/ ADaM specifications based on necessary information to create

Define.xml Version2.0 by Pinnacle21. Templates are designed to be programmer friendly and auto populated. Included all the variables in the templates fully compliant with guides published by CDISC (e.g., Study Data Tabulation Model Implementation Guide (SDTMIG), Analysis Data Model Implementation Guide (ADaMIG) and ADaM Structure for Occurrence Data (OCCDS)).

Reviewer's Guide:
We prepared our own templates for Study Data Reviewer's Guide (SDRG) and Analysis Data Reviewer's Guide (ADRG) based on the templates published by Pharmaceutical Users Software Exchange (PhUSE) to include rules for e-data submission to PMDA as much as possible. For example, we included descriptions for character sets and converting from original to SI units. However, these templates were not perfect because it was difficult to prepare one Reviewer's Guide that could be submitted to both FDA and PMDA. So that, we have created 2 sets of (for FDA and for PMDA) Reviewer's Guide for one study even after this standardization.

2. Updating folder structure
   We established our folder structure for programming activities based on Module 5 of eCTD in the first standardization of clinical data. At this time, we added folders related to Japanese data (e.g., adam_j, sdtm_j) and clinical pharmacology folder (e.g., cp) according to Technical Conformance Guide on Electronic Study Data Submissions in PMDA.

THE GLOBAL PROCESS FOR SMOOTH E-DATA SUBMISSIONS TO FDA&PMDA AUTHORITIES

We need to submit electronic study data to authorities at the time of application. As we all know that, notifications about e-data submission have been published by FDA and PMDA, respectively. Many rules and regulations about e-data submission are similar between the authorities. However, there are some different rules. The similarities and differences have already discussed in detail from many companies and/or various associations in various documents and presentations. We categorized in this paper as follows.

- Consulting process with authorities
- Preparation of submission deliverables
- Validation rules

When we prepare for submission according FDA or PMDA rules, the other requirement may not be met. It is desirable to prepare for submission more strategically and under a more optimal way.

THE MAIN DIFFERENCES OF E-DATA SUBMISSION BETWEEN FDA AND PMDA

Consulting Process with Authorities

Differences in consulting process with both authorities shown in below Figure 1 (Kitahara et al., 2018).

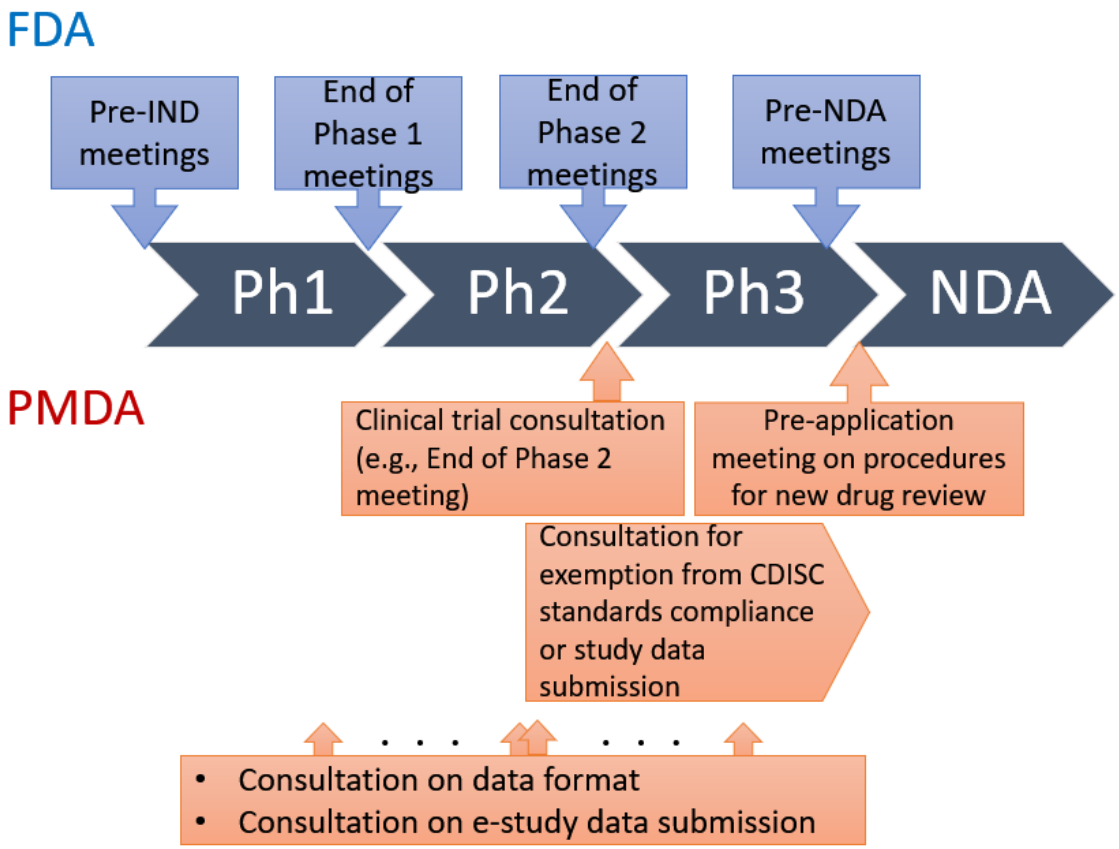

Figure 1. Consultation Process with Authorities

In Formal Meeting with FDA, there are Type A Meeting, Type B Meeting and Type C Meeting. As Type B Meeting, there are Pre-IND meetings, End of Phase 1 meetings, End of Phase 2 meetings and Pre-NDA meetings. Generally, we often consult about e-data submission in this Type B Meeting. When we consult with FDA about e-data submission, we need to prepare and submit Study Data Standardization Plan (SDSP) to FDA.

The notification of consultation related to e-data submission with PMDA has been updated at April 1, 2019 (Table 1). The purposes of clinical trial consultation and pre-application meeting on procedures for new drug review are the same as before. Besides, two meetings (consultation for exemption from CDISC standards compliance or study data submission, consultation on data format) have been added. Before April 1, 2019, we could discuss about technical issues/concerns for data format and share validation issues on Pinnacle 21 in the consultation for e-study data submission with PMDA. However, after the updating the notification, the purpose of this meeting is only to share Pinnacle 21 validation issues.

Consultation	Purpose	Status
Clinical trial consultation (e.g. End of Phase 2 meeting)	To agree with the PMDA about target data/studies and analyses of e-study data submission	
Consultation for exemption from CDISC standards compliance or study data submission	To agree with the PMDA about exemption from CDISC standards compliance or study data submission	New
Consultation on data format	To discuss technical issues/concerns for data format	New

Consultation for e-study data submission	To share Pinnacle 21 validation issues	Change
Pre-application meeting on procedures for new drug review	To confirm finalized submission package and application date (Should send finalized Appendix 8 to the PMDA beforehand)	

Table 1. Consultation related to e-Data Submission with PMDA

Preparation of Submission Deliverables

Target Date of e-Data Submission

FDA requires preparing e-data in accordance with CDISC standards and submission at NDA in all trials initiated after December 17, 2016 including SEND. On the other hand, PMDA has started to accept e-data from October 1, 2016 and they will be also mandatory after April 1, 2020. However, PMDA has not required to submit SEND yet.

We showed below the differences between FDA and PMDA regarding the studies that we need to submit e-data (Figure 2). If we assume we will applicant after April 2020, we submit only "Study B" to FDA. We do not need to submit e-data of "Study A" to FDA because the study initiated before December 17, 2016. In the case of PMDA, we need to submit e-data in both studies, "Study A" and "Study B" (under the agreement with PMDA). It is because the date of NDA for the product is after April 2020.

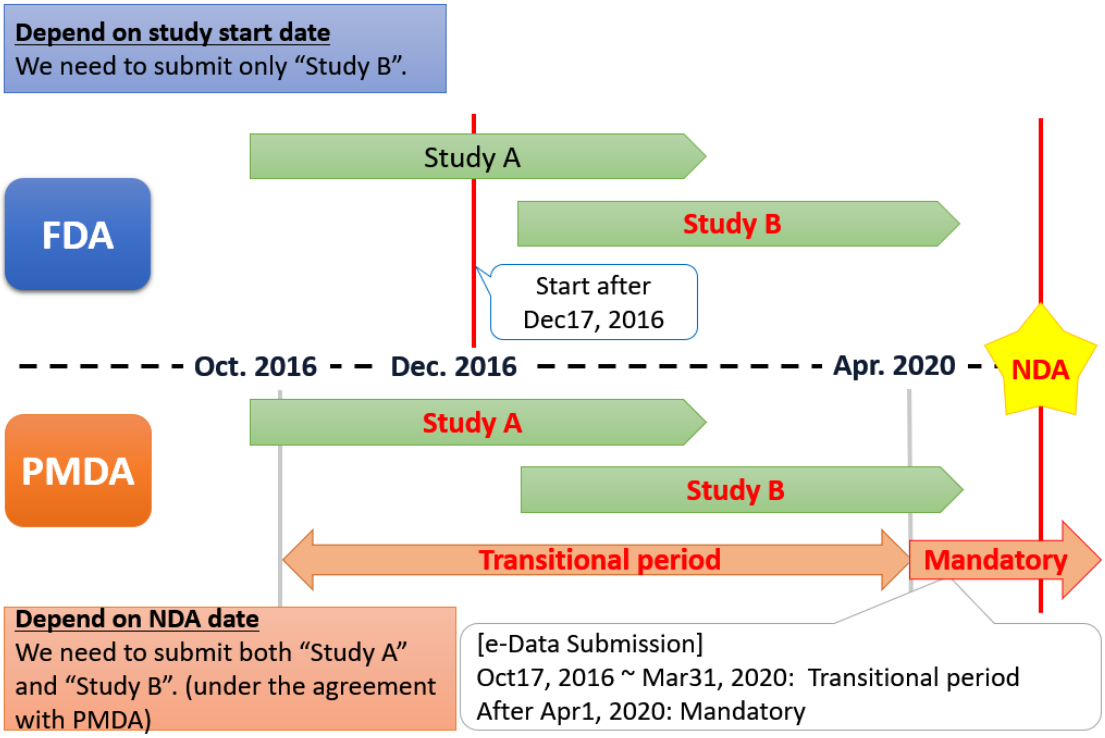

Figure 2. Target Date of e-Data Submission

Folder Structure

There are also differences between FDA and PMDA about folder structure (Figure 3). The structure proposed by FDA has a folder to store a split data (split). On the other hand, the structure proposed by PMDA has folders for Japanese data (adam_j, sdtm_j) and clinical pharmacology (cp).

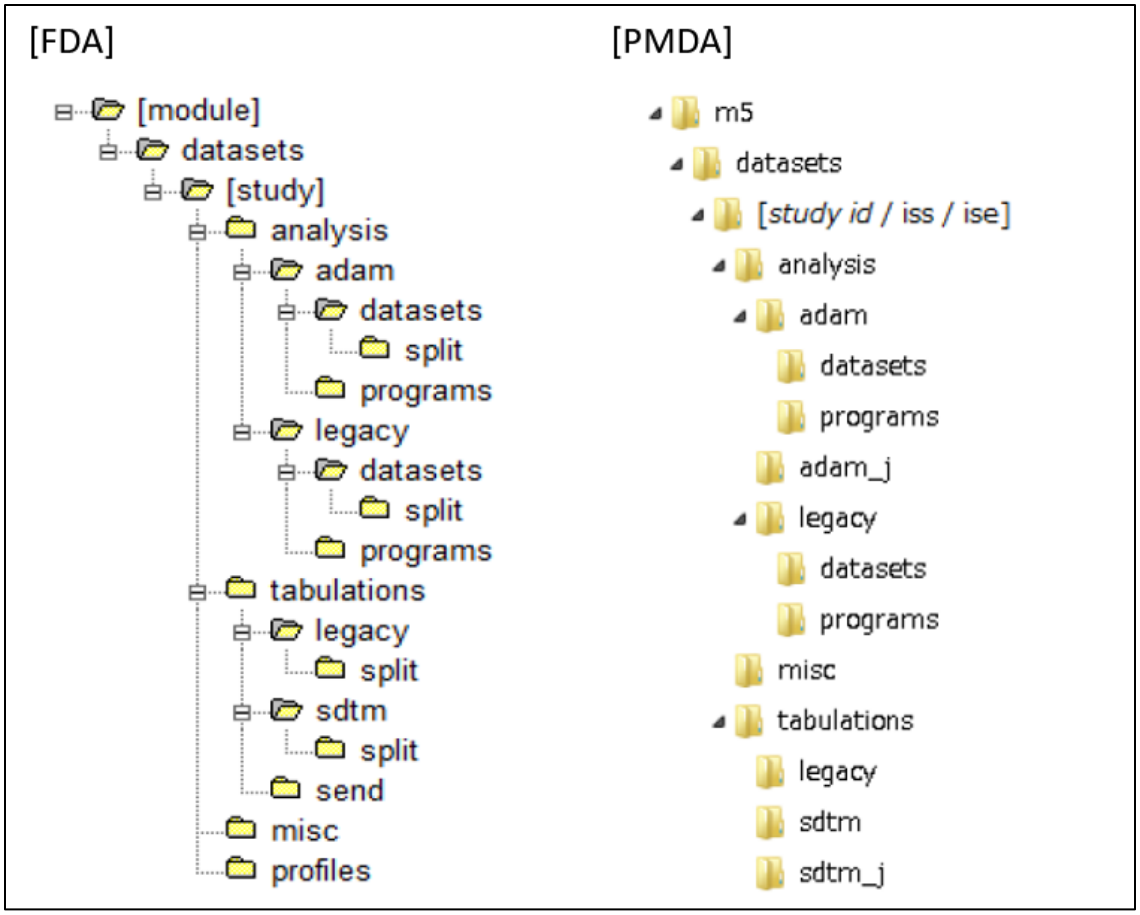

Figure 3. Folder Structure: FDA vs. PMDA

Other

There are other various differences between FDA and PMDA such as below.

- Analysis Results Metadata (ARM)
  FDA does not specifically mention of ARM requirement in their guidance. On the other hand, PMDA strongly recommend submitting the ARM.
- Japanese data
  In PMDA, if we have some Japanese datasets, we need to handle and submit them appropriately according to a notation of PMDA.
- Split datasets
  In FDA, we need to split more than 5GB dataset(s) and submit both the split and non-split datasets to them. In PMDA, we need to consult with them if we have 5GB dataset(s).
- Version of a validation tool (Pinnacle21)
  FDA does not specifically mention of the version of validation tool in their guidance. On the other hand, PMDA publishes they use Pinnacle 21 Enterprise 3.0.5 to validate for e-data in their website.
- Validation between SDTM domains and ADaM datasets
  FDA does not specifically mention of the check between SDTM domains and ADaM datasets. In PMDA, when they validate for ADaM datasets, they also check ADaM datasets with SDTM domains. We need to check between SDTM and ADaM using a validation tool before submitting e-data to PMDA.

Validation Rules

"Validation rules" and the "Severity" are different between both authorities. We showed some examples for SDTM below (Table 2).

There are two categories ("Error" and "Warning") in FDA's validation rule. On the hand, there are three categories ("Reject", "Error" and "Warning") in PMDA's validation rule. And, there are rules that exist only in either FDA or PMDA. Table 2 also showed all patterns of the combination.

We should be the most careful with the pattern of "Error" and "Reject" in FDA and PMDA Severity. Generally, if "Reject" is found in our e-data, PMDA will not accept our data until the data will be updated to resolve the "Reject" contents.

The next patterns to be cared are "Warning" and "Error" or Null and "Error" in FDA and PMDA Severity. In e-data submission to FDA, if we find the contents with "Error" and do not resolve that, we have to describe an explanation of "Error" in our Reviewer's Guide. However, in PMDA, we must share those "Error" contents and the counts with PMDA in consultation for e-study data submission before NDA. We should confirm issues with "Error" in PMDA Severity as soon as possible because we need to have enough time for consultation with PMDA.

Of course, the pattern of "Error" and "Error" in FDA and PMDA Severity is also important for us. However, we think that such "Error" can be found earlier than the above patterns. And, in that case, once we solve the "Error" issues, we can submit the e-data to both authorities.

P21/PMDA ID	FDA ID	Message	Domains	Combination		Shionogi Severity Level
				FDA Severity	PMDA Severity	
SD0002	FDAC018	NULL value in variable marked as Required	ALL	Error	Reject	High
SD1004	FDAC067	Invalid value for ARMCD	DM, TA, TV	Warning	Error	Middle
SD1132		AESER is not 'Y'	AE		Error	Middle
CT2003	FDAC342	Coded and Decoded values do not have the same Code in CDISC CT	ALL	Error	Error	Low
SD0051	FDAC091	Inconsistent value for VISIT within VISITNUM	SV, TV	Error	Warning	Low
SD0016	FDAC114	Missing value for --STRESC, when --DRVFL='Y'	FINDINGS	Warning	Warning	Low
SD1140		PMDA Expected variable not found	ALL		Warning	Low
SD2261	FDAC278	Invalid TSVALCD value for TRT	TS	Error		Low
SD1097	FDAC022	No Treatment Emergent info for Adverse Event	SUPPAE	Warning		Low

Table 2. Pattern of the Validation Results based on FDA and PMDA Severity

THE GLOBAL FLOW FOR PREPARATION OF E-DATA PACKAGE IN SHIONOGI

Please image that you will applicant a product in your company. It is a global product and you plan to applicant to US (FDA) and Japan (PMDA). When you apply in the order of US, Japan, you will first prepare for the application based on FDA notices. And then, you will prepare to submit e-data to PMDA based on the deliverables for FDA submission. If the order of application is reversed, the preparation is also reversed. Alternatively, you may be preparing for submission at the same time for FDA and for

PMDA, respectively. For example, US colleagues prepare the package for FDA and Japanese colleagues prepare that for PMDA. However, in any case, you will be preparing two packages (for FDA and for PMDA) for the same product.

We (both Japan and US Biostatistical members in SHIONOGI) believe that it is inefficiency to spend our resources to create the deliverables for each authority, respectively. Under this motivation, we have considered the process for preparing one e-data package that meets the rules of both authorities as much as possible. It might be difficult to prepare one package perfectly because FDA and PMDA have different notifications. However, we believe that it makes sense to "close" to one package. In our company, we have just started to consider one e-data package strategy recently and we will introduce our experience.

Validation by Pinnacle21 and Reviewer's Guide

As we mentioned above, "Validation rules" and the "Severity" are different between both authorities. We used to describe only the validation results of FDA rule in "Issue Summary" section of Reviewer's Guide when we prepare e-data for FDA submission. In the case of PMDA submission, we used to describe only the validation results of PMDA rule.

We have considered to describe the validation results of both authorities' rules in Reviewer's Guide for any of studies regardless of FDA and PMDA submission (Figure 4). Some other companies may have already applied the same resolution.

As the results of that, we can check the "Reject" and "Error" issues in PMDA at early stage. When we find "Reject" issues, we update at that time even if US colleagues driving the study. In addition, we need to consult and to agree about "Error" issues with PMDA before NDA. It is quite effective for us to be able to confirm which "Error" issues we should consult with PMDA at early step.

4. Data Conformance Summary

4.1 Conformance Inputs

Was OpenCDISC used to evaluate conformance? Yes

If yes, specify the versions of Pinnacle21 and the Pinnacle21 validation rules:

[For FDA] Pinnacle21 Community v2.2.0, SDTM v3.2 rules

[For PMDA] Pinnacle21 Community v2.1.3, SDTM v3.2 rules

Were sponsor-defined validation rules used to evaluate conformance? No

If yes, describe any significant sponsor-defined validation rules:

Were the SDTM datasets evaluated in relation to define.xml? Yes

Was define.xml evaluated? Yes

Provide any additional compliance evaluation information:

4.2 Issues Summary

Dataset(s)	Diagnostic Message	FDA ID	P21/PMDA ID	Severity [FDA]	Severity [PMDA]	Count	Explanation
VS	Variable length is too long for actual data	FDAC036	SD1082	Error	Warning	1	The allocated length for each column containing character (text) data was set to the maximum length of the variable used across all datasets in the study except for suppqual datasets according to STUDY DATA TECHNICAL CONFORMANCE GUIDE published by FDA.
VS	Inconsistent value for VSTPT		SD2239		Error	9	The time of the Vital measuring is not collected by CRF for the different VSTPT. Multiple results are set for the same value of VSDTC.

Figure 4. Example for SDRG

Folder Structure

Folder structure for e-data submission is also different between FDA and PMDA.

As we mentioned above, we established our folder structure based on Module 5 of eCTD in the first standardization of clinical data. At this time, we added folders related Japanese data (e.g., adam_j, sdtm_j) and clinical pharmacology folder (e.g., cp) according to Technical Conformance Guide on Electronic Study Data Submissions in PMDA (Figure5. “For programming activity”). We use this folder structure effectively in programming activities.

In addition, we have prepared a folder for e-data submission in our global server (Figure5. “For e-data submission”). We store the deliverables for submitting to authorities in each folder between each study completion and the NDA. According to guides of each authority, we have prepared two patterns (for FDA and PMDA respectively) of Module 5 folder structure per one product under the difference between both authorities. We have included “misc” in default folder structure for e-data submission, considering the case of storing external data. About “legacy” and “split” folder, we have not included in our default folder structure because these folders are very rarely used for us. When we will use these folders, we can add them manually.

We will consider that we move our deliverables from programming folder to e-data submission folder with the audit automatically using execution batch processing based on the SAS program in the near future.

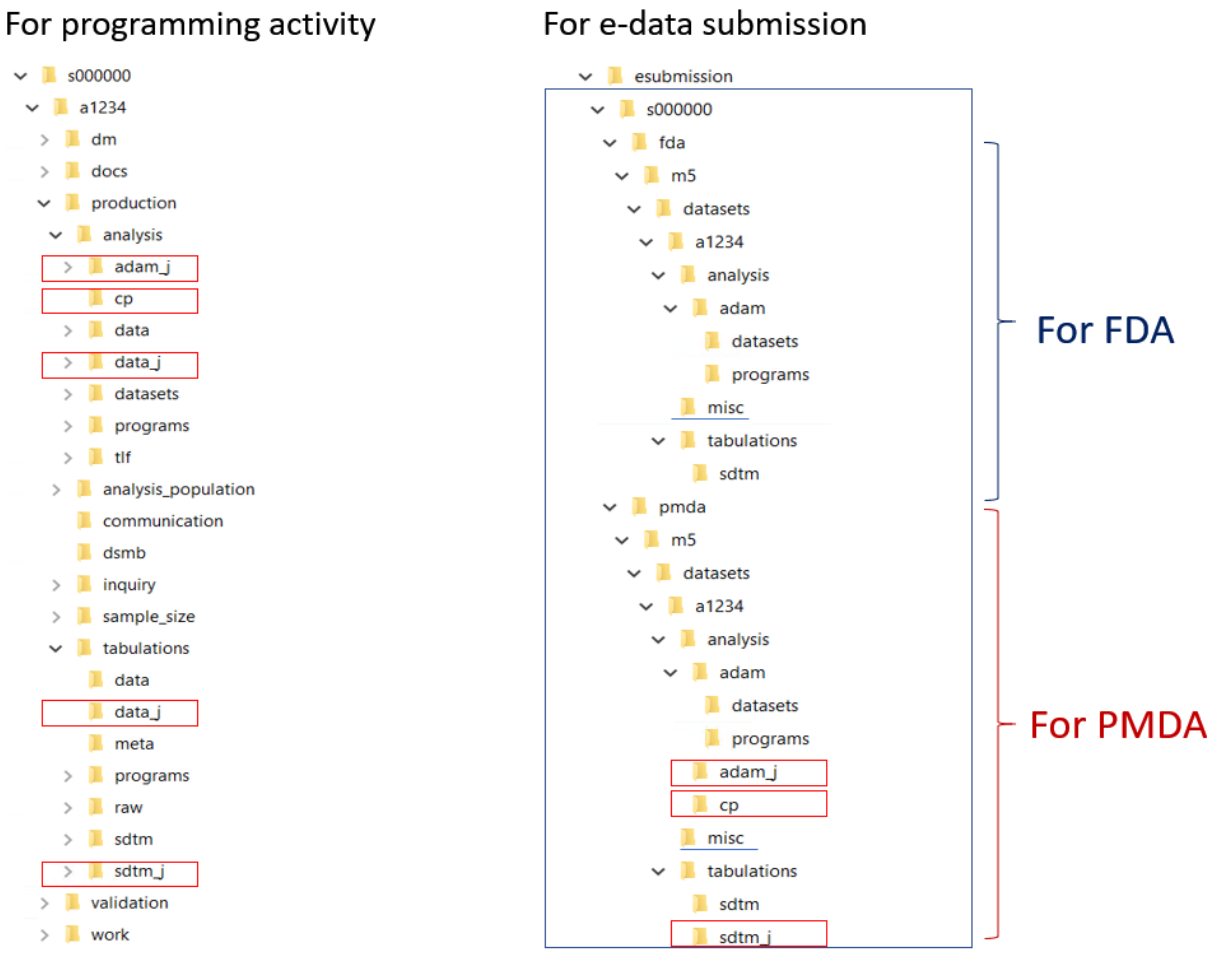

Figure 5. Folder Structure for e-Data Submission to FDA and PMDA

Document Control between SDRG/ADRG, Study Data Standardization Plan (SDSP), Appendix 8 and Information for e-Data Submission Gateway System

We need to submit SDSP to FDA, similarly Appendix 8 to PMDA and communicate with them towards IND and NDA. Additionally, there are SDRGs and ADRGs as deliverables for submission to both authorities. And, when we submit e-data to PMDA via e-data submission gateway system, information to keep in e-data system and documents (SDSP, Appendix 8, SDRG and ADRG) are very common, see below example.

- Study information
  e.g., Study Identifier, Trial title
- The information related to standardize of each deliverable
  e.g., The version of SDTM, SDTM IG, ADaM, ADaM IG, Controlled Terminology, WHO-DD and MedDRA

Actually, one of the issues of e-data submission to PMDA is the consistency between Appendix 8, SDRG, ADRG and study data information put in Gateway system. Sometimes, we need to update again those documents after the e-data submission due to conflicts between them. In addition, we need to assure the consistency between these documents and SDSP from the viewpoint of a global development.

To solve this issue, we have started to consider a uniform management of e-data for all studies in our company. We have also considered that we will get the e-data information using SAS and the other method automatically as much as possible. And, we will share it with those who are involved in e-data submission (e.g., Data Scientist, Programmer, Statistician, Clinical Pharmacology, Medical Writing, Regulatory Affairs, Project Managers).

The main purpose of this management tool is below.

- Creating SDSP, Appendix 8, SDRG/ADRG and the information for e-data submission semi automatically and maintain consistency among the documents
- Communication tool with those who are involved in e-data submission
- Prioritization our products to be submitted e-data by objectively evaluating various status of each study data (e.g., We use Shionogi Severity Level listed in Table 2.)

SECRET OF TEAM BUILDING AND COMMUNICATION FOR E-DATA SUBMISSION

In Shionogi, when we discussed the standardization and/or processes related to e-data submission and our programming activities, colleagues from US and Japan are assigned in the WG. While discussing with US and Japanese colleagues together, we can create better processes “for each other”. This makes it easier to work globally and allows each other to have a sense of responsibility for this work.

Notifications published by FDA and PMDA, or CDSIC guidance are updated on regular basis. It is very difficult for specific persons to check all updated information because there are many documents and we do not know the timing of update. Everyone who is involved in data science or programming activities always pays attention to these notification and guidance updates. And we share the information each other.

We store these notifications and guidance in our internal Sharepoint site which both US and Japan Biostatistical members can access (Figure 6). It is easy for us to access the information at central location and “One Stop Shop”. The latest notifications from PMDA are in Japanese. In that case, Japanese colleagues share with US colleagues about information that needs particular attention by e-mail, teleconference or face to face meeting.

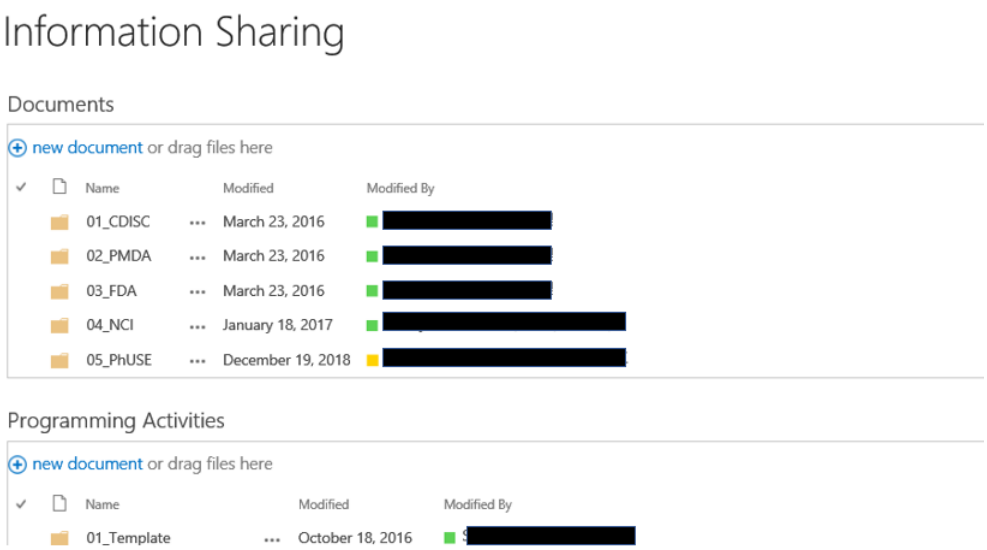

Figure 6. Example of Information Sharing

To keep our staff with up-to-date information related to submission, standards requirements, regularly organizing trainings, quiz, and lectures to understand key points related to CDISC standards and e-data submission.

CONCLUSION

Most rules related to e-data submission are common between FDA and PMDA. However, there are some different rules and they might not be fully harmonized in the future. We have considered our global processes for submitting to both FDA and PMDA. This enables us to submit e-data to both authorities efficiently. However, we think that we need to continue to consider better ways to submit e-data to both authorities.

We are trying to prepare the package that meets the most common rules for both authorities from the viewpoint of the greatest common divisor or least common multiple. As a result, we can reduce the time, cost and human resources for final adjustment before submission to each authority. We will be able to spend the time and resources for other important or creative work.

We think that optimal procedures and internal communication methods for e-data submission differ depending on the characteristics of each company. It should be noted that our process is not best practice for any company. However, we believe that this paper will be helpful for you to establish a better process for e-data submission.

REFERENCES

Clinical Data Interchange Standards Consortium. “CDISC website.” 2019. Available at https://www.cdisc.org/.

Food and Drug Administration. “FDA Data Standards Catalog.” 2018. Available at https://www.fda.gov/forindustry/datastandards/studydatastandards/default.htm#Catalog.

Food and Drug Administration. “STUDY DATA TECHNICAL CONFORMANCE GUIDE.” 2019. Available at https://www.fda.gov/media/122913/download.

Food and Drug Administration. “Technical Rejection Criteria for Study Data.” 2019. Available at https://www.fda.gov/media/100743/download.

Food and Drug Administration. “Validator Rules.” 2018. Available at https://www.fda.gov/downloads/ForIndustry/DataStandards/StudyDataStandards/UCM546468.xlsx.

Kitahara, T., Noda, A., Takanami, Y., Kurisu, A., Yamamura, A., Iijima, Y., Arita, Y., Shiraishi, T. and Nogawa, A. 2018. “Lessons Learned for Successful e-Study Data Submission to PMDA toward the End of Transitional Period.” *PhUSE EU Connect 2018*, SA08. Available at http://www.phusewiki.org/docs/Frankfut%20Connect%202018/SA/Papers/SA04-sa08-19185.pdf.

Koretaka, Y., Fujiwara, M., Yoshida, Y. and Kitanishi, Y. 2014. “Automatic Access Control via SAS: More Efficient and Smart.” *PharmaSUG 2014*, AD06. Available at https://www.pharmasug.org/proceedings/2014/AD/PharmaSUG-2014-AD06.pdf.

Ministry of Health, Labour and Welfare. “Notification on Practical Operations of Electronic Study Data Submissions.” 2015. Available at https://www.pmda.go.jp/files/000206451.pdf.

Ministry of Health, Labour and Welfare. “Revision of Notification on Practical Operations of Electronic Study Data Submissions.” 2019. Available at https://www.pmda.go.jp/files/000229311.pdf.

Ministry of Health, Labour and Welfare. “Question and Answer Guide Regarding “Notification on Practical Operations of Electronic Study Data Submissions”.” 2019. Available at https://www.pmda.go.jp/files/000229314.pdf.

Ministry of Health, Labour and Welfare. “Basic Principles on Electronic Submission of Study Data for New Drug Applications.” 2014. Available at https://www.pmda.go.jp/files/000160019.pdf.

Ministry of Health, Labour and Welfare. “Revision of Basic Principles on Electronic Submission of Study Data for New Drug Applications.” 2019. Available at https://www.pmda.go.jp/files/000229309.pdf.

Ministry of Health, Labour and Welfare. “Question and Answer Guide Regarding “Basic Principles on Electronic Submission of Study Data for New Drug Applications”.” 2019. Available at https://www.pmda.go.jp/files/000229313.pdf.

Pharmaceuticals and Medical Devices Agency. “Technical Conformance Guide on Electronic Study Data Submissions.” 2015. Available at https://www.pmda.go.jp/files/000206449.pdf.

Pharmaceuticals and Medical Devices Agency. “Revision of Technical Conformance Guide on Electronic Study Data Submissions.” 2019. Available at https://www.pmda.go.jp/files/000229312.pdf.

Pharmaceuticals and Medical Devices Agency. “PMDA Validation Rules.” 2015. Available at https://www.pmda.go.jp/files/000208341.zip.

Pharmaceuticals and Medical Devices Agency. “Appendix 8.” 2019. Available at https://www.pmda.go.jp/files/000228884.docx.

Pharmaceuticals and Medical Devices Agency. “FAQ website.” 2019. Available at https://www.pmda.go.jp/review-services/drug-reviews/about-reviews/p-drugs/0029.html.

Pharmaceuticals and Medical Devices Agency. “Website for Gateway.” 2019. Available at https://www.pmda.go.jp/review-services/drug-reviews/about-reviews/p-drugs/0030.html.

Pharmaceuticals and Medical Devices Agency. “PMDA Data Standards Catalog.” 2017. Available at https://www.pmda.go.jp/files/000216763.zip.

Pharmaceuticals and Medical Devices Agency. “Website for the notification of consultation related to e-data submission with PMDA.” 2019. Available at https://www.pmda.go.jp/review-services/f2f-pre/consultations/0040.html.

Pharmaceutical Users Software Exchange. “Website for Analysis Data Reviewer's Guide by PhUSE.” Available at https://www.phusewiki.org/wiki/index.php?title=Analysis_Data_Reviewer%27s_Guide.

Pharmaceutical Users Software Exchange. “Website for Study Data Standardization Plan by PhUSE.” Available at https://www.phusewiki.org/wiki/index.php?title=Study_Data_Standardization_Plan_(SDSP).

Pharmaceutical Users Software Exchange. “Website for Study Data Reviewer's Guide by PhUSE.” Available at https://www.phusewiki.org/wiki/index.php?title=Study_Data_Reviewer%27s_Guide.

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