PP16

FDA and PMDA Study Data Submission Distinctions

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ABSTRACT

The Food and Drug Administration (FDA) and the Pharmaceuticals and Medical Devices Agency (PMDA) require standardized study data for certain regulatory submissions. Industry approaches to meeting these requirements vary across sponsors and between regulatory review divisions. Within the PHUSE 'Optimizing the Use of Data Standards' working group, the 'Industry Experiences Submitting Standardized Study Data to Regulatory Authorities' sub team established a project to recommend best submission strategies and planning practices.

In the end-to-end process of drug development, it is essential to be aware of agency distinctions between the respective regulatory submission requirements. This poster addresses the similarities and differences in standards between the FDA and the PMDA covering mandates, data packages, dictionaries, validation rules, meetings and timelines. Additionally, questions to help sponsors plan for submitting to both agencies based on industry experiences are included.

OVERVIEW

The requirement to adhere to electronic submission guidance's from the FDA and PMDA and submit data in a standardized CDISC format is becoming critically important. The mandate, to submit data using the SDTM and the ADaM formats to the FDA, became effective as of 16 December 2016 for all study starts after this date. The mandate for submitting standardized data to the PMDA will become effective as of 1 April 2020, regardless when the study commenced.

In the end-to-end process of drug development best strategy, planning and communication practices, it is essential to be aware of the regulatory requirements to plan, develop, and submit the study data submission deliverables.

Although both health agencies require submission in CDISC SDTM and ADaM formats, there are some underlying differences in the data standard requirements that are to be addressed prior to submission. At present, it would be very difficult to submit the exact electronic submission data package to both agencies.

ACRONYMS

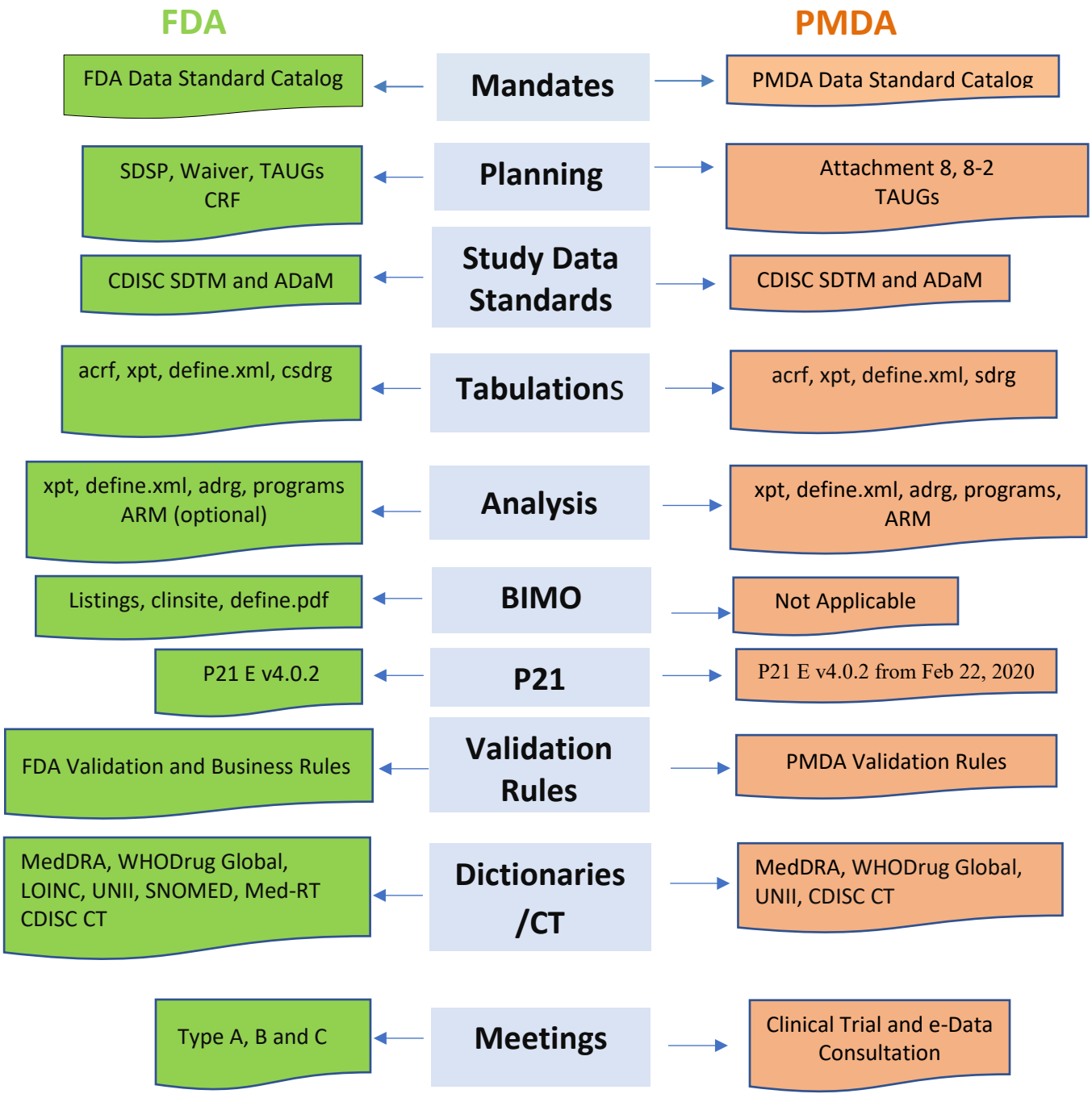
Term	Description
acrf	Annotated Case Report Forms
ADaM	Analysis Data Model
adrg	ADaM Data Reviewer's Guide
ANDA	Abbreviated New Drug Application
ARM	Analysis Results Metadata
ASCII	American Standard Code for Information Interchange
BE	Bioequivalence

BIMO	Bioresearch Monitoring
BLA	Biologic License Application
BMV	Bioanalytical Method Validation
CDISC	Clinical Data Interchange Standards Consortium
CBER	Center for Biologics Evaluation and Research
CDER	Center for Drug Evaluation and Research
CRF TOC	Case Report Forms Table of Contents
csdrg	clinical Study Data Reviewer's Guide
CSV	comma-separated values (CSV) file format
CT	Controlled Terminology
eCRF	Electronic Case Record Forms
eCTD	Electronic Common Technical Document
e-Data	Electronic Data
e-sub	Electronic Submission
FAQ	Frequently Asked Questions
FDA	Food and Drug Administration
GB	Gigabytes
HIV	Human immunodeficiency virus
ICH	International Conference on Harmonisation
IND	Investigational New Drug
ISE	Integrated Summary of Efficacy
ISS	Integrated Summary of Safety
LAB or LB	Laboratory
LOINC	Logical Observation Identifiers Names Codes
MedDRA	Medical Dictionary for Regulatory Activities
MED-RT	Medication Reference Terminology
NDA	New Drug Application
P1	Phase I

P2	Phase II
P21E	Pinnacle 21 Enterprise
pdf	Portable Document Format
PDUFA	Prescription Drug User Fee Act
PhUSE	Pharmaceutical Users Software Exchange
.phxproj	*Phoenix* Project file format
PMDA	Pharmaceutical and Medical Devices Agency
.pwo	*WinNonlin* Workbook Object
Q&A	Questions and Answers
SAS	Statistical Analysis Software
SDSP	Study Data Standardization Plan
SDTM	Study Data Tabulation Model
SDTMIG	Study Data Tabulation Model Implementation Guide
SI	Standardized International
SNOMED - CT	Systematized Nomenclature of Medicine – Clinical Terms
TAUG	Therapeutic Area User Guide
TCG	Technical Conformance Guide
txt	text
UNII	Unique Ingredient Identifiers
V	version
WHO	World Health Organization
WHO DD	World Health Organization Drug Dictionary
XLS	eXceL Spreadsheet
XLSX	eXceL Spreadsheet (a newer file format referred to as Open XML)
XML	eXtensible Markup Language
XPT	Transport File Format
XSL	eXtensible Stylesheet Language

CHART COMPARISON of FDA and PMDA STUDY DATA DISTINCTIONS

The diagram below shows the comparison of documents, standards and tools between the both agencies.



FDA and PMDA STUDY DATA DISTINCTIONS

The distinctions are classified into the following categories for ease of comparing mandates, standards, data packages, dictionaries, rules and requirements between FDA and PMDA.

MANDATES ACROSS FDA AND PMDA AGENCIES

FDA		PMDA	
Mandates Across Agencies			
References: [1]		References: [17] [22]	
New Drug Application (NDA) Abbreviated New Drug Application (ANDA) Biologics License Application (BLA)	17-Dec-2016	NDA	01-Apr-2020
Investigational New Drug (IND) Application	17-Dec-2017	Transition Period	01-Oct-2016 to 31-Mar-2020
• Studies starting on or after 17-December-2016 are to adhere to CDISC format for NDAs, ANDAs, and certain BLAs and subsequent submissions to these types of applications. • Studies starting on or after 17-December-2017 are to adhere to CDISC format for certain INDs. • All electronic submissions are to be compliant to the FDA 'Data Standard Catalog' requirements. • Waivers are possible for studies that started before 17-December-2016.		• Irrespective of study start date, study data is to adhere to the CDISC format as of 01-April-2020. Refer to the PMDA Data Standard Catalog for the supported CDISC standards. • Waiver/Exemptions are allowed under certain conditions based on the PMDA guidance updated on 24-January-2019. • Sponsors need to consult with PMDA for requesting a waiver/exemption.	

COMPARISION OF SIMILARITIES AND DIFFERENCES IN STUDY DATA SUBMISSIONS

FDA	PMDA
Study Data Planning	
References: [3] [11] [26]	References [18][21][24][25]
Study Data Standardization Plan (SDSP)	• Attachment 8 ('Consultation on Data Format of Submission of Electronic Study Data') • Attachment 8-2 'Consultation on Exemption of Submission of Electronic Study Data' is also available.
SDSP is a living document. Recommended to initiate and submit at pre-IND but no later than the end of Phase 2. Update and submit throughout development. For CBER submission, include CBER appendix within SDSP (template found in PHUSE website, 'SDSP Template with optional CBER appendix'.)	Attachment 8 is a living document. Submit prior to the eData Consultation as a preliminary meeting document. The finalized updated document is required for 'Pre-consultation meeting on review data format' that is planned 1 to 3 months prior to the application being submitted.
Therapeutic Area User Guides (TAUGs)	
References: [1]	References: [18]
TAUGs are expected to be followed if they are listed in the FDA TCG (Technical Conformance Guide - section 5.2 Supported Therapeutic Areas). TA standards that have been approved by the FDA are considered part of the CDISC foundational standards. Also refer to 'Technical Guides' - 'Therapeutic Area Information and Specifications' for additional information on the study data submissions to CDER and CBER (e.g. Next Generations Sequencing, QT Studies, BMV, HIV, Vaccines and Comparative	All Therapeutic Area Standards that have been published by CDISC may be used for submission and must be referenced in Attachment 8 and the SDTM and ADaM Data Reviewer's Guides. Sponsors need to consult with PMDA on Therapeutic Area Standards.

FDA	PMDA
Clinical Endpoint BE Studies)	
Case Report Forms (CRFs)	
CRFTOC (The CRF TOC is a list of subjects for four standard AE categories of interest required for a submission (death, discontinuation from AE, discontinuation due to any other reason, and serious AE). Additional AE categories may exist depending on protocol specific details (i.e. AE's of Interest).	Not included in initial e-sub data package but may be requested later.
Individual eCRFs (The eCRFs of the subjects from CRFTOC listing)	Not included in initial e-sub data package but may be requested later.
CRFTOC and individual eCRFs are not part of dataset folder but part of m5 eCTD folder	Not applicable
Tabulations	
References: [3]	References: [18]
SDTM Annotated blank CRF saved as acrf.pdf	Identical requirement
SDTM datasets are to use transport format (.xpt) version 5.0	Identical requirement
Study Data Reviewer's Guide is to be saved as csdrg.pdf (Include "Legacy Data Conversion Plan" for CBER, if applicable)	Study Data Reviewer's Guide is to be saved as 'study-data-reviewers-guide.pdf.' Discuss with PMDA alignment using csdrg.pdf
• Use define.xml v1.0 and define.pdf prior to 15-March-2018 • Use define.xml v2.0 on or after 15-March-2018. • A define.pdf is not required with v2.0 but recommend checking with the reviewer.	Both define.xml v1.0 and v2.0 are permissible to use. The define.pdf is not necessary.
Supplement Data Definition (optional) is provided for describing the complex computation algorithm. It is not recommended to describe the complex and lengthy derivation in the define.xml due to the style limitation of define.xml	Identical requirement
Analysis	
References: [3]	References: [18]
• Use define.xml v1.0 and define.pdf prior to 15-March-2018. • Use define.xml v2.0 on or after 15-March-2018. • A define.pdf is not required but recommend checking with the reviewer.	Identical requirement
ADaM datasets are to use transport format (.xpt) version 5.0 and prefix 'ad' for the dataset name (example: adxxxx.xpt).	Identical requirement
Analysis Data Reviewer's Guide is to be saved as adrg.pdf.	Analysis Data Reviewer's Guide is to be saved as 'analysis-data-reviewers-guide.pdf.' Discuss with PMDA alignment using adrg.pdf
Submit programs in .txt format (provide the software programs and macros used to create all ADaM datasets and tables and figures associated with primary and secondary efficacy analyses) Label: If applicable, submit data and programs for any additional analysis to support the Prescribing Information.	The file name should include the extension of the analysis software used (i.e. sas). If the file name does not contain an extension, an explanation about the file format should be included in the ADaM data guide. • Programs in txt format or pdf format have been allowed. Discuss this with the PMDA. • No specific information on label requirements but PMDA recommends providing any programs which supports the rationale for the setting of dosage and administration, which covers the label requirements.
Analysis-Results-Metadata (not required)	Analysis-Results-Metadata (as part of define.xml v2.0 or as a separate PDF file).

FDA	PMDA
Integrated Summary Safety (ISS)/Integrated Summary Efficacy (ISE)	
References: [3] [1]	References: [23] [24]
The same requirements of Analysis package stated in the above section applies to respective agencies	
Software Programs	
References: [3]	References: [18]
File names should only contain letters, numbers or hyphens, and no underscores or spaces.	Identical requirement
All file names should be in lower case.	Identical requirement
Does not require any specific software for statistical analyses. Sponsor should consult with agency to confirm the choice of software and document this in the ADaM Data Reviewer's Guide.	Does not require any specific software for statistical analyses. Sponsor to document what was used in both Attachment 8 and ADaM Data Reviewer's Guide.
Does not expect sponsor to submit executable programs, unless specifically requested by the agency.	Does not expect sponsor to submit executable programs.
No specific requirements for submitting standard company macros. Helpful in submitting analysis macros.	Prefers that macros be submitted when macros are used in programs submitted. If it is difficult to submit macros, specifications that describe algorithms can be documented in the ADaM Data Reviewer's Guide.
Files Types Accepted	
References: [14]	References: [18]
CSV, XLS, XLSX for non-patient data	CSV, XLS, XLSX acceptable (no specific rule defined in regulatory documents)
PDF	Identical requirement
XPT	Identical requirement
XML, XSL	Identical requirement
Programs in txt (ASCII)	Programs in .sas or software extension The following files can be submitted in the cp folder in the eCTD backbone. • ASCII Format Data Files • Phoenix Projects (*.phxproj) • WinNonlin Files (*.pmo、*.pwo)
Regulatory Documents	
Providing Regulatory Submissions In Electronic Format — Standardized Study Data [2]	Basic Principles on Electronic Submission of Study Data for New Drug Applications [17]
Study Data Technical Conformance Guide [3]	Technical Conformance Guide on Electronic Study Data Submissions [18]
FDA Data Standards Catalog [1]	PMDA Data Standards Catalog [19]
Business Rules [5]	No Business Rules
Validator Rules [5]	Study Data Validation Rules [20]
FDA Technical Rejection Criteria for Study Data [6]	Study Data Validation Rules [20]
Standardized Format for Electronic Submission of NDA and BLA Content for the Planning of Bioresearch Monitoring (BIMO) Inspections for CDER Submissions [7]	No information
Bioresearch Monitoring Technical Conformance Guide [8]	No information
No information	Notification on Practical Operations of Electronic Study Data Submissions [21]
No information	Question and Answer Guide Regarding "Basic Principles on Electronic Submission of Study Data for New Drug Applications" [22]
No information	Question and Answer Guide Regarding "Notification on

FDA	PMDA
	Practical Operations of Electronic Study Data Submissions" [23]
No information	FAQs on Electronic Study Data Submission (Excerpt) [24]
Portable Document Format (PDF) Spécifications [14]	Electronic Common Technical Document Specification [27]

DATASETS AND VARIABLE REQUIREMENT DIFFERENCES

FDA	PMDA
References: [3]	References: [18]
Datasets must be submitted using the SAS Transport Files v5 format.	Identical requirement
Dataset names (maximum 8 characters) should only contain lowercase letters, numbers and must start with a letter.	Identical requirement
No other symbols or special characters should be included in variable and dataset names.	Special characters can only use low line '_'
For legacy studies on/before 17 December 2016 it is permissible to use the underscore character (low line) '_' in variable names and dataset names.	Special characters can only use low line '_'
Variable names (maximum 8 characters) should only contain uppercase letters, numbers and must start with a letter.	Identical requirement
Variable names require use of ASCII text codes	ASCII alphanumeric text codes
The allotted length for each variable containing text is to be set to the maximum length needed by that variable.	SDTM datasets should be optimized for length due to the PMDA validation rule.
Variable labels (maximum 40 characters) and dataset labels (maximum 40 characters) can include ASCII text codes and punctuation characters but avoid: • Unbalanced apostrophe, • Unbalanced single and double quotation marks • Unbalanced parentheses, braces or brackets '(' '{' and '[' • '<' less than sign and '>' greater than sign.	Submission of data in the SAS v5 transport file format is required for data submission on the PMDA. Therefore, the limitations of SAS v5 transport file format is applicable. The limitations are as follows: • Variable name: max 8 characters • Variable label, dataset label: max 40 characters • Variable length: max 200 characters
Dataset > 5GB must be split and both the split and the non-split versions of the datasets must be submitted. Non-split dataset remains in the main dataset folder and split dataset goes to the sub folder (/split) within the main folder.	Consult the PMDA beforehand if the size of a dataset file is 5GB or greater.
Not Applicable	If variables had been collected in Japanese text then refer to PMDA TCG section 4.1.5 "Handling of data written in Japanese text" for the guidance.

Technical Conformance Guides	
Screen failures, when provided, should be included as a record in DM with the ARM, ARMCD, ACTARM and ACTARMCD fields left blank. This convention is inconsistent with the SDTMIG v3.2 and earlier versions.	No such specific requirements for PMDA. However, P21 PMDA Rule has a note for this inconsistent (violation): Violation of SD002 (Required variables cannot be NULL for any records) will be considered part of Rejection criteria, except for the following variables in DM domain that will be considered Errors. -ARMCD, ARM, ACTARMCD, and ACTARM.
For subjects who are randomized in a treatment group but not treated, the planned arm variables (ARM and ARMCD) should be populated, but actual treatment arm variables (ACTARM and ACTARMCD) should be left blank per TCG v4.2. This convention is inconsistent with SDTMIG.	No such specific recommendation. Refer to the above information from P21 PMDA Rule.

VALIDATION RULES

FDA	PMDA
References: [5][6]	References: [20] [20a]
Four rejection rules based on FDA technical rejection criteria. (Refer to FDA Technical Rejection Criteria).	Based on PMDA new validation rules: • 9 SDTM Rejects • 13 ADaM Rejects • 14 Define-XML Rejects
P21	
FDA uses and accepts latest P21 Enterprise version available.	PMDA uses P21 Enterprise v3.0.5 to check compliance, which has compatibility with P21 community v2.1.3. PMDA to update to v4.0.2 from 22-February-2020. PMDA announced the dates of new validation rules and P21 Enterprise version - Validation rules 1.0 support ends 31-March-2021 - Validation rules 2.0 requirement begins 01-April-2020 - Transition period for validation rule: 01-April-2020 to 31-March-2021 - PMDA to use P21 Enterprise 4.0.2 from 22-February-2020 -
REJECT	
• Rejects are reported as Errors in P21 tool. • The technical rejection criteria should be met before submission (not yet turned on).	• Rejects will cause the review to be suspended until corrections have been made. • All rejects must be resolved before submission.
ERROR	
• Errors that CAN be fixed SHOULD be fixed. • Errors that cannot be fixed should be documented and explained in the Data Reviewer's Guide with a clear rationale.	• Errors that CAN be fixed SHOULD be fixed. • Errors that cannot be fixed should be documented and explained in both the Data Reviewer's Guide and Attachment 8 with a clear rationale and explain them at the 'Consultation on Data Format' meeting. • Errors without any prior explanation will cause the review to be suspended until corrections have been made.
WARNING	

• Warnings that CAN be fixed SHOULD be fixed. • FDA does not require the explanation for warnings. But it is good practice to explain warnings that cannot be fixed in the Data Reviewer's Guide with a clear rationale.	• Warnings that CAN be fixed SHOULD be fixed. • PMDA does not require the explanation for warnings. • The reason for the violation may be requested separately from the perspective of the quality of the clinical study data.

FORMAL MEETINGS DURING DRUG DEVELOPMENT LIFECYCLE

FDA	PMDA
References: [13]	References: [24]
There are four different types of formal meetings (Type A, Type B, Type B (end of phase (EOP)), and Type C).	Consultation on data format meeting is divided into two meetings: • Clinical trial consultation (e.g. Pre-P1, Pre-P2, End of Phase 2, and Pre-NDA). • e-Data consultation meetings.
• Technical questions as part of Type C meeting. • Could also be part of Type B and Type B (EOP) meetings (e.g. Pre-IND, End of Phase 2, Pre-NDA/Pre-BLA meeting).	Clinical trial consultation: Sponsor needs to consult which study data/analysis will be submitted as part of the clinical trial consultation meeting. (Sponsors cannot consult this at e-data consultation meetings.) Three types of e-Data consultation meetings: • Consultation on **preparation** of submission of electronic study data for methods of storing data and/or submission; • Consultation on **data format** of submission of electronic study data for validation results; • Consultation on **exemption of submission** of electronic study data. • The Clinical trial and submission of electronic study data consultations meetings can be requested multiple times at any time during the drug development. • Please refer to the FAQ1-5 for the details on consultation meetings at "FAQs on Electronic Study Data Submission (Apr 2019)" document.

DICTIONARY COMPARISONS

Dictionary	FDA	PMDA
	References: [1]	References: [19] [24]
MedDRA Medical Dictionary for Regulatory Activities	Must use current version of MedDRA for SDTM AE domain for study starts by 15-March-2019 and for certain INDs by 15-March-2020 otherwise version 8 or earlier is acceptable.	Version 8.0 or later (Multiple versions accepted). Support began 01-October-2016.
WHODrug Global World Health Organization Drug Dictionary	B3 format will be required for all studies that start on 15-March-2019 otherwise, B2 format is acceptable.	WHO Drug Dictionary Enhanced version 2008:3 (01-Decemebr-2008 or later) data support begins 01-October-2016. Use of WHO Drug dictionary is required; if there are no WHO DD code available

		then sponsor-defined codes are acceptable but must document in the Data Reviewer's Guide.
LOINC Logical Observation Identifiers Names Codes	The latest version is to be used for the SDTM Lab domain. Required by 15-March-2020 and 15-March-2021 for certain INDs. .	No requirement for LOINC LB codes.
UNII Unique Ingredient Identifiers	Must use latest version for study starts 17-December-2016 or 17-December 17-2017 for certain INDs.	FDA Substance Registration System [Q4-6 in FAQs on Electronic Study Data Submission]
SNOMED CT Systematized Nomenclature of Medicine – Clinical Terms	As applicable to study starts 17-December- 2016 or 17-December-2017 for certain INDs.	No information found.

CONTROLLED TERMINOLOGY

FDA	PMDA
References: [1]	References: [19]
All versions; requirement began 17-December-, 2016 (for NDA, aNDAs) and 17-December-2017 (for certain INDs)	• Use versions 10-June-2011 or later • Support began 01-October-2016 • Consult PMDA for versions between 17-February- and 10-June-2011 •

QUESTIONS TO CONSIDER WHEN PLANNING FOR FDA AND PMDA SUBMISSIONS

1. **Can we create one single eSub Dataset Package and submit to both the FDA and the PMDA either at the same time or later?**

   Technically, both agencies use the same CDISC standards; however, there are still some differences between the two agency requirements. This limits the ability for a sponsor to create one package that satisfies both the FDA and PMDA requirements.

2. **What would you recommend if a study were filing to the FDA and PMDA?**

   Ensure that any SDTM/ADaM conformance issues (ERRORS and REJECTS) are addressed BEFORE the filing to any agencies and during the trial conduct before database lock. Execute the latest published P21 on an ongoing basis against both agencies validation rules and avoid late show stoppers.

3. **What if I do not know if we are submitting to the PMDA?**

   First of all, Find Out! The implications could be severe and could create a lot of re-work. Hence, plan ahead and be prepared. Ideally, ensure there are no 'REJECT' outcomes from running the CDISC validation rules, regardless of whether you are submitting to the FDA, PMDA or any other health authority.
   The SDTM and ADaM validations are in place to ensure standards are being adopted & implemented in the right way to enable faster analyses of the data.

RECOMMENDATIONS

- Plan early for planning, developing and submitting standardized study data
- Implement SDTM and ADaM standards early
- Convert any legacy study that is used for the filing into CDISC standards
- Ensure conformance checking performed early and on an on-going basis against CDISC and agencies conformance rules.
- Resolve issues and ensure there are no Reject validation outcomes early on and on-going basis.

- Complete the eSub data package at least 2 months prior to planned filing date.

CONCLUSION

FDA and PMDA have respective mandates, guidelines, validation rules and recommendations to submit the standardized data in CDISC standards. This paper provides a comprehensive similarities and differences highlights in study standardized data submission covering mandates, data standards catalog, data packages, dictionaries, validation rules, regulatory meetings and timelines for both agencies.

Additionally, a case study and questions to help sponsors plan for submissions based on industry experiences are included. These distinctions and experiences are intended to help the industry in the end to end process of drug development to plan, develop, and submit the study data submission deliverables.

Although agencies require CDISC standards and have similar guidelines, there are differences in the validation rules, other requirements and documentations, which limits the ability for a sponsor to create one package that satisfies both the FDA and PMDA requirements.

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REFERENCES

Reference Number	Title of Reference
	FDA
1	FDA Data Standards Catalog
2	Providing Regulatory Submissions in Electronic Format - Standardized Study Data
3	Study Data Technical Conformance Guide (October 2019)
4	Providing Regulatory Submissions in Electronic Format - Submissions Under Section 745A(a) of Federal Food, Drug and Cosmetic Act
5	Business Rules and Validator Rules
6	FDA Technical Rejection Criteria for Study Data
7	Standardized Format for Electronic Submission of NDA and BLA Content for the Planning of Bioresearch Monitoring (BIMO) Inspections for CDER Submissions (Draft Guidance)

8	Bioresearch Monitoring Technical Conformance Guide
9	Position on Use of SI Units for Lab Tests
10	SNOMED Healthcare Terminology
11	Study Data Standardization Plan Checklist Recommendations
12	Providing Regulatory Submissions in Electronic Format – Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications
13	Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products Guidance for Industry
14	Portable Document Format (PDF) Specifications (Sep 2016)
15	Submit using eCTD
16	Guidelines for Requesting Waiver to Current Supported Study Data Standard Versions
PMDA	
17	Notification on Basic Principles (Jan 2019)
18	Revision of Technical Conformance Guide on Electronic Study Data Submissions (Jan 2019)
19	Data Standards Catalog (2019) or http://www.pmda.go.jp/english/review-services/reviews/0002.html
20	PMDA Study Validation Rules v1.0 (2015-11-18) PMDA Study Validation Rules v2.0 (2019-09-27)
20a	PMDA announcement on Validation Rules v2.0 and P21 Enterprise upgrade (Japanese) Electronic Data Submission in Japan - Yuki Ando, PMDA
21	Notification on Practical Operations (Jan 2019)
22	Q&A Regarding Notification of Basic Principles (Jan 2019)
23	Q&A Regarding Notification on Practical Operations (Jan 2019)
24	FAQs on Electronic Study Data Submission (Apr 2019)
25	PMDA / Attachment 8 (April 2019) Attachment 8-2 (April 2019)
PHUSE	
26	PHUSE Regulatory Referenced Final Deliverables (Templates/Guidelines)
ICH	
27	Electronic Common Technical Document Specification (July 2008)