ACCOVION

A CLINIPACE WORLDWIDE Company

Comparison of FDA and PMDA Requirements for Electronic Submission of Study Data

Monika Kawohl

Statistical Programming

Accovion

References

- FDA Website: Study Data Standards Resources
  - Guidance for Industry: Providing Regulatory Submissions in Electronic Format – Submissions Under Section 745A(a) of the FD&C Act.
  - eStudy Data Guidance
  - Technical Conformance Guide
  - Data Standards Catalog
- PMDA Website: Advanced Review with Electronic Data Promotion Group
  - Basic Principles on Electronic Submission of Study Data for New Drug Applications
  - Notification on Practical Operations of Electronic Study Data Submissions
  - Technical Conformance Guide
  - Data Standards Catalog

Requirement Timelines

FDA

NDAs/ANDAs/ certain BLAs:

Studies starting at/after 17-Dec-2016

Certain INDs:

Studies starting at/after 17-Dec-2017

PMDA

NDAs:

Specific Studies submitted at/after 01-Apr-2020

Transition period:

01-Oct-2016 to 31-Mar-2020

ACCOVION

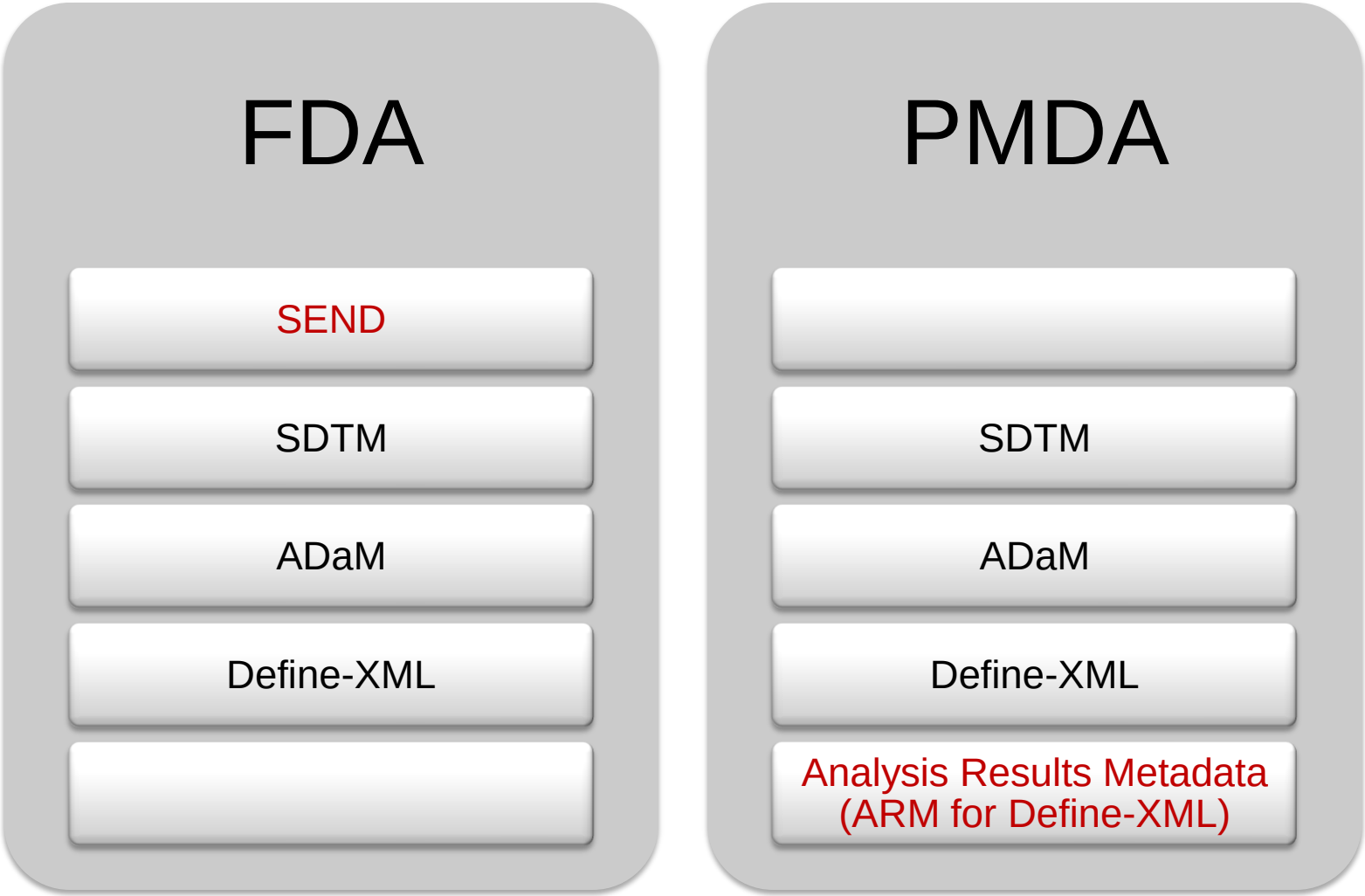
A CLINIPACE WORLDWIDE Company

PMDA: study types and submission formats of documents subject to electronic submission

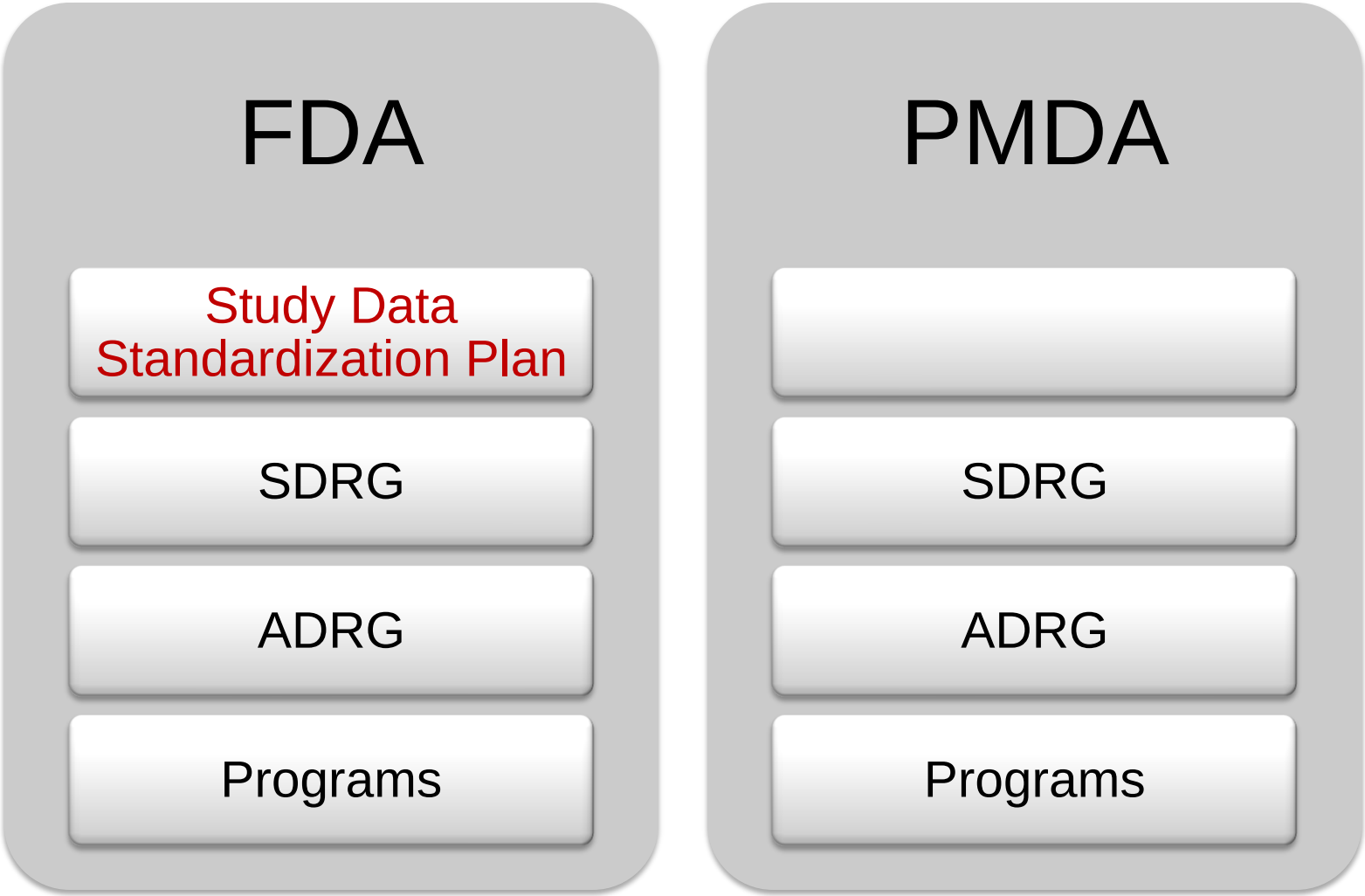
Section in notification of basic principles	Content		Individual clinical study data	Analysis dataset	
				Concerning efficacy and safety analysis	Concerning PK or PK/PD analysis
2. 2) a	Data on results from all phase II and phase III studies (including long-term studies) that are generally regarded to 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	Phase I studies of oncology drugs	SDTM	ADaM	ADaM
		Phase I studies that have been conducted in both Japanese and non-Japanese subjects (e.g.; in case of a strategy of global clinical trials and bridging studies)			In principle, ADaM, but other formats may be acceptable in certain cases
		QT/QTc studies based on ICH E14 guideline			ADaM
2. 2) Note	Phase I and clinical pharmacology studies other than a and b, which were deemed necessary by PMDA	Clinical studies where standard pharmacokinetic analysis was performed	SDTM	ADaM	ADaM is preferable, but other formats are acceptable
		Population analysies	formats other than CDISC standard would be sufficient		
		Physiologicallybased pharmacokinetic model analysies			
2. 2)	References other than a and b, which were deemed necessary by PMDA		SDTM*	ADaM*	
2. 2)	Integrated summary of safety and efficacy (ISS/ISE)		SDTM**	ADaM	

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

Required CDISC Standards



Supplemental Data Submission Documents



Other Selected Differences of Interest

Topic	FDA	PMDA
Dataset file size limit	1 GB	5 GB (no rules for splitting datasets)
Standardized Units	"CDER and CBER recognize that SI units are the worldwide standard and international trials regularly measure and report lab tests using SI units. … In the absence of a holistic transition within the U.S. healthcare community to SI units, conversion of certain lab test results to U.S. conventional units may be a necessary interim step toward a transition to full SI unit reporting."	"The use of SI units is recommended. If data were collected in units that are commonly used in guidelines … where conversion of the data to those in SI units is possible, separately store the converted data in SI units in the SDTM dataset as data in the standard units and submit them. The conventional units may be used in application documents. The ADaM dataset must include the units used in application documents."
Valid special characters in file names	Historically: "-" Per eCTD validation criteria V3.1: "-", "_"	"_" exclusively
Non-supported Standard Versions	Waiver possible	Conversion necessary

ACCOVION

A CLINIPACE WORLDWIDE Company

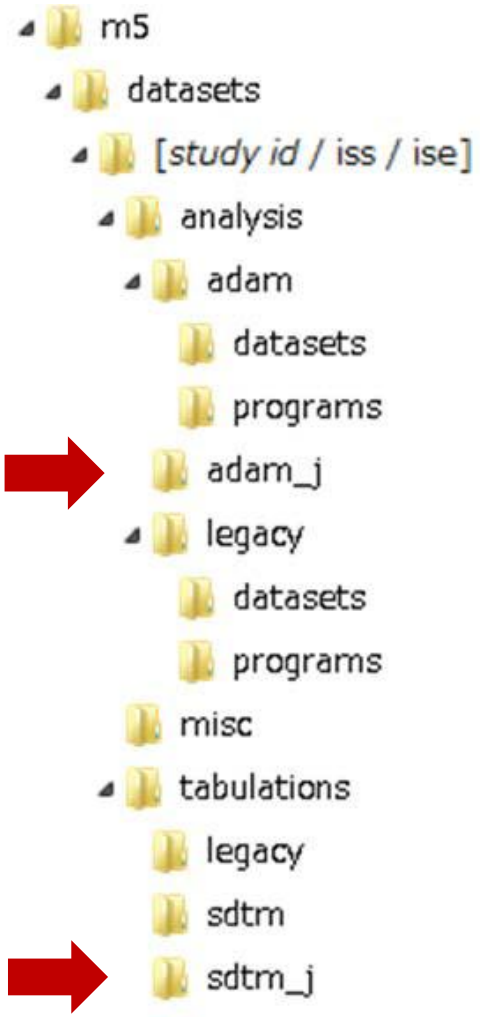
PMDA Data Standards Catalog

In general,
- less entries than in FDA's catalog
- No "Date Requirement Begins/Ends"

PMDA Data Standards Catalog (2015-07-30) - Data Exchange Standards

Use	Data Exchange Standard	Supported Version(s)	Implementation Guide Version	Exchange Format	Date Support Begins (YYYY-MM-DD)	Date Support Ends (YYYY-MM-DD)	Notes
Clinical study datasets - Transport	SAS Transport (XPORT)	5	-	XPT	2016-10-01		
Clinical study datasets	SDTM	1.4	3.2	XPT	2016-10-01		
Clinical study datasets	SDTM	1.3	3.1.3	XPT	2016-10-01		
Clinical study datasets	SDTM	1.2	3.1.2 Amendment1	XPT	2016-10-01		
Clinical study datasets	SDTM	1.2	3.1.2	XPT	2016-10-01		
Clinical study datasets	ADaM	2.1	1.0	XPT	2016-10-01		
Clinical study data definition files	Define	2.0	-	XML	2016-10-01		
Clinical study data definition files	Define	1.0	-	XML	2016-10-01		
Documents	PDF	1.4-1.7	-	PDF	2016-10-01		In principle, eCTD PDF specification should be referenced for details.

PMDA Option: Verbatim Terms in Japanese Language



Primary reference for review: English datasets

When data collected as free text should not/cannot be translated to English without loss of information, proceed as illustrated below:

AE in folder sdtm

Row	STUDYID	DOMAIN	USUBJID	AESEQ	AETERM
1	ABC123	AE	123101	1	*JAPANESE TEXT IN SOURCE DATABASE*
2	ABC123	AE	123101	2	*JAPANESE TEXT IN SOURCE DATABASE*
3	ABC123	AE	123101	3	*JAPANESE TEXT IN SOURCE DATABASE*

AE in folder sdtm_j

Row	STUDYID	DOMAIN	USUBJID	AESEQ	AETERM
1	ABC123	AE	123101	1	*頭痛*
2	ABC123	AE	123101	2	*背部痛*
3	ABC123	AE	123101	3	*肺塞栓*

Topics Specific to PMDA Technical Conformance Guide

- Submission process technical details
  - System requirements necessary for submission of electronic study data
  - Method and basic flow of the submission of electronic study data
  - Relationship between electronic study data and eCTD
- Electronic study data on phase I and clinical pharmacology study results and clinical pharmacology analyses
  - Specific deliverables to be stored in folder “cp“

➢ Respective guidance from FDA is stored in a set of different other documents

Summary

- Overall, FDA and PMDA requirements are quite similar
- Still, differences exist
- Know where to find the smallprint
- Watch out for updates
- Keep in mind the common theme in FDA/PMDA docs:
  "Consult with the regulatory agency prior to submission"

- BTW, have you seen the following PharmaSUG 2015 paper?
  „ Japanese submission/approval processes from programming perspective" (Ryan Hara)