Effective collaboration between the global and Japan team for eData submission to PMDA

Considerations from the global team's point of view

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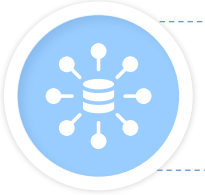
Agenda

eData submission governance and processes in BI



eData submission strategy in our project

Feedback about “eData submission to PMDA” from the global team’s point of view

Lessons learned from the collaboration with the global team

eData submission governance and processes in BI

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Governance – Task team for eData submission to PMDA

Role in eData submission	*Global project team*	*Japan team*
Project management	Global Submission manager	Subject Matter Expert in eData submission to PMDA
Make strategies for (s)NDA, (supplemental) New Drug Application submission	Project statistician	Statistician, Clinical PK/PD (PK part)
SDTM	Project data manager	Data manager
ADaM	Project programmer	Programmer
SDTM and ADaM for PK part	Programmer in PK/PD	Clinical PK/PD
Gateway submission		Global submission services in Regulatory affairs

Communicate with each counterpart in the global/Japan team

Development of CSR/CTD and CDISC deliverables

Study data in SDTM/Legacy format

Pooled database in SDTM format

- *Define XML*
- *Pinnacle 21 validation*
- *SDRG, Study reviewers' guide*

- *Define XML*
- *ARM, Analysis result metadata*
- *Pinnacle 21 validation*
- *ADRG, Analysis data reviewers' guide*
- *SAS programs for statistical analyses*

Data management

Programmer

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eData submission strategy in our project

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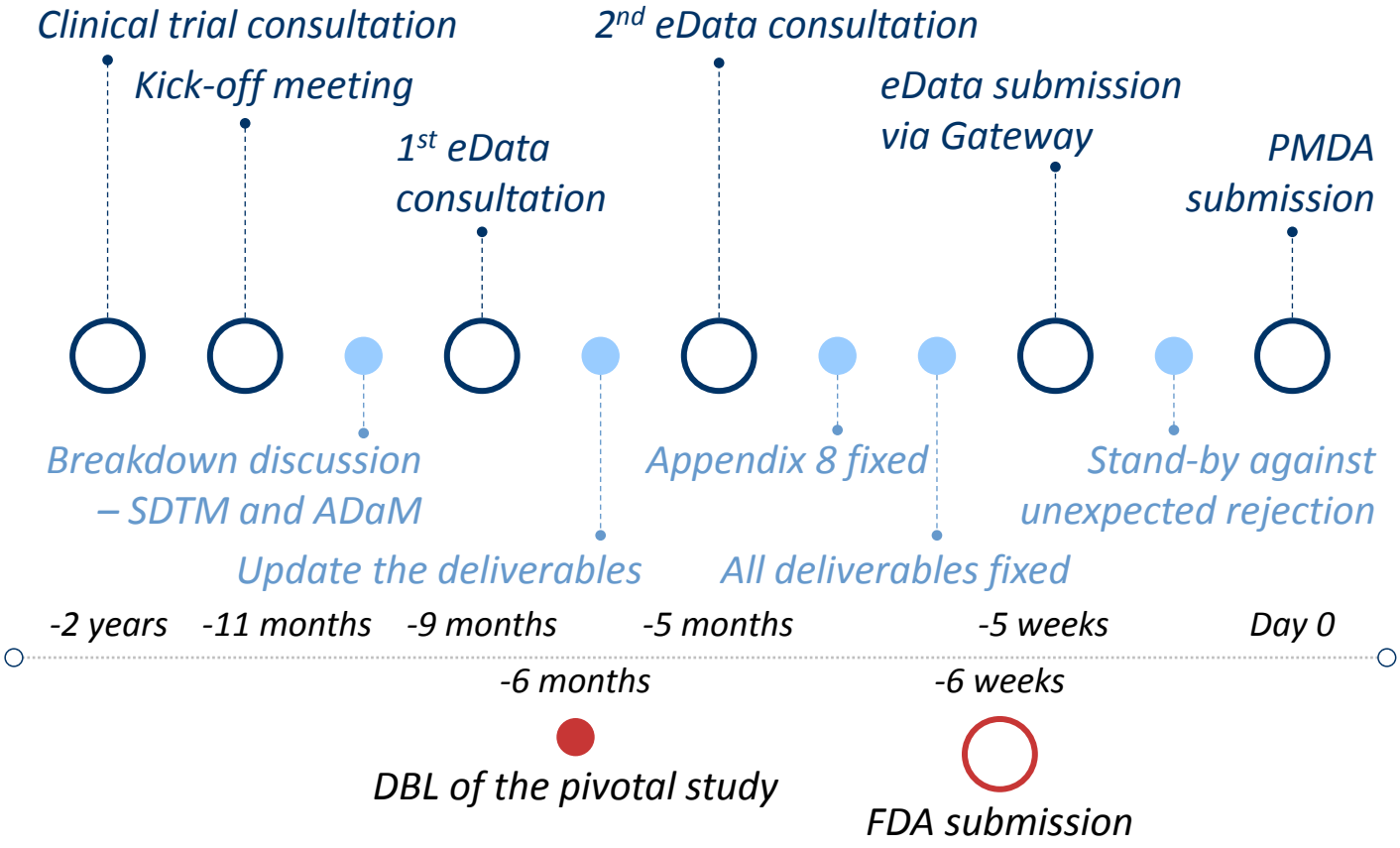
Project schedule



Kick-off meeting

At the kick-off meeting, Japan team achieved a consensus with the global team for effective collaboration

- Introduced importance of challenging the eData submission during the transition period
- Introduced differences about eData submission regulatory requirements between PMDA and FDA, e.g. PMDA's rejection policy
- Shared overview of the timeline
- Proposed the "All-in-one" concept for preparing deliverables

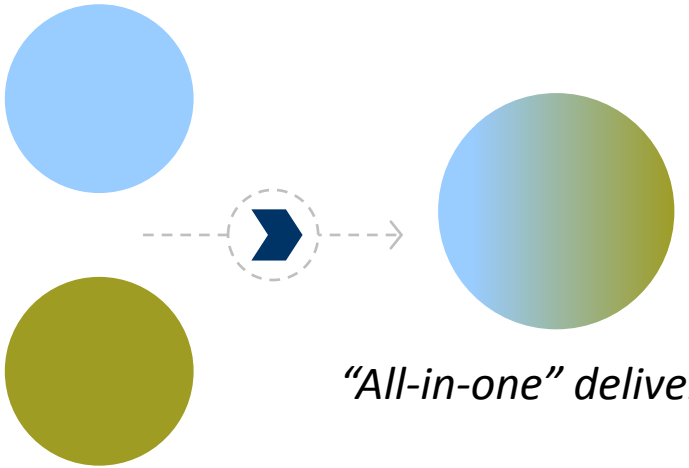
Proposals from the local team – “All-in-one” concept

What is the “All-in-one” concept?

Making combined deliverables adapted for both FDA’s and PMDA’s requirements. It allows reducing workload

Deliverables based on PMDA’s requirements

Deliverables based on FDA’s requirements



“All-in-one” deliverables

“All-in-one” deliverables adapted for both regulatory requirements

“All-in-one ” deliverables submitted to both regulatory agencies

Objective		Requirements/ Recommendations		Submitted deliverables to FDA and PMDA	Details
		FDA	PMDA		
Pinnacle 21		V 2.2	V 2.1.3		
SDTM		x	x	**x**	TS domain updated for PMDA
Annotated CRF		x	x	x	
SDRG		x	x	x	Combined issue summary table (V2.2 and V2.1.3)
ADaM		x	x	x	
Define.xml	SDTM	x	x	x	
	ADaM	x	x	x	
ARM			x*	x	
ADRG		x	x	x	Combined issue summary table (V2.2 and V2.1.3)
SAS programs	ADaM	x*	x	x	
	Analyses	x*	x	x	

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＊: Recommendations from authorities

“All-in-one” deliverables adapted for both regulatory requirements

Example: The combined issue summary table described on the SDRG

4.2 Issues Summary

Dataset	Diagnostic Message	Severity	Count	Explanation
DC	(Pinnacle21 ID : SD1212) DCSTRESN does not equal DCSTRESC	Error	1	Values are not different in SAS dataset, XPT is generating the difference
DM	(Pinnacle21 ID : SD2003) Invalid value for ACTARM	Error	106	Subjects are not assigned to an ARM -because those patients are entered but not randomized in the trial.
EX	(Pinnacle21 ID : SD1205) EXSTDTC date is before RFXSTDTC	Error	338	Treatment in Run-in or Open-Label treatment. Trial drug starts in Blinded treatment
EX	(Pinnacle21 ID : SD1207)	Error	917	Treatment in Run-in or Open-Label treatment. Trial drug starts in Blinded

The table has two columns for both validation rules

Dataset	FDA Validation Rules		PMDA Validation Rules		Diagnostic Message	Count	Comment
	Pinnacle 21 ID	Severity	Pinnacle 21 ID	Severity			
DA	SD0065	Warning	SD0065	Warning	USUBJID/VISIT/VISITNUM values do not match SV domain data	162	For subject numbers 1152002007, 1276001001 a wrong or surrogate visit number was taken instead to document medication kits assigned/dispensed. For subject numbers 1392015002, 1724012001, 1840027002 medication was assigned/dispensed at or after end of treatment. For all other subjects medication kits are assigned by IRT for a visit, but the visit data and dispense data is not yet completed in BRAVE.
DA	SD1076	Warning	SD1076	Warning	Model permissible variable added into standard domain	1	Ok as is. Permissable variable EPOCH has been added.
DA	SD1082	Error	SD1082	Warning	Variable length is too long for actual data	1	Ok as is for VISIT. Shrinking is done according to the Technical Conformance Guide, i.e. maximum length of the variable used across all datasets. However, the CDISC Validator does only check the maximum length of the variable within one dataset and not across all datasets.
DA	SD1117	Warning	SD1117	Warning	Duplicate records	16416	Ok as is. Variable DAREFID is used as additional key variable. This variable is not considered as key variable in the validator.
DI	SD9999	Error	SD9999	Error	Dataset DI class not recognized	1	Device Identifiers (DI) Domain has been defined according the given definion in the 'Implementation Guide for Medical Devices'. Structure of this domain is not recognized by the current validator version.

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“All-in-one” deliverables adapted for both regulatory requirements

SNOMED CT terminology is used when populating the indication in the TS domain

TSPARMCD	*TSPARM*
INDIC	Trial Indication
TDIGRP	Diagnosis Group

- BI should remove the related data from the TS domain submitted to PMDA in the absence of a SNOMED license.

Handled by:

Japan team

PMDA consultation → *The confirmation from PMDA* → *SNOMED values are removed* → *Submitted to PMDA*

Global team

All-in-one package → *Submitted to FDA*

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Collaboration to make “All-in-one” deliverables

eData consultation meeting (combined with technical and methodology)

Preparation *Involve the global team*

- Filled-in the Appendix 8(translated in English) together
- Specified what the scope, questioners and required deliverables are
- Finally translated the Appendix 8 into Japanese and submitted it along with the required deliverables
- Input the latest information about the requirement, e.g. Pascal issue (mmHg)

Collaboration to make “All-in-one” deliverables – Continued

Post meeting

Agile feedback

- Arranged meetings with the global team within the same day to provide feedback in a timely manner

Timeline/Risk management

- Timeline for deliverables should be agreed with the global team beforehand
  - When can ADaM and the related documents be fixed?
  - Possibility of receiving additional analyses requested by FDA before the eData submission to PMDA
- Booked the schedule of the global team for unexpected reworks due to rejections after the Gateway submission

Feedback about “eData submission to PMDA” from the global team’s point of view

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Feedback from the global team's point of view

- Nice communication and collaboration played a part in our achievement!
- The global team tried to recognize the local requirements
  - Consider the PMDA's requirements seriously
  - The rejection policy is acceptable
  - Importance of involvement of the Japan team members and their expected contributions
- Complicated specific requirements
  - Is Appendix 8 redundant? Some of the questionnaires are duplicated with the reviewers' guides
  - What are the deliverables for the eData consultation meeting? Only the Appendix 8?
  - Are Pinnacle 21 results, based on non validated data, sufficient?

Lessons learned from the collaboration with the global team

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Lessons learned from collaboration

- Involve the global team in eData submission to PMDA
  - Submission to PMDA is a part of the global submission activity
  - The Japan team's proactive contribution is expected
- Share accurate information with counterparts in a timely manner
- Timeline planning
  - By when are the required deliverables being finalized?
- Contingency plan
  - Block the global team's resources after the eData submission via Gateway in the case of unacceptance

Lessons learned from collaboration – Continued

Respect each other!

How to get to know about your counter part?

- Working together with the global team as a member of them
- Communicate with each other frequently via effective communication tools, e.g. Skype
- Increase opportunities to meet colleagues directly, e.g. extended business trip