e-Data Submission Tips and Insights from More-experienced Point of View

Tomotaro Shiraishi
A2 Healthcare Corporation

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A2 Healthcare
The Life First Company

エイツーヘルスケア株式会社

Purpose of this presentation

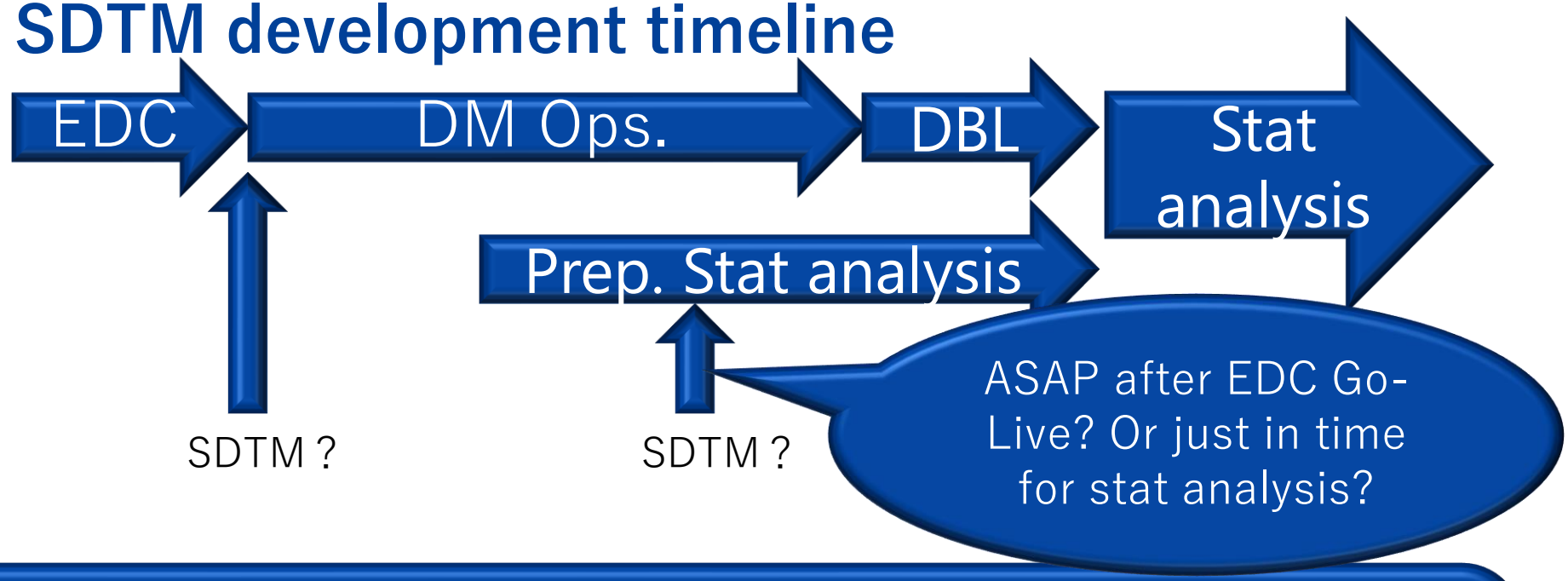
- eData submission will become mandatory in April 2020
- A2Healthcare has been supporting eData Submission in Japan a lot.
- With sharing our experiences, hoping to encourage exchange of information and experience among PHUSE community, including discussion for further improvement.

Agenda

1 Tips : SDTM/ADaM Creation

Tips : SDTM/ADaM Creation (1) - Timing

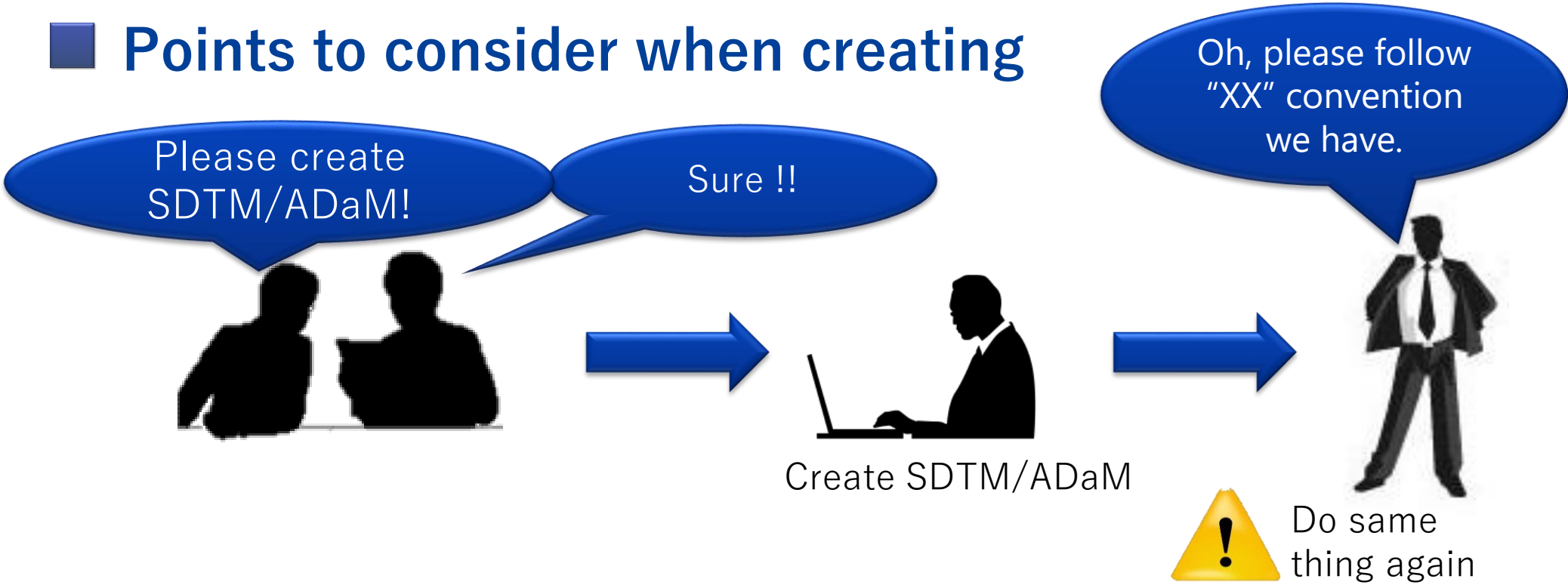
SDTM development timeline



If CRF modules are standardized, the standardized conversion programs can be implemented.
SDTM could be created at the same timing of EDC Go-live, if only protocol specific information can be handled for SDTM preparation.

Tips : SDTM/ADaM Creation (2) - Clarification

Points to consider when creating



Develop study-specific checklist before creation of datasets.
E.g., company standards, IG/CT versions, checklists for QC, description level of Define.xml

Tips : SDTM/ADaM Creation (3) - Integration

- **When considering integration, specification should be used for multiple studies within a submission**

Study 1

Study 2

Variable Name	Variable Label	Variable Type	Codelist / Controlled Terms	*CDISC-01*	*CDISC-02*
AGE	Age	num		DM.AGE;	DM.AGE;
AGEU	Age Units	text	AGEU	DM.AGEU;	DM.AGEU;
AGEGR1	Pooled Age Group 1	text	AGEGR1	If 20 <= AGE < 30 then AGEGR1 = "20 <= - < 30"; Else If 30 <= AGE < 40 then AGEGR1 = "30 <= - < 40"; Else If 40 <= AGE < 50 then AGEGR1 = "40 <= - < 50"; Else If 50 <= AGE then AGEGR1 = "50 <=";	N
AGEGR1N	Pooled Age Group 1 (N)	num	AGEGR1N	Coded from AGEGR1;	N
AGEGR2	Pooled Age Group 2	text	AGEGR2	N	If 10 <= AGE < 20 then AGEGR2 = "10 <= - < 20"; Else If 20 <= AGE < 30 then AGEGR2 = "20 <= - < 30"; Else If 30 <= AGE then AGEGR2 = "30 <=";

This template enables to highlight differences between studies within a submission

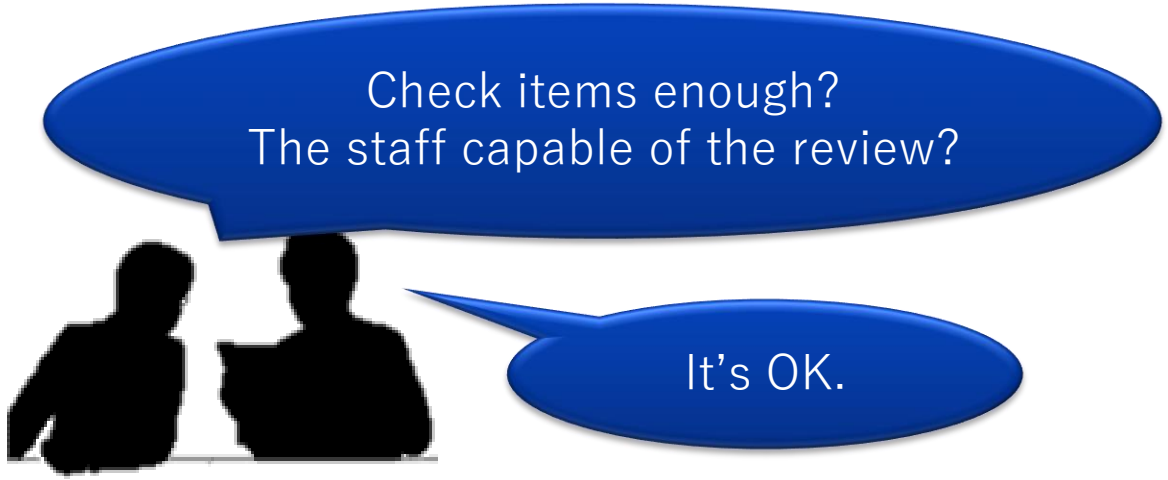
2 Quality of deliverables : SDTM/ADaM

Quality of deliverables : SDTM/ADaM (1)

Standardization of quality checklist

- Checkpoints are defined in the template including
  - Things not checked programmatically by Pinnacle21

Prepare checklist for a project based on standardized template



Check items are shared/reviewed,
and appropriate staff is assigned before work starts.

Quality of deliverables : SDTM/ADaM (2)

Considerations when submitting via Gateway

- File names could be problematic
- E.g. programs for ADaM creation and statistical analysis “T14.2.3.1.sas”

“T” – NG
“.” -- NG

*Technical Conformance Guide Section 3.5

PDF

- Validation according to eCTD requirement

Scope: PDFs submitted to PMDA (such as SDRG/ADRG)

*Technical Conformance Guide
Section 4.1.2.1, 4.1.2.2, 4.1.2.3, 4.2.2.1

3 Frequently encountered issues/Qs (data conversion of legacy trials/Pinnacle21)

Frequently encountered issues (data conversion of legacy trials)

Typical issues

Issues	Frequency
Specification not written in SAP	Very often
Difference of validation results due to software version	Very often
External data not defined in any documents	Rare
Insufficient information due to missing analysis programs and macros	Sometimes
Errors in CSR	Sometimes

Time consuming cases

- Not able to get answers to questions about data/program because of in-license products
- Need to amend CSR

Frequently encountered issues (Pinnacle21) – 1

Difference b/w Community and Enterprise

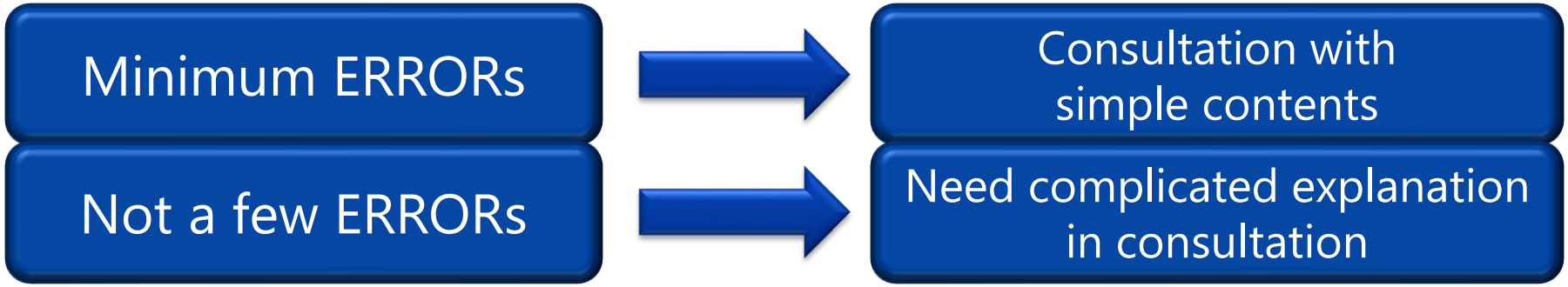
*FAQs on Electronic Study Data Submission Q1-16

The importance :
The tool should be used correctly in the right environment.

- File name of Controlled Terminology (deletion of date)
- No double-byte character in the path for the target files
- Cross-checks with Define.xml and cross checks b/w SDTM and ADaM

Frequently encountered issues (Pinnacle21) – 2

To which extent the ERRORs should be resolved



Situation	Approach and merit

Newly create SDTM/ADaM	• Minimize ERRORs
	  • Consultation could be via TC
	  • Can shorten timeline towards submission

Check and modify existing SDTM/ADaM	• Explain ERRORs in consultation • Minimize workload for modification

4 Tips :PMDA Consultation/Gateway

PMDA Consultation

Consultation which A2 participated

Contents of Consultation	Frequency
Confirmation of ERRORs detected by Pinnacle	Very often
Contents of simulation approach of PPK, structure of CP folder and the contents in them	Sometimes
Data to be submitted by study level	Sometimes
Exemption of orphan drug submission	Not yet

It's getting more frequent that PMDA accepts explanation of ERRORs via TC.

In case of PPK, CP folder is confirmed in "consultation on preparation of submission of e-study data"

PMDA Consultation

How to prepare briefing materials

- Important to determine owns which section
  - E.g. Attachment 8

Section	Responsible
1	Regulatory, PM
2	DM/Biostats/CP, etc.
3	Regulatory, PM
4	DM/Biostats/CP, etc.

Need to determine the scope of briefing materials in advance

- ERRORs description in Attachment 8
  - Attach Pinnacle report or SDRG/ADRG?

Gateway

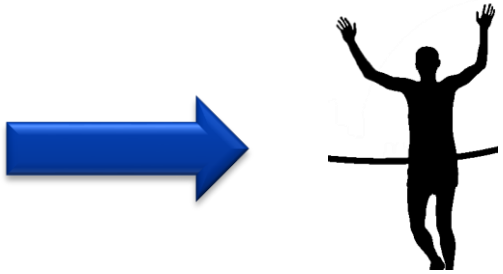
- **Clarify who does what**
  - Gateway Operation: Regulatory?, partially DM/BM/CP?
  - Use of TSV file: how do you use in future?
    - Information currently entered in TSV file will be included in xml message file for eCTD v4.0

Need to discuss process for future
(e.g., which function should enter the information about CDISC)

Gateway

Resubmission of files

Completion of submission via Gateway



Complete validation Status changes as "acceptable"

Discrepancy b/w RG and attachment 8 is found

The way to submit is different depending on resubmission timing

Timing	The way to submit
Before NDA	Revise RG, and submit m5 folder including revised RG (overwrite) again
After NDA	Revise RG, and submit revised RG only

*FAQs on Electronic Study Data Submission Q3-10

5 Summary

Summary

We have faced several issues…

Someone else must also have faced same issues.
YOU in this world would help me.

It is very helpful to have someone whom we can talk/share lessons learned

Summary

Most important thing is:

Facilitate smooth review by eData submission and deliver new drugs to patients as early as possible

So…

Discuss regarding efficient eData submission and enable to utilize them in review process.
Offer information to contribute to this industry.

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