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AGENDA

- INTRODUCTION
- PLANNING
- EXECUTION
- CLOSE-OUT ACTIVITIES

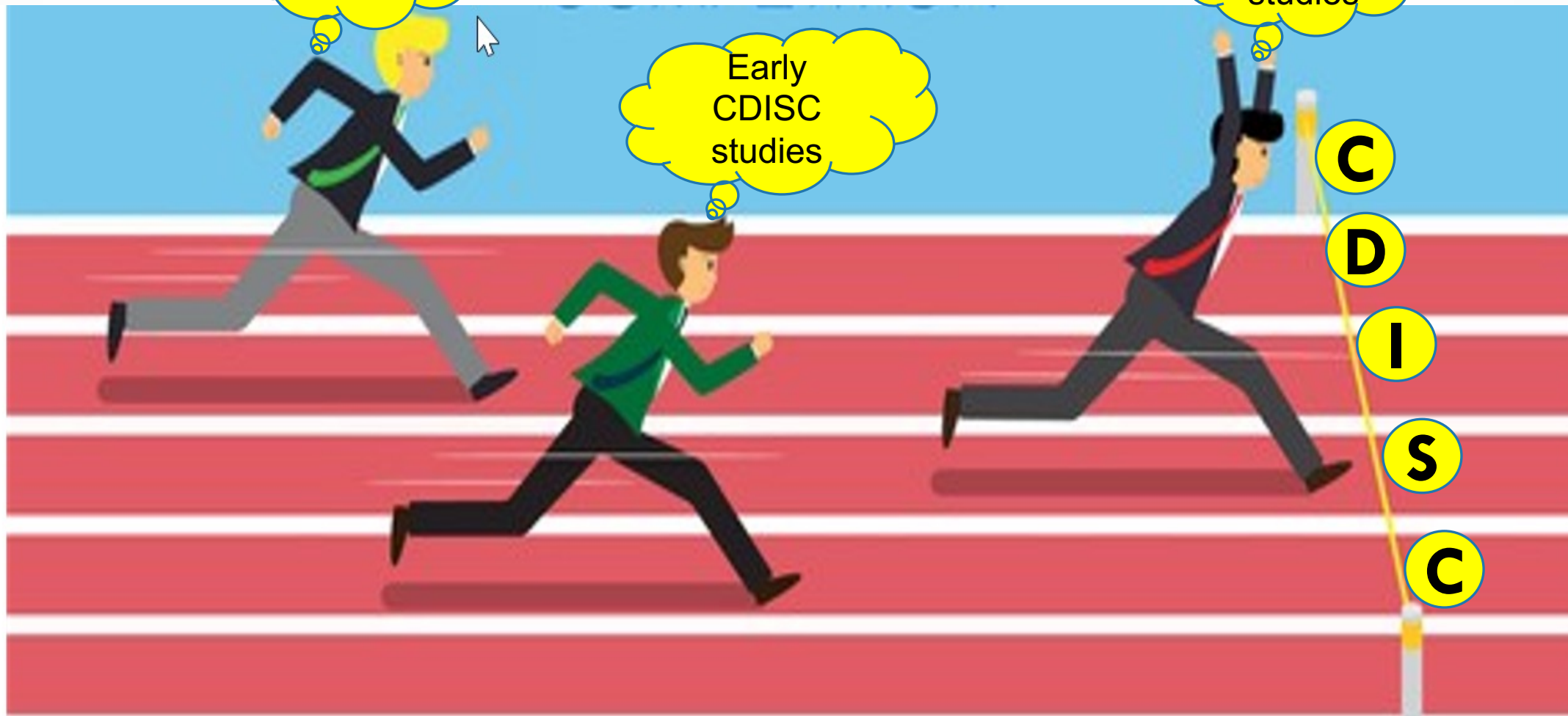
INTRODUCTION

Legacy
studies

Early
CDISC
studies

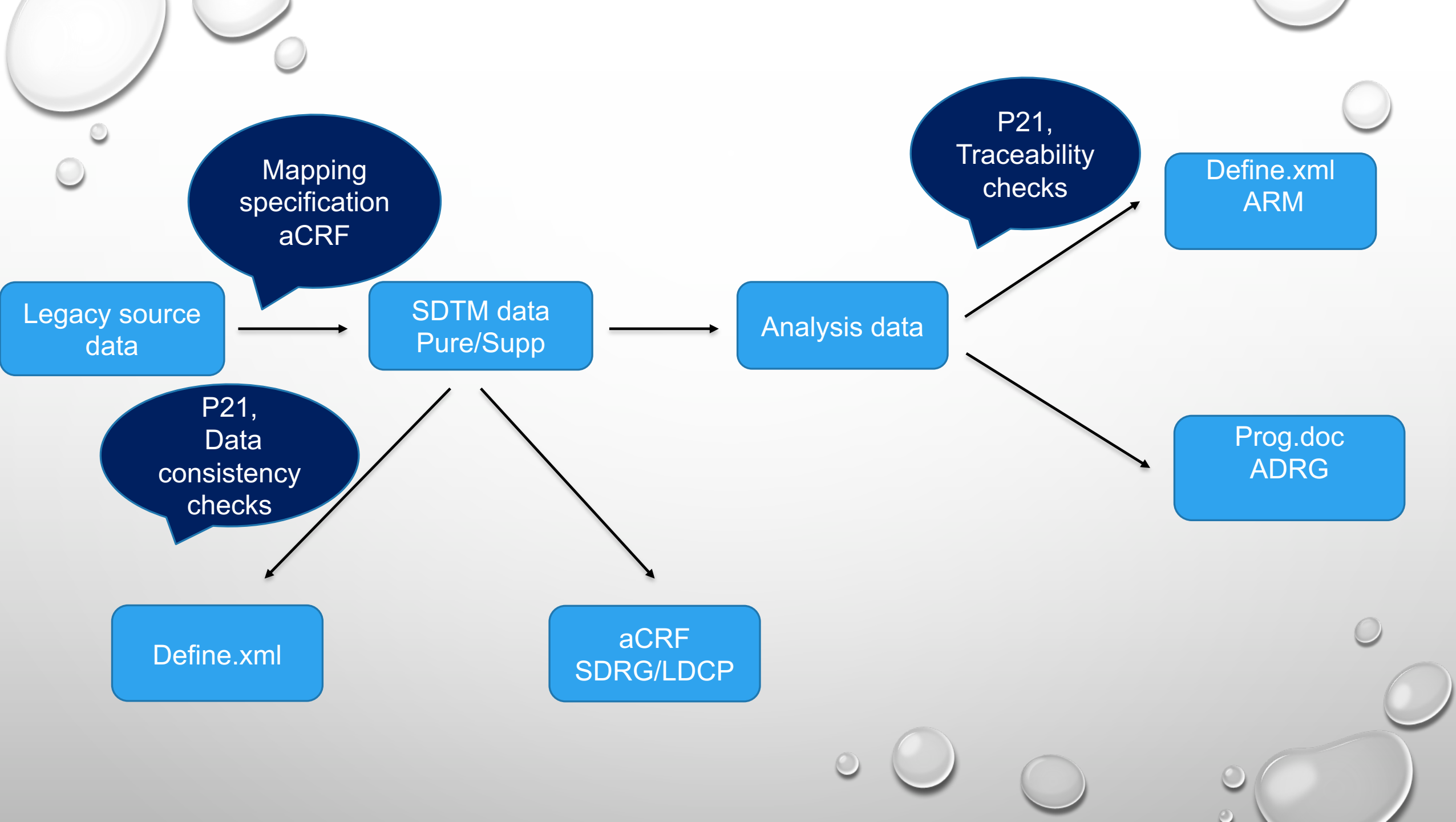
New
CDISC
studies

C
D
I
S
C



Planning

- Defining scope of submission package
- Pooling strategy
- Identification of critical activities
- Timelines and collaboration
- Submission management

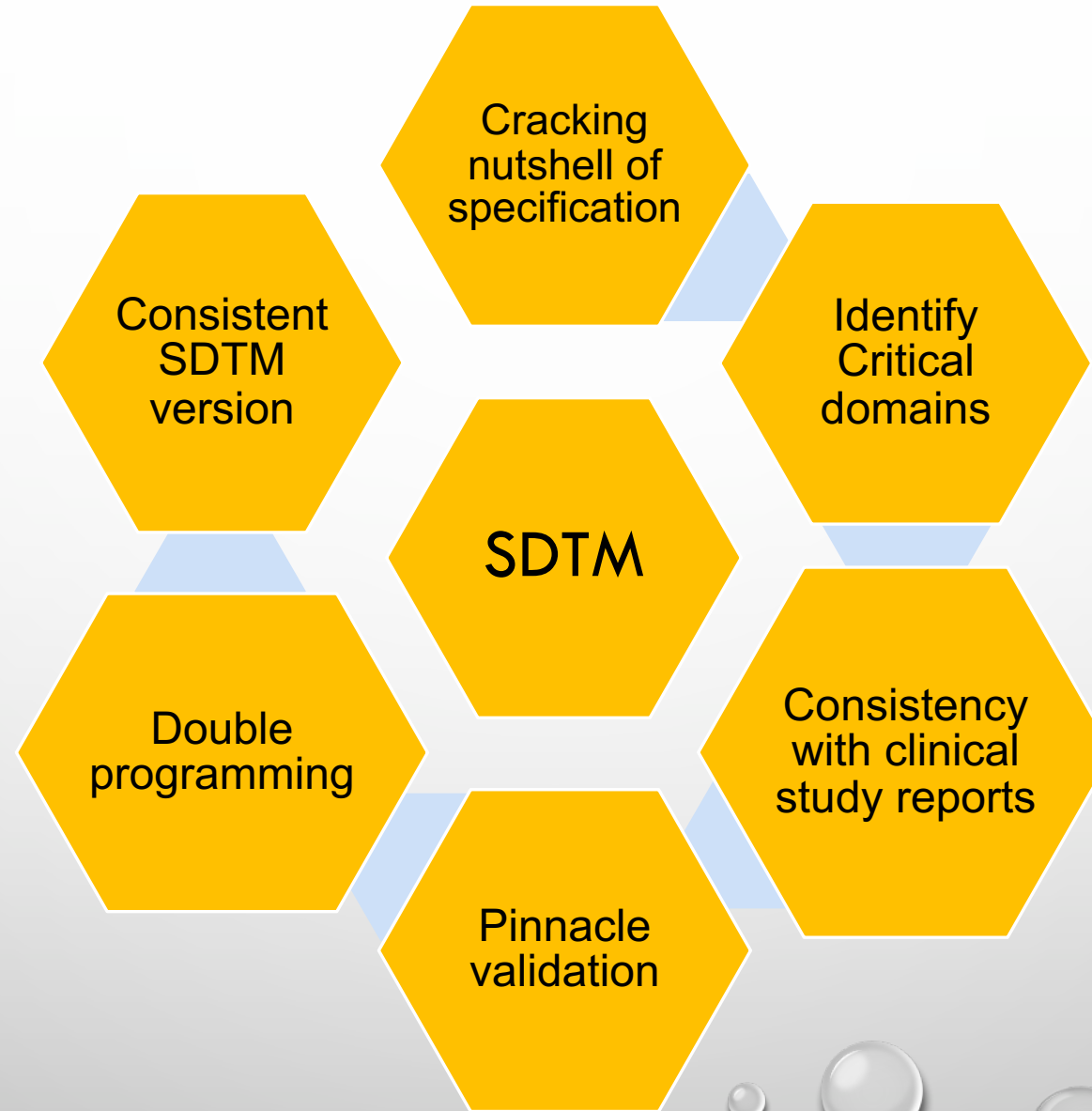


Mapping specification

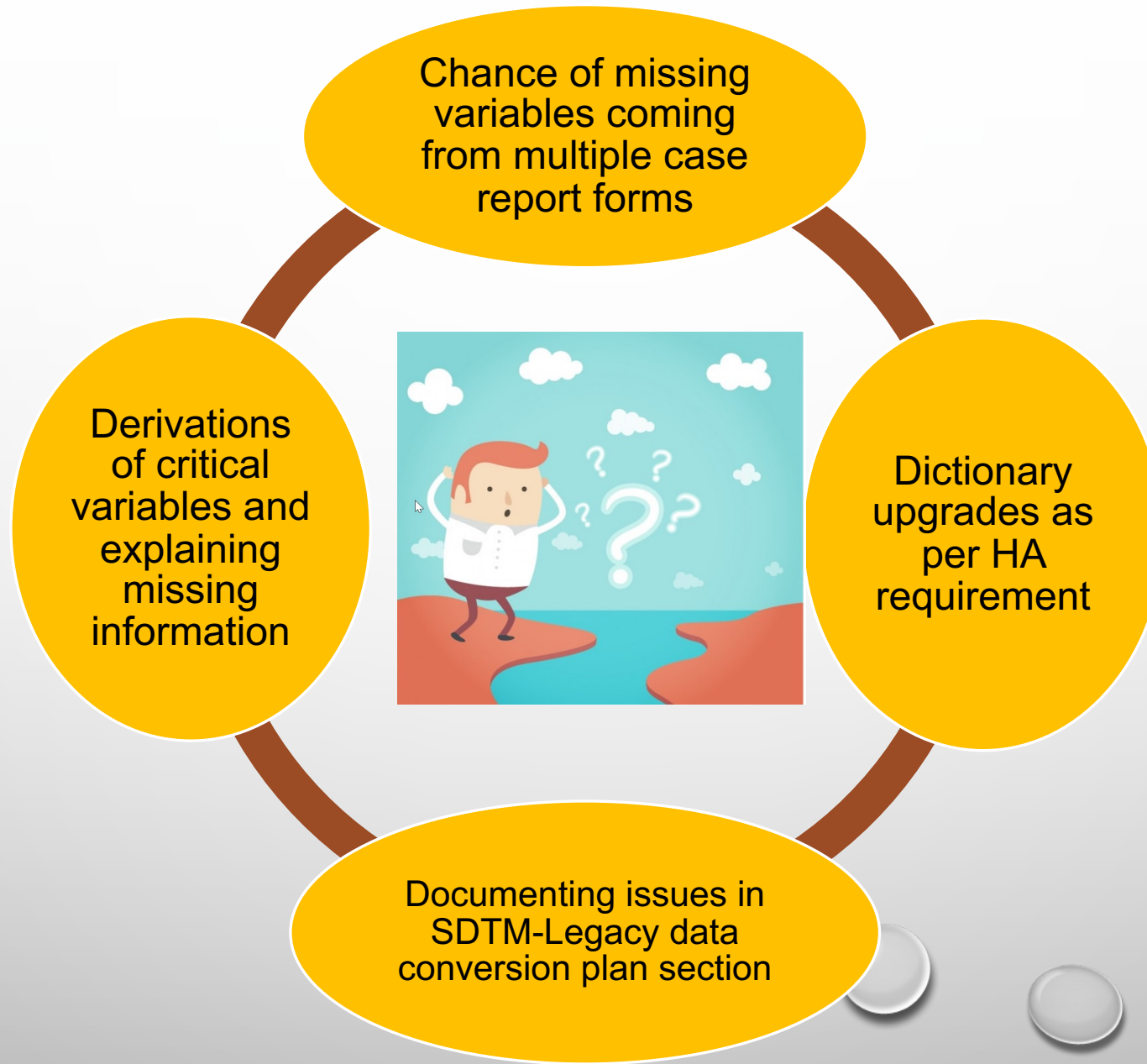
- What is mapping specification
- Importance
- Planning ahead
- Challenges

	A	B	C	L	M	N	O	P	Q	R	S	T	U	V
1	C1	C2	C3	C12	C13	C14	C15	C16	C17	C18	C19	C20	C21	C22
2	DOMAIN PREFIX	VARIABLE NAME	... - FORMAT - CDISC CONTR. TERMINOLOGY - COMP. ALGORITHM - EXT. DICTIONARY	DOMAIN PREFIX	VARIABLE NAME	CODELIST	NOT MAPPED	ONE TO X or 99 or	ONLY DIRS	DATE FD ND or NT	RELAT ED	VARIA BLES RELAT	CATGO ORY	
3							X		X		n	n	FIXED VALUE	Additional programming comments
4														
47	AE	AECAT	AECATS	AEV				99					GENERAL	CC
48	AE	AECAT	AECATS	ADJ				99					ANGIOEDEMA OR ANGIOEDEMA-LIKE EVENT	CC
49	AE	AESCAT	AESCATS					X						
50	AE	AEBODSYS	MEDDRA	AEV	SOC_TXT			X						TN
51	AE	AESOCCD	MEDDRA	AEV	SOC_CODE			X						TN
52	AE	AESOABR	MEDDRA	AEV	SOC_ABBR			X						TN
53	AE	AELOC	BODLOCS					X						
54	AE	AESEV	AESEVS	AEV	AEVSEV1C			X						
55	AE	AESER	NOYESS	AEV	AEVSEV1C			X						
56	AE	AESER	NOYESS	ADJ	AEVSEV2C			X						
57	AE	AEACN	AEACNS	AEV	ACNTAK1N\ACNTAK2N \ACNTAK3N			D						Only one value will be present in ACNTAK1N, ACNTAK2N or ACNTAK3N. Need to determine which source variable has a value present and set the output AEACN variables based on that one value using the codelist specified.

SDTM



SDTM-Challenges



SDTM

Example from SDTM-LDCP section:

ISSUES ENCOUNTERED AND RESOLVED

➤ Was any recoding done for meddra and was there any impact on the analysis?

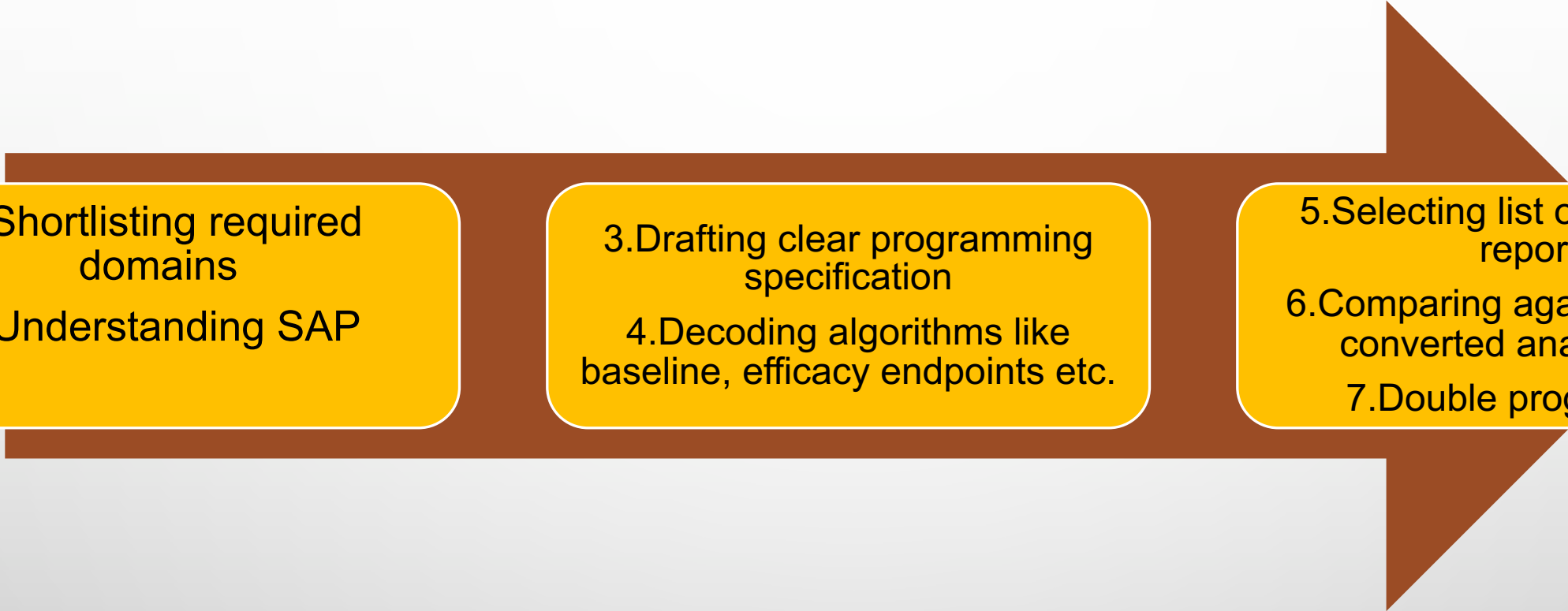
No

➤ Was any recoding done for whodrug and was there any impact on the analysis?

Yes, terms coded by novdtd march 2004 were upgraded based on WHODD version march 2017. Novdtd is a Novartis in-house dictionary used to classify or code medications, procedures, and non-drug therapies. Classification system is based on the WHODDE (B2 format). NOVDTD has been solely maintained by Novartis and systematic updates have been performed for march version and usually once per year. Novartis used novdtd march 2004 version which was based on march 2004 version of WHODDE B2 format. Therefore all code / term coded by novdtd were upgraded by novdtd 17.3, based on WHODD version march 2017.

Concomitant medications which were not coded by WHODD were summarized.

Analysis data



```
graph LR; A[1. Shortlisting required domains  
2. Understanding SAP] --> B[3. Drafting clear programming specification  
4. Decoding algorithms like baseline, efficacy endpoints etc.]; B --> C[5. Selecting list of traceability reports  
6. Comparing against legacy & converted analysis data  
7. Double programming];
```

1.Shortlisting required domains
2.Understanding SAP

3.Drafting clear programming specification
4.Decoding algorithms like baseline, efficacy endpoints etc.

5.Selecting list of traceability reports
6.Comparing against legacy & converted analysis data
7.Double programming

Define package

- Define XML
- SDRG/aCRF
- ARM (if planned to be included)
- ADRG
- Sharing sas programs: prog.doc
- Form 8 and planning timelines [PMDA]

DEFINE-Challenges

- Being consistent across multiple submission documents having same data sections

データセット Dataset	提出するものにチェック☑を記載。使用するバージョンでドメインに正式採用されていない場合にはカスタムドメイン欄に記載すること。 Need to check for dataset to be submitted	該当する場合にチェック☑を記載			備考
		SUPP	日本語 使用	SUPP 日本語 使用	
AE	☒	☒	☐	☐	
CE	☐	☐	☐	☐	
CM	☒	☐	☐	☐	
CO	☒	☒	☐	☐	

Table 3-1 List of SDTM Subject-Level Domains

Dataset – Dataset Label	Efficacy	Safety	Other	SUPP --	Custom	Related Using RELREC	Observation Class
AE - Adverse Events		X		X			Events
FAAE - Findings About Adverse Events		X		X			Findings
CM - Concomitant Medications		X		X			Interventions
CO - Comments			X	X			Special Purpose

- Cautious with regards to pinnacle21 conformance report based on the HA data is being submitted to.
- Explaining mismatches against the study analysis reports with converted data.
- Submitting ARM

Issue category		
Reject	<i>Rules which, if violated, will cause the review to be suspended until corrections have been made</i> → <u>Must be corrected</u> (it should be noted that the PMDA won't proceed with evaluation without correcting)	Based on FDA technical rejection criteria
Error	<i>Rules which, if violated without any prior explanation, will cause the review to be suspended until corrections have been made</i> → <u>Need to explain in RG and explain to the PMDA at Consultation on data format</u> (it should be noted that the PMDA won't proceed with evaluation without agreement)	Need to explain in RG
Warning	<i>Rules which, even when violated, will not necessarily require any explanation</i> → <u>NOT necessarily need to explain in RG and explain to the PMDA at Consultation on data format.</u>	Need to explain in RG

PMDA-The Pharmaceuticals and Medical Devices Agency

FDA -The United States Food and Drug Administration

RG - Reviewers Guide

Handling early CDISC studies

- What are early CDISC studies
- Estimating the scope of work
- Performing P21 checks on old data
- Update SDTMs as per latest CDISC standards
- Translating these updates in SDTM to ADaM
- Annotated CRF to be updated as per the updated SDTM programs
- Critical part in checking the SDTM-ADaM traceability

Handling early CDISC studies

- Reports selected for submission
- Preparing prog.doc for the reports selected.
- Updating programs of reports with respect to updated analysis datasets.

Challenges:

- a. Dependency from SDTM-ADaM
- b. Dictionary upgrades
- c. Traceability with analysis reports

CONCLUSION

Foresee
caveats

Multiple
quality
checks

Identification
of critical
components

Planning as
per number of
stakeholders



Collaboration

Timelines
with good
buffer

References

- Challenges for implementing legacy data conversion plan (LDCP) in electronic data submission-pharma SUG 2018 - paper SS-05
- Challenges of submitting electronic study data to two authorities: PMDA and FDA-paper SA02 PHUSE EU connect 2018
- Documenting traceability for the FDA: clarifying the legacy data conversion plan & introducing the study data traceability guide-pharma SUG 2017 - paper SS11
- Study data technical conformance guide –U.S. FDA



THANK
You! 😊