



PP10: Implementation of the ICH E9(R1) Estimands Framework Using Data Standards

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About Estimands

ICH E9(R1)

Addendum on Estimands and Sensitivity Analysis in Clinical Trials to the Guideline on Statistical Principles for Clinical Trials

Finalized in November 2019 (Step 4)

Has been or is in the process of being adopted by Health Authorities

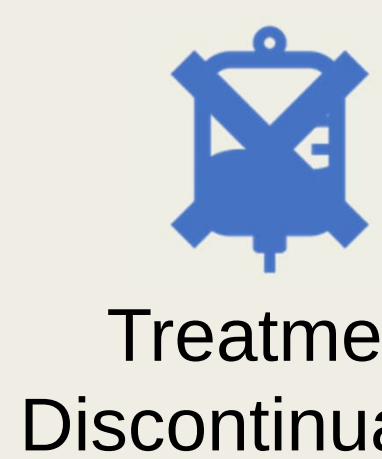
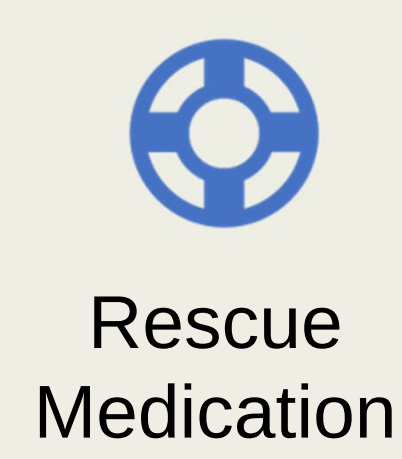
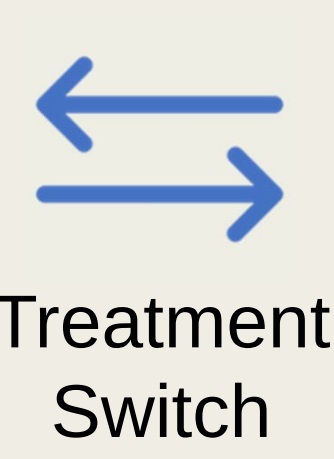
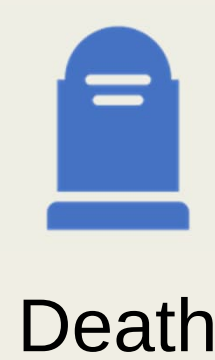
Covers the important multidisciplinary considerations relating to the implementation of the ICH E9(R1) estimands framework for clinical trial planning, design, conduct, analysis and interpretation

The technical implementation in the data flow was not in scope

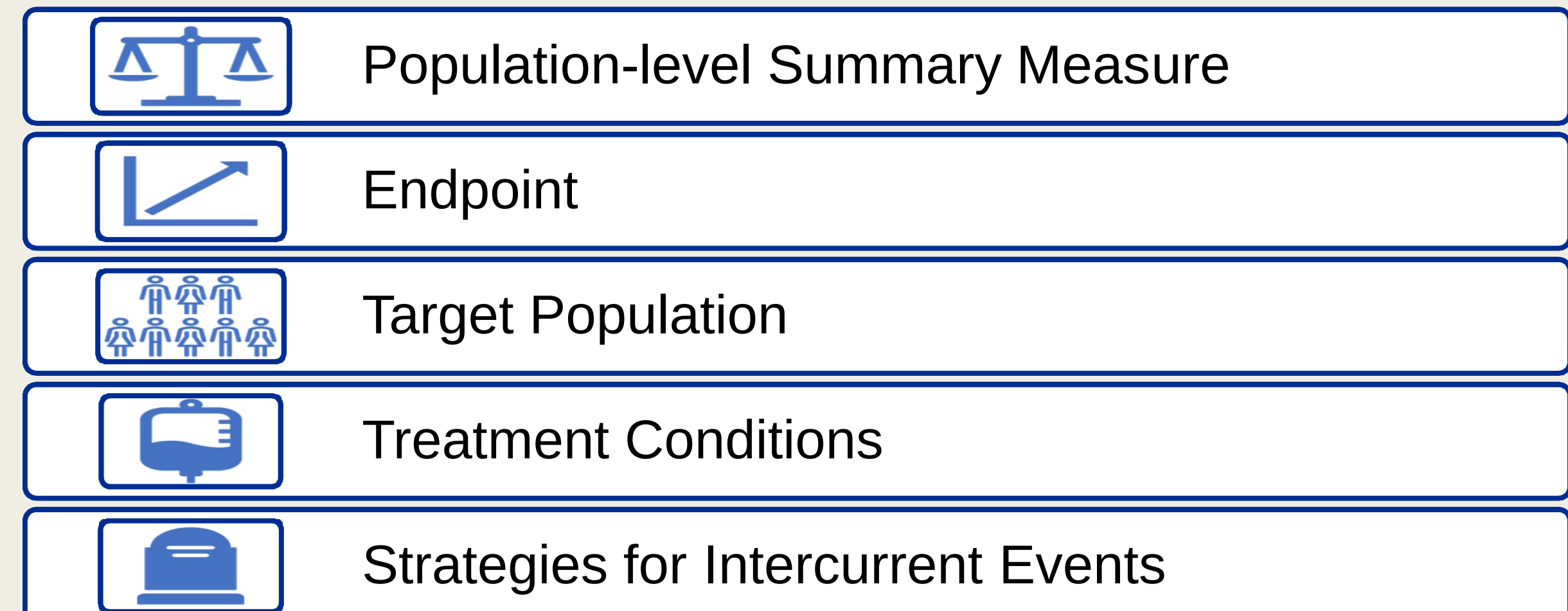
Additional guidance for the implementation of the estimands framework in the data flow is necessary

Intercurrent Events = Events occurring after treatment initiation that affect either the interpretation or the existence of the measurements associated with the clinical question of interest

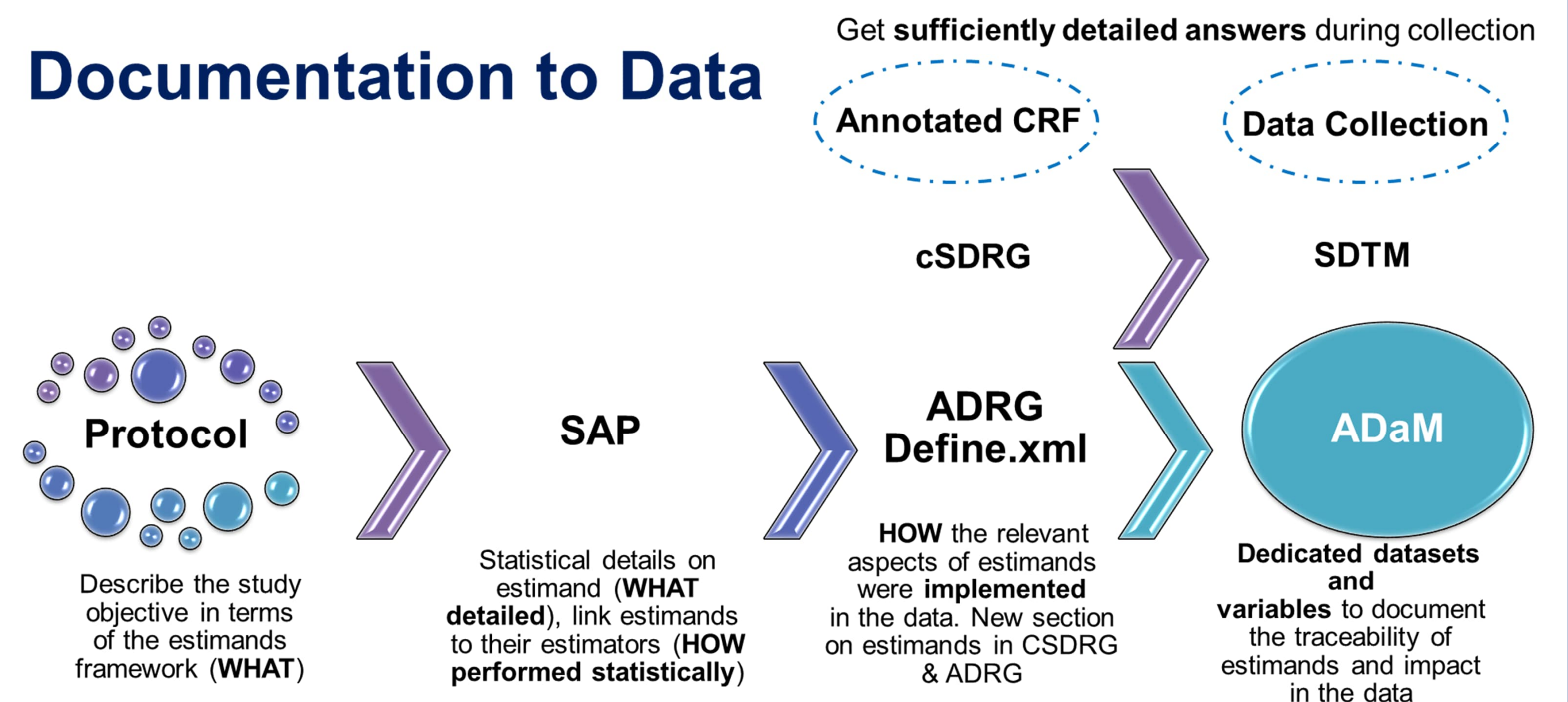
Examples:



Estimand = A precise description of the treatment effect reflecting the clinical question posed by the trial objective

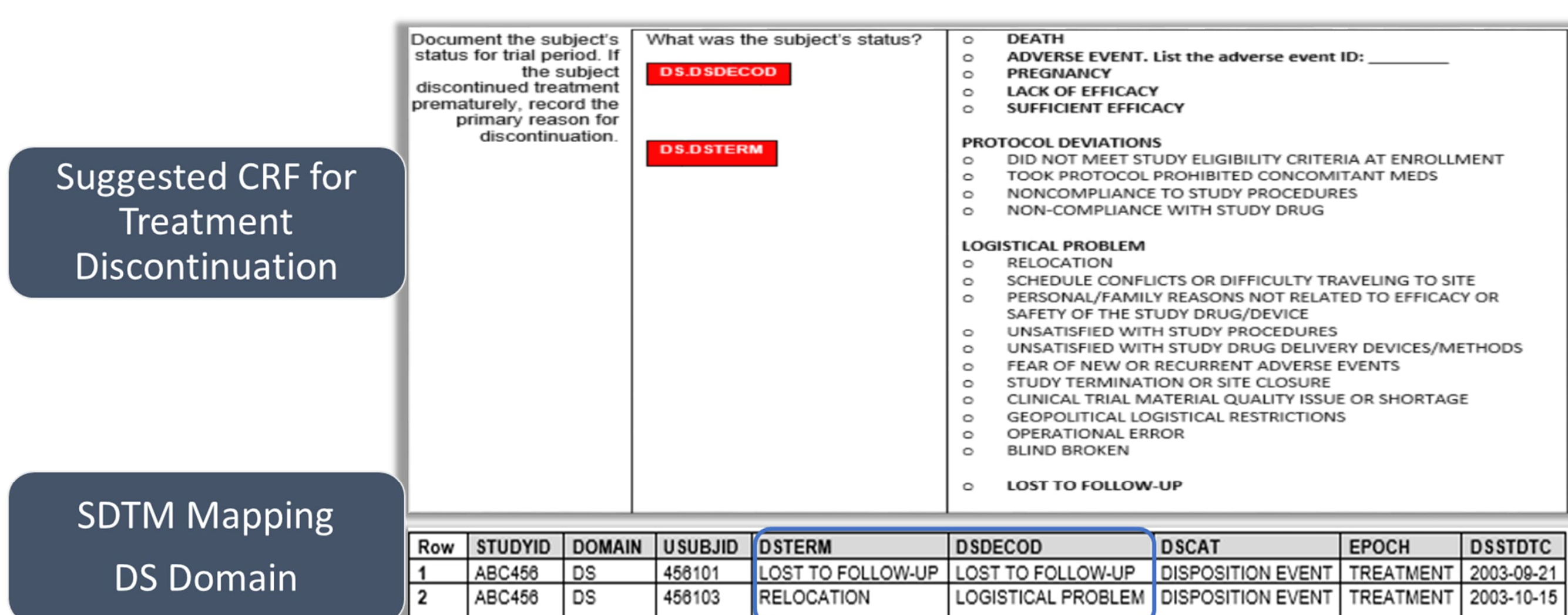
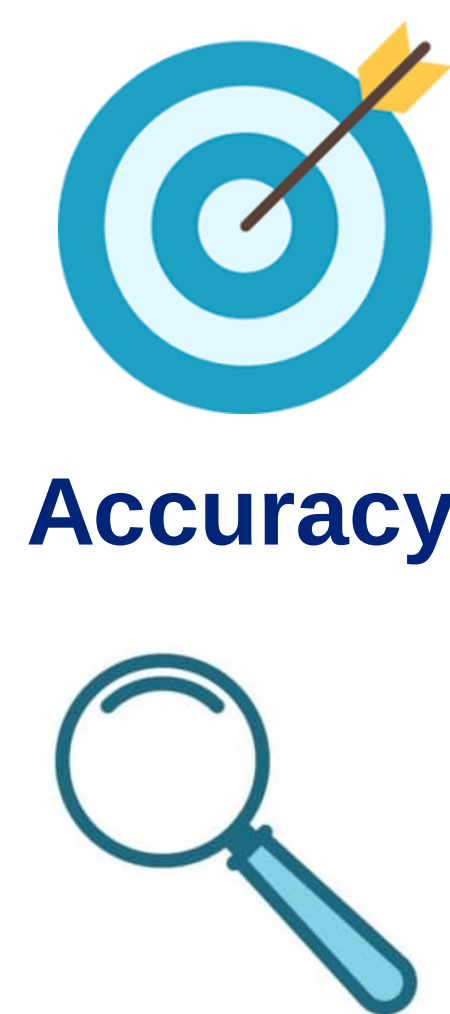


Documentation to Data



Data Collection & Tabulation

Intercurrent Events – Treatment Discontinuation



Accuracy

Granularity

Intercurrent Events – Concomitant Medication

Suggested CRF for Concomitant Medication

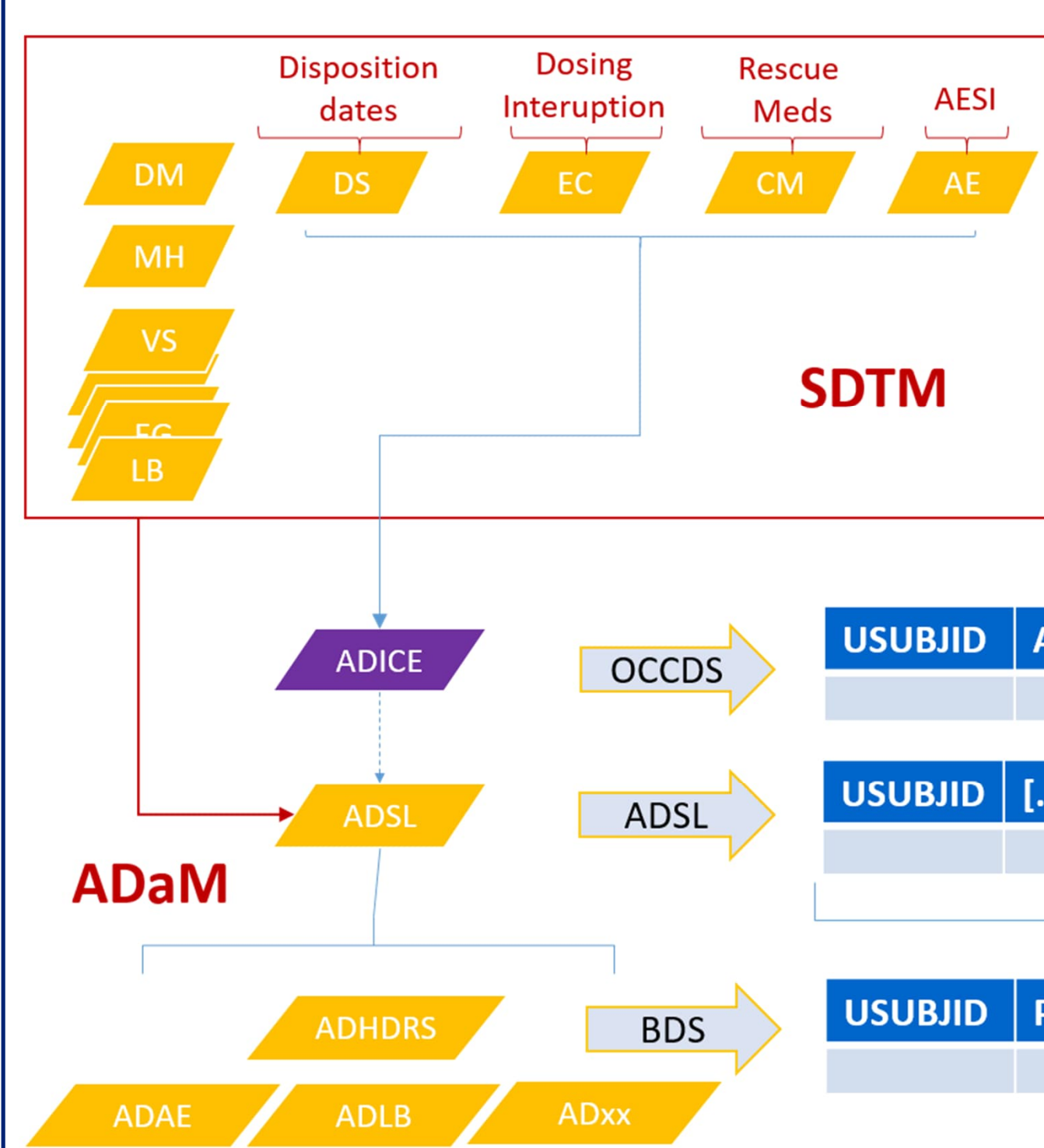
SDTM Mapping CM Domain

Indicate if the subject took any concomitant medication/treatment.	Were any concomitant medications taken? (Not submitted)	Yes	No
Record only one treatment per time point. Provide full name, name of the medication/treatment.	What was the medication? (Not submitted)		
Record specific reasons the medication was taken.	For what indication was the medication taken? (Not submitted)		
Start Date	End Date		
Is the medication ongoing?	End Date	Yes	No

Row	STUDYID	DOMAIN	USUBJID	CMTRT	CMINDC	CMSTDT	CMENRF	CMENDTC
1	ABC456	CM	456101	ASPIRIN	PROPHYLAXIS FOR INFECTION	2003-07-21	ONGOING	
2	ABC456	CM	456103	ANTACIDS	RESOLVE THERAPY	2003-08-15		2003-09-01

Enhancing CRF standards to improve the accuracy of data collection for intercurrent events (notably those relating to medications) is necessary

Data Analysis



Depending on the definition of the estimand, subjects and/or certain data points may be included or excluded from data point sets (increased granularity).

To allow full traceability of intercurrent events a new ADaM OCCDS domain ADICE is proposed

Proposed ADaM Implementation

USUBJID	ASEQ	UTERM	ATERM	ADECODEy	ASTDT	AENDT	SRCDOM	SRCSEQ
USUBJID	[...]	FASFL	SAFFL	EST01FL	EST02FL	ESTzzFL		
USUBJID	PARAMCD	AVISIT	[...]	AVAL	CHG	DTYPE	ICESEQzz	ESTzzRFL

Conclusions

