



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

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Get Involved



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 (Step 5)

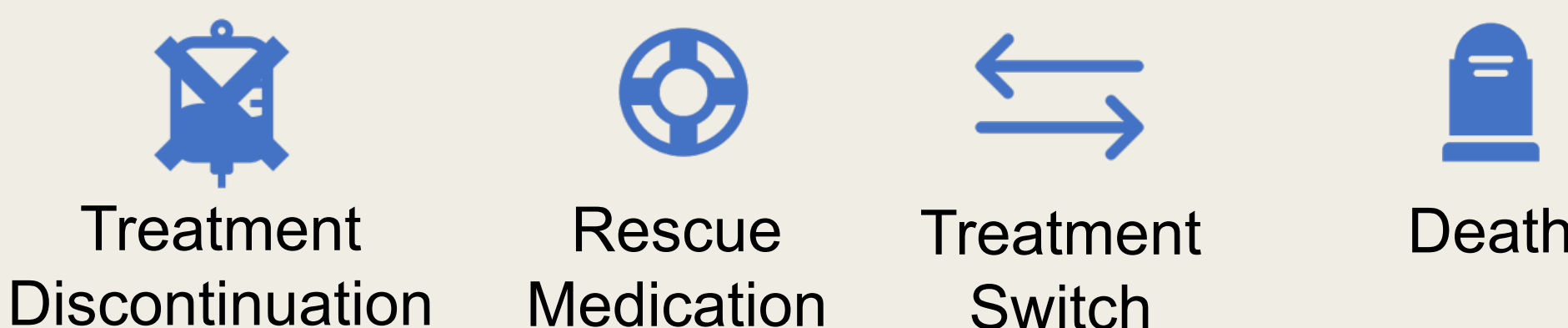
Covers the important multidisciplinary considerations relating to the implementation of the ICH E9(R1) estimands framework for clinical trial planning, design, conduct, analysis and interpretation

The technical implementation in the data flow was not in scope

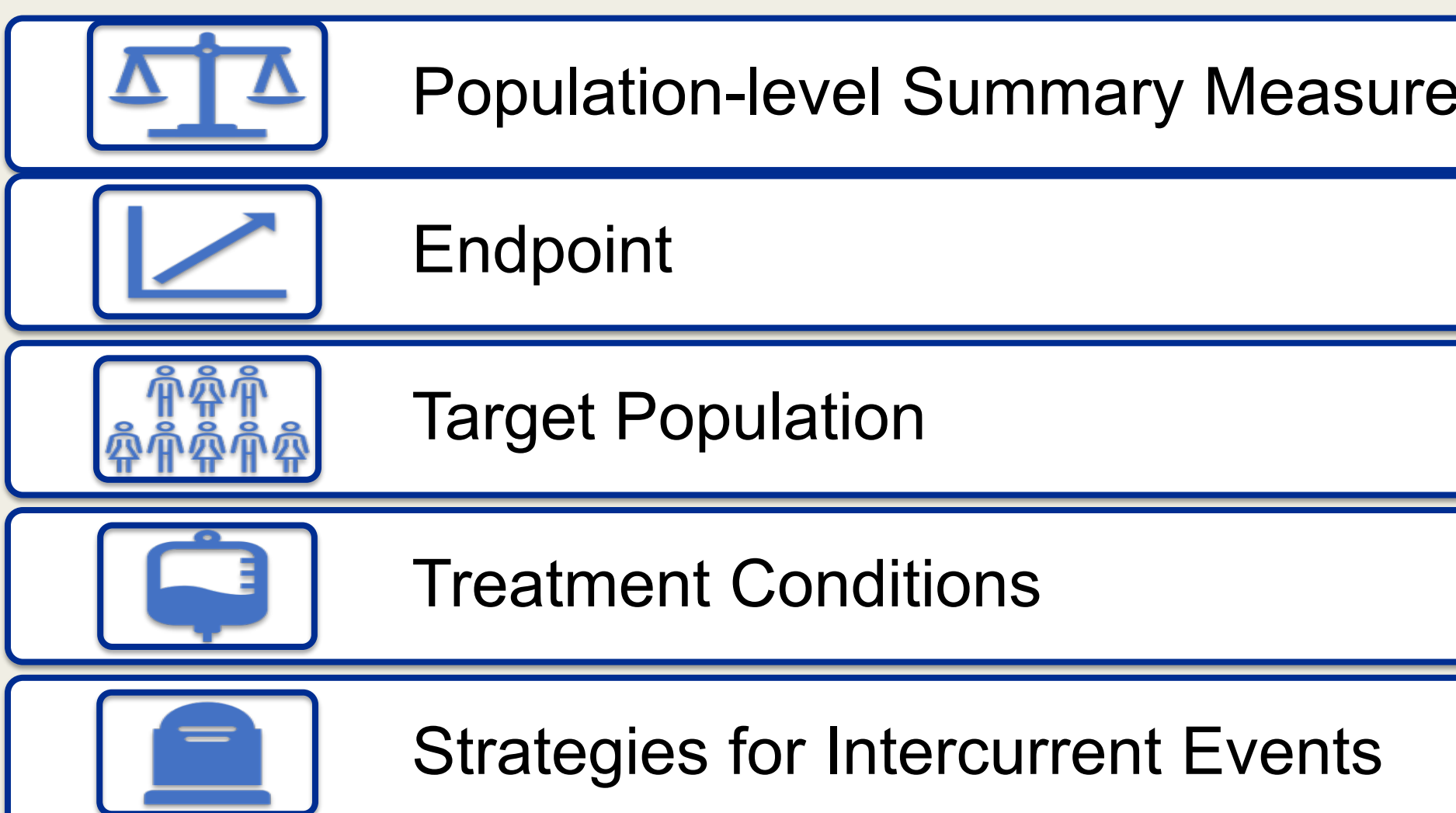
Additional guidance for the implementation of the estimands framework in the data flow is necessary

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

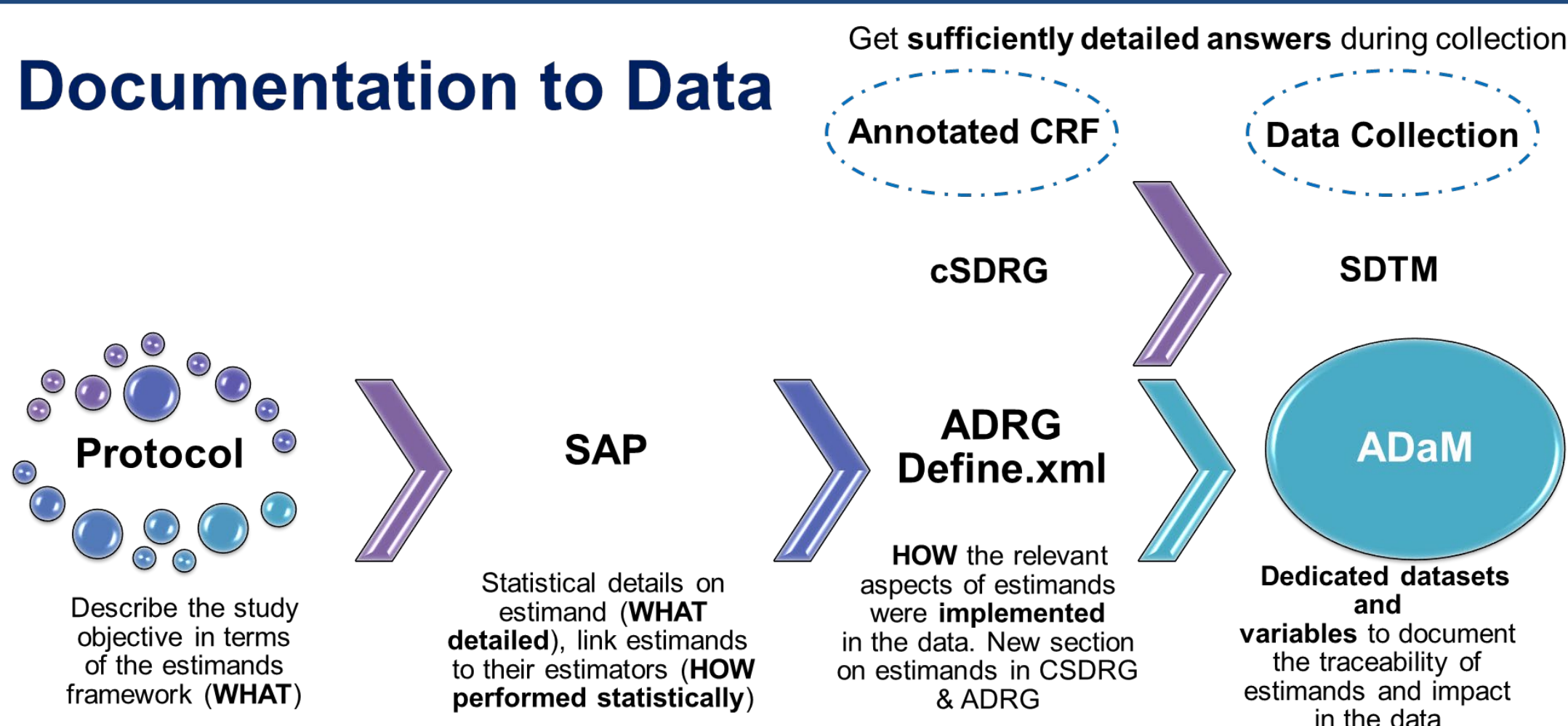
Examples:



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



Documentation to Data



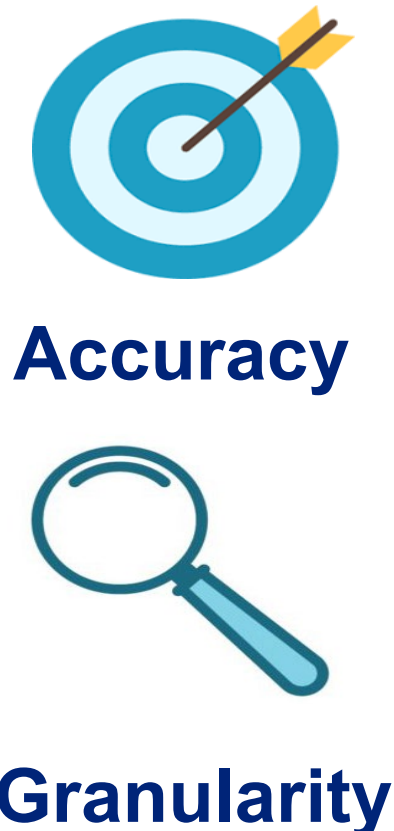
Data Collection & Tabulation

Intercurrent Events – Treatment Discontinuation

Suggested CRF for Treatment Discontinuation

SDTM Mapping DS Domain

Document the subject's status for trial period. If the subject discontinued treatment prematurely, record the primary reason for discontinuation.	What was the subject's status?		DS.DSDECODE DS.DSTERM o DEATH o ADVERSE EVENT. List the adverse event ID: _____ o PREGNANCY o LACK OF EFFICACY o SUFFICIENT EFFICACY PROTOCOL DEVIATIONS o DID NOT MEET STUDY ELIGIBILITY CRITERIA AT ENROLLMENT o TOOK PROTOCOL PROHIBITED CONCOMITANT MEDS o NONCOMPLIANCE TO STUDY PROCEDURES o NON-COMPLIANCE WITH STUDY DRUG LOGISTICAL PROBLEM o RELOCATION o SCHEDULE CONFLICTS OR DIFFICULTY TRAVELING TO SITE o PERSONAL/FAMILY REASONS NOT RELATED TO EFFICACY OR SAFETY OF THE STUDY DRUG/DEVICE o UNSATISFIED WITH STUDY PROCEDURES o UNSATISFIED WITH STUDY DRUG DELIVERY DEVICES/METHODS o FEAR OF NEW OR RECURRENT ADVERSE EVENTS o STUDY TERMINATION OR SITE CLOSURE o CLINICAL TRIAL MATERIAL QUALITY ISSUE OR SHORTAGE o GEOLOGICAL LOGISTICAL RESTRICTIONS o OPERATIONAL ERROR o BLIND BROKEN LOST TO FOLLOW-UP					
Row	STUDYID	DOMAIN	USUBJID	OSTERM	DSDECODE	DSCAT	EPOCH	DSSTDTC
1	ABC456	DS	456101	LOST TO FOLLOW-UP	LOST TO FOLLOW-UP	DISPOSITION EVENT	TREATMENT	2003-08-21
2	ABC456	DS	456103	RELOCATION	LOGISTICAL PROBLEM	DISPOSITION EVENT	TREATMENT	2003-10-15



Accuracy

Granularity

Intercurrent Events – Concomitant Medication

Suggested CRF for Concomitant Medication

SDTM Mapping CM Domain

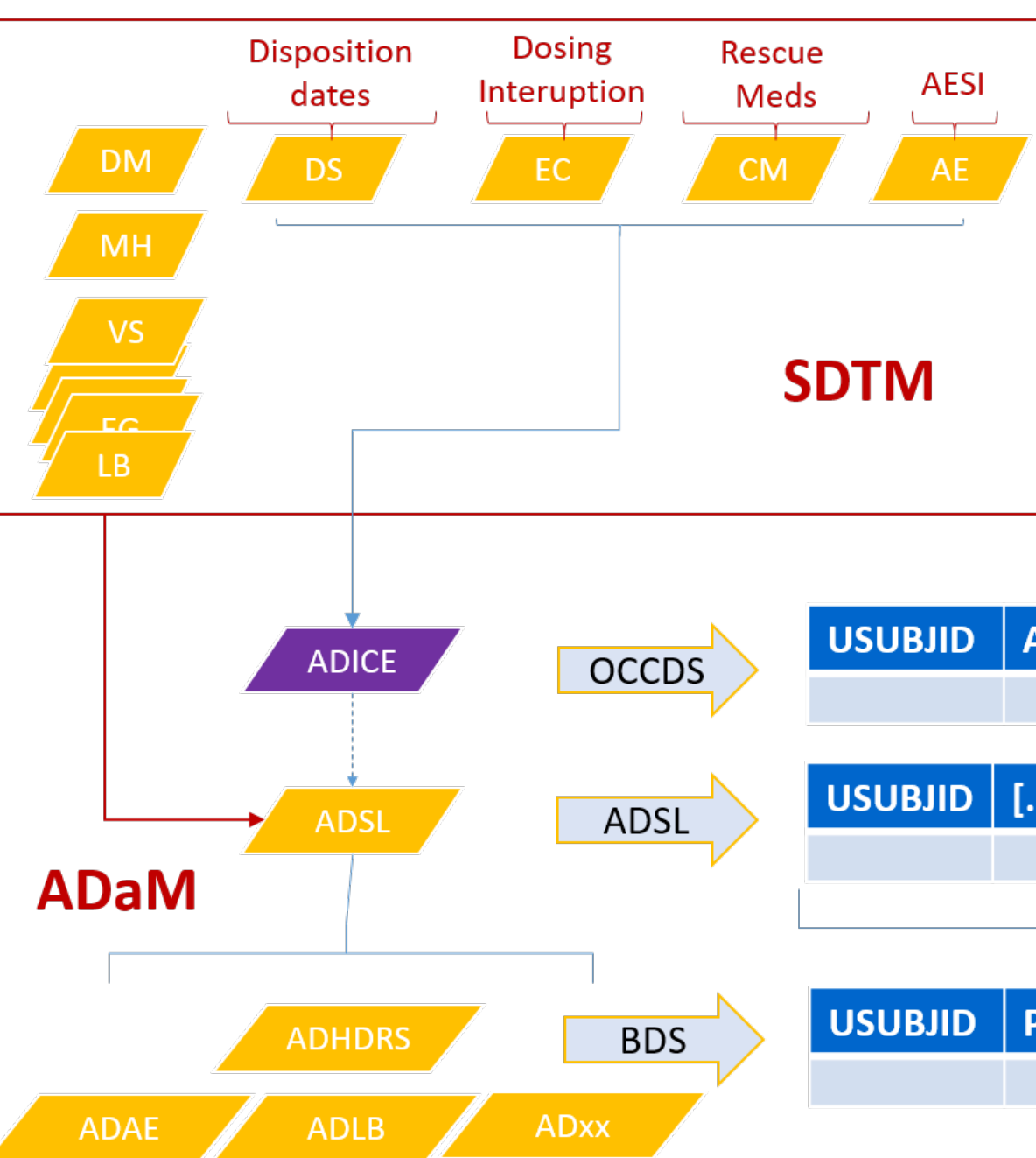
Indicate if the subject took any concomitant medication/treatment. Record only one treatment per line. Provide full trade name of the medication/treatment. Record specific reasons the medication was taken.	Were any concomitant medications taken? CM.CMTRT	☐ Yes ☐ No
For what indication was the medication taken? CM.CMNDC	What was the medication? CM.CMTRT	
Start Date CM.CMSTDT	End Date CM.CMENDT	
Is the medication ongoing? CM.CMENRF		☐ Yes ☐ No

Row	STUDYID	DOMAIN	USUBJID	CMTRT	CMNDC	CMSTDT	CMENRF	CMENDT
1	ABC456	CM	456101	ASPIRIN	PROPHYLAXIS FOR INFECTION	2003-07-21	ONGOING	
2	ABC456	CM	456103	ANTACIDS	RESCUE THERAPY	2003-08-15		2003-08-01

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

Data Analysis

Proposed ADaM Implementation



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 dataset ADICE is proposed

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

Conclusions

