Submission Success: Navigating the Maze of Documentation and Checks for Seamless Regulatory Submissions

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Meet the Speakers

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Disclaimer and Disclosures

- *The views and opinions expressed in this presentation are those of the authors and do not necessarily reflect the official policy or position of CDISC or Certara.*

Agenda

1. Introduction
2. Overview of Submission Requirements
3. Key Documentation for FDA and PMDA
4. Items to Review and Cross-Checks
5. Q&A

The Challenge of Submission Preparation

What and Where?

Preparing SDTM and ADaM data packages can be daunting.

Numerous guidance documents and checks are required.

The process can be overwhelming without proper guidance.

Goals of This Presentation

Discuss key documentation for submissions to FDA and PMDA.

Provide a list of items to review and cross-check.

Empower attendees to enhance their organization's submission process.

Submission Requirements

FDA & PMDA Website Links

FDA

- Study Data Standards Resources (https://www.fda.gov/industry/fda-data-standards-advisory-board/study-data-standards-resources)
- Study Data for Submission to CDER and CBER (https://www.fda.gov/industry/study-data-standards-resources/study-data-submission-cder-and-cber)
- Electronic Regulatory Submission and Review (https://www.fda.gov/drugs/electronic-regulatory-submission-and-review/electronic-submissions-presentations)

PMDA

- New Drug Review with Electronic Data (https://www.pmda.go.jp/english/review-services/reviews/0002.html)

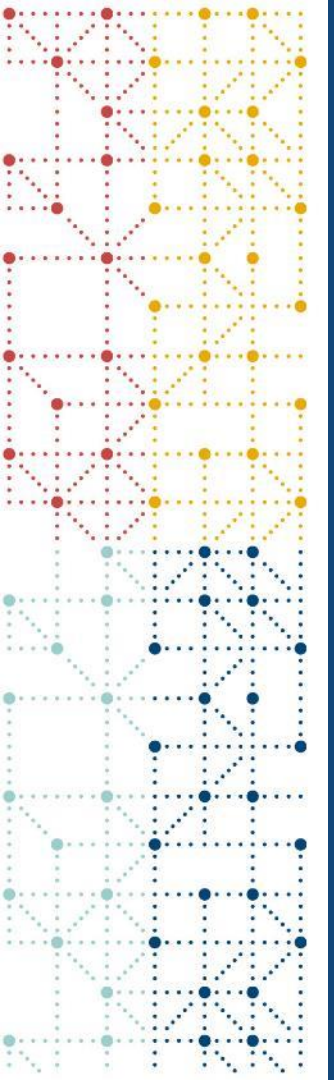
Agency Requirements

FDA	PMDA
Data Standards Catalog	Data Standards Catalog
Study Data Technical Conformance Guide	Technical Conformance Guide
Technical Specifications	Study Data Validation Rules
Business Rules	Notification on Electronic Study Data + its Q&A
Validator Rules	Notification on Gateway Application
Providing Regulatory Submissions In Electronic Format – Standardized Study Data	FAQs on Electronic Study Data Submission

Contents Within Documents

Document Type	Contents
Data Standards Catalog (FDA, PMDA)	Currently accepted versions of standards, dictionaries, file formats
Study Data Technical Conformance Guide (FDA, PMDA)	Provides specifications and guidance on how to use data standards to submit standardized study data
Technical Specifications (FDA)	Information on implementation of specific types of study data
Business (FDA) & Validator Rules (FDA, PMDA)	Validation rules used to assess standardized study data conformance
Notification on Electronic Study Data + its Q&A (PMDA)	Guidance on submitting standardized electronic study data
Notification on Gateway Application (PMDA)	Guidance on submitting using Gateway system
FAQs on Electronic Study Data Submission (PMDA)	Q&A on submitting electronic study data

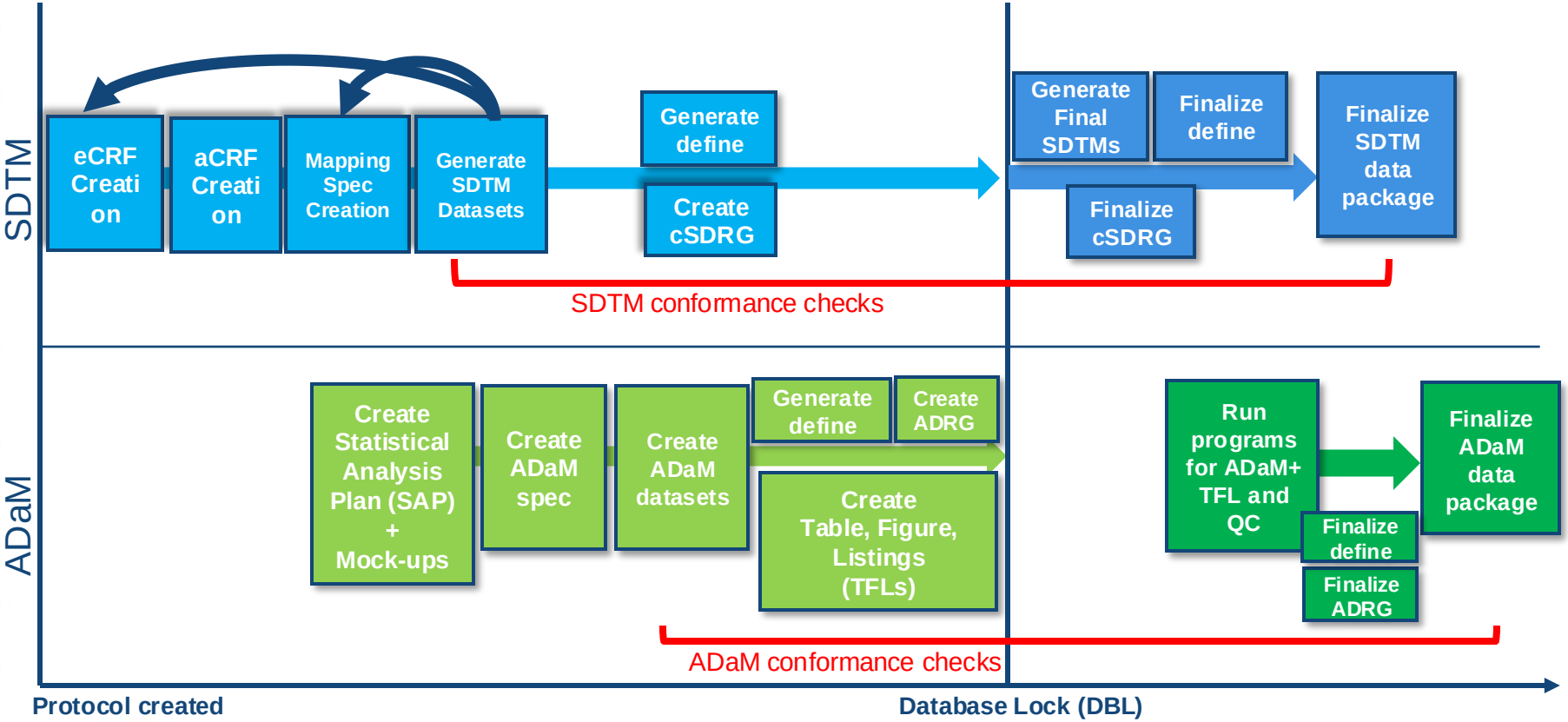
What goes into a submission?



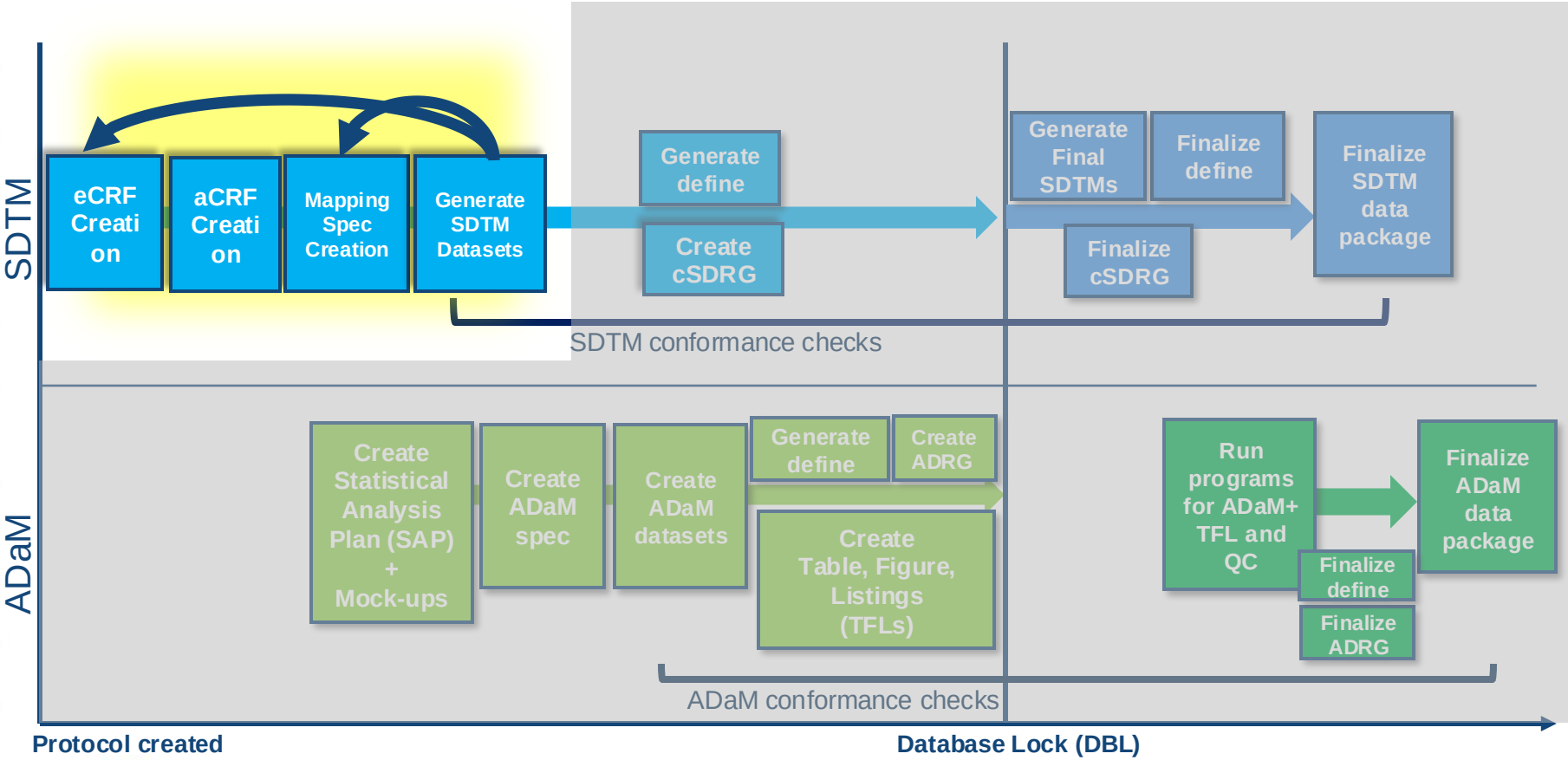
Examples

Slides Using Images

General Process Flow



Checks when creating aCRF and SDTM datasets



Checks When Creating the aCRF and SDTM Datasets

- Ensure variables populated from data collected via eCRF have annotations on the aCRF and are present in the datasets
- Ensure consistency of SUPPQUALs between domains, documentation, and studies in the submission and the use of CDISC fragments have been used
- Ensure consistency of TESTCD/TEST pairings between domains and studies in the submission
- Ensure study follows any regulatory guidance specific to the type of study data being submitted
- Ensure study follows any Therapeutic Area Guides specific to the type of study data being submitted

Example: Check aCRF Fields for Annotations and Verify Mapping

HO (Healthcare Encounters)

ryze

Protocol

Site Number

Subject Number

Form HO - Healthcare Encounters

1 HO - Healthcare Encounters

1.1	No text has been found for the specified Locale	( ) No [NOT SUBMITTED] ( ) Yes
1.2	No text has been found for the specified Locale	( ) EMERGENCY ROOM VISIT ( ) HOSPITAL STAY ( ) INTENSIVE CARE UNIT STAY ( ) PRIMARY CARE PHYSICIAN'S OFFICE VISIT ( ) SKILLED NURSING FACILITY STAY ( ) OTHER [NOT SUBMITTED] HOTERM
1.3	No text has been found for the specified Locale	HOTERM
1.4	What was the [healthcare encounter/HOTERM] [start/admission] date? (DD-MMM-YYYY)	HOSTDTC
1.5	What was the [healthcare encounter/HOTERM] [end/discharge] date? (DD-MMM-YYYY)	HOENDTC
1.6	Was the [healthcare encounter/HOTERM] ongoing (as of the [study-specific timepoint or period])?	( ) No [NOT SUBMITTED] ( ) Yes HOENRTPT=ONGOING
1.7	What was the reason for the [healthcare encounter/HOTERM]?	HOREAS in SUPPHO

	STUDYID	DOMAIN	USUBJID	HOSEQ	HOSPID	HOTERM	EPOCH	HOSTDTC	HOENDTC	HOSTDY	HOENDY
1	CDISCA	HO	CDISC001-01	1	1	HOSPITAL STAY	TREATMENT	2009-04-23T17:37	2009-04-26T10:59	200	203
2	CDISCA	HO	CDISC001-01	2	2	HOSPITAL STAY	TREATMENT	2009-05-21T12:06	2009-05-22T11:53	228	229
3	CDISCA	HO	CDISC001-01	3	3	HOSPITAL STAY	TREATMENT	2009-05-28T20:04	2009-05-29T19:55	235	236
4	CDISCA	HO	CDISC001-01	4	4	HOSPITAL STAY	TREATMENT	2009-09-05T12:13	2009-09-08T17:34	335	338
5	CDISCA	HO	CDISC001-01	5	5	HOSPITAL STAY	TREATMENT	2010-01-27T17:01	2010-02-07T17:05	479	490
6	CDISCA	HO	CDISC001-01	6	6	HOSPITAL STAY	TREATMENT	2010-02-18T11:19	2010-02-21T21:14	501	504
7	CDISCA	HO	CDISC001-01	7	7	HOSPITAL STAY	TREATMENT	2010-05-17T13:43	2010-05-25T14:07	589	597
8	CDISCA	HO	CDISC001-01	8	8	HOSPITAL STAY	TREATMENT	2011-06-03T14:54	2011-06-05T17:25	971	973
9	CDISCA	HO	CDISC001-01	9	9	HOSPITAL STAY	TREATMENT	2013-02-08T18:10	2013-02-11T17:48	1587	1590
10	CDISCA	HO	CDISC001-01	10	10	HOSPITAL STAY	FOLLOW-UP	2013-04-30T12:53	2013-05-02T18:13	1668	1670
11	CDISCA	HO	CDISC001-01	11	11	HOSPITAL STAY	FOLLOW-UP	2013-08-21T08:20	2013-08-28T10:16	1781	1788
12	CDISCA	HO	CDISC001-03	1	1	HOSPITAL STAY	TREATMENT	2000-05-13T08:15	2000-05-15T22:45	23	25
13	CDISCA	HO	CDISC001-03	2	2	HOSPITAL STAY	FOLLOW-UP	2000-07-06T20:13	2000-07-11T14:51	77	82
14	CDISCA	HO	CDISC001-03	3	3	HOSPITAL STAY	FOLLOW-UP	2000-07-20T14:39	2000-07-26T09:12	91	97
15	CDISCA	HO	CDISC001-03	4	4	HOSPITAL STAY	FOLLOW-UP	2000-09-19T09:50	2000-09-21T16:11	152	154
16	CDISCA	HO	CDISC001-03	5	5	HOSPITAL STAY	FOLLOW-UP	2001-01-20T20:00	2001-01-24T15:10	275	279
17	CDISCA	HO	CDISC001-03	6	6	HOSPITAL STAY	FOLLOW-UP	2001-09-20T15:10	2001-10-24T14:57	518	552
18	CDISCA	HO	CDISC001-03	7	7	HOSPITAL STAY	FOLLOW-UP	2001-11-19T14:28	2001-11-30T19:09	578	589
19	CDISCA	HO	CDISC001-03	8	8	HOSPITAL STAY	FOLLOW-UP	2001-12-06T18:21	2001-12-09T15:04	595	598
20	CDISCA	HO	CDISC001-03	9	9	HOSPITAL STAY	FOLLOW-UP	2002-03-22T21:18	2002-03-25T20:55	701	704

Example: Consistency of Supplemental Qualifiers

Appendix D: CDISC Variable-naming Fragments

aCRF Field

1.12. Other Prior Therapy [ ] PTHEROTH in SUPPCM

define.xml

SUPPCM (Supplemental Qualifiers for CM, Concomitant/Prior Medications) - [Non Standard] Location: suppcm.xpt

Related Parent Dataset: CM (Concomitant/Prior Medications)

Variable	Label / Description	Type	Role	Length or Display Format	Controlled Terms or ISO Format	Origin / Source / Method / Comment
STUDYID	Study Identifier	text	Identifier	6		Protocol
RDOMAIN	Related Domain Abbreviation	text	Identifier	2		Assigned
USUBJID	Unique Subject Identifier	text	Identifier	18		Derived
IDVAR	Identifying Variable	text	Identifier	5	Identifying Variable in SUPPCM • "CMSEQ"	Assigned
IDVARVAL	Identifying Variable Value	text	Identifier	2		Assigned
QNAM	Qualifier Variable Name	text	Topic	8	Qualifier Variable Name for SUPPCM • "PRTHEROTH" = "Other Prior Therapy"	Assigned
QLABEL	Qualifier Variable Label	text	Synonym Qualifier	39	Qualifier Variable Label for SUPPCM • "Other Prior Therapy"	Assigned
QVAL VLM	Data Value	text	Result Qualifier	60		
➤ QNAM = "PTHEROTH"	Other Prior Therapy	text		60		Collected (Source: Investigator) Annotated Case Report Form [22]

SUPPQUAL table in cSDRG for CM

QNAM	Description
PTHERO	Other Prior Therapy

Example: Consistency of Sponsor Defined –TESTCD / –TEST Values

STUDYID	DOMAIN	USUBJID	FASEQ	FATESTCD	FATEST	FAOBJ	FAORRES	FASTRESC	VISITNUM	FADTC
STUDY1	FA	STUDY1-001	1	DXSUB	Diagnosis Subgroup	ALZHEIMER'S DISEASE	HYPERPLASTICITY	HYPERPLASTICITY	1	2023-05-04

STUDYID	DOMAIN	USUBJID	FASEQ	FATESTCD	FATEST	FAOBJ	FAORRES	FASTRESC	VISITNUM	FADTC
STUDY2	FA	STUDY2-001	1	DIAGSUB	Diagnosis Subgroup	ALZHEIMER'S DISEASE	HYPERPLASTICITY	HYPERPLASTICITY	1	2023-05-04

- Consistency of sponsor created terms, SUPPQUALS, TESTCD/TEST, PARMCD/PARM values *between datasets and documents* within a study is *necessary*.
- Consistency of these values *between studies within a submission* helps make review of the data *easier and faster*.

Example: Use FDA Technical Specifications When Applicable

FDA U.S. FOOD & DRUG ADMINISTRATION

Submitting Study Datasets for Vaccines to the Office of Vaccines Research and Review

Guidance for Industry

Technical Specifications Document

If a reactogenicity event should happen to continue beyond the assessment interval, it should also be represented in the AE domain, with the CE domain record indicating that the event extended beyond the assessment interval, using the variables Clinical Event End Reference Time Point (CEENTPT) (e.g., "Day 7") and Clinical Event End Relative to Reference Time Point (CEENRTPT) ("Ongoing"). A check box in the CRF, indicating whether the reactogenicity event is ongoing after the assessment period, is recommended. The event should be categorized in the Adverse Event Category (AECAT) variable as "reactogenicity." The start day/date (--STDY/--STDTC) and the end day/date (--ENDY/--ENDTC) of the reactogenicity event should be identical in both the CE and AE domain; whereas the duration (--DUR) should report the time that the event occurred as part of the assessment interval and as part of the continuance separately (e.g., an event that lasted 6 days in the assessment interval and 3 days beyond the assessment would be reported as Clinical Event Duration (CEDUR) = 6 days and Adverse Event Duration (AEDUR) = 3 days). We recommend one or more check boxes in the CRF, indicating the duration of the reactogenicity event in the assessment period and the duration of the reactogenicity event beyond the assessment period.

STUDYID	DOMAIN	USUBJID	CESEQ	CETERM	CECAT	CESCAT	CEOCCUR	CESTDTC	CEENDTC	CEDUR	CEENRTPT	CEENTPT
VAC1	CE	VAC1-01	1	HEADACHE	REACTOGENICITY	SYSTEMIC	Y	2024-03-18	2024-03-27	P6D	ONGOING	DAY 7

STUDYID	DOMAIN	USUBJID	AESEQ	AETERM	AECAT	AESCAT	AESTDTC	AEENDTC	AEDUR
VAC1	AE	VAC1-01	1	HEADACHE	REACTOGENICITY	SYSTEMIC	2024-03-18	2024-03-27	P3D

Example: Use FDA Technical Specifications When Applicable

Appendix B: Trial Summary (TS) Parameters for Submission – Clinical

FDA Desired - Clinical	TSPARMCD	TSPARM	FDA Notes
Conditional	FDATCHSP	FDA Technical Specification	If applicable. the value should be the exact listing as in the appendix of the Technical Conformance Guide. Use as many rows as needed.

TS

STUDYID	DOMAIN	TSSEQ	TSGRPID	TSPARMCD	TSPARM	TSVAL	TSVALNF	TSVALCD	TSVCDREF	TSVCDVER
VAC1	TS	1		FDATCHSP	FDA Technical Specification	Submitting Study Datasets for Vaccines to the Office of Vaccines Research and Review				

5.3 List of FDA Technical Specification Documents

5.3.6 Submitting Study Datasets for Vaccines to the Office of Vaccines Research and Review

Example: Use Accepted Therapeutic Area User Guides When Applicable

5.2 Supported Therapeutic Areas

Sponsors may use new TA extensions of a CDISC standard, but are not required to until the extensions have been incorporated into a SDTMIG version supported by FDA (the supported SDTMIGs are listed in the Catalog). Sponsors should explain the rationale in the cSDRG for using TA extensions that are not currently listed in this document.

If the study data submitted follows a Therapeutic Area User Guide (TAUG), include the values for TSPARM/TSPARMCD and TSVAL indicated in the table from section 4.1.1.3 in the TS domain.

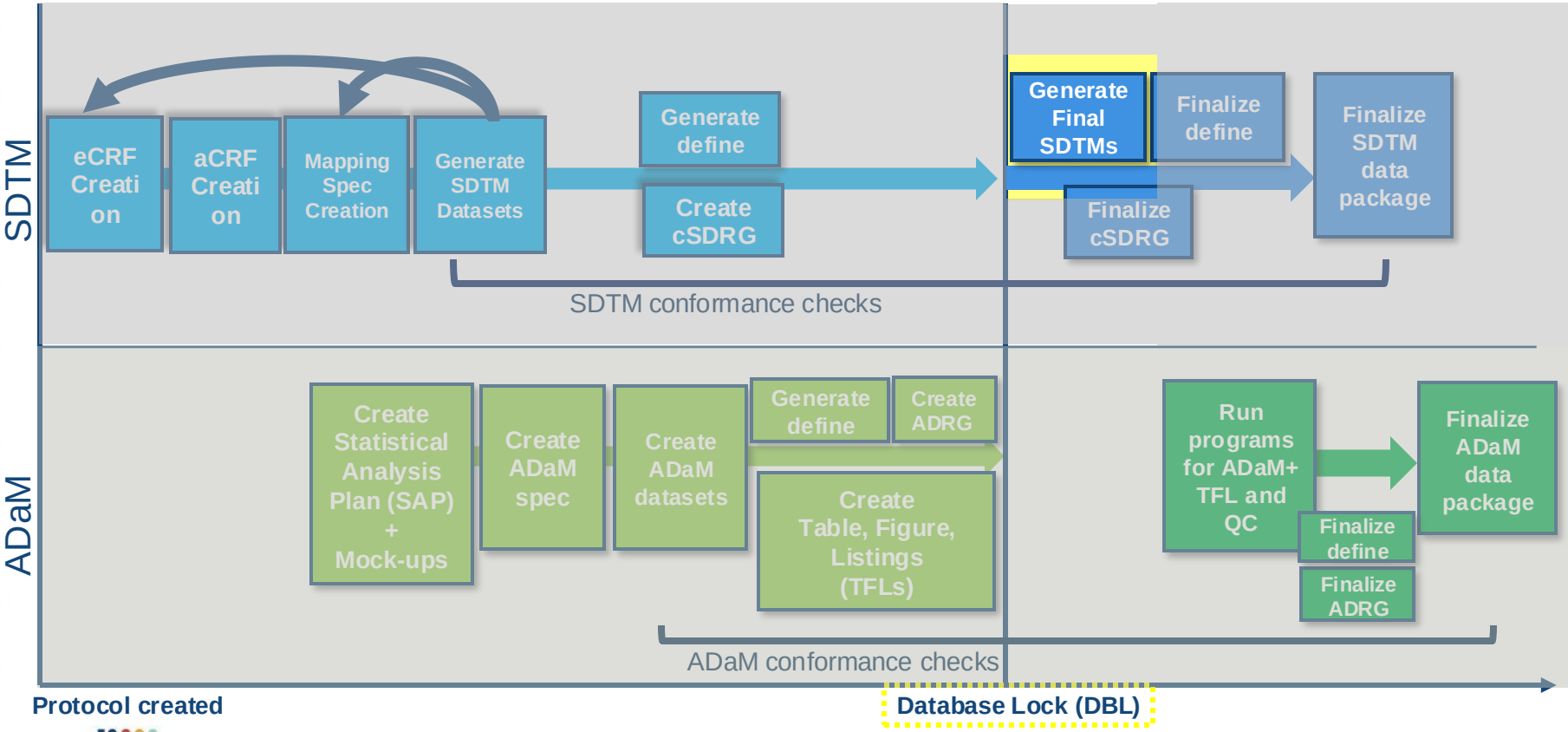
The TA extensions that are currently incorporated into FDA supported CDISC foundational standards include:

- Dyslipidemia Therapeutic Area User Guide v1
- Chronic Hepatitis C Therapeutic Area Data Standard User Guide v1
- QT Studies Therapeutic Area User Guide v1
- Diabetes Therapeutic Area User Guide v1.0 – Supplement for ADaM
- Tuberculosis Therapeutic Area User Guide v2.0
- Diabetic Kidney Disease Therapeutic Area User Guide v1.0
- Ebola Therapeutic Area User Guide v1.0
- Rheumatoid Arthritis Therapeutic Area User Guide v1.0
- Malaria Therapeutic Area User Guide v1.0
- Kidney Transplant Therapeutic Area User Guide v1.0
- TAUG-Influenza v1.1
- Virology Therapeutic Area User Guide v2.1
- Prostate Cancer Therapeutic Area User Guide v1.0
- Schizophrenia Therapeutic Area User Guide v1.1
- Major Depressive Disorder Therapeutic Area User Guide v1.0
- Major Depressive Disorder Therapeutic Area User Guide v1.0
- Duchenne Muscular Dystrophy Therapeutic Area User Guide v1.0
- Vaccines Therapeutic Area User Guide v1.1
- Chronic Obstructive Pulmonary Disease Therapeutic Area User Guide v1
- Colorectal Cancer Therapeutic Area User Guide v1.0
- Huntington's Disease Therapeutic Area User Guide v1.0
- Post Traumatic Stress Disorder Therapeutic Area User Guide v1.0
- Clostridium Difficile Associated Diarrhea Therapeutic Area User Guide v1.0
- Acute Kidney Injury v1.0

TS

STUDYID	DOMAIN	TSSEQ	TSGRPID	TSPARMCD	TSPARM	TSVAL	TSVALNF	TSVALCD	TSVCDREF	TSVCDVER
VAC1	TS	1		CTAUG	CDISC Therapeutic Area User Guide	Vaccines Therapeutic Area User Guide v1.1		C161455	CDISC	2024-03-29

Checks when creating final SDTMs after DBL



Helpful When Creating Final SDTMs After DBL

Ensure that final randomization info is properly incorporated into SDTM DM.ARM/ARMCD at unblinding

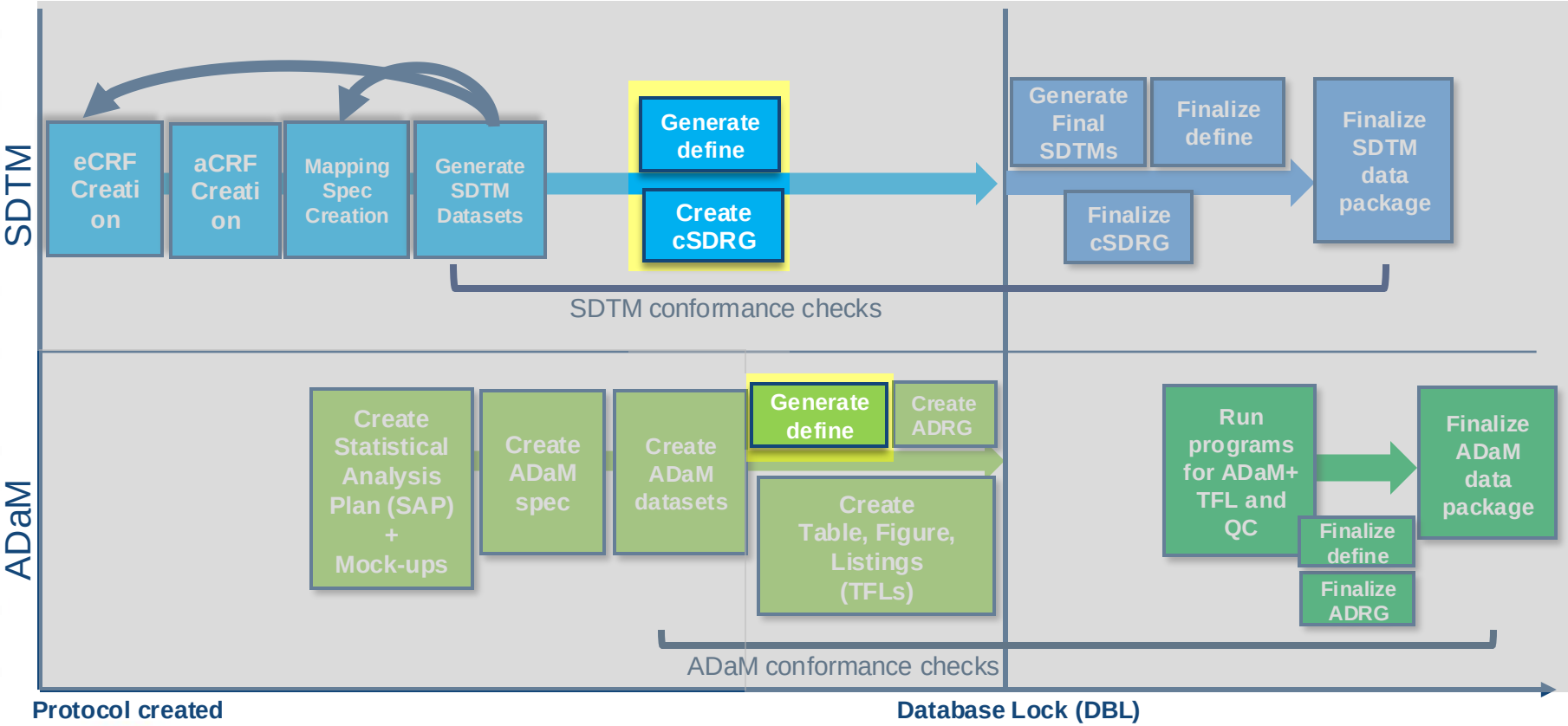
Ensure that any misallocations of planned treatments are properly accounted for in SDTM DM.ACTARM/ACTARMCD at unblinding

Ensure that any 3rd party data that was blinded during the study (e.g., PK concentrations, particular lab tests, etc.) is delivered properly unblinded and are properly incorporated into final SDTMs

Ensure WHODrug coding is consistent for same values of --TRT

Ensure DUNS and Sponsor Name are completed correctly in TS

Checks when creating define.xml



Helpful when creating define.xml

- Ensure Methods and Comments in define.xml are present without references to raw datasets or variables
- Ensure all variables used for reference in Methods and Comments are present in the datasets and define.xml
- Ensure accuracy of Core variables in an ADaM define.xml
- Ensure when ARM is created, selection criteria is accurate (especially due to updates)
- Update ADaM define.xml and ADaM Datasets for any SDTM variables that are copied as-is to ADaM datasets when SDTM variables are updated. (e.g., SDTM variable names and labels can be changed and must cascade to ADaM)
- Ensure all annotated variables on aCRF are present in define.xml with an Origin of CRF (if define-xml v2.0) or Collected (if define-xml 2.1)
- Ensure match between dataset metadata and SDTM/ADaM dataset content (e.g., dataset labels, key variables)
- Ensure match between variable metadata and SDTM/ADaM dataset content (e.g., variable labels)
- Ensure all codelists and C-codes that are needed are present

Example Methods

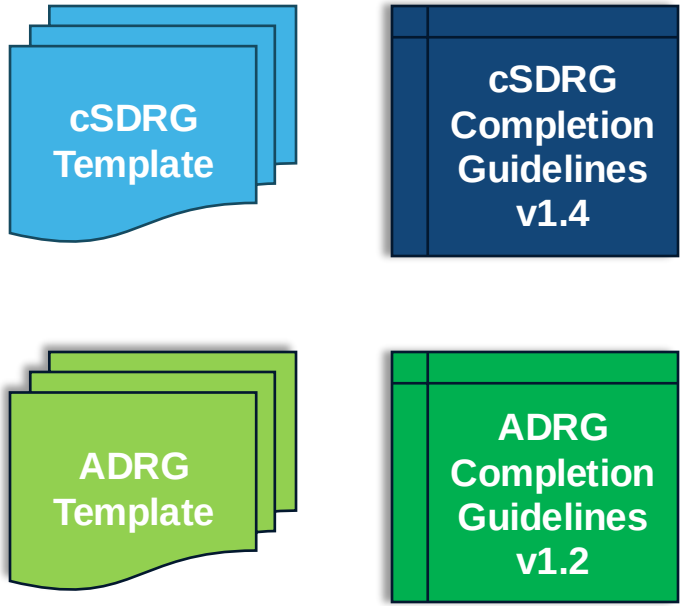
Concatenated value of demog.site + demog.sub

STUDYID + SITEID + SUBJID

Set to “Y” when AESTDTC > EXSTDTC

Y when ae1.aestdat is after ex4.exstdat

Documentation for the Creation of Reviewer's Guides



https://phuse.global/Deliverables

Helpful when creating cSDRG

Ensure section 3.1 of cSDRG is completed correctly:

- List datasets that include data for screen failure subjects
- Ensure any planned but not submitted datasets are reported
  - If yes and dataset is present in define.xml v2.1, ensure the Has No Data attribute has been set to Y
- Verify if submitted data is a subset of collected data
- Verify if adjudication data is present

Ensure section 3.3 is completed with explanations for all non-leading-question-fields annotated as NOT SUBMITTED on the aCRF

Review issue explanations in section 4.2 to make sure all information has been included and the explanation addresses the issue found by the validator

Ensure section 3.1 of cSDRG is completed correctly

3.1 Overview

Are the submitted data taken from an ongoing study? <Yes> <No>

If yes, describe the data cut or database status:

(Text here)

Were the SDTM datasets used as sources for the analysis datasets? <Yes> <No>

If no, what were the sources of analysis datasets?

(Text here. Include the following text if applicable:

Please refer to Legacy Data Conversion Plan and Report Appendix for details.)

Do the submission datasets include screen failures? <Yes> <No>

If yes, which datasets include screen failure data?

(Text here)

Were any domains planned, but not submitted because no data were collected? <Yes> <No>

If yes, list domains not submitted:

(Text here)

Are the submitted data a subset of collected data? <Yes> <No>

If yes, describe the reason that all collected data were not provided:

(Text here)

Is adjudication data present? <Yes> <No>

If yes, describe the implementation approach and location of the adjudication data:

(Text here)

Additional Content of Interest

(See cSDRG Completion Guidelines for additional content of interest, and include text here).

Ensure section 3.3 is completed with explanations for all non-leading-question-fields annotated as NOT SUBMITTED on the aCRF

3.3 Annotated CRFs

(Text here or indicate this section is not applicable)

Explanation of data fields [Not Submitted]

aCRF page Number(s)	Data Collection Field	Explanation of why [NOT SUBMITTED]

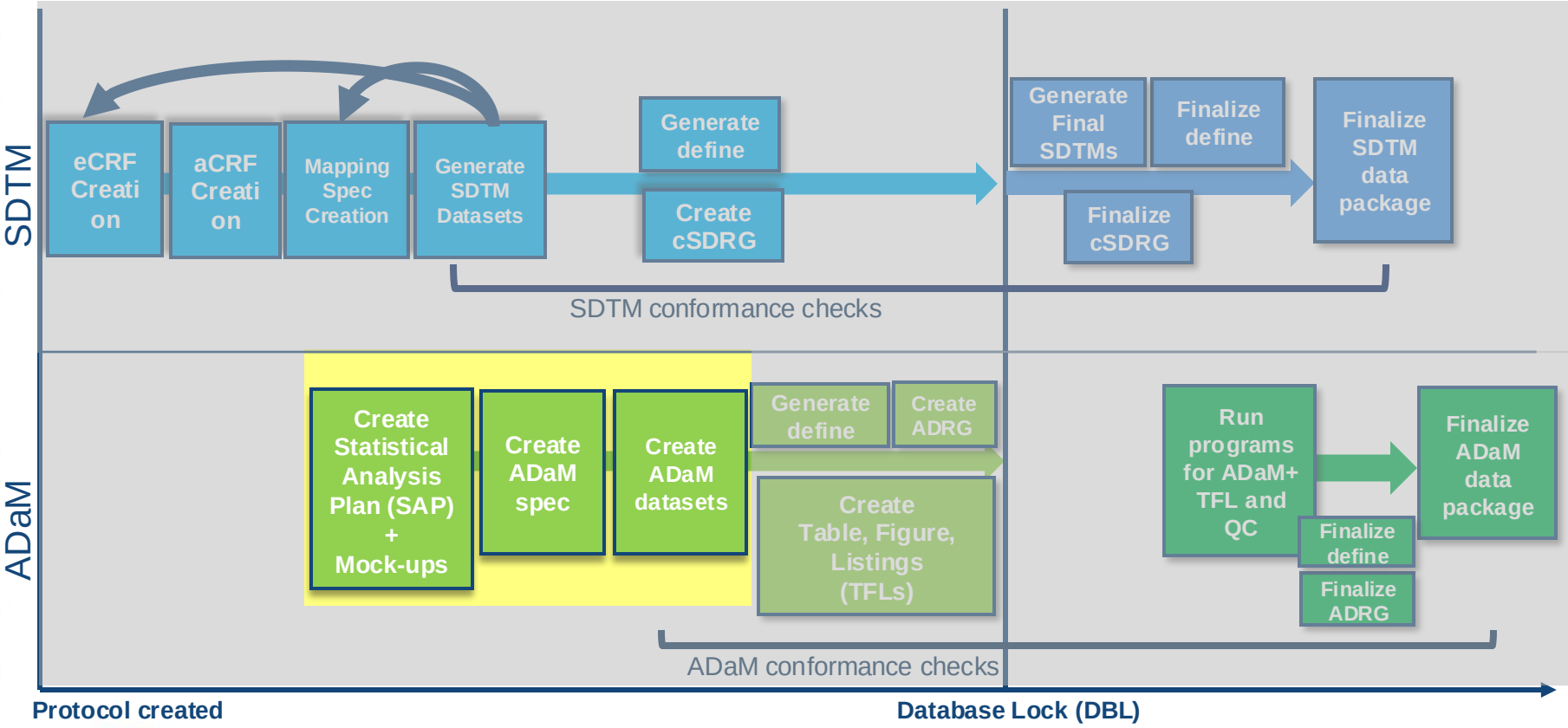
Review issue explanations in section 4.2 to make sure all information has been included and the explanation addresses the issue found by the validator

4.2 Issues Summary

(text here and/or use following table)

Dataset	Diagnostic Message	Severity	Count	Explanation

Checks when creating ADaM datasets



Helpful when creating ADaM datasets

	✓ Ensure all population flags defined in the Statistical analysis plan are derivable and those flags are created in ADaM datasets
	✓ Ensure AVAL and AVALC have a 1:1 relationship
	✓ If date or time imputation is done, are date or time imputation flags created in ADaM datasets?
	✓ Ensure all tables and figures defined in mock-up plan can be created by ADaM datasets
✓	Ensure values and units needed for analysis are stored in ADaM datasets (If units that are stored in SDTM are different from ones needed for analysis, think about how to prepare those values in needed units)
	✓ Check how unscheduled visits are populated in SDTM if there are any issues to make analysis visits. Check SDTM Treatment variables, study periods, visits at the beginning of SDTM creation
	✓ Check if any SDTM variables can be usable in ADaM (ex., ADY and --DY, ABLFL and --BLFL). It would be nicer if the definition of a reference data can be matched between SDTM and ADaM.
	✓ If some data are not ready at this moment, do you need to prepare dummy data/variables for preparing for programs?
	✓ For any sponsor-defined variables, including supplemental qualifiers, check to ensure CDISC naming fragments have been used

Refer to 2023 slides

ADaM Datasets: Balancing Automated and Manual Conformance Check:
https://www.cdisc.org/sites/default/files/2023-08/2023_CDISC-Slide-Template_Non-CDISC%20Staff_02_China_seiko%20yamazaki.pdf

Check units in SDTM

LB domain

LBTEST	LBORRES	LBORRESU	LBSTRESN	LBSTRESU	LBNAM
Calcium	4.688	mEq/L	2.3441	mmol/L	Hospital **A**
Calcium	4.986	mEq/L	2.4938	mmol/L	Hospital **A**
Calcium	9.695	mg/dL	2.4189	mmol/L	Hospital **B**
Calcium	9.595	mg/dL	2.394	mmol/L	Hospital **B**

Mock-up

Table x Summary of Laboratory Data

Calcium (mg/dL)

	Active	Placebo
Baseline		
N	x	x
Mean (SD)	x.xx (x.xxx)	x.x (x.xxx)
Median	x.xx	x.xx
Min, Max	x.xx, x.xx	x.xx, x.xx
<Visit>		
N	x	x
Mean (SD)	x.xx (x.xxx)	x.x (x.xxx)
Median	x.xx	x.xx
Min, Max	x.xx, x.xx	x.xx, x.xx

Examples

1: Create a row for the value in the needed units and make --DRVFL =Y

LB domain

LBTEST	LBORRES	LBORRESU	LBSTRESN	LBSTRESU	LBDRVFL	VISIT	LBNAM
Calcium	4.688	mEq/L	2.3441	mmol/L		Week 1	Hospital A
Calcium			9.3947	mg/dL	Y	Week 1	Hospital A
Calcium	4.986	mEq/L	2.4938	mmol/L		Week 2	Hospital A
Calcium			9.9955	mg/dL	Y	Week 2	Hospital A
Calcium	9.695	mg/dL	2.4189	mmol/L		Week 1	Hospital B
Calcium			9.695	mg/dL	Y	Week 1	Hospital B
Calcium	9.595	mg/dL	2.394	mmol/L		Week 2	Hospital B
Calcium			9.595	mg/dL	Y	Week 2	Hospital B

Examples

2: Create a SUPP domain and store the values in the needed units

LB domain

LBSEQ	LBTEST	LBORRES	LBORRESU	LBSTRESN	LBSTRESU	LBNAM
1	Calcium	4.688	mEq/L	2.3441	mmol/L	Hospital A
2	Calcium	4.986	mEq/L	2.4938	mmol/L	Hospital A
3	Calcium	9.695	mg/dL	2.4189	mmol/L	Hospital B
4	Calcium	9.595	mg/dL	2.394	mmol/L	Hospital B

SUPPLB domain

RDOMAIN	IDVAR	IDVARVAL	QNAM	QLABEL	QVAL
LB	LBSEQ	1	LBCNRES	Result in conventional unit	9.3947
LB	LBSEQ	1	LBCNRESU	Conventional unit	mg/dL
LB	LBSEQ	2	LBCNRES	Result in conventional unit	9.9955
LB	LBSEQ	2	LBCNRESU	Conventional unit	mg/dL
LB	LBSEQ	3	LBCNRES	Result in conventional unit	9.695
LB	LBSEQ	3	LBCNRESU	Conventional unit	mg/dL
LB	LBSEQ	4	LBCNRES	Result in conventional unit	9.595
LB	LBSEQ	4	LBCNRESU	Conventional unit	mg/dL

Another option

3: Convert units in ADaM

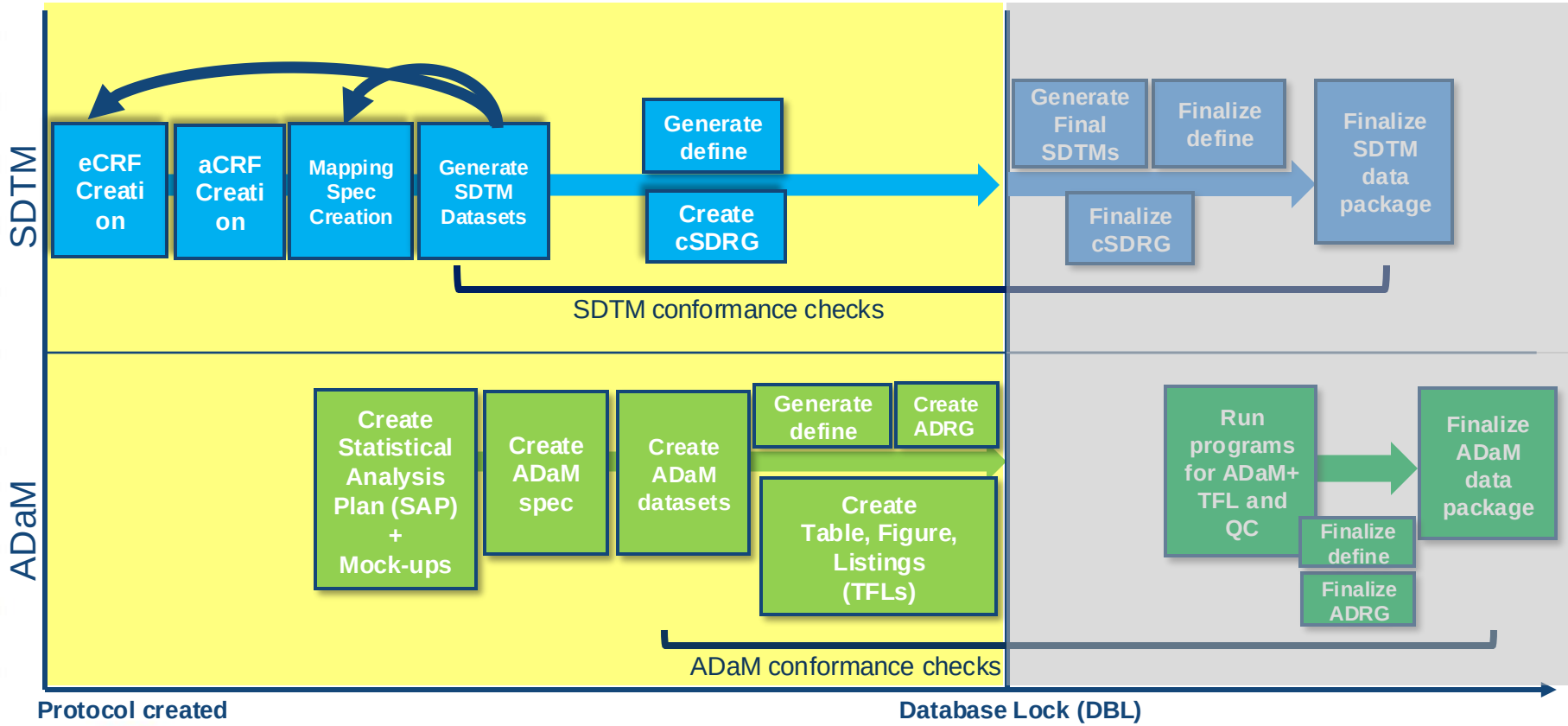
ADLB

PARAM	PARAMCD	AVAL
Calcium (mg/dL)	CA	9.3947
Calcium (mg/dL)	CA	9.9955
Calcium (mg/dL)	CA	9.6949
Calcium (mg/dL)	CA	9.5947

Make sure to check units in SDTM

- Find out if the units of values that are stored in SDTM are matching with the ones defined in SAP.
- If not, discuss with those who create SDTM how values of different units would be stored in SDTM.
- Decide that values in SDTM can be simply copied to ADaM without unit conversion or units of values have to be converted in ADaM.

Checks when all documents have been created



Helpful when all documents have been created

✓	✓ Cross-check the dataset content: Section 3.4.x in cSDRG/Section 5.2.x in ADRG, define.xml dataset metadata, and XPT datasets
	✓ Cross-check versions of IGs and validation tool configuration Section 1.3 in cSDRG/ADRG and versions of SDTM/ADaM and its IG
	✓ Cross-check versions of CT and dictionaries used and validation tool configuration Section 1.3 in cSDRG/ADRG
✓	✓ If define v2.1 is used, make sure all IG versions and CT versions are specified Section 1.3 in cSDRG/ADRG and standards section in define.xml
	✓ For SDTM: Is study ongoing? If yes, this question in section 3.1 of the cSDRG should be answered as “Yes”, and in TS: • TSVAL when TSPARMCD=SENDTC should be null • TSVAL=Y when TSPARMCD=ONGOSIND (Ongoing Study Indicator) • Verify correct date is present in TSVAL when TSPARMCD=DCUTDTC (Data Cutoff Date)

Cross-check XDRG, define, and xpt

ADRG

5.2 Analysis Datasets

Dataset - Dataset Label	Class	Efficacy	Safety	Baseline or other subject characteristics	PK/PD	Primary Objective	Structure
ADSL - Subject Level Analysis	SUBJECT LEVEL ANALYSIS DATASET			X			one record per subject
ADAE - Adverse Events Analysis	OCCURRENCE DATA STRUCTURE		X				one record per subject per adverse event
ADQSADAS - ADAS-Cog Analysis	BASIC DATA STRUCTURE	X					One record per subject per parameter per analysis visit per analysis date

XPT Dataset contents

adqsadas.xpt ×

Key	Value
Path	C:\Users\81804\Docum
Dataset	ADQSADAS
Label	ADAS-Cog Analysis
Created On	2013-11-20T20:55:18
Modified On	2013-11-20T20:55:18

Define

Datasets

Dataset	Description	Class - SubClass	Structure	Purpose	Keys
ADSL [ADaMIG 1.1]	Subject-Level Analysis	SUBJECT LEVEL ANALYSIS DATASET	one record per subject	Analysis	STUDYID, USUBJID
ADQSADAS [ADaMIG 1.1]	ADAS-Cog Analysis	BASIC DATA STRUCTURE	One record per subject per parameter per analysis visit per analysis date	Analysis	STUDYID, USUBJID, PARAMCD, AVISIT, ADT

When define v2.1 is used, check all IG versions and CT versions are specified

Define

Study Name	CDISC-Sample
Study Description	CDISC-Sample Data Definition
Protocol Name	CDISC-Sample
Metadata Name	Study CDISC-Sample Data Definitions

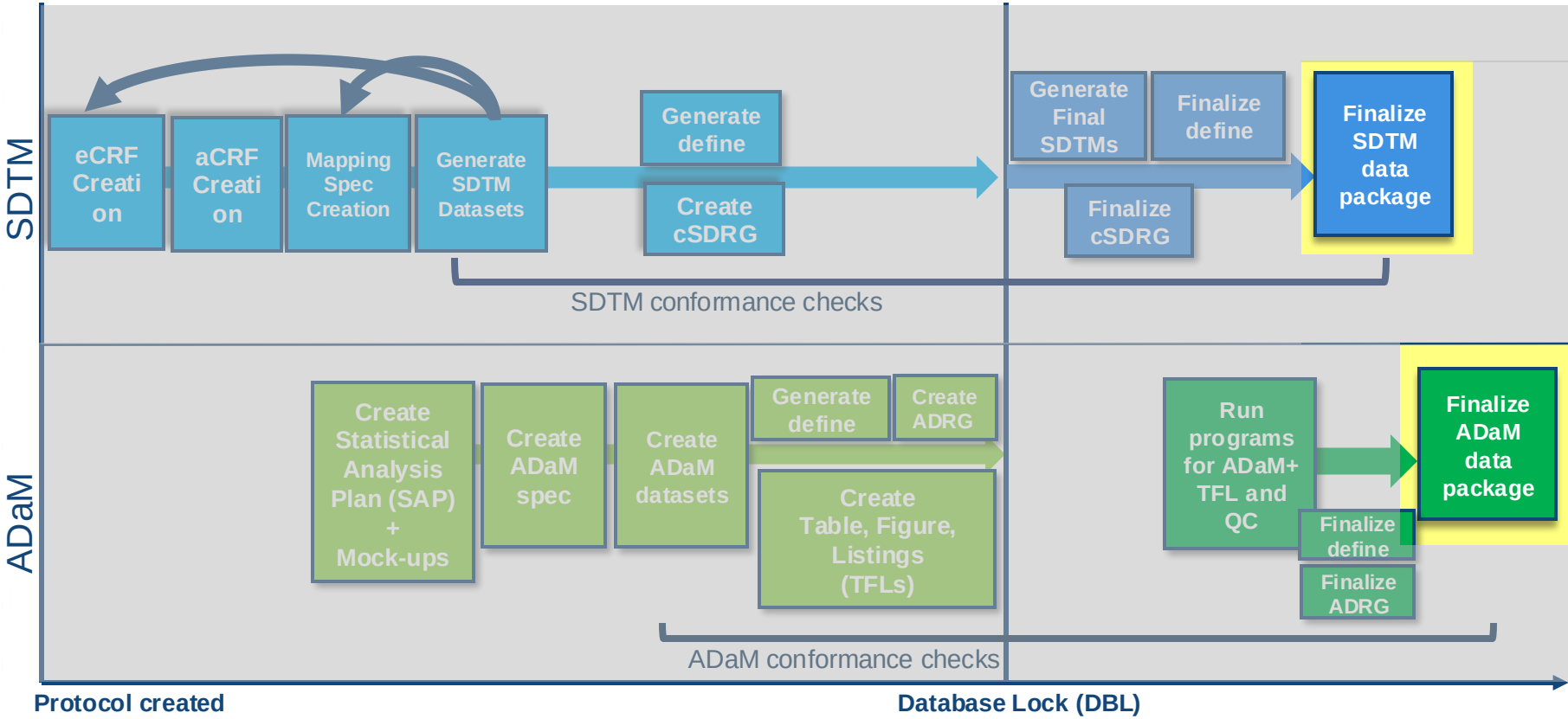
Standards for Study CDISC-Sample

Standard
ADaMIG 1.1
ADaMIG 1.3
CDISC/NCI ADaM 2022-06-24
CDISC/NCI ADaM 2023-03-31
CDISC/NCI SDTM 2023-03-31

1.3 Study Data Standards and Dictionary Inventory

Standard or Dictionary	Versions Used
SDTM	•SDTM v1.7 •SDTMIG v3.3
SDTM Controlled Terminology	CDISC SDTM Controlled Terminology, 2023-03-31
ADaM	•ADaM v2.1 •ADaMIG v1.1 •ADaMIG v1.3
ADaM Controlled Terminology	CDISC ADaM Controlled Terminology, 2022-06-24 CDISC ADaM Controlled Terminology, 2023-03-31
Data Definitions	Define-XML v2.1
TAUG (if applicable)	
Medical Events Dictionary	MedDRA 24.1
Other standards (optional)	

Checks immediately before submission



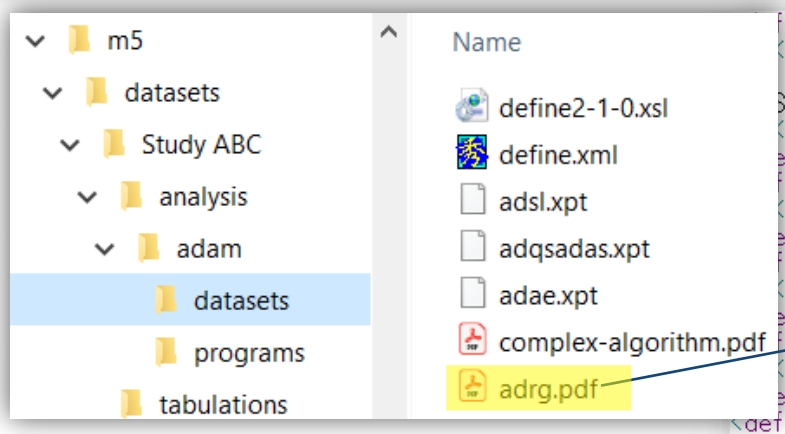
Helpful immediately before submission

	✓ To aid your own review of studies in the submission, create a master table of studies in the submission with details on the versions of Implementation Guides, Models, Dictionaries, and Important dates
	✓ Ensure aCRFs for submission are flattened but still contain SDTM annotations
✓	✓ Ensure links and bookmarks are clickable and provide accurate navigation
	✓ Ensure MedDRA coding is consistent for same values of –TERM for studies that are using the same MedDRA version
	✓ Ensure files are placed in the appropriate module and folder, especially wrt split datasets
	✓ Ensure that all submitted programs are the final versions used, are well-documented, reasonably understandable in terms of logic and flow, and error-free. Named as xxx.sas or xxx.r.
	✓ Ensure that any subsidiary macros and auxiliary files used in any analysis logic in the submitted programs are available in some form (program, dataset, adrg, etc.)
	✓ Ensure that all submitted datasets are the final versions used in all submitted analyses (submitted .xpts are created from the final versions of datasets used in analysis)
	✓ Create inventory of TFL objects submitted, including the programs used to create each, and the datasets referenced from all programs, so that final submission inventory is known.
	✓ Create programs inventory document as programs.pdf, including program name, brief description of purpose and links to all submitted ADaM and TFL programs. Submit with programs and link to it from adrg (and define.xml).
	✓ Ensure that Study Tagging Files (stf.xml) account for all submitted datasets, programs and associated documentation (define.xml, csdrg, adrg, etc.)

Can you open documents after placing data packages into a specific file directory structure?

Datasets

Dataset	Description	Class - SubClass	Structure	Purpose	Keys	Documentation	Location
ADSL [ADaMIG 1.1]	Subject-Level Analysis	SUBJECT LEVEL ANALYSIS DATASET	one record per subject	Analysis	STUDYID, USUBJID	Screen Failures are excluded since they are not needed for this study analysis. See Analysis Data Reviewer's Guide, page 6. Analysis Data Reviewer's Guide	adsl.xpt

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```

Summary

Know the key documentation for submissions to regulatory agencies and ensure compliance with regulatory requirements

Go through the checklist of items at the right time for efficient preparation

- When creating aCRF and SDTM datasets
- When creating final SDTMs after DBL
- When creating define.xml
- When creating cSDRG
- When creating ADaM datasets
- When all documents have been created
- Immediately before submission

Please utilize the checklist for your organization's submission process

Thank You!