Therapeutic Area User Guides

LPO Support Webinar

29 May 2019

NIH NATIONAL CANCER INSTITUTE

Upon Completion of This Webinar You Should Be Able To

- Describe the purpose of CDISC Therapeutic Area User Guides (TAUG) and how they are developed
- Find the published and “in development” TAUGs
- Describe the contents of a typical CDISC TAUG
- Explain the relationship of CDISC TAUGs to CDISC Foundational Standards (CDASH, SDTM, ADaM)
- Explain the origin and purpose of FDA TA Specifications

Why Do We Need Therapeutic Area User Guides (TAUG)?

- CDISC Foundational Standards (CDASH, SDTM, ADaM)
  - "Generic" - useful for all kinds of studies, any therapeutic area
  - Primarily focused on showing examples of typical **safety** data
  - ➢ Not well understood how to apply to **efficacy** data
- Therapeutic Area User Guides (TAUG)
  - Developed to show examples of typical data in studies for specific diseases, e.g.,
    - Tuberculosis
    - Malaria
    - Breast Cancer
    - Lung Cancer
    - HIV

https://www.cdisc.org/standards/therapeutic-areas

32 published TAUGs

Listed alphabetically and by "disease area"

FDA Priority Therapeutic Areas “55 in 5”

Therapeutic Area (Disease/Domain) Data Standards Prioritization

This document is a tabular representation of the data graphically shown in the Roadmap for Development of Priority Therapeutic Area (TA) Standards document. It has been developed so additional information can be easily added periodically to communicate information regarding TA development projects.

Number	TA	Roadmap Grouping[1]	Status[6]	Start Date	Added to List[2]	Removed from List[2]	Tier[3]	Stage[4,5]
1	Alzheimer's	1	Published				Tier 1	Public Release, v2.0
2	Cardiovascular (CV)	1	Published				Tier 1	Public Release, v1.0 Provisional
3	CV Imaging (Echo)	1	Started		version 1			CFAST: Development
4	Pain	1	Published				Tier 1	Public Release, v1.1 Provisional
5	Parkinson's	1	Published				Tier 1	Public Release, v1.0 Provisional
6	Polycystic Kidney Disease	1	Published				Tier 1	Public Release, v1.0
7	Schizophrenia	1	Published				Tier 1	Public Release, v1.0 Provisional
8	Tuberculosis	1	Published				Tier 1	Public Release, v2.0
9	Virology	1	Published		version 1			Public Release, v2.0
10	Diabetes (previously Anti-diabetic agents)	2	Published	Q3 FY13			Tier 1	Public Release, v1.0 Provisional
11	Irritable bowel syndrome (IBD): Crohn's disease & Ulcerative colitis	2	Started	Q3 FY14	version 4	version 1	Tier 1	FDA: Requirements Definition
12	Major Depressive Disorder	2	Published	Q4 FY12			Tier 2	Public Release, v1.0
13	Complicated Urinary Tract Infections (cUTI)	2	Started	Q2 FY14			Tier 1	FDA: Requirements Definition
14	Acne	3	Started	Q1 FY13			Tier 1	FDA: Requirements Definition
15	Prevention of Pregnancy	3	Started	Q3 FY14			Tier 1	FDA: Requirements Definition
16	Rheumatoid Arthritis (RA)	3	Published	Q1 FY14			Tier 1	Public Release, v1.0
17	Complicated Skin and Skin Structure Infections (ABSSSI) (formerly Infection of Skin and/or Subcutaneous Tissue)	4	Started	FY15			Tier 1	FDA: Requirements Definition; CFAST: Proposed
18	QT Studies	4	Published	Q4 FY13			Tier 1	Public Release, v1.0 Provisional
19	Solid Organ Transplantation - Kidney	4	Published	Q1 FY14			Tier 1	Public Release, v1.0

https://www.fda.gov/media/83082/download

version 10

March 2, 2018

FDA Priority Therapeutic Areas “55 in 5”

Number	TA	Roadmap Grouping[1]	Status[6]	Start Date	Added to List[2]	Removed from List[2]	Tier[3]	Stage[4,5]
20	Influenza	5	Published	Q1 FY14			Tier 2	Public Release, v1.0 Provisional
21	Treatment of Postmenopausal Osteoporosis	5	Started	Q2 FY14			Tier 1	FDA: Requirements Definition
22	Anticonvulsants	6	Started	Q2 FY14			Tier 2	FDA: Requirements Definition
23	Dyslipidemia (formerly Lipid-altering Drug Groups)	6	Published	Q1 FY13			Tier 2	Public Release, v1.0 Provisional
24	Oncology - Breast	6	Published	Q2 FY14	version 5			Public Release, v1.0
25	Asthma	7	Published	Q1 FY13			Tier 2	Public Release, v1.0 Provisional
26	Bipolar Disorder	7	Started	Q4 FY14			Tier 2	Duke University: Development; CFAST: Proposed
27	Clostridium Difficile associated Diarrhea (formerly Clostridium Difficile Colitis)	7	Started	FY15			Tier 2	FDA: Requirements Definition; CFAST: Development
28	Muscular Dystrophy	7	Started	Q4 FY14	version 5			FDA: Requirements Definition; CFAST: Proposed
29	Oncology - Prostate	8	Published	Q4 FY14	version 5			FDA: Requirements Definition; CFAST: Development
30	Chemotherapy-induced Nausea and Vomiting	8	Started	FY15			Tier 3	Research Triangle Institute: Requirements Definition
31	COPD	8	Published	Q4 FY14			Tier 3	Public Release, v1.0 Provisional
32	Complicated Intra-Abdominal Infections (formerly Infectious Diseases of Abdomen)	8	Started					Definition
33	General Anxiety Disorder	9	Started	Q4 FY14			Tier 3	Duke University: Development; CFAST: Proposed
34	Treatment of Hepatitis C	9	Published	Q2 FY13			Tier 1	Public Release, v1.0 Provisional
35	Diabetic Nephropathy (also called Diabetic Kidney Disease)	9	Published	Q3 FY14			Tier 2	Public Release, v1.0
36	Attention Deficit Hyperactivity Disorder (ADHD)	9	Started	Q2 FY14			Tier 3	FDA: Requirements Definition
37	Treatment of Overactive Bladder	10	Started	Q1 FY13			Tier 2	FDA: Requirements Definition
38	Oncology - Colorectal	10	Published	FY15	version 5			FDA: Requirements Definition; CFAST: Development

Published

Published

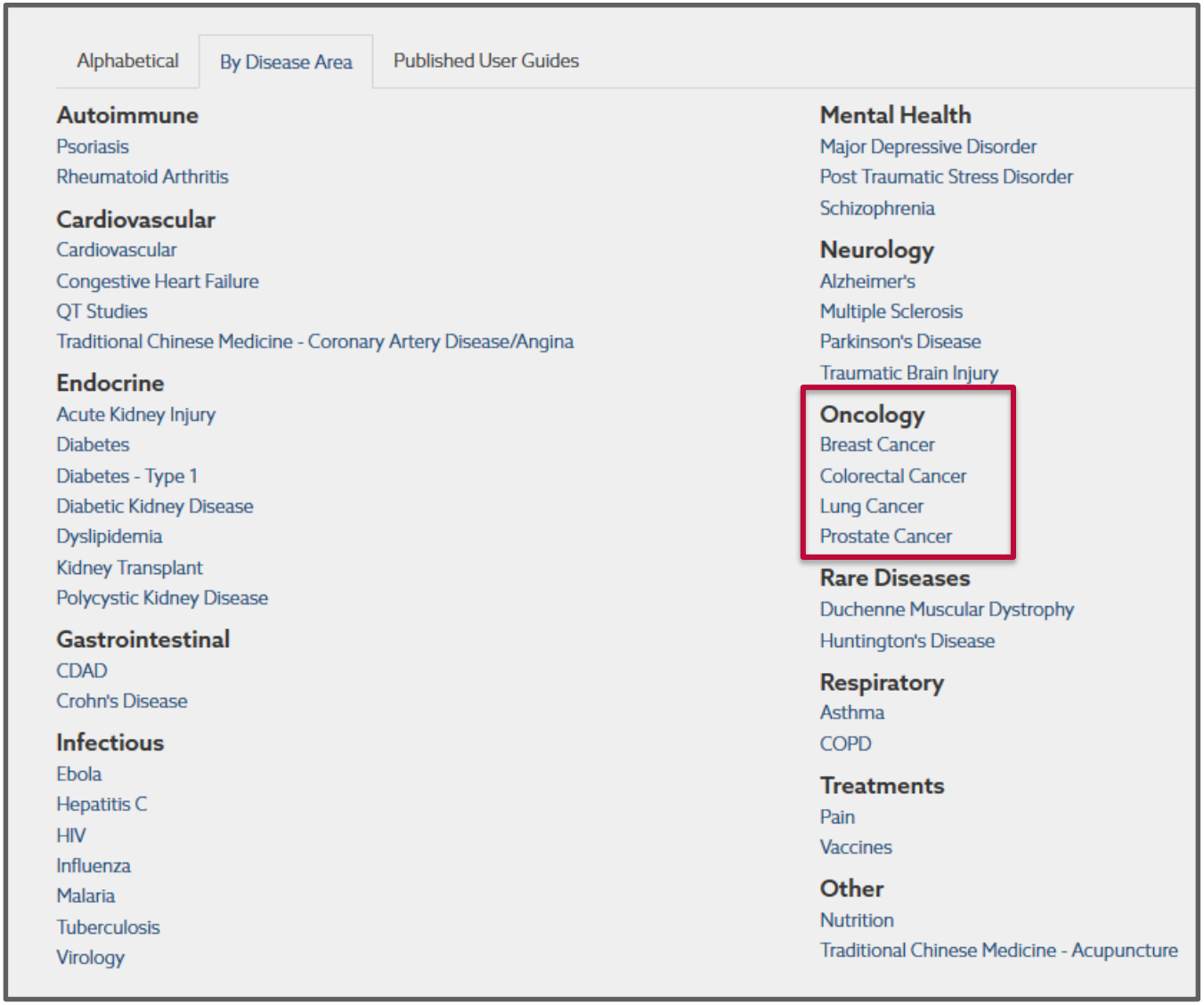
V10 is Not completely up to date

FDA Priority Therapeutic Areas “55 in 5”

Number	TA	Roadmap Grouping[1]	Status[6]	Start Date	Added to List[2]	Removed from List[2]	Tier[3]	Stage[4,5]
39	Oncology - Lung	10	Published	FY15	version 5			FDA: Requirements Definition; CFAST: Scoping
40	Oncology - Brain	10	Started		version 7			FDA: Requirements Definition
41	Anticoagulants for Atrial Fibrillation (formerly Atrial Fibrillation)	11	Started	Q2 FY14			Tier 3	FDA: Requirements Definition
42	Traumatic Brain Injury	11	Published	Q4 FY14			Tier 3	Public Release, v1.0
43	Psoriasis	12	Interest in 2018		version 6	version 4	Tier 1	CFAST: Proposed
44	Oncology – Cervical Cancer	12	Next Year		version 8			
45	Decompensated Congestive Heart Failure (CHF)	12	Interest in 2018				Tier 3	
46	Acute Kidney Injury	12	Interest in 2018					
47	Opioid Induced Constipation	13	Next Year		version 1			
48	Treatment of Hepatitis B	13	Next Year				Tier 3	
49	Tinea Pedis	13	Next Year				Tier 3	
50	Chronic Idiopathic Constipation	14	Next Year		version 1			
51	Treatment of HIV*	14	Started	2016			Tier 2	CFAST: Development
52	Prevention of HIV*	14	Started	2016			Tier 2	CFAST: Development
53	Treatment of Vasomotor Symptoms Due to Menopause	15	Interest in 2018				Tier 2	
54	Actinic Keratoses	15	Next Year				Tier 3	
55	Huntington's Disease	15	Started		version 10			CFAST: Development
Removed from List								
	Sedation	15			version 1	version 8		
	Pneumonia	6				version 6	Tier 2	
	Treatment of Cough	9				version 6	Tier 3	
	Bacterial Vaginosis	9				version 6	Tier 3	
	Aerosolized Antimicrobials for Cystic Fibrosis	10				version 6	Tier 3	
	Helicobacter Pylori Ulcer Disease	13				version 6	Tier 3	

Therapeutic Area User Guide (TAUG)

Published on the CDISC website: https://www.cdisc.org/standards/therapeutic-areas



Therapeutic Area User Guide (TAUG) *in Development*

Published on the CDISC website: https://www.cdisc.org/standards/in-development

Therapeutic Area	Development	Public Review	Release Notes	Projected Publication Date
Acute Kidney Injury Therapeutic Area User Guide v1.0	In Progress	No	In Development.	2020
Congestive Heart Failure Therapeutic Area User Guide v1.0	In Progress	No	In Development.	2020
Crohn's Disease Therapeutic Area User Guide v1.0	In Progress	No	In Development.	2020
Diabetes - Type 1 Therapeutic Area User Guide v1.0	In Progress	No	In Development.	2020
Nutrition Therapeutic Area User Guide v1.0	Completed	Completed	Preparing for Publication.	2019
Psoriasis Therapeutic Area User Guide v1.0	In Progress	No	In Development.	2020
Traditional Chinese Medicine - Acupuncture	In Progress	No	In Development.	2020
Traditional Chinese Medicine - Coronary Artery Disease/Angina Therapeutic Area User Guide v1.0	Completed	Completed	Preparing for Publication.	2019

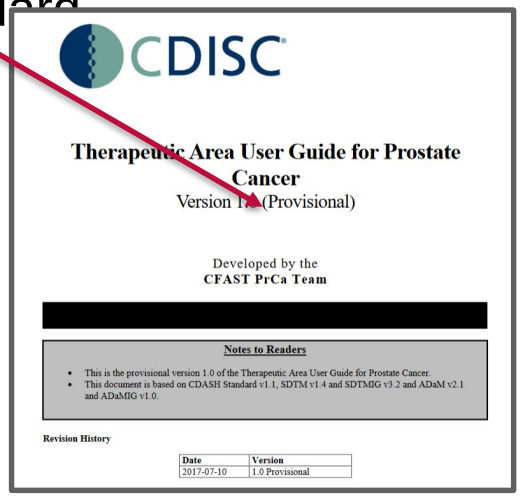
8 more TAUGs currently in development

Therapeutic Area User Guide (TAUG) Development

12-18 months

- "Short term" (usually grant-funded) projects led by CDISC staff/consultants, working with volunteers (including SME **clinicians**, foundational standards SMEs) and other organizations (e.g., C-Path)
  - Developed in CDISC Wiki (like all other CDISC standards)
  - Published as they are completed (not on the annual publication schedule)
  - TAUGs often include **proposed** domains, variables and terminology
  - Published as **Provisional** until everything in them is in a published version of the foundational standard

As a result, TAUG development has had a significant effect on the evolution of **foundational** standards


CDISC

Therapeutic Area User Guide for Prostate Cancer

Version 1.0 (Provisional)

Developed by the
CFAST PrCa Team

[redacted]

Notes to Readers

- This is the provisional version 1.0 of the Therapeutic Area User Guide for Prostate Cancer.
- This document is based on CDASH Standard v1.1, SDTM v1.4 and SDTMIG v3.2 and ADaM v2.1 and ADaMIG v1.0.

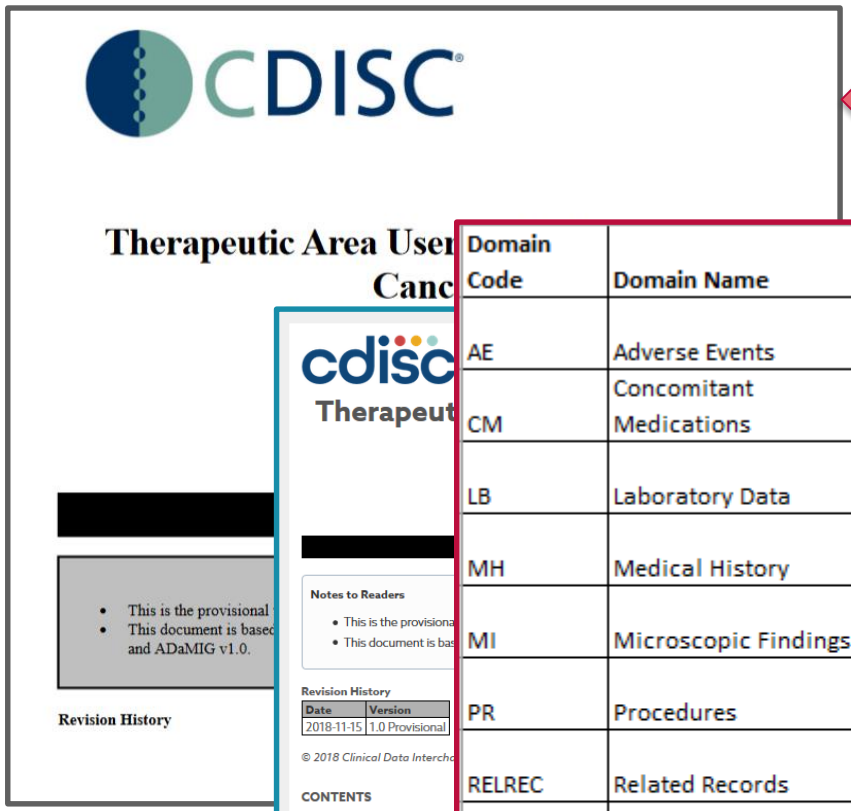
Revision History

Date	Version
2017-07-10	1.0 Provisional

Therapeutic Area User Guide (TAUG)

- TAUGs provide examples of how to implement the foundational standards (CDASH, SDTM, etc.) for a particular indication or therapy
- Used *in conjunction with / on top of foundational standards*
  - TAUGs do not replace CDASH, SDTM or ADaM
  - They show how to use CDASH, SDTM, ADaM for TA-specific data
- CDISC TAUGs do **not** represent additional requirements
  - What you collect in your studies should be based on
    - Science
    - Regulatory requirements
    - Data needed for your analysis
- TAUGs just provide *examples* of how to model *TYPICAL* data in the CDISC foundational standards

TAUGs and TA Specifications

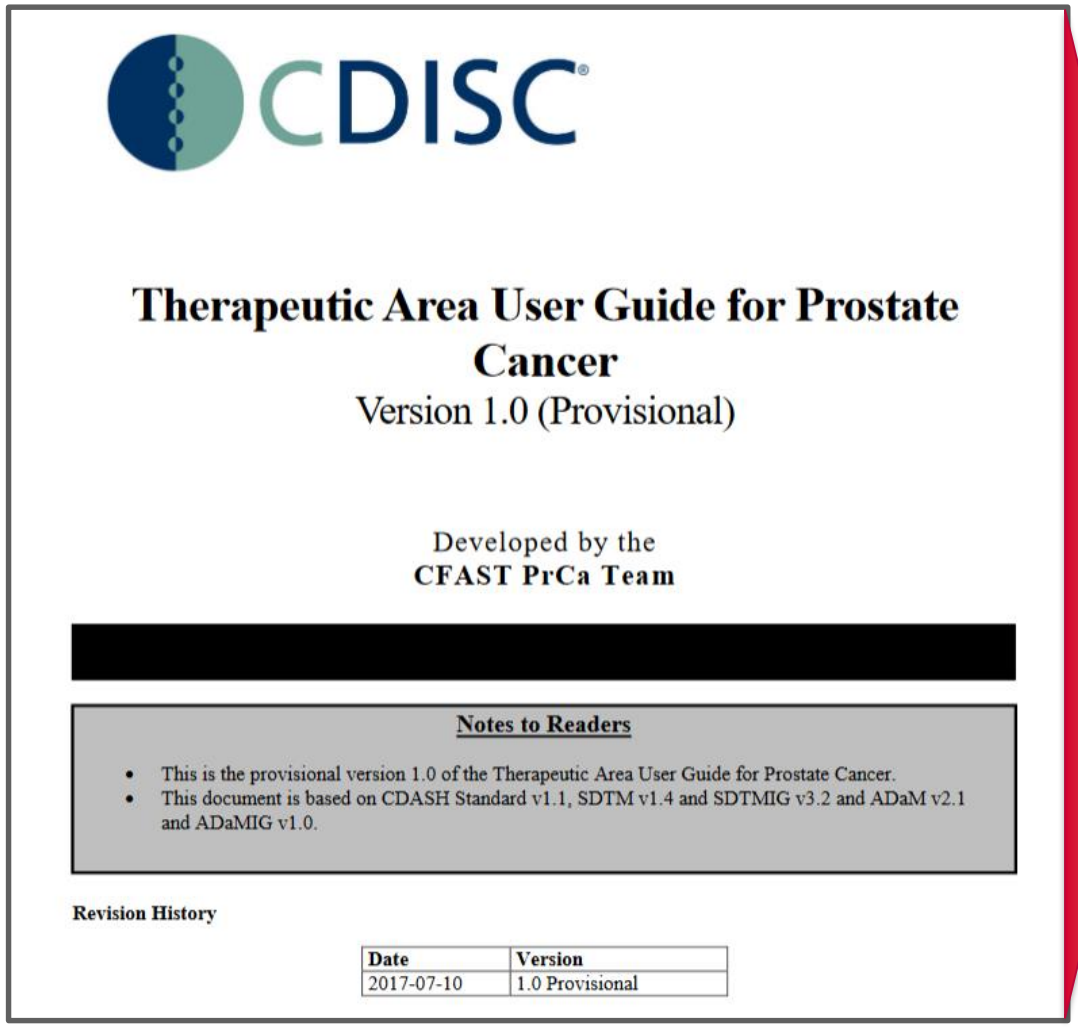


TAUGs are PDF or HTML documents

Domain Code	Domain Name	SDTMIG v3.1.2	SDTMIG v3.1.2 Amendment 1	SDTMIG v3.1.3	SDTMIG v3.2	Future SDTMIG
AE	Adverse Events	Standard Domain	Standard Domain	Standard Domain	Standard Domain	Standard Domain
CM	Concomitant Medications	Standard Domain	Standard Domain	Standard Domain	Standard Domain	Standard Domain
LB	Laboratory Data	Standard Domain	Standard Domain	Standard Domain	Standard Domain	Standard Domain
MH	Medical History	Standard Domain	Standard Domain	Standard Domain	Standard Domain	Standard Domain
MI	Microscopic Findings	Custom Domain	Custom Domain	Custom Domain	Standard Domain	Standard Domain
PR	Procedures	Custom Domain	Custom Domain	Custom Domain	Standard Domain	Standard Domain
RELREC	Related Records	Standard Domain	Standard Domain	Standard Domain	Standard Domain	Standard Domain
RS	Disease Response	Custom Domain	Custom Domain	Standard Domain	Standard Domain	Standard Domain
SM	Subject Disease Milestor	Custom Domain	Custom Domain	Custom Domain	Custom Domain	Standard Domain
	stones	Custom Domain	Custom Domain	Custom Domain	Custom Domain	Standard Domain
		Custom Domain	Custom Domain	Standard Domain	Standard Domain	Standard Domain
TU	Tumor Id cation	Custom Domain	Custom Domain	Standard Domain	Standard Domain	Standard Domain

They are accompanied by TA Specifications in Excel

TAUG Contents



CDISC

Therapeutic Area User Guide for Prostate Cancer

Version 1.0 (Provisional)

Developed by the
CFAST PrCa Team

Notes to Readers

- This is the provisional version 1.0 of the Therapeutic Area User Guide for Prostate Cancer.
- This document is based on CDASH Standard v1.1, SDTM v1.4 and SDTMIG v3.2 and ADaM v2.1 and ADaMIG v1.0.

Revision History

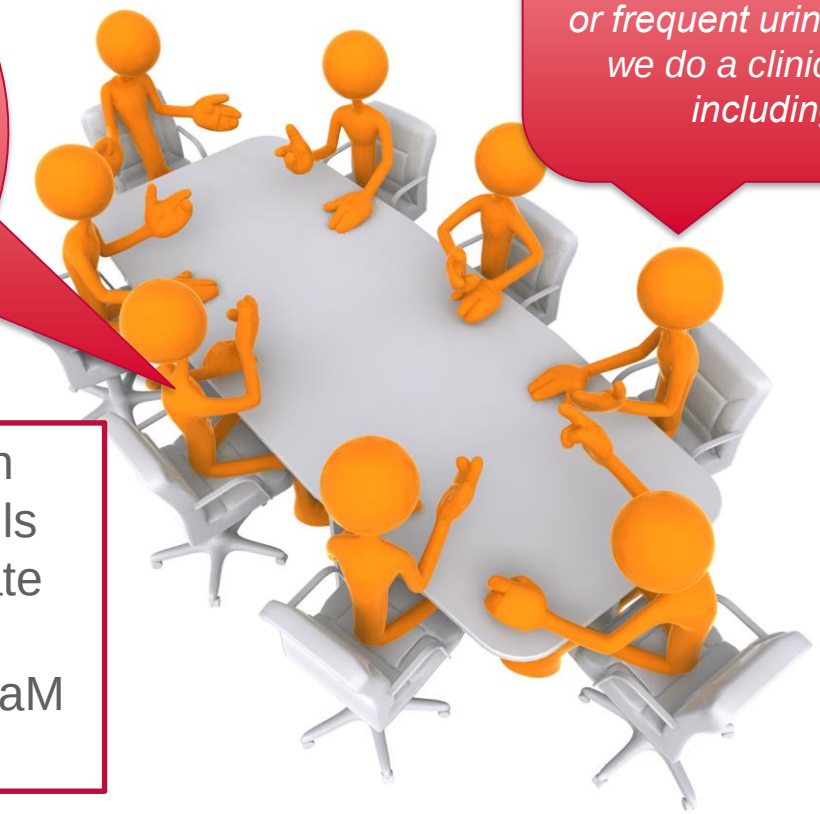
Date	Version
2017-07-10	1.0 Provisional

TAUG TOC

TAUG Development Process

"When we diagnose prostate cancer, the patient usually reports certain symptoms such as painful or frequent urination…then we do a clinical exam, including…"

"Tell me more about the specific tests, what tools are used,how they are performed, what kind of results are obtained."



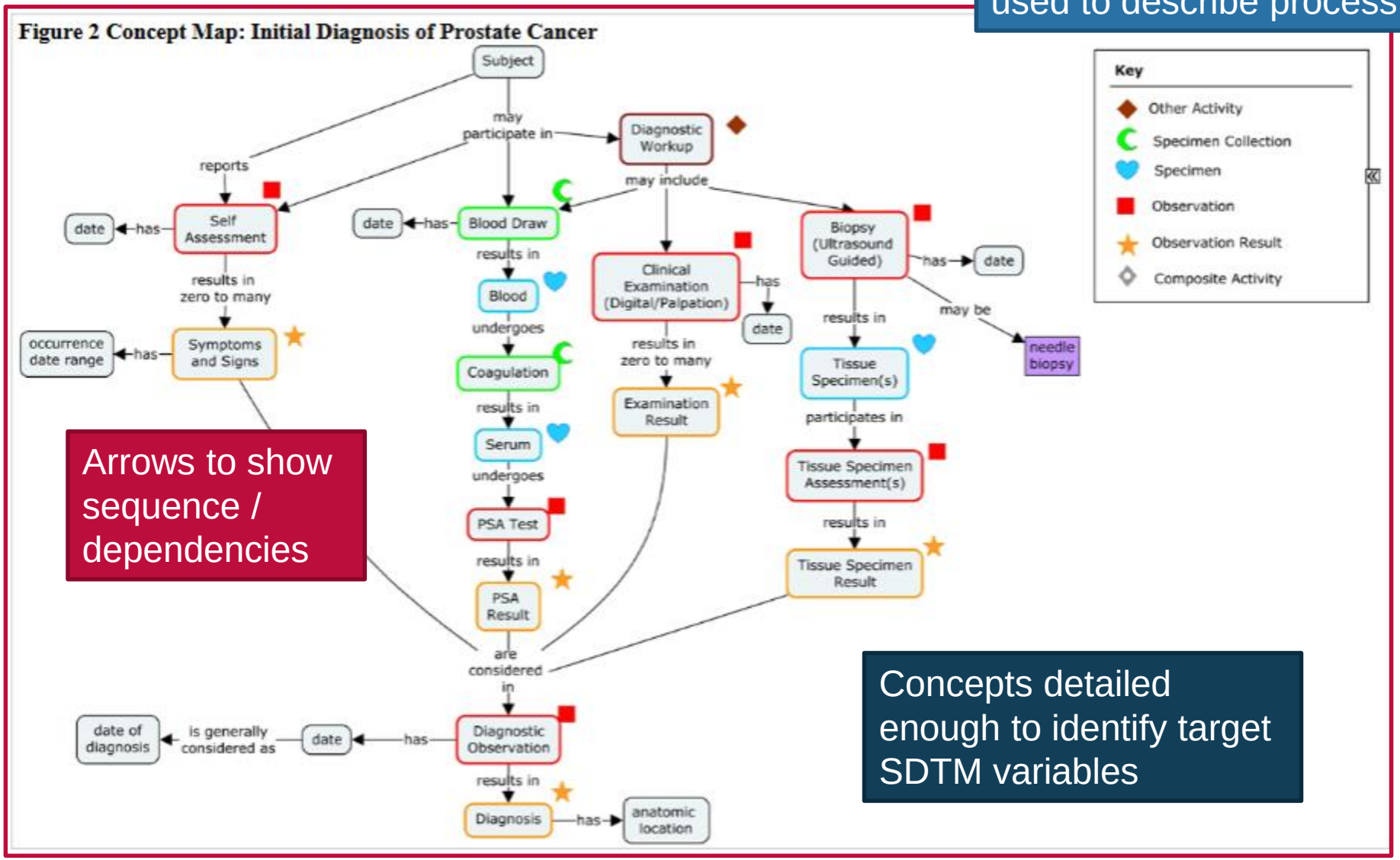
Clinical experts describe the disease population, the diagnostic process, typical treatments, etc.

Data experts listen and probe for details so they can translate the concepts into CDASH/SDTM/ADaM structures

The result of conversations like this are "Concept Maps". Concept Maps are produced for any complex concept to help the standards SMEs translate it to the right data structures.

TAUG Concept Maps

Key to color and shapes used to describe process



TAUG Concept Maps

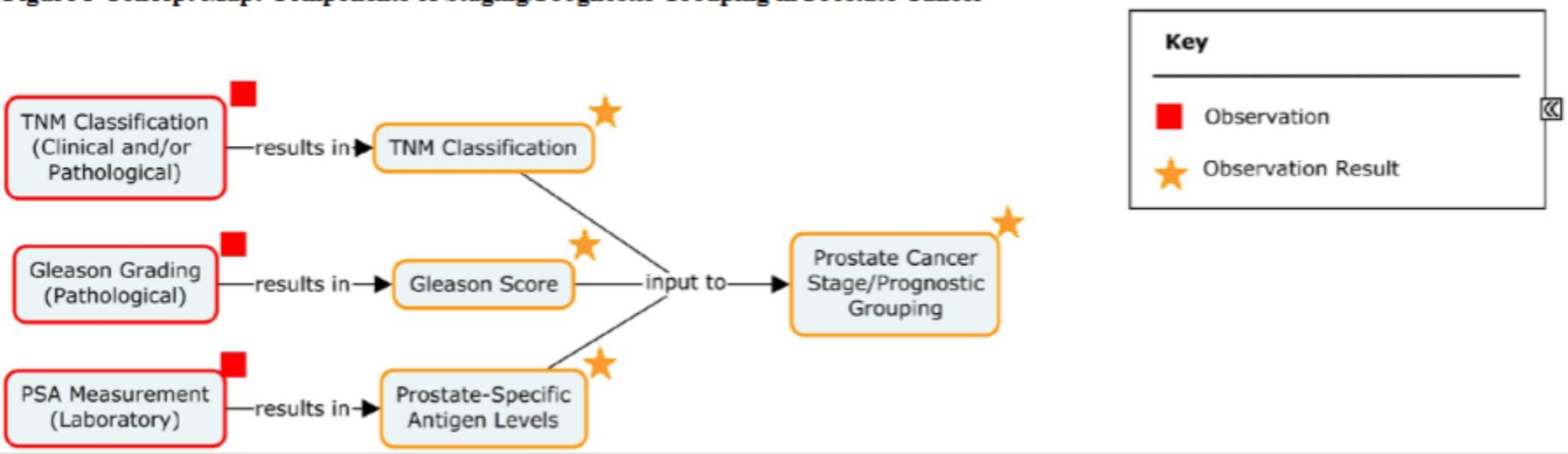
3.2 Staging

Disease staging describes the extent to which the malignancy has spread in the body. It contributes to the determination of treatment options and to the estimation of a patient's prognosis. Below are three components that can be used in prognostic cancer staging/prognostic grouping:

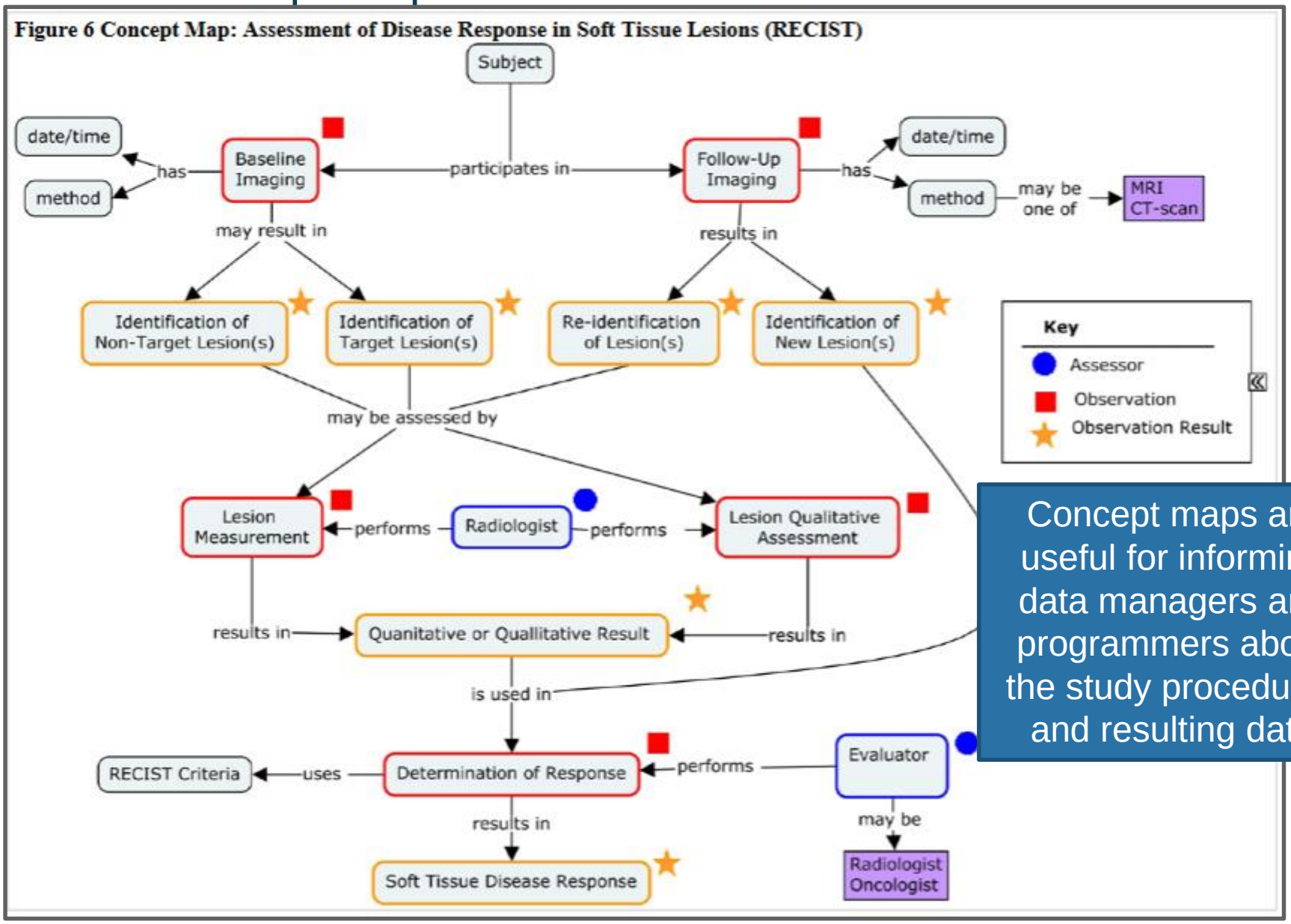
1. TNM Classification based on the American Joint Committee on Cancer (AJCC)'s Cancer Staging Manual
2. Gleason Score that results from microscopic examination of prostate tissue
3. Blood prostate-specific antigen (PSA) level

Concept maps typically have explanatory text published with them.

Figure 3 Concept Map: Components of Staging/Prognostic Grouping in Prostate Cancer

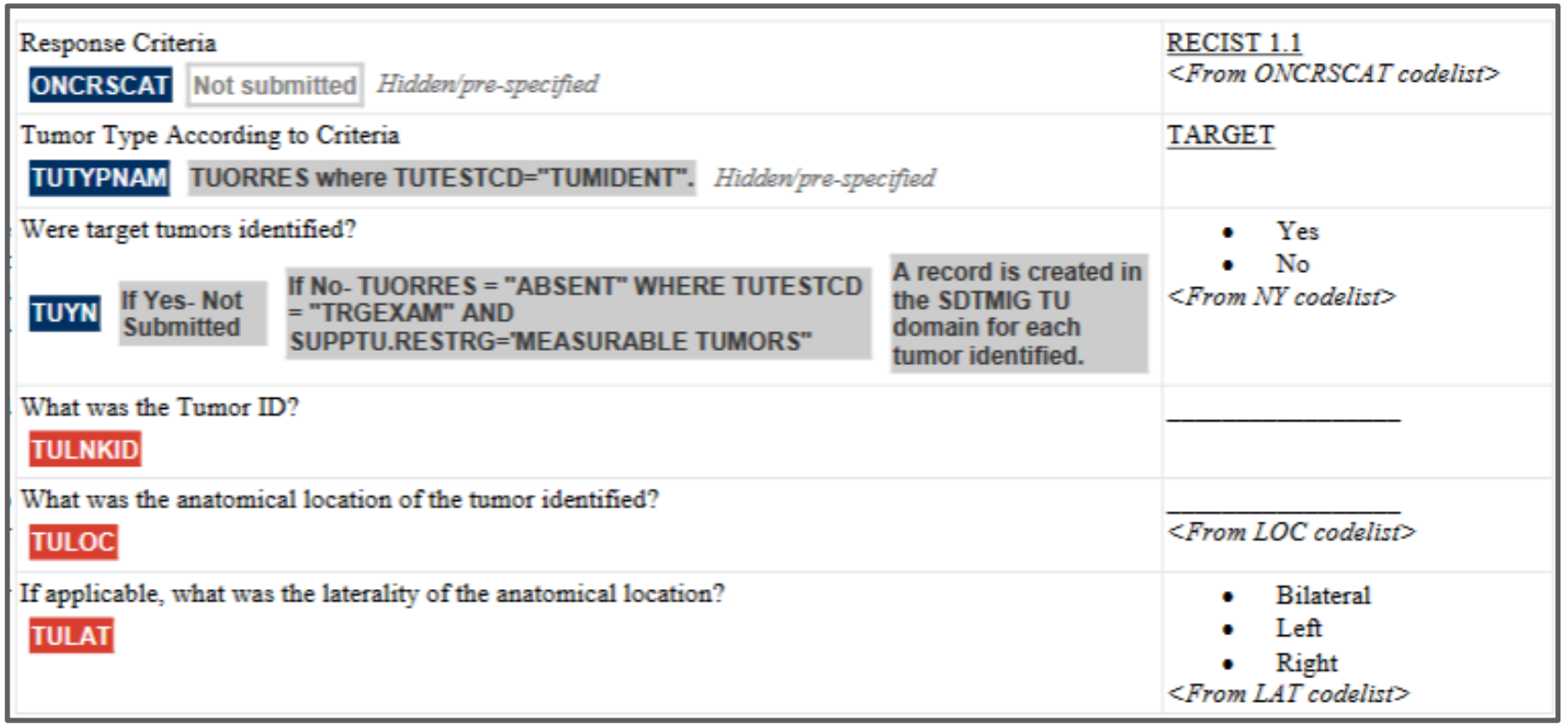


TAUG Concept Maps



Concept maps are useful for informing data managers and programmers about the study procedures and resulting data

TAUG Example Annotated CRFs



Response Criteria ONCRSCAT Not submitted *Hidden/pre-specified*			RECIST 1.1 *<From ONCRSCAT codelist>*
Tumor Type According to Criteria TUTYPNAM TUORRES where TUTESTCD="TUMIDENT". *Hidden/pre-specified*			TARGET
Were target tumors identified? TUYN	If Yes- Not Submitted	If No- TUORRES = "ABSENT" WHERE TUTESTCD = "TRGEXAM" AND SUPPTU.RESTRG='MEASURABLE TUMORS"	A record is created in the SDTMIG TU domain for each tumor identified.	• Yes • No *<From NY codelist>*
What was the Tumor ID? TULNKID				_____
What was the anatomical location of the tumor identified? TULOC				_____ *<From LOC codelist>*
If applicable, what was the laterality of the anatomical location? TULAT				• Bilateral • Left • Right *<From LAT codelist>*

Example CRFs are created and annotated with existing SDTM and CDASH variables.

Prostate Cancer Data Examples - Standard SDTMIG Domains

rs.xpt

Rows 1-2: Show a patient who did not have pre-study radiologic progression but did have PSA progression.

Rows 3-4: Show a patient who had pre-study radiologic progression but not PSA progression.

Rows 5-6: Show a patient who had both radiologic progression and PSA progression pre-study.

rs.xpt

Row	STUDYID	DOMAIN	USUBJID	RSSEQ	RSTESTCD	RSTEST	RSCAT	RSORRES	RSSTRESC	VISITNUM	VISIT	RSDTC	RSDY
1	PRC1220	RS	9001	1	RDIORESP	Radiologic Response	PCWG SCHER PROSTATE CANCER 2016	NON-PD	NON-PD	1	SCREENING	2010-12-03	-5
2	PRC1220	RS	9001	2	TMRESP	Tumor Marker Response	PCWG SCHER PROSTATE CANCER 2016	PD	PD	1	SCREENING	2010-12-03	-5
1	PRC1220	RS	9002	1	RDIORESP	Radiologic Response	PCWG SCHER PROSTATE CANCER 2016	PD	PD	1	SCREENING	2010-11-03	-3
2	PRC1220	RS	9002	2	TMRESP	Tumor Marker Response	PCWG SCHER PROSTATE CANCER 2016	NON-PD	NON-PD	1	SCREENING	2010-11-03	-3
1	PRC1220	RS	9003	1	RDIORESP	Radiologic Response	PCWG SCHER PROSTATE CANCER 2016	PD	PD	1	SCREENING	2010-06-03	-10
2	PRC1220	RS	9003	2	TMRESP	Tumor Marker Response	PCWG SCHER PROSTATE CANCER 2016	PD	PD	1	SCREENING	2010-06-03	-10

Disease specific data examples using existing SDTMIG domains are provided.

lb.xpt

Row	STUDYID	DOMAIN	USUBJID	LBSEQ	LBTESTCD	LBTEST	LBCAT	LBORRES	LBORRESU
1	ABC	LB	ABC-001-001	1	PCA3MRNA	Prostate Cancer Antigen 3 mRNA	URINALYSIS	164.6	10^3 RNA copies/mL
2	ABC	LB	ABC-001-001	2	PSAMRNA	Prostate-Specific Antigen mRNA	URINALYSIS	1870.6	10^3 RNA copies/mL
3	ABC	LB	ABC-001-001	3	PC3MPSAM	PCA3 mRNA/PSA mRNA		88	RATIO
4	ABC	LB	ABC-001-001	4	PRCTC	Prostate Circulating Tumor Cell Count	CHEMISTRY	7	/7.5 mL

Row	LBSTRESC	LBSTRESN	LBSTRESU	LBSPEC	LBSPCCND	LBMETHOD	LBDTC	VISITNUM	VISIT
1 (cont)	164.6	164.6	10^3 RNA copies/mL	URINE		REVERSE TRANSCRIPTASE PCR	2013-02-16	2	Week 2
2 (cont)	1870.6	1870.6	10^3 RNA copies/mL	URINE		REVERSE TRANSCRIPTASE PCR	2013-02-16	2	Week 2
3 (cont)	88	88	RATIO			CALCULATION	2013-02-16	2	Week 2
4 (cont)	7	7	/7.5 mL	BLOOD	ROOM TEMPERATURE	FLUORESCENT IMMUNOASSAY	2013-02-16	2	Week 2

Prostate Cancer Analysis Examples - TTE

6.1 Analysis Endpoints

In oncology trials, many of the commonly used analysis endpoints are based on the derivation of the time to an event, such as death or progression. The derivation of these time-to-event endpoints is based on dates that define the start of the observation period and dates that define the occurrence of the event or the end of the observation period, in the case of censoring. In oncology trials, the date of the start of the observation period is generally easy to identify, but the date associated with the event or censoring may require a detailed comparison of multiple candidate dates. The analysis issues associated with censoring are common to all time-to-event endpoints. Therefore, in the discussion below, issues associated with censoring are discussed within Section 6.1.1.1, Progression-free Survival, and not repeated for subsequent sections.

In addition to time-to-event endpoints, other commonly used analysis endpoints are based on a measure associated with a response, such as best overall response or duration of response. The derivation of these endpoints is based on classification of subjects according to their response to treatment. A typical prostate cancer

Common endpoints for studies in the disease area are used to create ADaM examples

6.1.1 Time to Event

The primary endpoint for a prostate cancer phase III study is typically either overall survival or progression-free survival. These endpoints are usually analyzed using survival analysis methods. The time to the event is usually defined as the time from the start of the study, such as the date of randomization, until an event such as progression disease (PD) or death occurs. The types of events that identify the end of the survival interval in combination with the associated censoring definitions are generally the key differentiators among the different time-to-event endpoints. Other time-to-event endpoints typically include: Event Free Survival, Disease Free Survival, Time to PSA progression: Time to Initiation of Non-Protocol Therapy, Time to First Skeletal-Related Event, Time to Opiate Use, and Time to Pain Progression.

To support the key analysis endpoints, normally the following assessments of prostate cancer status are collected during the course of the trial:

- Overall survival
- Soft tissue on computed tomography (CT) scan or on magnetic resonance imaging (MRI)
- Bone disease on radionuclide bone scans
- Skeletal-related events
- Brief Pain Inventory
- FACT-P and EQ-5D quality of life questionnaires
- PSA

Prostate Cancer Analysis Examples - ADTTE Specification

Example 1

This is an example of ADTTE variable metadata used for time-to-event variables. Note that this example uses the proposed variable PARQUAL and is therefore highlighted in italics. Please refer to the Known Issues section for more information on this variable.

ADTTE Dataset Metadata

Dataset	Description	Class	Structure	Purpose	Keys	Location	Documentation
ADTTE	Time-to-Event Analysis Dataset	BASIC DATA STRUCTURE	One record per subject per parameter	Analysis	STUDYID, USUBJID, PARAMCD	ADTTE.xpt	ADTTE.SAS/SAP

ADTTE Variable Metadata

Variable Name	Variable Label	Type	Codelist/Controlled Terms	Source/Derivation/Comment
STUDYID	Study Identifier	text		ADSL.STUDYID
USUBJID	Unique Subject Identifier	text		ADSL.USUBJID
TRTP	Planned Treatment	text		*Planned Treatment*
PARAM	Parameter	text	Progression-free Survival (months); Overall Survival (months)	*Name of the analysis parameter*
PARQUAL	Parameter Qualifier	text	INVESTIGATOR REVIEW; INDEPENDENT REVIEW	*This identifies the source of the Parameter. "INVESTIGATOR REVIEW" for investigator-based assessments; "INDEPENDENT REVIEW" for Independent Review assessments. Null for OS*
PARAMCD	Parameter Code	text	PFS; OS	Analysis code name corresponding to PARAM. Set to "PFS" if it is progression-free survival based on investigator/independent review data; set to "OS" if it is overall survival.
AVAL	Analysis Value	integer		The numeric value representing the duration (in weeks, months or days) from the original date of risk (such as randomization date or first dose date) to the event or censoring date of the analysis (it could be the last tumor assessment, death, progression disease, or discontinuation from the study date as described in the ADDATE dataset). In this example, randomization date (RANDDT) is used as the initial date of risk and ADT is the date of event or censoring. Thus, AVAL (in months) can be calculated as (ADT - RANDDT + 1)/30.4375

ADaM Specifications for the examples accompany ADaM dataset examples.

Prostate Cancer Analysis Examples - ADTTE Data Example

adtte.xpt

Row	STUDYID	USUBJID	TRTP	PARAM	PARQUAL	PARAMCD	AVAL	CNSR	ADT	EVNTDESC
1	ABC-123	ABC-123-001	A	Progression-free survival (months)	INDEPENDENT REVIEW	PFS	10.8090349075975	0	15OCT2014	Radiographic PD
2	ABC-123	ABC-123-001	A	Progression-free survival (months)	INVESTIGATOR REVIEW	PFS	15.8090349075975	0	20OCT2014	Radiographic PD
3	ABC-123	ABC-123-002	A	Progression-free survival (months)	INDEPENDENT REVIEW	PFS	3.81108829568789	0	07APR2014	Radiographic PD
4	ABC-123	ABC-123-002	A	Progression-free survival (months)	INVESTIGATOR REVIEW	PFS	3.81108829568789	1	07APR2014	No PD or Death
5	ABC-123	ABC-123-003	A	Progression-free survival (months)	INDEPENDENT REVIEW	PFS	25.7905544147844	1	20OCT2016	No PD or Death
6	ABC-123	ABC-123-003	A	Radiographic Progression-free survival (months)	INVESTIGATOR REVIEW	PFS	25.7905544147844	1	20OCT2016	No PD or Death
7	ABC-123	ABC-123-004	A	Progression-free survival (months)	INDEPENDENT REVIEW	PFS	7.68788501026694	1	22MAY2015	No PD or Death
8	ABC-123	ABC-123-004	A	Progression-free survival (months)	INVESTIGATOR REVIEW	PFS	7.68788501026694	1	22MAY2015	No PD or Death
9	ABC-123	ABC-123-005	A	Progression-free survival (months)	INDEPENDENT REVIEW	PFS	11.006160164271	0	13JAN2015	Radiographic PD
10	ABC-123	ABC-123-005	A	Progression-free survival (months)	INVESTIGATOR REVIEW	PFS	11.006160164271	0	13JAN2015	Radiographic PD
11	ABC-123	ABC-123-006	A	Progression-free survival (months)	INDEPENDENT REVIEW	PFS	29.4702258726899	1	19SEP2016	No PD or Death
12	ABC-123	ABC-123-006	A	Progression-free survival (months)	INVESTIGATOR REVIEW	PFS	29.4702258726899	1	19SEP2016	No PD or Death
13	ABC-123	ABC-123-007	A	Progression-free survival (months)	INDEPENDENT REVIEW	PFS	3.21971252566735	1	11AUG2014	No PD or Death
14	ABC-123	ABC-123-007	A	Progression-free survival (months)	INVESTIGATOR REVIEW	PFS	3.21971252566735	1	11AUG2014	No PD or Death

ADaM Specifications for the examples accompany ADaM dataset examples.

Prostate Cancer Analysis Examples - PSA Analysis

The analysis of PSA normally includes the following topics:

Baseline serum PSA	Summarized in the baseline characteristics.
PSA response>=50%	Equal to or more than a 50% reduction in PSA from baseline to any post-baseline PSA values.
PSA response>=50% Confirmed	Equal to or more than a 50% reduction in PSA from baseline to any post-baseline PSA values with a consecutive value that also has a decrease from baseline >= 50%, taken >=3 weeks later.
PSA response>=90%	Equal to or more than a 90% reduction in PSA from baseline to any post-baseline PSA values.
PSA response>=90% Confirmed	Equal to or more than a 90% reduction in PSA from baseline to any post-baseline PSA values with a consecutive value that also has a decrease from baseline >= 90%, taken >=3 weeks later.
Time to PSA progression	PSA progression is defined according to Prostate Cancer Working Group 2 (PCWG2) guidelines. Time to PSA progression is defined as the time from randomization to the date of first PSA value demonstrating progression, which is subsequently confirmed.

Detailed analysis dataset specification and metadata example for PSA analysis can be found in Section 6.3.3, Efficacy Analysis Datasets, Example 2.

Another Prostate Cancer-specific ADaM example

Prostate Cancer Analysis Examples - PSA Analysis

Example 2

This is an example of the ADPSA variable metadata used for analyses associated with PSA assessments.

ADPSA Dataset Metadata

Dataset	Description	Class	Structure	Purpose	Keys	Location	Documentation
ADPSA	PSA Analysis Dataset	BASIC DATA STRUCTURE	One record per subject per parameter	Analysis	STUDYID, USUBJID, PARAMCD	ADPSA.xpt	ADPSA.SAS/SAP

ADPSA Variable Metadata

Variable Name	Variable Label	Type	Codelist/Controlled Terms	Source/Derivation/Comment
STUDYID	Study Identifier	text		ADSL.STUDYID
USUBJID	Unique Subject Identifier	text		ADSL.USUBJID
TRTP	Planned Treatment	text		Planned Treatment
PARCAT1	Parameter Category 1	text	PSA Response; PSA Time to Event	PSA Response if PARAM contains "Response", PSA Time to Event if PARAM contains "Time to"
PARAM	Parameter	text	PSA Response >=50% Total; PSA Response >=50% Confirmed; PSA Response >=90% Total; PSA Response >=90% Confirmed;	These are the parameters used for efficacy analysis. Note that the two percentage values are given only as examples of response levels that may be analyzed

Another Prostate Cancer-specific ADaM example

Prostate Cancer Analysis Examples - PSA Analysis

adpsa.xpt

Rows 1-5: Subject ABC-001002 has PSA response for all definitions (50%, 90%, confirmed, and total) and does not have PSA progression.

Rows 6-10: Subject ABC-001007 has no PSA response but has PSA progression.

adpsa.xpt

Row	STUDYID	USUBJID	TRTP	PARCAT1	PARAM	PARAMCD	AVALC	AVAL	ADT	CNSR	EVNTDESC
1	ABC	ABC-001002	A	PSA Response	PSA Response >=50% Confirmed	PSA50CNF	PSA Response	1	8-Apr-11	.	
2	ABC	ABC-001002	A	PSA Response	PSA Response >=50% Total	PSA50TOT	PSA Response	1	8-Apr-11	.	
3	ABC	ABC-001002	A	PSA Response	PSA Response >=90% Confirmed	PSA90CNF	PSA Response	1	8-Apr-11	.	
4	ABC	ABC-001002	A	PSA Response	PSA Response >=90% Total	PSA90TOT	PSA Response	1	8-Apr-11	.	
5	ABC	ABC-001002	A	PSA Time to Event	Time to PSA Progression (Months)	PSAPROG		30.6201	2-Aug-13	1	Censored - No PSA Progression
6	ABC	ABC-001007	B	PSA Response	PSA Response >=50% Confirmed	PSA50CNF	No PSA Response	0		.	
7	ABC	ABC-001007	B	PSA Response	PSA Response >=50% Total	PSA50TOT	No PSA Response	0		.	
8	ABC	ABC-001007	B	PSA Response	PSA Response >=90% Confirmed	PSA90CNF	No PSA Response	0		.	
9	ABC	ABC-001007	B	PSA Response	PSA Response >=90% Total	PSA90TOT	No PSA Response	0		.	
10	ABC	ABC-001007	B	PSA Time to Event	Time to PSA Progression (Months)	PSAPROG		5.8152	13-Jul-11	0	PSA Progression

PSA could be tracked on a visit level and sponsors could create an intermediate dataset to show the course of PSA values. It is up to the sponsor to create this additional dataset.

Another Prostate Cancer-specific ADaM example

TAUG Custom Domains, NSVs and New Terminology

- When the standards SMEs dive into the details of a particular disease with the clinical experts, they will frequently identify new concepts (i.e. concepts that have not yet been addressed in a CDISC standard).
- When this happens there will be proposed new terminology, new variables or new domains in the TAUG
  - E.g. in the Ebola TAUG we have concepts that are unique to public health: Source Case Investigations and Contact Investigations.
    - A proposed ER domain is published in the Ebola TAUG for this

er.xpt

Row	STUDYID	DOMAIN	USUBJID	ERSEQ	ERTERM	ERCAT	ERPRESP	EROCCUR	ERDTC	ERSTDTC	ERENDTC
1	CDC-11	ER	CDC-01-101	1	Contact with a known or suspect case, or with any sick person	SOURCE CASE INVESTIGATION	Y	Y	2015-02-10	2015-01-15	2015-01-15
2	CDC-11	ER	CDC-01-101	2	Attend a funeral	SOURCE CASE INVESTIGATION	Y	Y	2015-02-10	2015-01-15	2015-01-15
3	CDC-11	ER	CDC-01-101	3	Travel outside their home or village/town	EVD RISK FACTORS	Y	Y	2015-02-10	2015-01-13	2015-01-18
4	CDC-11	ER	CDC-01-101	4	Hospitalized or go to a clinic or visit anyone in the hospital	EVD RISK FACTORS	Y	N	2015-02-10		
5	CDC-11	ER	CDC-01-101	5	Consult a traditional/spiritual healer	EVD RISK FACTORS	Y	N	2015-02-10		
6	CDC-11	ER	CDC-01-101	6	Direct contact (hunt, touch, eat) with animals or uncooked meat	EVD RISK FACTORS	Y	N	2015-02-10		

The ER domain has not yet been published in SDTMIG, so it is a custom domain in any published version of SDTMIG.

Prostate Cancer Data Examples - Custom Domains

tm.xpt

Row 1: Defines the date of the initial diagnosis of prostate cancer as a disease milestone, assigning it the name (MIDSTYPE) "INITDX."

Row 2: Defines the date of the diagnosis of metastatic prostate cancer as a disease milestone.

Row 3: Defines the date of progression after being treated with docetaxel-based chemotherapy as a disease milestone.

tm.xpt

Row	STUDYID	DOMAIN	MIDSTYPE	TMDEF	TMRPT
1	PRC1222	TM	INITDX	Initial Prostate Cancer Dx	N
2	PRC1222	TM	DXMCRPC	Diagnosis of metastatic castration-resistant prostate cancer	N
3	PRC1222	TM	PDAFTDOX	Progression after docetaxel-based chemotherapy regimen	N

sm.xpt

Row 1: Shows the date of initial diagnosis of prostate cancer for Subject 9001.

Row 2: Shows the date of the diagnosis of metastatic castration-resistant prostate cancer for Subject 9001.

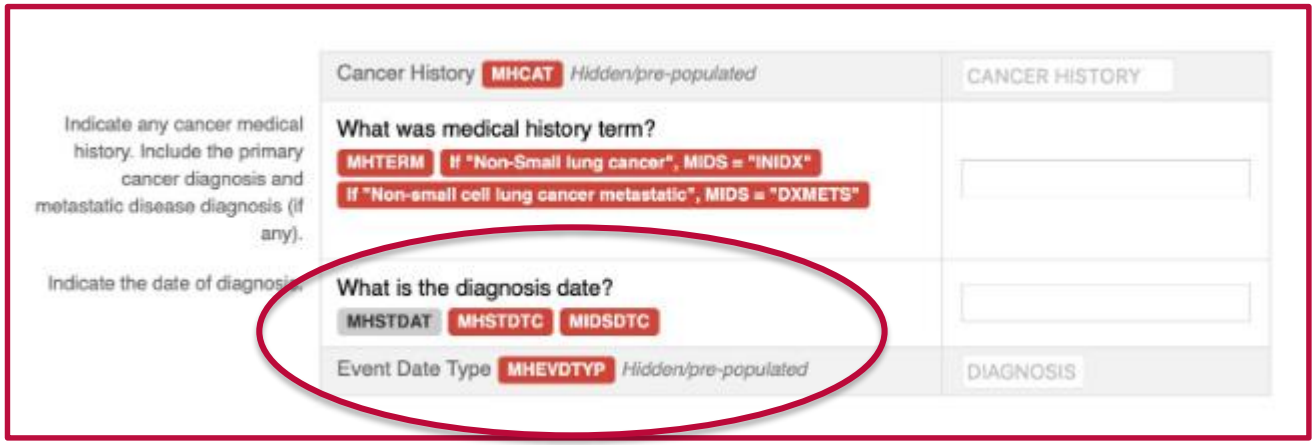
Row 3: Shows the date of diagnosis of progression after being treated with a docetaxel-based chemotherapy for Subject 9001.

sm.xpt

Row	STUDYID	DOMAIN	USUBJID	SMSEQ	MIDSTYPE	MIDS	SMSTDTC	SMENDTC	SMSTDY	SMENDY
1	PRC1222	SM	9001	1	INITDX	INITDX	2007-01-23		-1441	
2	PRC1222	SM	9001	2	DXMCRPC	DXMCRPC	2009-03-08		-666	
3	PRC1222	SM	9001	3	PDAFTDOX	PDAFTDOX	2010-12-03		-32	

Subject Milestone (SM) was a custom domain when the Prostate Cancer TAUG was published (2017), but is now a standard domain in SDTMIG V3.3

TAUG Example Annotated CRFs

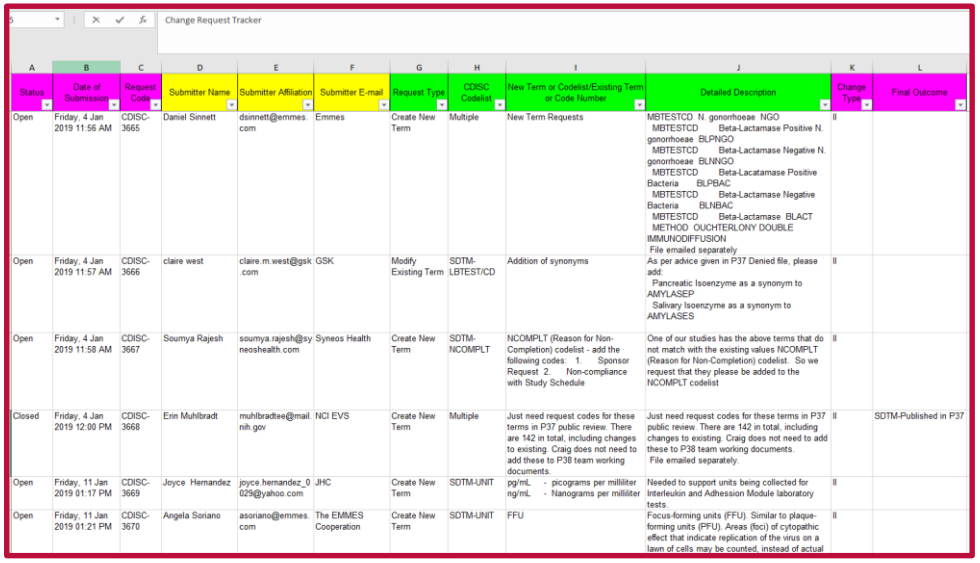


New variables may be identified during this process

e.g., MHEVDTYP was identified through TAUG development and is now a standard SDTM variable.

New Terminology

- Many of the New Term Requests for controlled terminology come from TAUG development
- Terminology liaison is part of every TAUG team
  - Responsible for submitting new term requests for the TAUG team, interfacing with Terminology team to respond to requests for information



Change Request Tracker

Status	Date of Submission	Request Code	Submitter Name	Submitter Affiliation	Submitter E-mail	Request Type	CDISC Codelist	New Term or Codelist/Existing Term or Code Number	Detailed Description	Change Type	Final Outcome
Open	Friday, 4 Jan 2019 11:56 AM	CDISC-3665	Daniel Sinnett	dsinnett@emmes.com	Emmes	Create New Term	Multiple	New Term Requests	MBTESTCD N. gonorrhoeae NGO MBTESTCD Beta-Lactamase Positive N. gonorrhoeae BLPNGO MBTESTCD Beta-Lactamase Negative N. gonorrhoeae BLNNGO MBTESTCD Beta-Lacatamase Positive Bacteria BLPBAC MBTESTCD Beta-Lactamase Negative Bacteria BLNBAC MBTESTCD Beta-Lactamase BLACT METHOD OUCHTERLONY DOUBLE IMMUNODIFFUSION File emailed separately	II	
Open	Friday, 4 Jan 2019 11:57 AM	CDISC-3666	claire west	claire.m.west@gsk.com	GSK	Modify Existing Term	SDTM-LBTEST/CD	Addition of synonyms	As per advice given in P37 Denied file, please add: Pancreatic Isoenzyme as a synonym to AMYLASEP Salivary Isoenzyme as a synonym to AMYLASES	II	
Open	Friday, 4 Jan 2019 11:58 AM	CDISC-3667	Soumya Rajesh	soumya.rajesh@syneoshealth.com	Syneos Health	Create New Term	SDTM-NCOMPLT	NCOMPLT (Reason for Non-Completion) codelist - add the following codes: 1. Sponsor Request 2. Non-compliance with Study Schedule	One of our studies has the above terms that do not match with the existing values NCOMPLT (Reason for Non-Completion) codelist. So we request that they please be added to the NCOMPLT codelist	II	
Closed	Friday, 4 Jan 2019 12:00 PM	CDISC-3668	Erin Muhlbradt	muhlbradtee@mail.nih.gov	NCI EVS	Create New Term	Multiple	Just need request codes for these terms in P37 public review. There are 142 in total, including changes to existing. Craig does not need to add these to P38 team working documents.	Just need request codes for these terms in P37 public review. There are 142 in total, including changes to existing. Craig does not need to add these to P38 team working documents. File emailed separately.	II	SDTM-Published in P37
Open	Friday, 11 Jan 2019 01:17 PM	CDISC-3669	Joyce Hernandez	joyce.hernandez_0029@yahoo.com	JHC	Create New Term	SDTM-UNIT	pg/mL - picograms per milliliter ng/mL - Nanograms per milliliter	Needed to support units being collected for Interleukin and Adhession Module laboratory tests.	II	
Open	Friday, 11 Jan 2019 01:21 PM	CDISC-3670	Angela Soriano	asoriano@emmes.com	The EMMES Cooperation	Create New Term	SDTM-UNIT	FFU	Focus-forming units (FFU). Similar to plaque-forming units (PFU). Areas (foci) of cytopathic effect that indicate replication of the virus on a lawn of cells may be counted, instead of actual	II	

TA Specifications (Excel)

User Guide Section Number	Section Name	Examples, Concept Maps, Tables, Lists	SDTM Domains used	"New" SDTM variables used	Comments
		Concept Map: Initial Diagnosis of Prostate Cancer			
3.2	Staging				
		Concept Map: Components of Staging/Prognostic Grouping in Prostate Cancer			
3.3	Prior Disease Progression or Response Patterns				
		Example 1	RS		
3.4	Pathology				
		Table: Pre-specified Findings			See 3.3 Example 3
		Table: Laboratory and Microscopic Assessments			See 3.3 Example 1
		Table: Genetic/Molecular Analysis			See 3.3 Example 2
		Table: Histology for Prostate Cancer			See 3.3 Example 4
	PCA3 mRNA, PSA mRNA, PCA3 Score, Prostate Circulating Tumor Cell Count	Example 1 (SDTM dataset)	LB		
	Gleason Grading	Concept Map: Detailed Process for Determination of the Gleason Score			
		Example 2 (SDTM databset)	MI		
	Infiltration of the membrane/Extent of the cancer	Example 3 (SDTM dataset)	MI	RESTRG	
	Prostate tissue cores	Example 4 (SDTM dataset)	MI	NUMCOR	
4	Disease assessments				
4.1	Treatments				
		Concept Map: Description of Treatment Options Following Prostate Cancer Diagnosis			
4.2	Disease Assessments and Response for Metastatic Disease				
		Concept Map. Assessment of Disease Response in Soft Tissue Lesions			
		Concept Map: Assessment of Response in Bone Lesions			
		Annotated CRF: Tumor Identification/Results Target Lesions	TU, TR	LNKID, LOCDTL, EVALID	
		Annotated CRF: Tumor Identification/Results Non-Target Lesions	TU, TR	LNKID, LOCDTL, EVALID	

A structured description of content in that TAUG

Important tool for FDA and PMDA to use for testing new TAUGs before they put them in their Technical Conformance Guides as *supported* standards.

When a TAUG is final, the team creates a TA Specification

TA Specification - Summary

TA Specifications (Excel)

Domain Code	Domain Name	SDTMIG v3.1.2	SDTMIG v3.1.2 Amendment 1	SDTMIG v3.1.3	SDTMIG v3.2	Future SDTMIG
AE	Adverse Events	Standard Domain	Standard Domain	Standard Domain	Standard Domain	Standard Domain
CM	Concomitant Medications	Standard Domain	Standard Domain	Standard Domain	Standard Domain	Standard Domain
LB	Laboratory Data	Standard Domain	Standard Domain	Standard Domain	Standard Domain	Standard Domain
MH	Medical History	Standard Domain	Standard Domain	Standard Domain	Standard Domain	Standard Domain
MI	Microscopic Findings	Custom Domain	Custom Domain	Custom Domain	Standard Domain	Standard Domain
PR	Procedures	Custom Domain	Custom Domain	Custom Domain	Standard Domain	Standard Domain
RELREC	Related Records	Standard Domain	Standard Domain	Standard Domain	Standard Domain	Standard Domain
RS	Disease Response	Custom Domain	Custom Domain	Standard Domain	Standard Domain	Standard Domain
SM	Subject Disease Milestones	Custom Domain	Custom Domain	Custom Domain	Custom Domain	Standard Domain
TM	Trial Disease Milestones	Custom Domain	Custom Domain	Custom Domain	Custom Domain	Standard Domain
TR	Tumor Results	Custom Domain	Custom Domain	Standard Domain	Standard Domain	Standard Domain
TU	Tumor Identification	Custom Domain	Custom Domain	Standard Domain	Standard Domain	Standard Domain

List of **domains** used in TAUG and whether they are standard or custom by version of SDTMIG..

TA Specification - Domains

TA Specifications (Excel)

Domain	Variable	Variable Label	Data Type	Controlled Term, Codelist, or Format	SDTM v1.2	SDTMIG v3.1.2 Amendment 1	SDTM v1.3	SDTM v1.4	Future SDTM	Description
AE	LAT	Laterality	Char		NSV (SuppQual)	NSV (SuppQual)	NSV (SuppQual)	Standard	Standard	
AE	CAUSE	Cause of the Event	(text)		NSV (SuppQual)	NSV (SuppQual)	NSV (SuppQual)	NSV (SuppQual)	NSV (SuppQual)	
LB	LNKGRP	Link Group ID	Char		NSV (SuppQual)	NSV (SuppQual)	Standard	Standard	Standard	
MH	EVDTYP	Event Date Type	(text)		NSV (SuppQual)	NSV (SuppQual)	NSV (SuppQual)	NSV (SuppQual)	NSV (SuppQual)	
MH	MIDS	Disease Milestone Instance Name	Char		NSV (SuppQual)	NSV (SuppQual)	NSV (SuppQual)	NSV (SuppQual)	Standard	
MI	TSTDTL	Measurement, Test or Examination Detail	Char		NSV (SuppQual)	NSV (SuppQual)	NSV (SuppQual)	Standard	Standard	
MI	NUMCOR	Number of Cores Collected	(integer)		NSV (SuppQual)	NSV (SuppQual)	NSV (SuppQual)	NSV (SuppQual)	NSV (SuppQual)	The number of core samples ta biopsy procedure.
MI	RESTRG	Pre-Specified Result Targeted by Test	(text)		NSV (SuppQual)	NSV (SuppQual)	NSV (SuppQual)	NSV (SuppQual)	NSV (SuppQual)	Describes the result targeted by the test identified in TESTCD. Used when the measurement, test, or examination indicates the presence or absence of a pre-specified result value.
PR	LAT	Laterality	Char		NSV (SuppQual)	NSV (SuppQual)	NSV (SuppQual)	Standard	Standard	
PR	LNKID	Link ID	Char		NSV (SuppQual)	NSV (SuppQual)	Standard	Standard	Standard	

List of **variables** used in the TAUG that may be non standard in some (or all) published versions of SDTMIG

TA Specification - Variables

TA Specifications (Excel)

CDASH Variable Name, Question Text, and Prompt: The CRF annotations were developed considering the CDASHIG 2.0, and CDASH Model 1.0 that are anticipated to be published. The user is cautioned that the CRF prompt, question text, and CDASH variable name used in this TAUG are subject to change.
Collection of Date of Birth: In several countries, the collection of date of birth is restricted in order to protect patient confidentiality. There are some concepts, for example "Age at Diagnosis," that rely on the date of birth in order for that concept to be derived. Collection of age for these critical age-related data points has been raised to the CDISC SDS committee for discussion on the best way to represent this in SDTM. Guidance on how to collect this information will be provided in future versions of this user guide.
TESTCD= "TRGEXM" and NSV variable RESTRG: RESTRG (Pre-Specified Result Targeted by Test) is used when the finding is pre-specified, and it should be populated with the pre-specified finding of interest. This variable is always used in combination with a --TESTCD of "TRGEXM" and a --TEST of "Targeted Examination". The variable --ORRES is then populated with a value indicating whether or not the pre-specified finding was observed. This modelling strategy was used in the TU domain to indicate whether or not measurable, or non-measurable tumors were "ABSENT" at the initial assessment (e.g., TUTESTCD="TRGEXM" and RESTRG="Measurable Tumors" and TUORRES ="ABSENT"). These variables were also used in the MI domain where TRGEXM is used as the MITESTCD and RESTRG is used to specify the "findings" that were pre-specified. Typically, this was used to model questions of the type "did you see the specified finding". This proposed modelling is under discussion and subject to change.
Use of the PARQUAL Variable: Some ADaM examples make use of PARQUAL, a proposed variable with restricted defined usage currently under consideration by the CDISC ADaM team. Note, however, that this variable is incompatible with the current ADaMIG, which states, "PARAM must include all descriptive and qualifying information relevant to the analysis purpose of the parameter."

Some informative content: **List of Known Issues**

Explanations and caution that what you see in the TAUG may be Provisional until these issues are resolved in a published version of the relevant foundational standard.

TA Specification - Known Issues

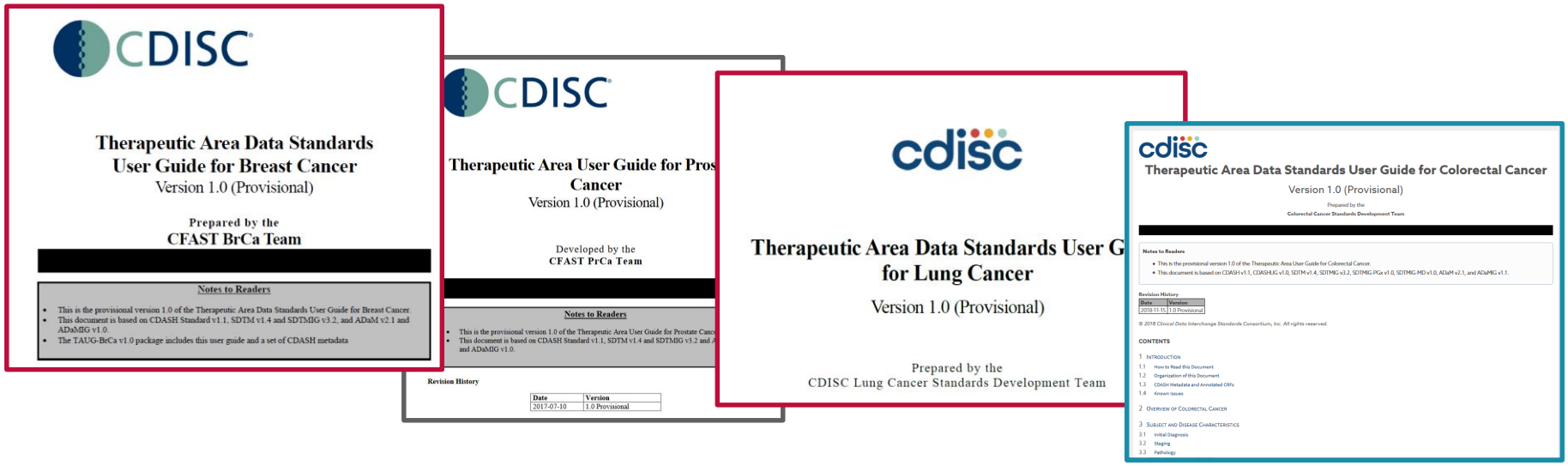
When do TAUGs become Final?

- TAUGs are published as Provisional if there are
  - Custom Domains
  - Non-standard variables
- TAUGs can be published as Final
  - Once non-standard content in a TAUG has been published in the relevant standard(s)
  - No more often than annually (November) when other Final standards are published

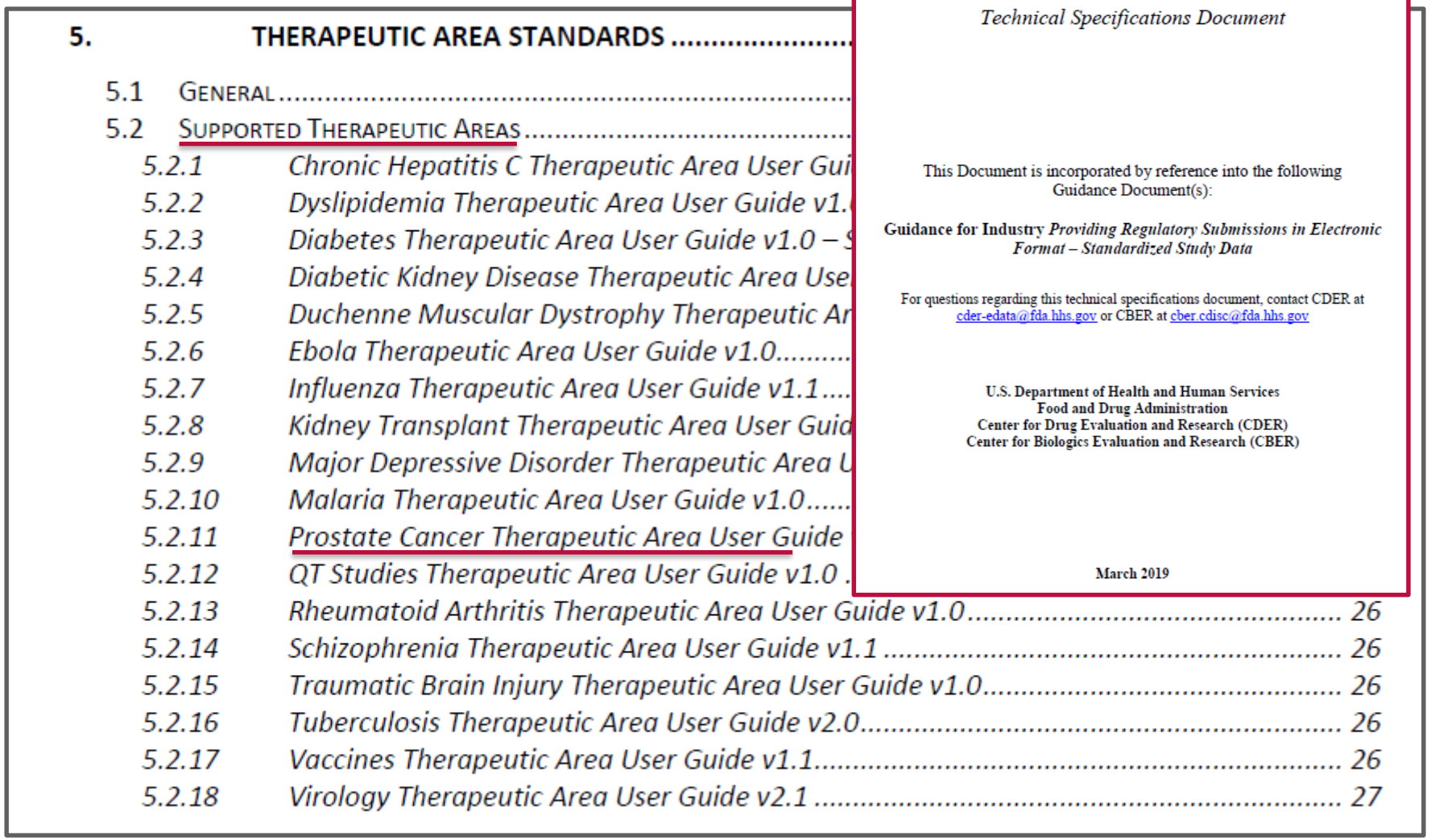
Current Published Oncology TAUGs

- All solid tumor
  - Breast Cancer
  - Lung Cancer
  - Prostate Cancer
  - Colorectal Cancer

Only PrCa currently listed in FDA TCG as “supported”



FDA - Supported TAUGs in Technical Conformance Guide



STUDY DATA
TECHNICAL CONFORMANCE GUIDE

Technical Specifications Document

This Document is incorporated by reference into the following Guidance Document(s):

Guidance for Industry ***Providing Regulatory Submissions in Electronic Format – Standardized Study Data***

For questions regarding this technical specifications document, contact CDER at cder-edata@fda.hhs.gov or CBER at cber.cdisc@fda.hhs.gov

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

March 2019

Current Published Oncology TAUGs

- Breast Cancer
- Lung Cancer
- Prostate Cancer
- Colorectal Cancer

"Supported" means that FDA has tested the TAUG Specification and determined they can accept data modeled after the examples in the TAUG.

Other oncology TAUGs can also be informative and useful for reviewing how the TAUG team handled commonly collected data in these oncology areas.

Some non-oncology TAUGs may have useful information, too.

Tip*: Create a Master File

- Compile a searchable PDF file with all TAUGs included
  - Allows searching by domain or keywords
- Compile a master Excel file from all published TAUG Specifications
  - Allows filtering and sorting

Courtesy of Melissa Mineo, Theradex 2019-05-29

FDA Specifications

- FDA has also published some of their own “TA Specifications”
- These FDA TA Specifications were not developed by CDISC and did not follow the CDISC TAUG development process
  - They were developed “in-house” by FDA
- They address Data and Analysis Specifications that are important to FDA
  - Specifications come from published Guidance
- Published on FDA Study Data Standards Resources page

https://www.fda.gov/industry/fda-resources-data-standards/study-data-standards-resources

FDA TA Specifications

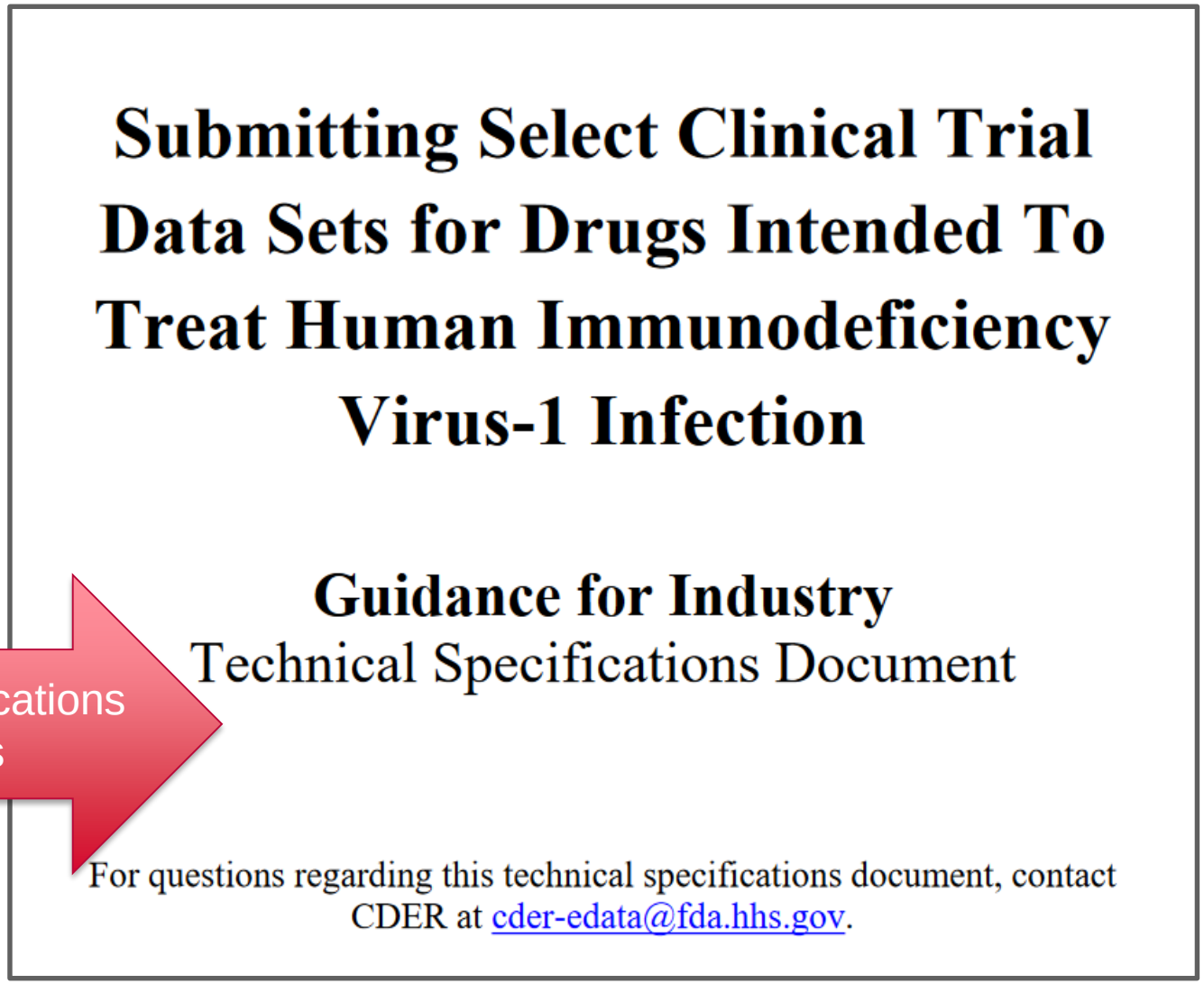
- More prescriptive than CDISC standards because they
  - List the SDTM datasets that are expected
  - Are more focused on what they want to see in ADaM
- Because they are from FDA, they should be considered more as “additional requirements” (unlike CDISC TAUGs)
- Currently only 3 FDA TA Specifications are published
  - HIV (CDER)
  - Vaccines (CBER)
  - BE Clinical Endpoints - ANDAs (CDER)

https://www.fda.gov/industry/fda-resources-data-standards/study-data-standards-resources

FDA TA Specifications

- **Human Immunodeficiency Virus**
  HIV Technical Specifications Guidance v. 1.0 (PDF – 296 KB) (March 2018) - This document provides detailed information and specifications for the content of data sets that should be submitted as part of the sponsor's/applicant's application for drugs intended to treat human immunodeficiency virus (HIV). These specifications also provide an opportunity for dialogue between the sponsor/applicant and reviewers to discuss issues with trial design or study conduct that may affect the content of these analysis data sets. These specifications were built to support the recommendations provided in the guidance for industry entitled "Human Immunodeficiency Virus-1 Infection: Developing Antiretroviral Drugs for Treatment" and reflect the data standards and processes described in the FDA Study Data Technical Conformance Guide.
- **Vaccines**
  Vaccines Technical Specification Guidance v1.0 - This document provides detailed information and specifications for the content of datasets submitted to FDA's CBER Office of Vaccines Research and Review (OVRR). These specifications reflect current CBER OVRR thinking, are built to be consistent with the FDA Study Data Technical Conformance Guide, and are generally consistent with the Therapeutic Area User Guide (TAUG) for Vaccines.
- **Comparative Clinical Endpoint Bioequivalence Studies**
  Clinical Endpoint BE Studies v1.0 – This document provides recommended technical specifications and general considerations on how certain comparative clinical endpoint bioequivalence study data and skin adhesion and irritation/sensitization study data for Abbreviated New Drug Applications (ANDAs) should be submitted using FDA-supported data standards located in the FDA Data Standards Catalog.

FDA TA Specifications



Submitting Select Clinical Trial Data Sets for Drugs Intended To Treat Human Immunodeficiency Virus-1 Infection

Guidance for Industry

Technical Specifications Document

For questions regarding this technical specifications document, contact CDER at cder-edata@fda.hhs.gov.

FDA TA Specifications are PDFs

FDA TA Specifications

FDA TA Specifications

3.1 Baseline Demographic Variables

Variable Name	Variable Label	Type	Comments
STUDYID	Study Identifier	Char	
USUBJID	Unique Subject Identifier	Char	
SUBJID	Subject Identifier for the Study	Char	
SITEID	Study Site Identifier	Char	
SITEGRy	Pooled Site Group y	Char	Character description of the grouping of clinical sites for analysis purposes. All sponsors should start with SITEGR1 and include additional 'y' variables as needed.
INVID	Investigator Identifier	Char	
INVNAM	Investigator Name	Char	
RANDDT	Date of Randomization	Num	
BRTHDTC	Date/Time of Birth	Char	Date/time of birth of the subject in ISO 8601 character format. This date may be partial.
BRTHDT	Date of Birth	Date	Numeric date of birth of the subject with imputation as necessary to account for the collection of a partial date.
AGE	Age	Num	Age expressed in AGEU. Can be derived as (RFSTDTC-BRTHDTC), but BRTHDTC may not be available in all cases (because of subject privacy concerns).
AGEU	Age Units	Char	Expected value: 'Years' Units associated with age. Should be the same across studies when appropriate.
SEX	Sex	Char	Expected values: 'M', 'F' Sex of the subject.
RACE	Race	Char	
RACEGR1	Race Group 1	Char	Expected values: 'WHITE', 'BLACK', 'ASIAN', 'OTHER' This race grouping is required and it is requested that sponsors use this variable name, label, and values.
ETHNIC	Ethnicity	Char	Expected values: 'HISPANIC OR LATINO', 'NOT HISPANIC OR LATINO', 'NOT REPORTED', 'UNKNOWN' Ethnicity of the subject
COUNTRY	Country	Char	Expected values should follow NCI-EVS controlled terminology.
REGION1	Continental Region	Char	This variable indicates the Continent where the study was done
REGIONy	Geographical Region y	Char	This variable indicates the grouping of investigator sites into the "yth" geographical region (REGIONy=REGION2,

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3.4 Study Discontinuation Variables

Variable Name	Variable Label	Type	Comments
EOSSTT	End of Study Status	Char	Expected Values: 'COMPLETED', 'ONGOING', 'DISCONTINUED' End of study status. This should be populated for all subjects. If by the last scheduled visit date before database cutoff date the subject is ongoing, the value of this variable should be set to 'ONGOING'. If the subject completed the study according to the protocol, then the variable should be set at 'COMPLETED'. Otherwise, 'DISCONTINUED'.
EOSDT	End of Study Date	Num	For subjects that discontinued the study, this is the date of study discontinuation. For subjects that completed the study, this is the date of the end of study completion. For ongoing subjects, this should be null.
DCSREAS	Reason for Discontinuation From Study	Char	This variable will be populated only when EOSSTT='DISCONTINUED'.
DCSREASP	Reason Spec for Discont From Study	Char	This optional variable further describes the reason for discontinuation from the study.
DSCCOMM	Comments for Discontinuation	Char	Post-hoc findings of the reasons for discontinuation should be described. For example, It is helpful to provide details for "Withdrawal of consent", "Physician decision", "Patient decision", and "Other" categories.
DSCAEON	Any Ongoing AEs When Study Disc	Char	Expected Values: 'Y', 'N' This variable indicates if there were any AEs that were ongoing at the time of study discontinuation.
DSCAETX	Max Tox Grade of Ongoing AE	Char	Expected Values: '1', '2', '3', '4', '5' The highest toxicity level of any adverse event that was ongoing at the time of study discontinuation.
CDCAEDY	Study Day of First CDC Class C Event	Num	This is the study day of the first treatment emergent CDC Class C event.
DTHDTC	Date of Death	ISO8601	The source of this variable should be DM.DTHDTC.
DTHDT	Date of Death	Num	Numeric date of death based on DM.DTHDTC, using imputation as necessary.

Summary

- We are required to submit to FDA standardized study data tabulations and standardized analysis datasets (Ref: Data Standards Catalog)
  - We *first* have to follow all the rules for foundational standards found in the published SDTMIG, ADaMIG, Controlled Terminology, etc.
  - We also have to follow all the FDA business rules
- TAUGs and TA Specifications are *based on* the CDISC foundational standards and provide specific information about **how to apply the CDISC foundational standards to typical data for specific diseases** and therapy areas
  - https://www.cdisc.org/standards/therapeutic-areas
    - CDISC TAUGs (PDF or HTML)
    - CDISC TA Specifications (Excel)
- Additional FDA TA Specifications are based on FDA Guidance
  - https://www.fda.gov/industry/fda-resources-data-standards/study-data-standards-resources

Q&A

NCICDISCSupport@nih.gov