CHILTERN

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Use TA Guidelines to Optimize Your Standardization Efforts

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New Delhi

Agenda

- **The Therapeutic Area Standards Initiative**
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  - Guidance to Industry
  - Governance
- **Therapeutic Area User Guide (TAUG)**
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  - Resolution of SDTM Modeling Issues
  - Relationship to Other Standards
  - Conclusion

The Therapeutic Area Standards Initiative

- Launched by the Food and Drug Administration as part of Prescription Drug User Fee Act V (PDUFA V) performance goals.
- Ensure engagement and input of key authoritative clinical and medical professional societies in TA projects.
- Adopt or adapt existing standards where possible.
- Use a well-defined data standards governance function.

The Therapeutic Area Standards Initiative Project Plan: Objectives

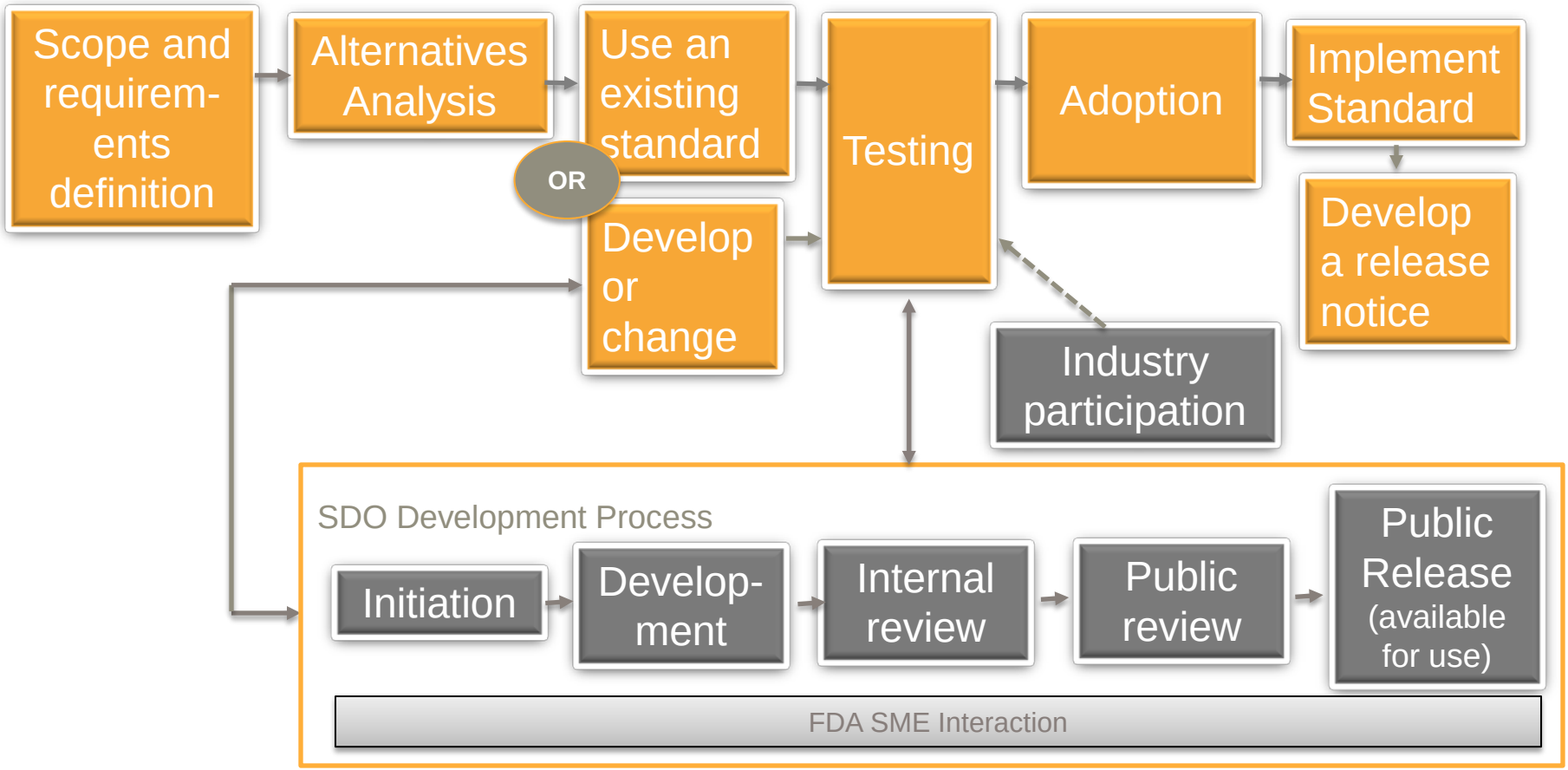
Establish and implement standards that support FDA's recommendations

Use an open and transparent process

Express TA recommendations in sustainable standards

Implement in guidance

Collaborative Standard Development Process



Selection of Therapeutic Areas (TAs)

- FDA's Center for Drug Evaluation and Research (CDER) and Center for Biologics Evaluation and Research (CBER) compiled a prioritized list of disease and therapeutic areas (TAs) for additional data standardization.

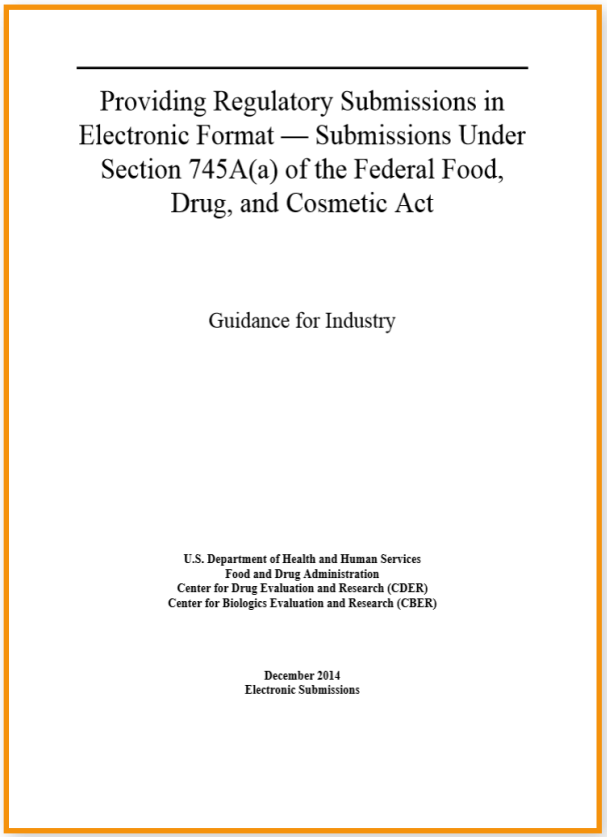
- Key factors considered in the identification and prioritization of these areas:

Number and type of active investigational new drug applications (INDs)

Existing standardization projects underway

Industry input on drug development pipeline activity

Guidance to Industry

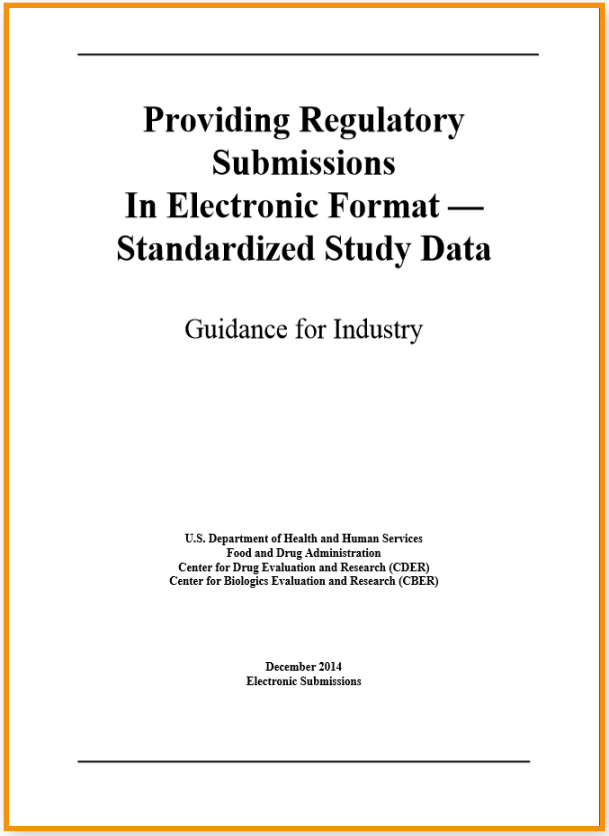


Providing Regulatory Submissions in Electronic Format — Submissions Under Section 745A(a) of the Federal Food, Drug, and Cosmetic Act

Guidance for Industry

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)

December 2014
Electronic Submissions

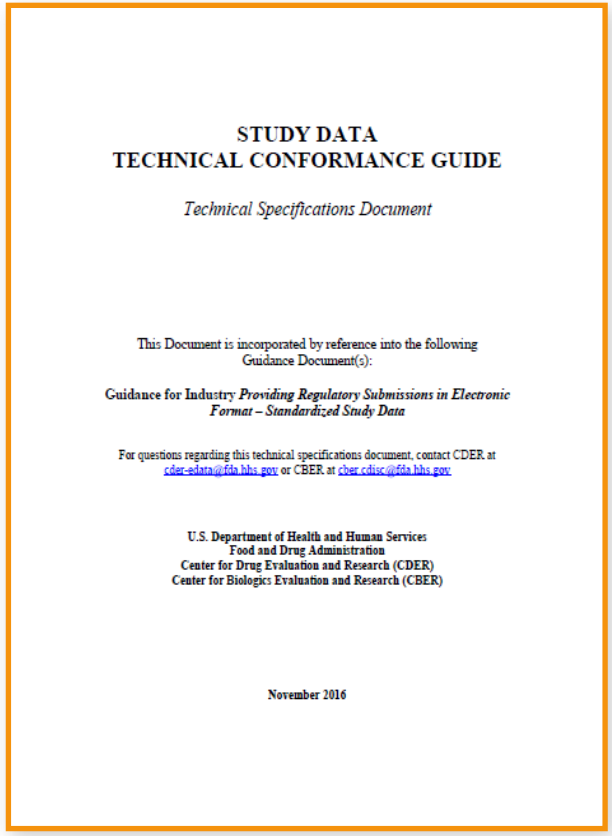


Providing Regulatory Submissions In Electronic Format — Standardized Study Data

Guidance for Industry

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)

December 2014
Electronic Submissions



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)

November 2016

Governance

- Data Standards Program Board (DSPB)
- The DSPB provides the leadership and oversight to guide FDA's overall data standards strategy, and ensures that its objectives are accomplished.

Internal Governance

- The Coalition for Accelerating Standards & Therapies (CFAST)
- Drives development of Therapeutic Area User Guides (TAUGs).

External Governance

Risk Management

FDA's recommendations for TAS have not been clearly articulated and vetted internally and/or externally.

SCOPE

Accountability for the TAS development process may not be clear across all stakeholders.

PROCESS

Personnel with the requisite skills to complete all project deliverables on time and with the highest quality may not be available.

RESOURCES

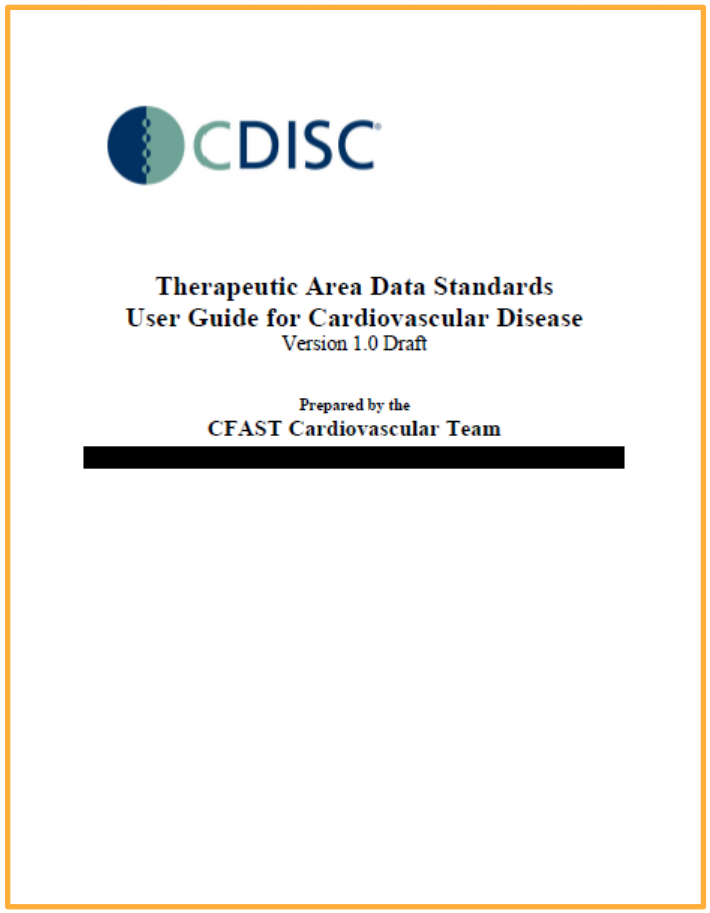
External stakeholder partnerships may not be able to sustain the development of TA projects due to financial constraints and/or insufficient staffing

STAKEHOLDER MANAGEMENT

Therapeutic Area User Guide (TAUG)

- Focus – identify core TA concepts and translate into CDISC standards
- SDTM mapping of key TA endpoints results in
  - New domains/variables
  - New control terminology
  - Modelling strategies
- Domains used in TAUGs are distributed across:
  - SDTMIG v3.2
  - SDTMIG Medical Devices v1.0
  - SDTMIG Associated Persons v1.0
  - TAUG draft domains not in any SDTMIG

Cardiovascular Therapeutic Area User Guide (TAUG-CV)



- The CV TAUG describes the most common data needed for CV studies for reporting of endpoints.
- Defines research concepts unambiguously, to allow use of consistent terminology in CV studies to enable aggregation and comparison of data across studies and drug programs.
- New draft domain - Cardiovascular Physiology (CV).

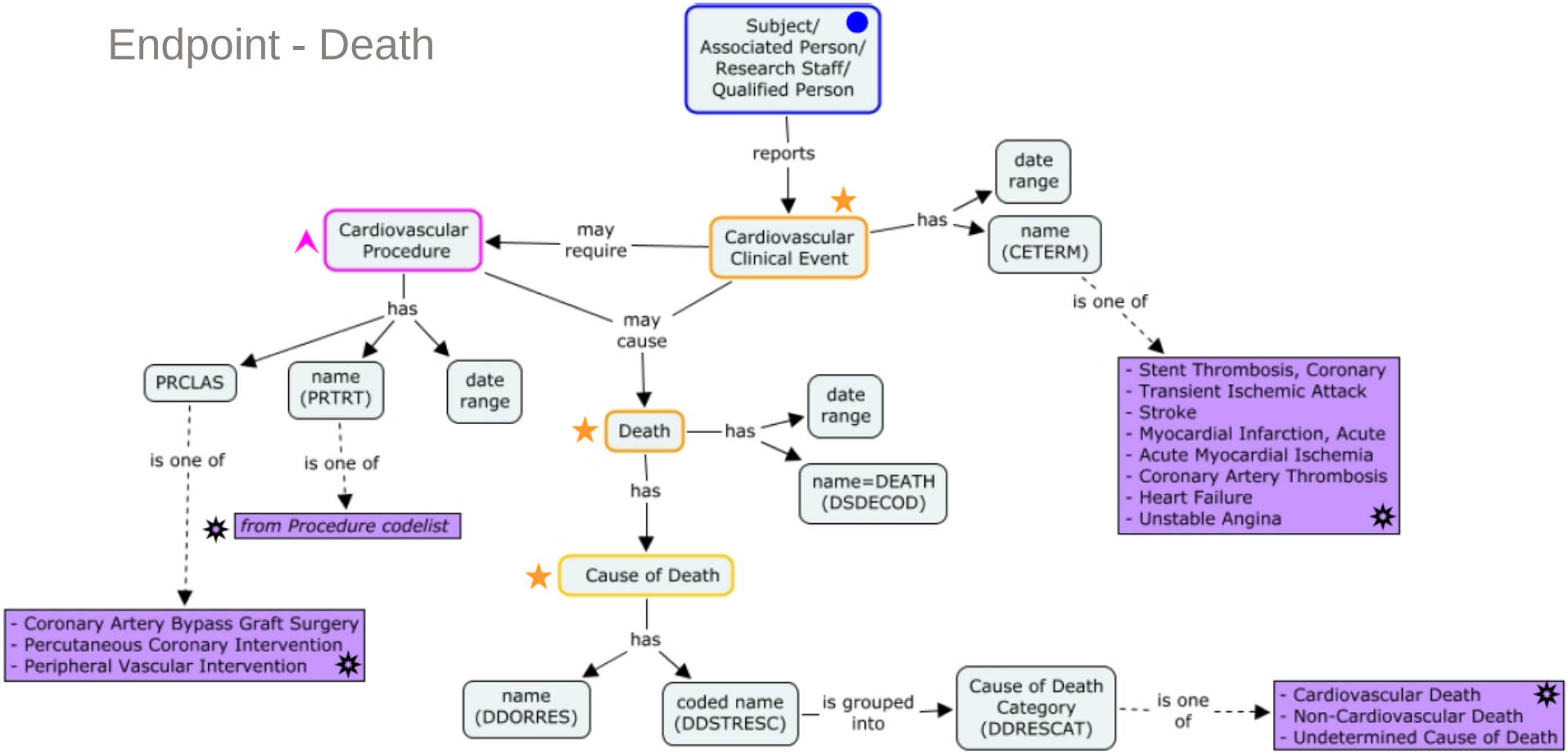
Disease Assessments

- Acute Coronary Syndrome (ACS)

- Cardiovascular Endpoints:
  - Death
  - Adjudication of Events
  - Myocardial Infarction
  - Percutaneous Coronary Intervention
  - Peripheral Vascular Intervention
  - Heart Failure Event
  - Unstable Angina Hospitalization Event

Disease Assessments – Concept Maps

Endpoint - Death



Disease Assessments – Dataset Representation

- Representation of the examples in form of datasets – quick reference to programmers
- Ease the understanding of data and provides guidance of accurate representation of therapeutic area specific data in SDTM domains.

ds.xpt

Row	STUDYID	DOMAIN	USUBJID	DSSEQ	DSLNKID	DSTERM	DSDECOD	DSCAT	DSDTC	DSSTDTC
1	STUDY01	DS	40945	1	DTH-1	Death due to stroke	DEATH	DISPOSITION EVENT	2007-11-27	2007-11-27

dd.xpt

Row	STUDYID	DOMAIN	USUBJID	DDSEQ	DDLNKID	DDTESTCD	DDTEST	DDORRES	DDSTRESC
1	STUDY01	DD	40945	1	DTH-1	PRCDTH	Primary Cause of Death	DEATH DUE TO STROKE	CARDIOVASCULAR: STROKE
2	STUDY01	DD	40945	2	DTH-1	SECDTH	Secondary Cause of Death	KIDNEY FAILURE	RENAL FAILURE

Row	DDRESCAT	VISITNUM	DDDTC
1 (cont)	CARDIOVASCULAR DEATH	9	2007-11-27
2 (cont)	NON-CARDIOVASCULAR DEATH	9	2007-11-27

Endpoint – Death

Disposition domain captures death as an event and Death Details captures death category and other details

Resolution of SDTM Modelling Issues

Cardiovascular Lesions

Issue

- The TU (Tumor Identification) and TR (Tumor Results) domains are specific to oncology data. Where should the Cardiovascular Lesions mapped?

Solution

- Populate the lesion data in the existing (Tumor Identification) TU and (Tumor Results) TR domains instead of creating new domains for non oncology data.
- The TU and TR domain names will be revised in the next version of the SDTMIG to Tumor and Lesion Identification (TU) and Tumor and Lesion Results (TR).

Resolution of SDTM Modelling Issues

Adverse Events vs Clinical Event

Issue

- Cardiovascular events expected in CV Endpoint studies should be recorded as an adverse event or a clinical event in SDTM?

Solution

- They should be clinical events when being evaluated as a CV Endpoint, since they are expected to occur in CV Endpoint studies.
- They should be mapped to CE domain and not AE.

Resolution of SDTM Modelling Issues

Adjudicated Data

Issue

- The SDTM IG doesn't provide guidance on adjudicated events and findings.

Solution

- Following variables are added in the relevant domains:
  - --EVAL (Evaluator Identification)
  - --EVALID (Multiple Evaluator Identification)
  - --ACPTFL (Accepted Evaluation)

Relationship to Other Standards

- This TAUG does not replace the foundational CDISC standards or their implementation guides.
- The user should be well versed with SDTM IG before applying the advice in this user guide.
- The TAUG uses the Cardiovascular Physiology (CV) domain, which is draft domain that has not appeared prior to TAUG-CV. Being a draft domain, it is subject to change or deletion without formal notice.

Conclusion

- The development of Therapeutic Area Data Standards is accelerating the data standards optimization.
- Several new domains, variables and modeling strategies are evolving with the development of these Therapeutic Area User Guidelines.
- The TA standards can also aid in standardizing the designing of e-CRF for the TA specific elements and hence cover the gaps for a successful clinical trial life cycle.

References

- Therapeutic Area Standards Initiative Project Plan

http://www.fda.gov/downloads/drugs/developmentapprovalprocess/formssubmissionrequirements/electronicsubmissions/ucm371691.pdf

- CV Therapeutic Area User Guideline

https://www.cdisc.org/cardiovascular-studies-therapeutic-area

- FDA Guidance to Industry

http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm064994.htm

- Study Data Technical Conformance Guide

http://www.fda.gov/ForIndustry/DataStandards/StudyDataStandards/default.htm

Questions?

Thank you!

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