A Synopsis of Study Data Technical Conformance Guide

- Make sure Nothing is lost during submission

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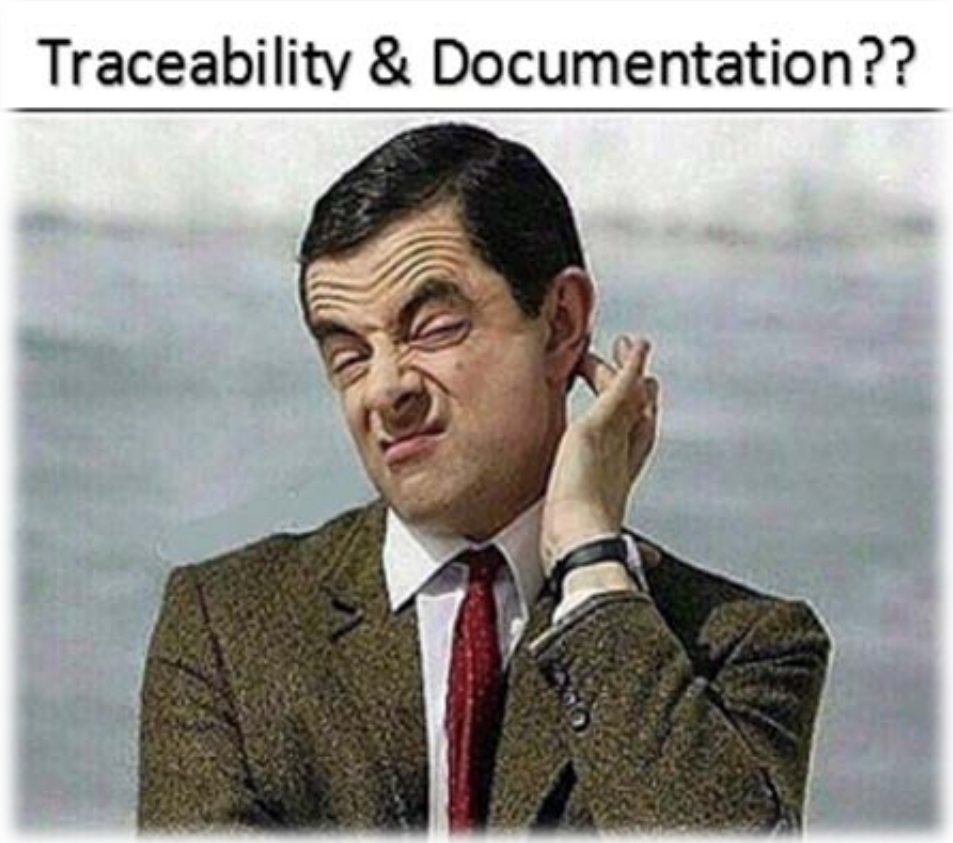
PhUSE SDE
22nd April, 2017
Bengaluru, India

CHILTERN
Designed Around You®

Data Standardization & Traceability

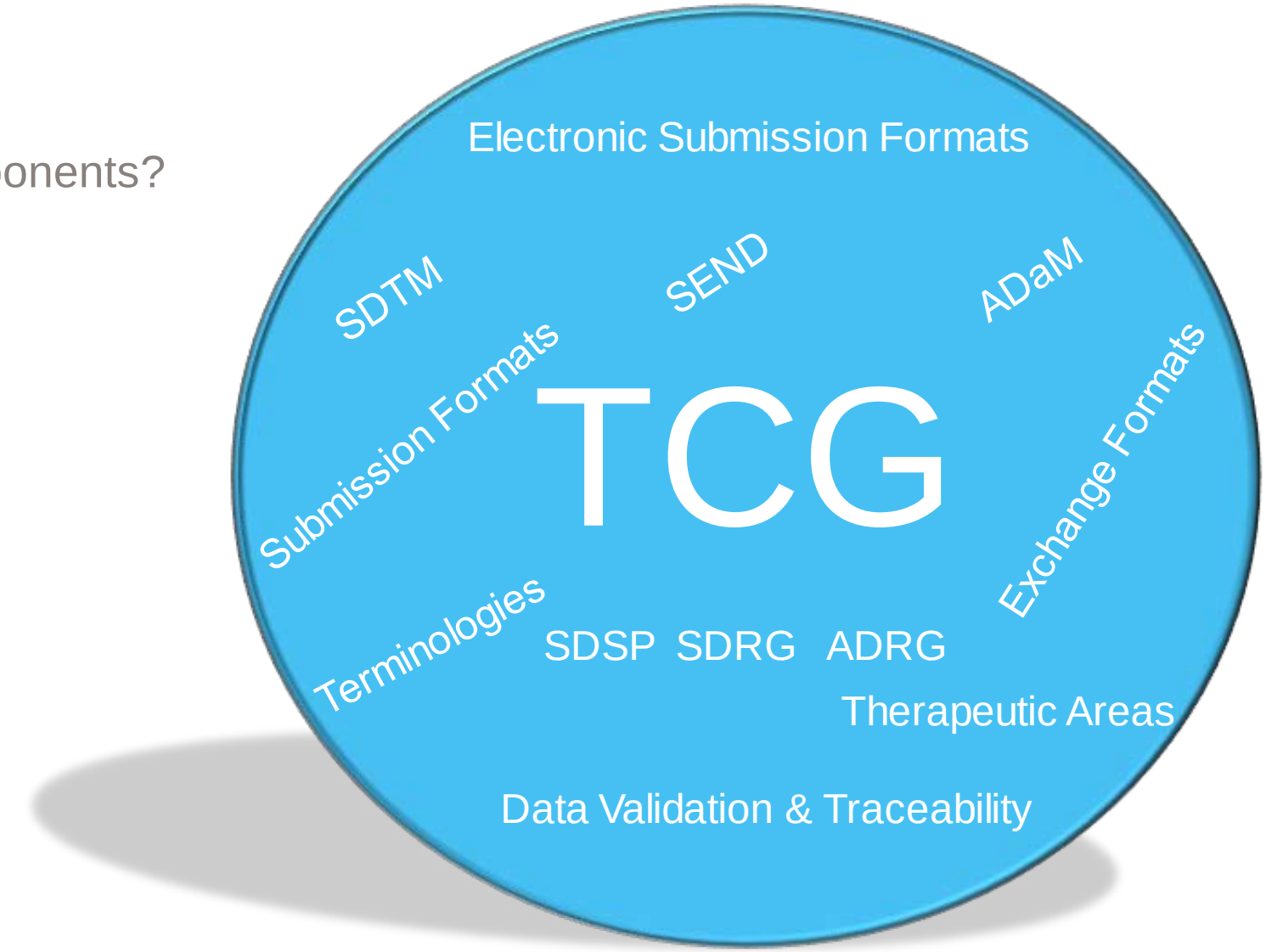
```
Number of Observations with Some Compared Variables Unequal: 0.
Number of Observations with All Compared Variables Equal: 135.

NOTE: No unequal values were found. All values compared are exactly equal.
```

"No unequal values" messages are NOT just sufficient!!!



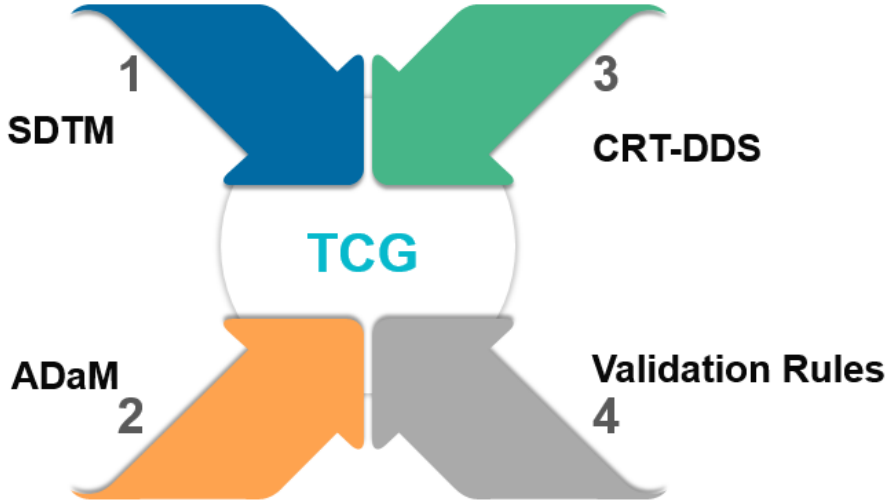
The Agenda

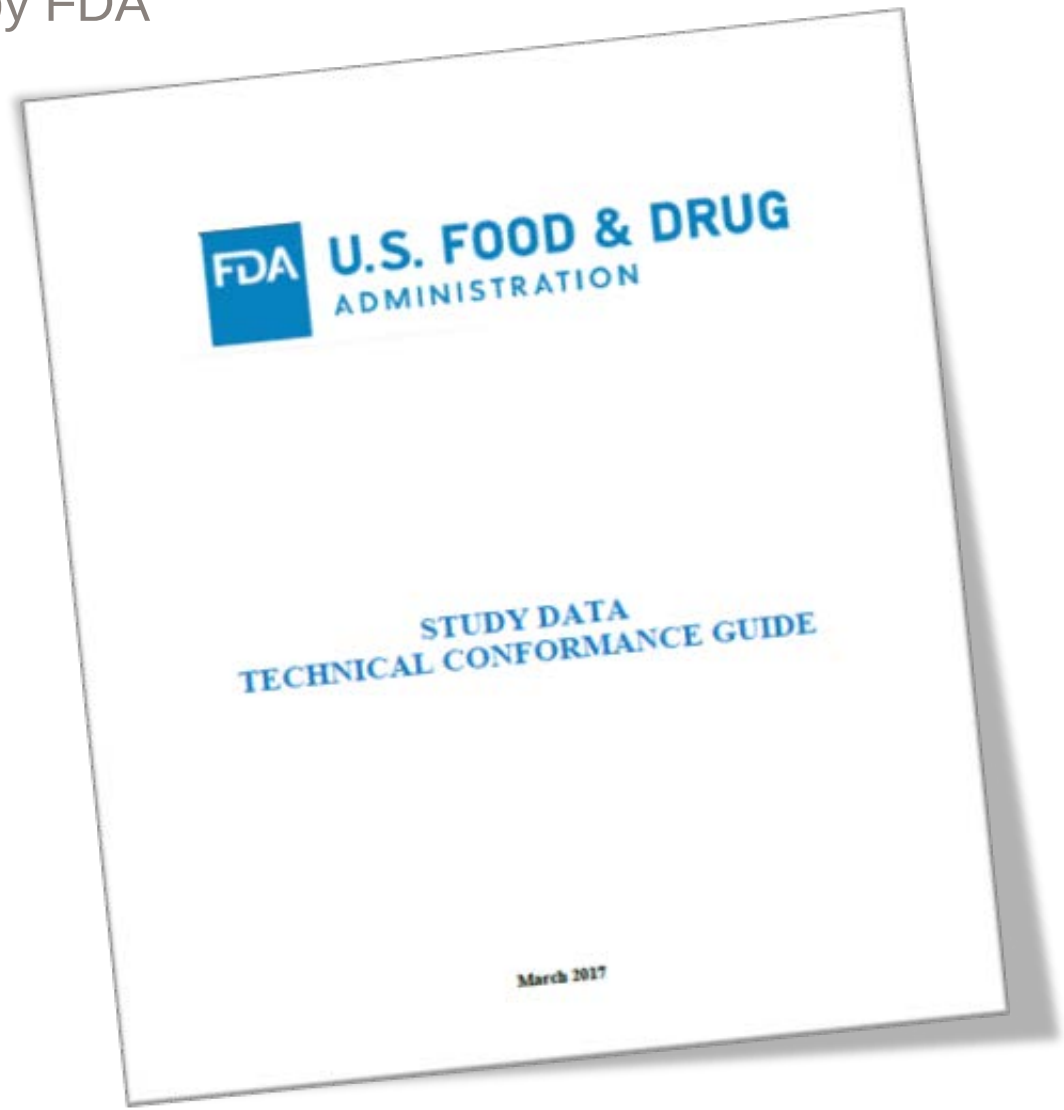
- What is TCG?
- Why do we need?
- How to apply the core components?
- What is new in v3.3?
- Conclusion



What is TCG?

- Study Data Technical Conformance Guide published by FDA
- Provides technical specifications, recommendations and general considerations on standardized data in IND, NDA, ANDA and BLA
- Promotes interactions between sponsors and FDA

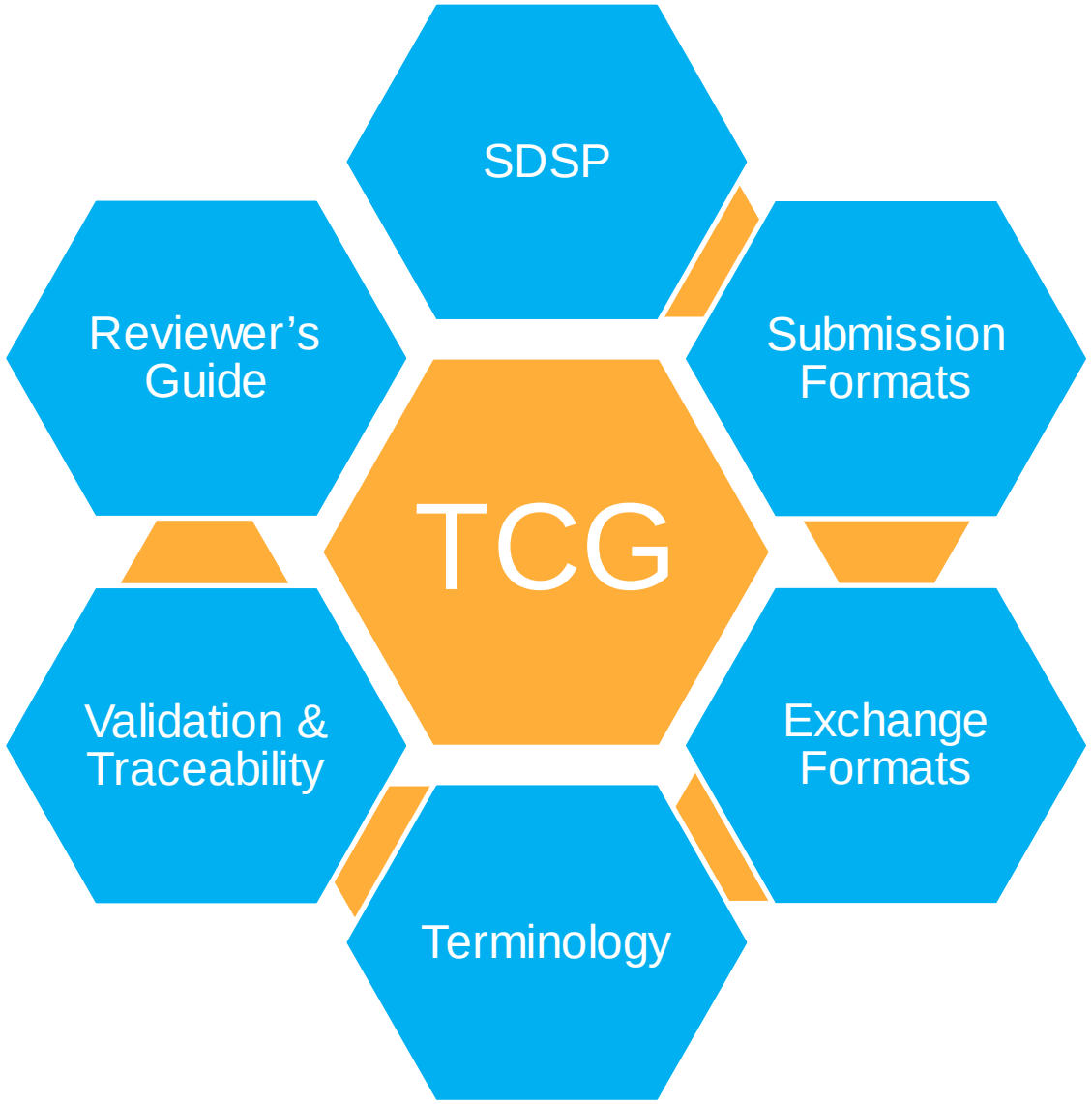




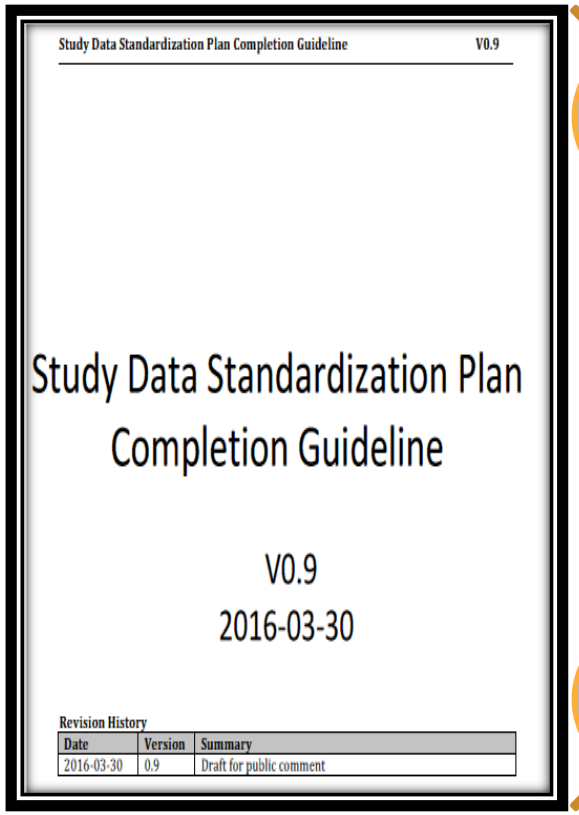
Why do we need?

- To ensure that submitted data are both compliant and useful
- From **December 17th, 2016** - CDISC compliant data is mandatory
- The FDA may refuse to file (RTF) for NDAs and BLAs, or refuse to receive (RTR) for ANDAs
- In 2015, FDA refused to receive 14 % of submissions.
- Around 71 submissions are refused due to Technical reasons

Core components of TCG



Study Data Standardization Plan


Study Data Standardization Plan Completion Guideline V0.9

Study Data Standardization Plan Completion Guideline

V0.9

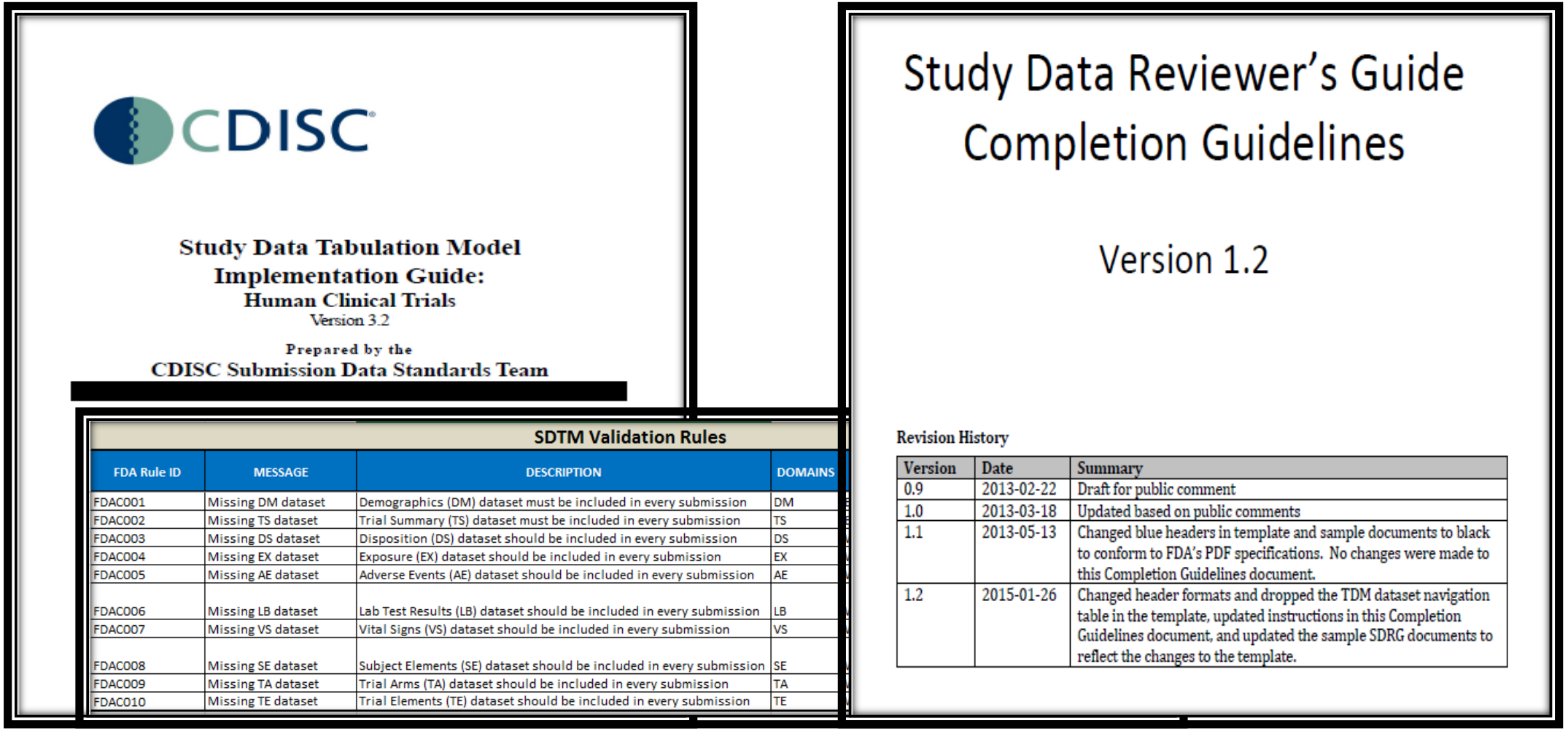
2016-03-30

Revision History

Date	Version	Summary
2016-03-30	0.9	Draft for public comment

- Planned studies
- Study type
- Study design
- Data standards, Formats, Terminologies & their versions

SDTM Outlook



CDISC

Study Data Tabulation Model Implementation Guide:
Human Clinical Trials
Version 3.2

Prepared by the
CDISC Submission Data Standards Team

SDTM Validation Rules

FDA Rule ID	MESSAGE	DESCRIPTION	DOMAINS
FDAC001	Missing DM dataset	Demographics (DM) dataset must be included in every submission	DM
FDAC002	Missing TS dataset	Trial Summary (TS) dataset must be included in every submission	TS
FDAC003	Missing DS dataset	Disposition (DS) dataset should be included in every submission	DS
FDAC004	Missing EX dataset	Exposure (EX) dataset should be included in every submission	EX
FDAC005	Missing AE dataset	Adverse Events (AE) dataset should be included in every submission	AE
FDAC006	Missing LB dataset	Lab Test Results (LB) dataset should be included in every submission	LB
FDAC007	Missing VS dataset	Vital Signs (VS) dataset should be included in every submission	VS
FDAC008	Missing SE dataset	Subject Elements (SE) dataset should be included in every submission	SE
FDAC009	Missing TA dataset	Trial Arms (TA) dataset should be included in every submission	TA
FDAC010	Missing TE dataset	Trial Elements (TE) dataset should be included in every submission	TE

Study Data Reviewer's Guide
Completion Guidelines

Version 1.2

Revision History

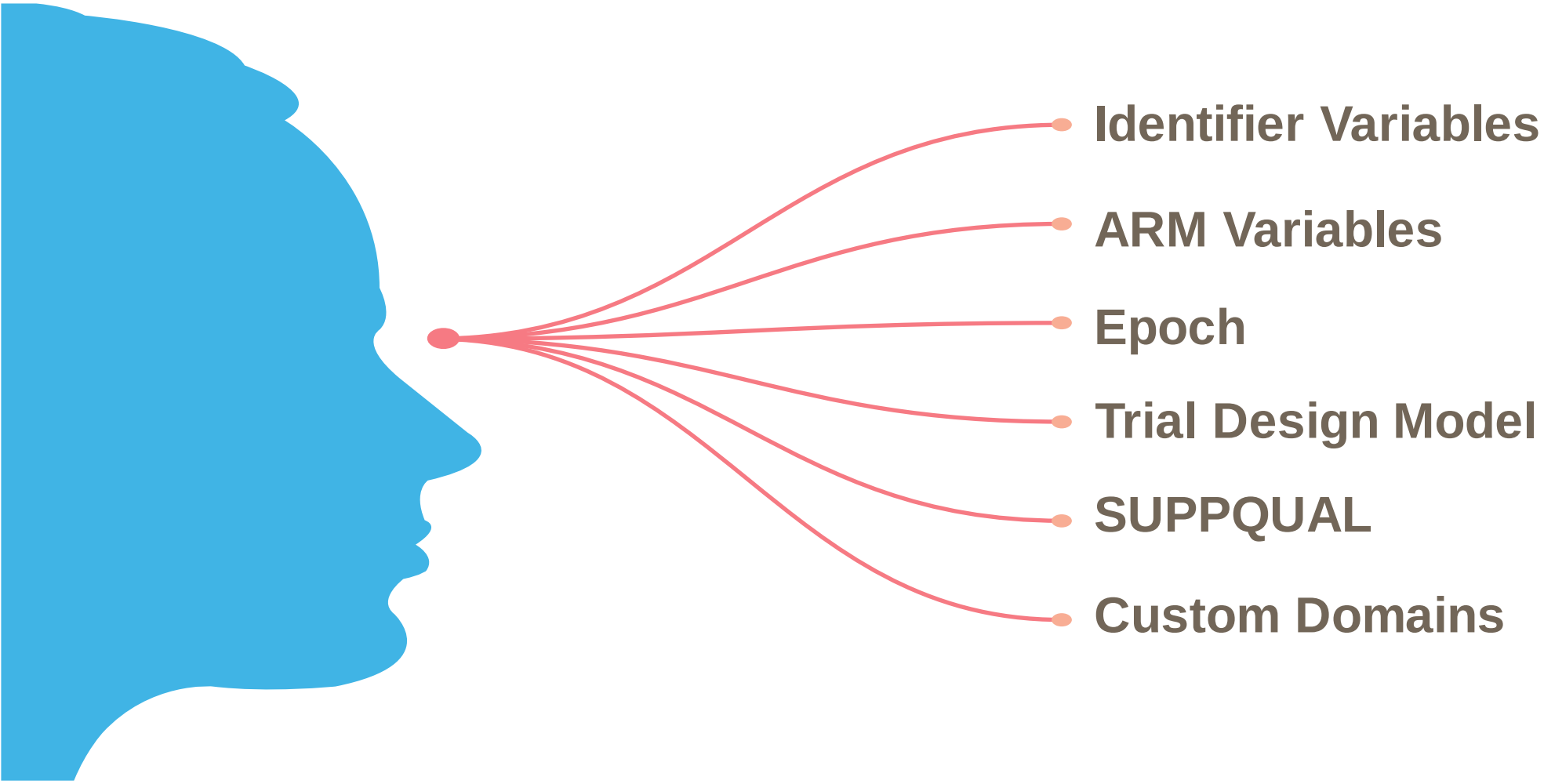
Version	Date	Summary
0.9	2013-02-22	Draft for public comment
1.0	2013-03-18	Updated based on public comments
1.1	2013-05-13	Changed blue headers in template and sample documents to black to conform to FDA's PDF specifications. No changes were made to this Completion Guidelines document.
1.2	2015-01-26	Changed header formats and dropped the TDM dataset navigation table in the template, updated instructions in this Completion Guidelines document, and updated the sample SDRG documents to reflect the changes to the template.

SDTM Outlook - Exchange Formats

Exchange Formats					
Use Case	**Standard**	**Format**	**Supported Version**	**IG Version / Reference sources**	**Requirement Begins (MM/DD/YYYY)**
Documents	PDF	PDF	1.4 - 1.7	For CDER and CBER only: Portable Document Format (PDF) Specifications	
Clinical study data sets - Transport	XPORT	XPT	5	SAS Technical Support TS-140	
Clinical study datasets	SDTM	XPT	1.4	3.2	03/15/2018 [1] 03/15/2019 [2]
Clinical study datasets	SDTM	XPT	1.3	3.1.3	12/17/2017 [2]
Clinical study datasets	SDTM	XPT	1.2	Version 3.1.2 Amendment 1	12/17/2016 [1] 12/17/2017 [2]
Clinical study datasets	SDTM	XPT	1.2	3.1.2	12/17/2016 [1] 12/17/2017 [2]
Study data definition	Define	XML	2	N/A	12/17/2016 [1] 12/17/2017 [2]
Terminology					
Use Case	**Standard**	**Type**	**SDO**	**Version(s)**	**Requirement Begins (MM/DD/YYYY)**
SDTM domains	CDISC CT	General Clinical Data	NCI	2011-06-10 or later	12/17/2016 [1] 12/17/2017 [2]
AE Domain	MedDRA	Adverse Events	MSSO	8 or later	12/17/2016 [1] 12/17/2017 [2]
CMDECOD and CMCLAS	WHO DD	Medication	WHO	Latest Version	03/15/2018 [1] 03/15/2019 [2]
LBLOINC	LOINC	Laboratory Tests	Regenstrief Institute	Latest Version	03/15/2018 [1] 03/15/2019 [2]
CMDECOD and TSVAL where TSPARMCD is TRT or CURTRT or COMPTRT.	UNII	Substances, ingredients & moieties	FDA	Latest Version	12/17/2016 [1] 12/17/2017 [2] 05/06/2004 [3]
CMCLAS, TSVAL where TSPARMCD=PCLAS and TSPARM = Pharmacologic Class.	NDF-RT	Pharmacological Class	VHA	Latest Version	12/17/2016 [1] 12/17/2017 [2]
TSVAL where TSPARMCD=INDIC	SNOMED CT	Indication and Usage	IHTSDO		12/17/2016 [1] 12/17/2017 [2]

[1] For NDAs, ANDAs, and certain BLAs.
[2] For certain INDs.

SDTM Outlook - Submission Format



SDTM Outlook - .xpt Format

Dataset

- Size: Should be < 5 GB (if >5 then split by - -CAT and - -SCAT)
- Length: Name – 8, Label - 40

Variable

- Length: Name – 8, Label - 40
- Set to maximum length of the variable used across all datasets

Value

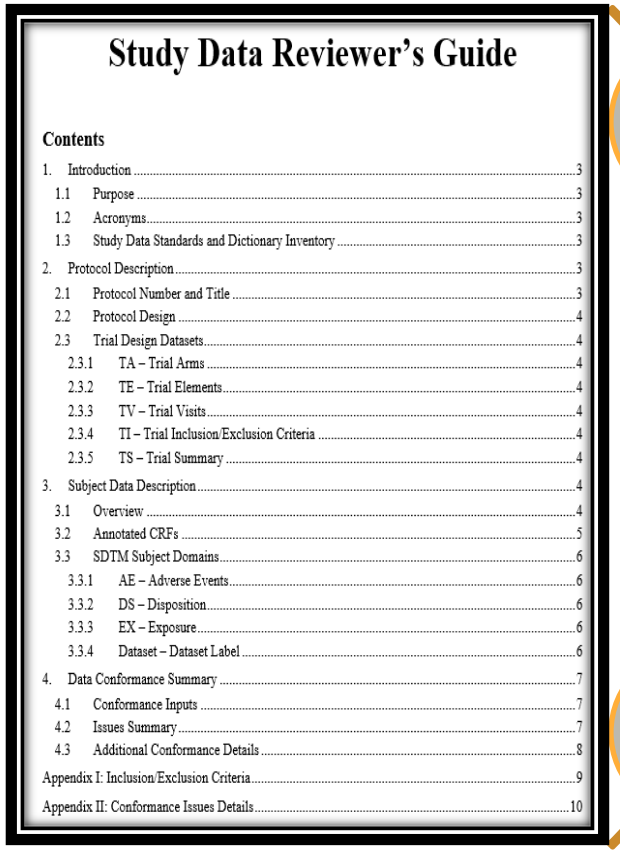
- - -TESTCD/ETCD: 8
- ARMCD/ACTARMCD: 20

Avoid

- Name: Punctuation, Dashes, Spaces, Non-alphanumeric
- Label: Unbalanced apostrophe, parenthesis, “<“ , “>”

Use ASCII text codes only!

SDTM Outlook - SDRG



Study Data Reviewer's Guide

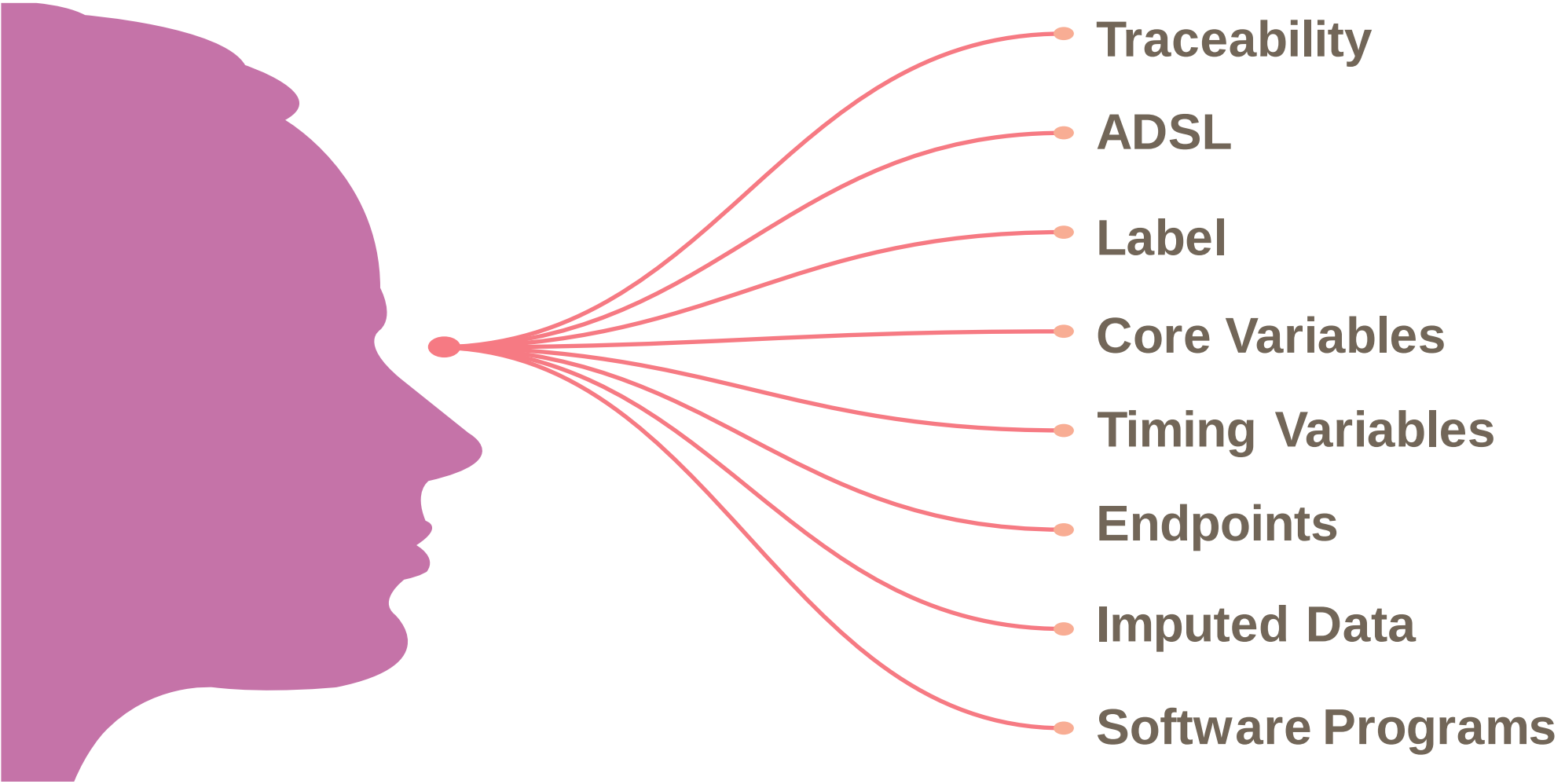
Contents

- Introduction
- Protocol Description
- Subject Data Description
- Data Conformance Summary

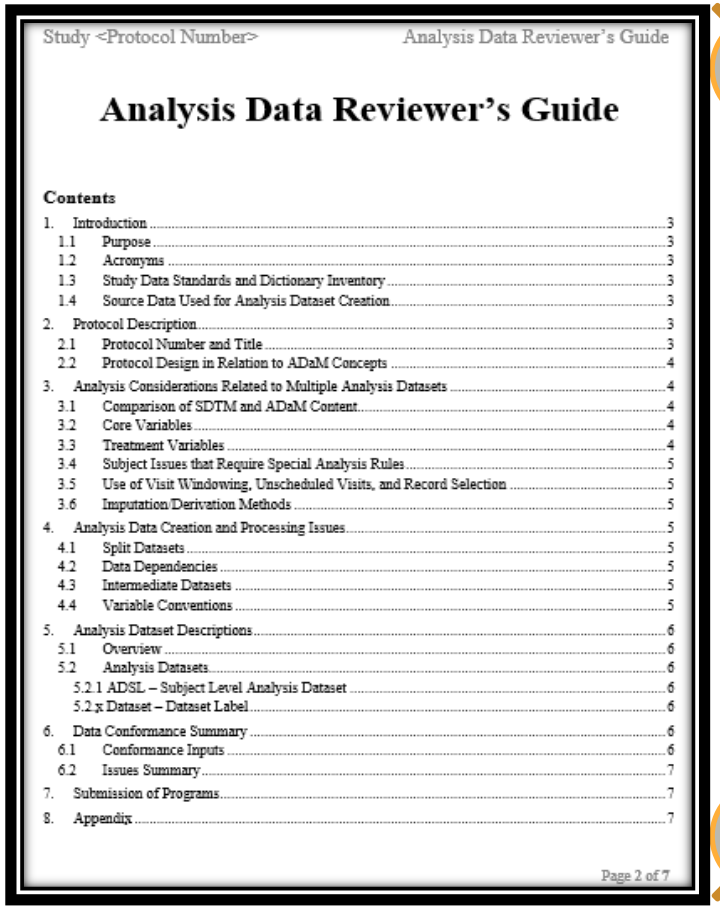
ADaM Outlook

- ADaM datasets should be used
  - To create and to support the results in CSR
  - Integrated Summaries of Safety (ISS) and Integrated Summaries of Efficacy (ISE)
  - Analysis required for a thorough regulatory review
- ADaM datasets can contain imputed data or data derived from SDTM datasets
- Intention is to perform minimal programing while reporting
- Attributes to be kept unchanged for SDTM variables in ADaM

ADaM Outlook



ADaM Outlook - ADRG


Study <Protocol Number> Analysis Data Reviewer's Guide

Analysis Data Reviewer's Guide

Contents

Page 2 of 7

- Introduction
- Protocol Description
- Considerations related to Multiple Analysis
- Data Creation and Processing Issues
- Dataset Descriptions
- Data Conformance Summary
- Submission of Programs

Electronic Submission Package

- aCRF
- Define.xml + SDRG
- SDTM Datasets
- Overall Reviewer's Guide
- ADaM Datasets
- Define.xml + ADRG
- Subject Profiles
- Miscellaneous Datasets

What's new in v3.3?

Naming convention:

- For the reviewer's guide the file names are modified as cSDRG.pdf, nSDRG.pdf and adrg.pdf

Clarification on DS:

- When there is more than one disposition event, the EPOCH or DSSCAT variable should be used to aid in distinguishing between them

Use case of VISITDY:

- For MA, MI, OM, to Indicate groupings of grace day data collections using the VISITDY variable in the DS domain
- For in-life findings, to indicate grouping of measurements across grace days when measurements are grouped in the Study Report

New supported TAs added:

- Diabetic Kidney Disease, Ebola, Kidney Transplant, Malaria and Rheumatoid Arthritis

Recap & Conclusion

- FDA will validate submissions upon receipt and will assess conformance to required study data standards
- Benefits from Good submission package: Less agency questions and Accelerate approval
- Technical Conformance Guide is a key document to help you get it right
- Some of documents or rules are only recommended in current version, but it may be changed in the future version
- **"In your data submissions, you should follow the most recent Technical Conformance Guide."**

Glossary

- **ANDA:** Abbreviated New Drug Application
- **ASCII:** American Standard Code for Information Interchange
- **BLA:** Biologics License Application
- **CBER:** Center for Biologics Evaluation and Research
- **CDER:** Center for Drug Evaluation and Research
- **eCTD:** Electronic Common Technical Document
- **IHTSDO:** International Health Terminology Standards Development Organization
- **IND:** Investigational New Drug
- **LOINC:** Logical Observation Identifiers Names and Codes
- **MSSO:** Maintenance and Support Services Organization
- **NCI:** National Cancer Institute
- **NDA:** New Drug Application
- **NDF-RT:** National Drug File – Reference Terminology
- **SNOMED:** Systematized Nomenclature of Medicine
- **UNII:** FDA Unique Ingrédient Identifier
- **VHA:** Veterans Health Administration

Questions & Discussion

Contact

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