FDA-CTP AND CDISC DEVELOP TOBACCO DATA STANDARDS TO ACHIEVE EFFICIENCIES FOR ALL STAKEHOLDERS

Presented by
Chrissie Cai
Data Quality Management Team Supervisor
Division of Regulatory Science Informatics
Office of Science, CTP, FDA

Presented by
Christine Connolly
Head of Standards Projects, CDISC

19 October 2023

CENTER FOR TOBACCO PRODUCTS

CTP Data Standards

- Regulatory Background
- CTP Data Standards Strategy
- Benefits

CDISC Data Standards

- Tobacco Implementation Guide (TIG v1.0)
- TIG v1.0 Progress and Innovation Highlights
- TIG v1.0 Examples

CTP DATA STANDARDS

THE TOBACCO CONTROL ACT BECAME LAW ON JUNE 22, 2009

FDA's goal is to reduce the harm from all regulated tobacco products across the entire U.S. population:

- Reducing the number of people who start using tobacco products
- Encouraging more people to stop using these products
- Reducing the adverse health impact for those who continue to use these products

THE TOBACCO CONTROL ACT'S AUTHORITIES

The Tobacco Control Act amended the Federal Food, Drug, and Cosmetic Act (FD&C) to provide FDA authority for:

- Premarket review of new and modified risk tobacco products
- Postmarket surveillance
- Product standards
- Testing and reporting of ingredients
- Reporting of harmful and potentially harmful constituents
- Adverse event reporting
- New warning labels
- Advertising and promotion restrictions
- User fees

FDA'S TOBACCO REGULATORY AUTHORITIES

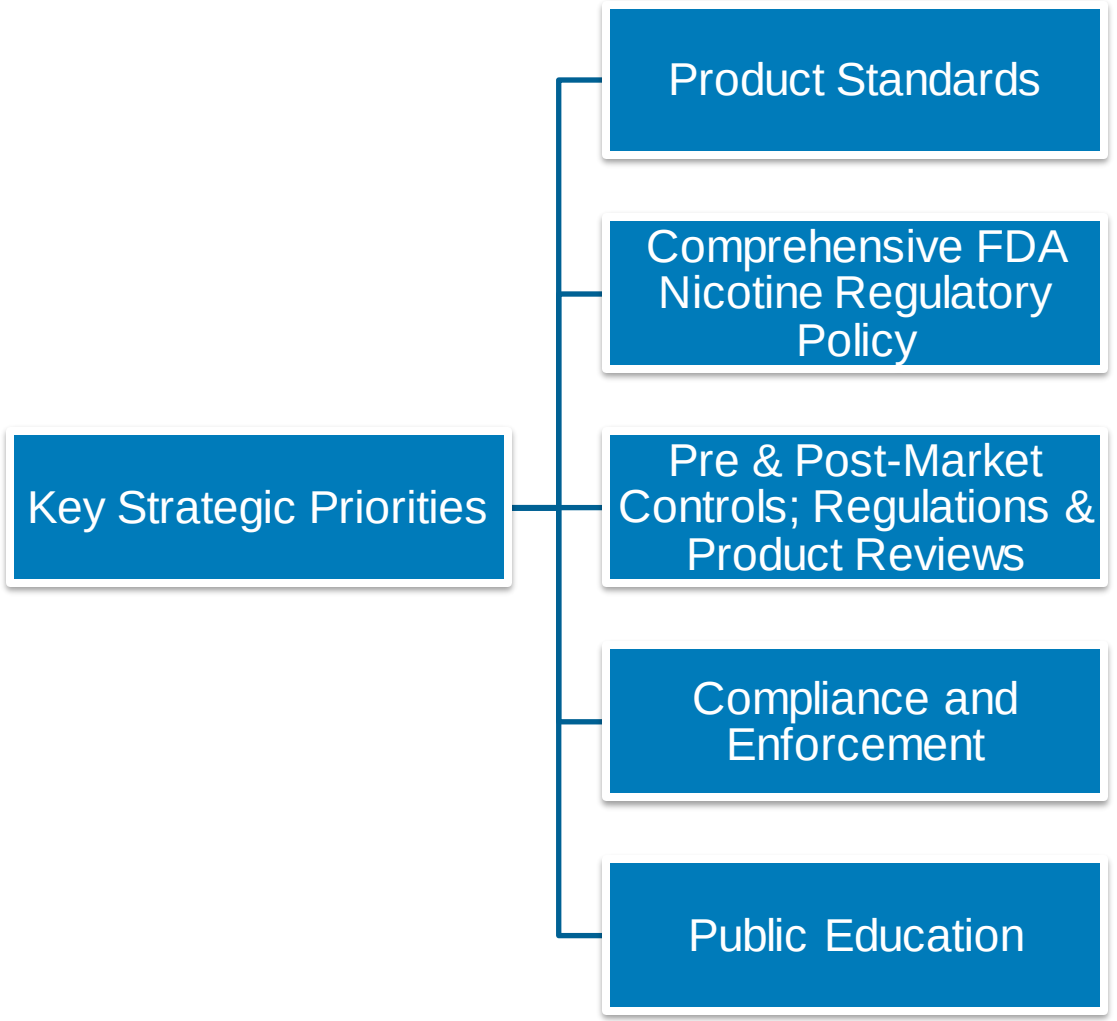
In general, FDA's tobacco regulatory authorities do not extend to:

- Setting tax rates for tobacco products
- Regulating therapeutic products, such as those marketed to treat tobacco dependence
- Setting clean indoor air policies
- Regulating tobacco growing
- Requiring the reduction of nicotine yields to zero
- Providing cessation services
- Banning all cigarettes, smokeless tobacco products, little cigars, other cigars, pipe tobacco, or roll-your-own tobacco products
- Changing the minimum age of sale for tobacco products

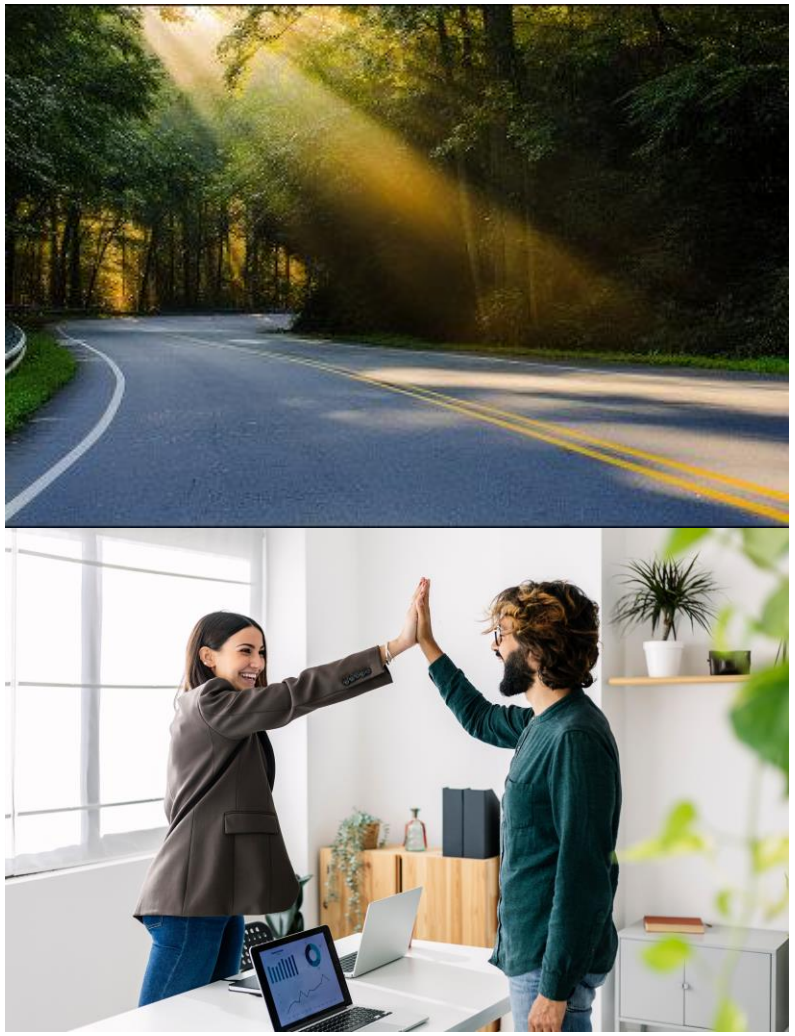
ABOUT CTP

Mission Statement

To protect Americans from tobacco-related death and disease by regulating the manufacture, distribution, and marketing of tobacco products and by educating the public, especially young people, about tobacco products and the dangers their use poses to themselves and others



CTP DATA STANDARDS STRATEGY



CTP Data Standards Strategy 2021-2025

- Outlines strategies for the development and dissemination of data standards to better support the programs of CTP through better, more meaningful data
- Supports CTP's public health mission through predictable, consistent, and high-quality data standards
- Areas that are included
  - **Electronic Data Exchange Standards**
  - **Premarket and Postmarket Review**
  - Quality
  - Policy
  - Planning and Governance

CTP DATA STANDARDS

Electronic Data Exchange Standards

- Technical Specification Document
- Electronic Submissions through CTP Portal or Electronic Submission Gateway (ESG)
- Utilize the Appendix A example for Organization of Folders and Documents
- Electronic submissions must be packaged using eSubmitter
- Data files such as Excel (xls, xlsx) or sas transport files (xpt or xport) should not be converted to a PDF

CTP DATA STANDARDS

Premarket and Postmarket Review

- OMB Forms
- Best Practices
  - Always obtain the most recent form from FDA.gov. Do not re-use previously downloaded forms.
  - Submit 4057b with all PMTA applications.
  - Complete the required fields defined by product category and sub-category.
  - Do NOT change form fields, data drop downs or file format. Submit the file as an .xlsx

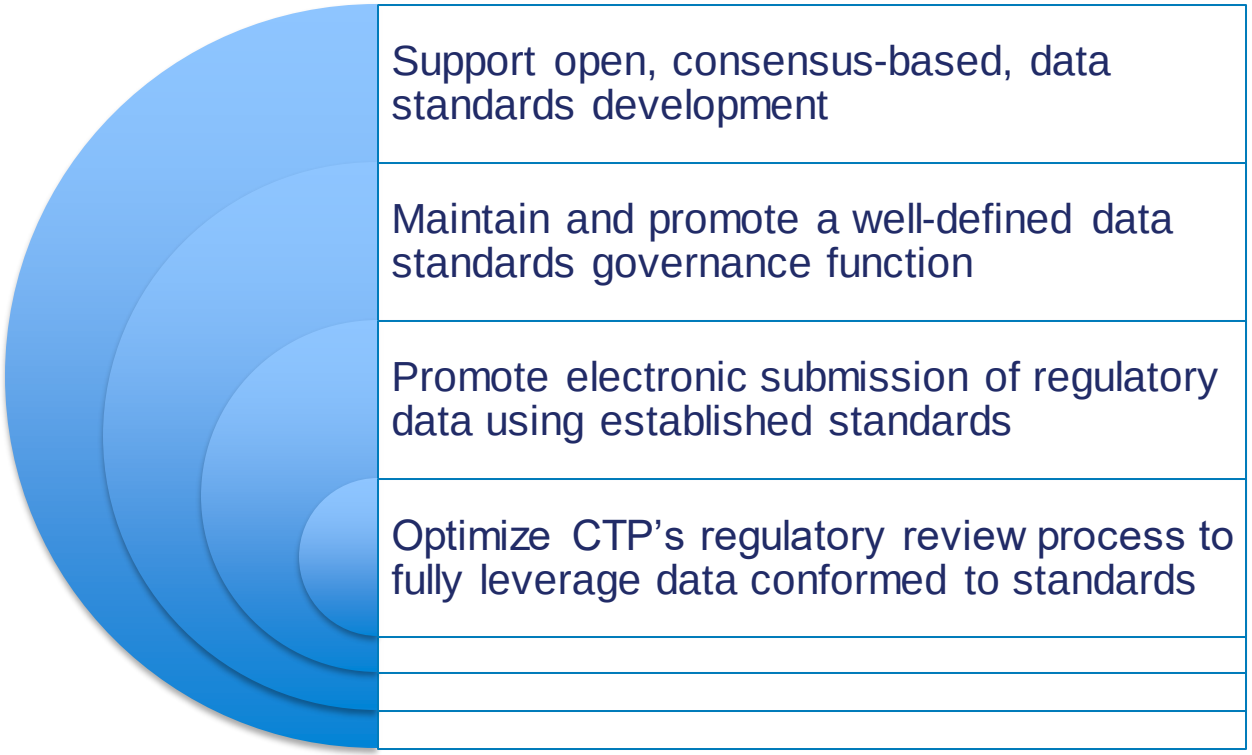
Form Number	Title	Edition Date	Format	Contact	Center
4057	Premarket Tobacco Product Application (PMTA) Submission	12/2022	FDA-Form-4057 12-2022.pdf1.76 MB	CTP 1-877-CTP-1373 (1-877-287-1373)	Center for Tobacco Products
4057a	Premarket Tobacco Product Amendment and General Correspondence Submission	12/2022	FDA-Form-4057a 12-2022.pdf977.82 KB	CTP 1-877-CTP-1373 (1-877-287-1373)	Center for Tobacco Products
4057b	Premarket Tobacco Product Application Grouping Product Submission Spreadsheet	12/2022	FDA-4057b 12.2022.xlsm82.82 KB	CTP 1-877-CTP-1373 (1-877-287-1373)	Center for Tobacco Products

CTP DATA STANDARDS GRANT PROGRAM

The Grant program has published for public participation under RFA-FD-22-002

This is a **Cooperative Agreement** grant which is a support mechanism used when there will be substantial Federal scientific or programmatic involvement. Substantial involvement means that, after award, FDA scientific or program staff will assist, guide, coordinate, or participate in project activities.

Strategic Goals



DATA STANDARDS BENEFITS

Reduce time in finding data

Ensure the same words mean the same thing *(Controlled Terminology)*

Reinforce validations *(Conformance Rules)*

Empower search and automation capabilities

Re-use data is easier

Enhance transparency & Stakeholder **E**ngagement

CDISC DATA STANDARDS

Clinical Data Interchange Standards Consortium

TOBACCO IMPLEMENTATION GUIDE (TIG)

- Tobacco Implementation Guide (TIG):
  - Supports the CTP Data Standards Strategy 2021-2025 through provision of standards and terminologies to facilitate tobacco research, scientific review, harm reduction, and information exchange
  - Is a collaborative initiative with FDA-CTP, CDISC, and industry stakeholders
  - To develop non-proprietary, consensus-based, vendor-neutral, platform-independent submission data standards for tobacco product data
  - Will develop a set of standards, collectively referred to as **TIG v1.0**, to be freely available on the CDISC website in 2024

TOBACCO IMPLEMENTATION GUIDE (TIG) V1.0

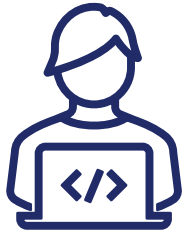
A single, comprehensive implementation guide designed for use cases unique to tobacco studies

An overview of standards and general implementation

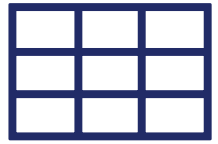
With guidance by topics and use cases; e.g.

- Product Description
- Nonclinical
- Individual Health
- Population Health

Key scientific concepts and maps



Data Collection (*CDASH eCRFs*, *ODM-XML*)



Data Tabulation (*SEND*, *SDTM Human Clinical*, *Define-XML*)

Analysis (*ADaM, Define-XML*)

Common Language (*Controlled Terminology*)

Measures of Adherence (*Conformance Rules*)

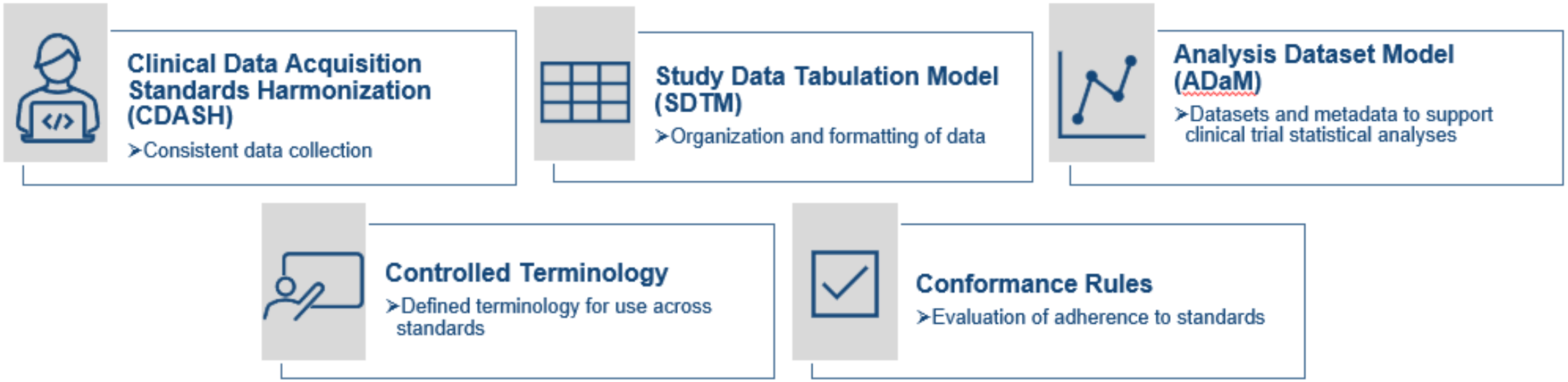
Accessible in platforms which optimize use (including *CDISC website*, *CDISC Library*)

Education and Outreach (including *webinars*, *formal training*)

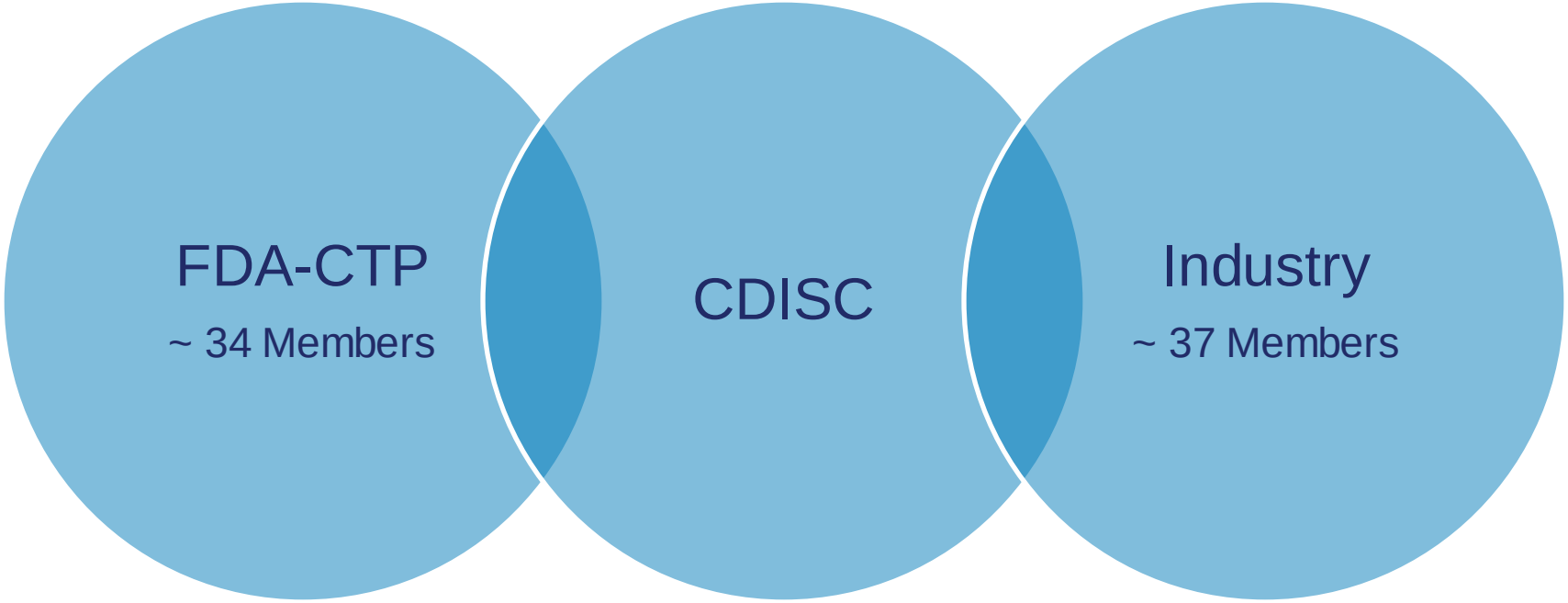
DATA STANDARDS

- Addresses concepts for tobacco studies and translates them into CDISC standards for both:
  - Established CDISC standards
  - New CDISC standards to fill gaps identified by FDA-CTP and Industry SMEs

- Standards you will see as part of this project include:



TIG TEAM AND TIMELINES

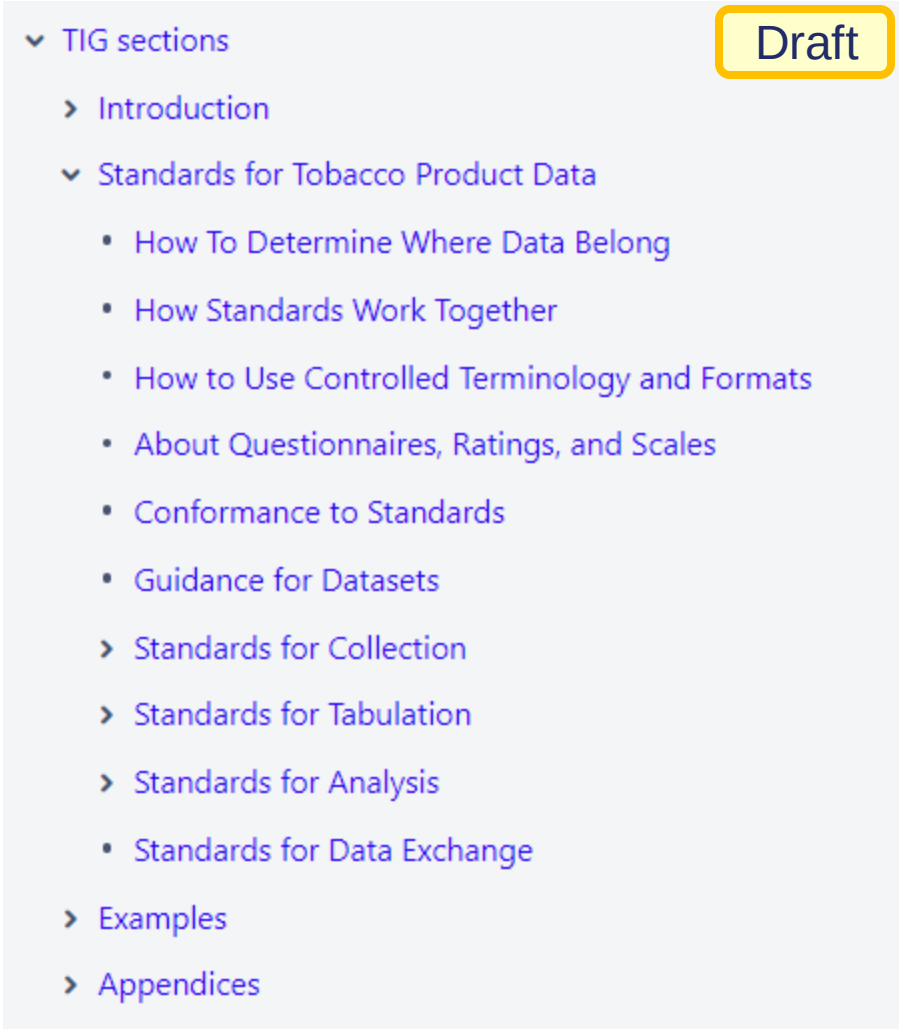


23-Jan	23-Feb	23-Mar	23-Apr	23-May	23-Jun	23-Jul	23-Aug	23-Sep	23-Oct	23-Nov	23-Dec	24-Jan	24-Feb	24-Mar	24-Apr	24-May
					Education											
Standards Development			Internal Review						Public Review						Publication	Wrap-up
QRS Development																
Data Science																

❑ Start of Public Review

PROGRESS

- ✓ Scope and Requirements for TIG v1.0 are complete
- ✓ Key concepts are identified
- ✓ Standards development is complete via four workstreams
- ✓ Internal Review comment resolution is concluding
- ❑ Public Review is commencing
- ❑ Data Science strategy/platforms are in progress
- ❑ Education & Communication in progress
- ✓ Conference presentations in 2022 and 2023 to raise awareness



INNOVATION HIGHLIGHTS

The TIG v1.0 is CDISC's first *hybrid* implementation guide

- Developed in partnership with the FDA-CTP, the TIG v1.0 is a stand-alone CDISC **foundational standard** that serves as a comprehensive resource for the collection, tabulation, analysis, and exchange of tobacco product data for submissions to FDA-CTP.

- The TIG v1.0 implements the following models:
  - CDASH Model v1.2
  - SDTM v2.1
  - ADaM v2.1
  - With references to standards and resources including Define-XML v2.1 and CDISC eCRF Portal

HYBRID IMPLEMENTATION GUIDE STRATEGY

Philosophy for development:

- Adhere to Plain Writing: It's the Law! | FDA
  - https://www.plainlanguage.gov/guidelines/, as much as possible
- Orient implementation guide to 1) Data, 2) Users, and 3) Standards - in this order
- Ensure guidance is simplified, concise, and organized from highest level concepts to detailed concepts
- Adhere to scope of implementation of standards only (i.e., like an instruction manual)
- Limit content best described in other resources (e.g., other CDISC and regulatory documentation)

Suggested in team kick-off.

INNOVATION HIGHLIGHTS

The TIG v1.0 focuses on implementation for use cases identified by one or more stakeholders as important in the context of tobacco product submissions

The following use cases are specifically addressed in the TIG: Draft

- *Product Description*, which refers to concepts used to characterize tobacco products.
- *Nonclinical*, which refers to concepts used to identify potential risks and effects on biological processes for tobacco products via in vitro and in vivo nonclinical studies.
- *Product Impact on Individual Health*, which refers to concepts used to assess the impact of tobacco products on individuals.
- *Product Impact on Population Health*, which refers to concepts used to assess the impact of tobacco products on populations of individuals.

PRODUCT DESCRIPTION EXAMPLE

Tobacco Product Identifiers and Descriptors – New, Predicate, Original, and Comparison Products (TO)

Draft

to.xpt

Row	STUDYID	DOMAIN	SPTOBID	TOSEQ	TOPARMCD	TOPARM	TOCAT	TOSCAT	TOVAL	TOVALU
1	TOB07	TO	CIG01a	1	TBPRDCAT	Tobacco Product Category	NEW PRODUCT	PRODUCT IDENTIFIER	Cigarette	
2	TOB07	TO	CIG01a	2	TBPRSCAT	Tobacco Product Subcategory	NEW PRODUCT	PRODUCT IDENTIFIER	Filtered, Combusted	
3	TOB07	TO	CIG01a	3	MANUF	Manufacturer	NEW PRODUCT	PRODUCT IDENTIFIER	Joes Cigs USA	
4	TOB07	TO	CIG01a	4	TRADENAM	Trade Name	NEW PRODUCT	PRODUCT IDENTIFIER	Treetop Menthol King Size	
5	TOB07	TO	CIG01a	5	PACKTYP	Package Type	NEW PRODUCT	PRODUCT DESCRIPTOR	HARD PACK	
6	TOB07	TO	CIG01a	6	PRDQUAN	Product Quantity	NEW PRODUCT	PRODUCT DESCRIPTOR	20	CIGARETTE
7	TOB07	TO	CIG01a	7	LENGTH	Length	NEW PRODUCT	PRODUCT DESCRIPTOR	86.0	mm
8	TOB07	TO	CIG01a	8	CIRCUMF	Circumference	NEW PRODUCT	PRODUCT DESCRIPTOR	26.0	mm
9	TOB07	TO	CIG01a	9	VENTLTN	Ventilation	NEW PRODUCT	PRODUCT DESCRIPTOR	10.0	%
10	TOB07	TO	CIG01a	10	CHARFLAV	Characterizing Flavor	NEW PRODUCT	PRODUCT DESCRIPTOR	MENTHOL	

NONCLINICAL IN VITRO EXAMPLE

Bacterial Reverse Mutation Test (Ames) (GT) Draft

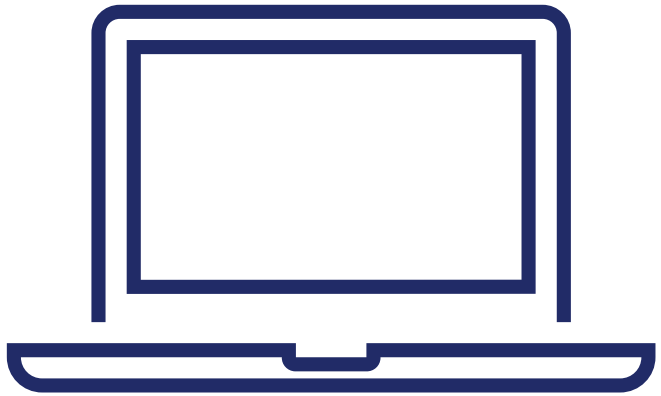
gt.xpt

Row	STUDYID	GNTXAID	DOMAIN	GTSEQ	GTREFID	GTTESTCD	GTTEST	GTORRES	GTORRESU	GTCOLSRT	GTSTRESC	GTSTRESN	GTSTRESU	GTSTAT	GTREASND	GTMETHOD	GTDTC
1	8325064	Ames	GT	1	1_1	RPP	Revertant Colony Numbers Per Plate	26	NOT APPLICABLE		26	26	NOT APPLICABLE			INSTRUMENT COUNTED	2015-08-03
2	8325064	Ames	GT	2	1_2	RPP	Revertant Colony Numbers Per Plate	35	NOT APPLICABLE		35	35	NOT APPLICABLE			INSTRUMENT COUNTED	2015-08-03
3	8325064	Ames	GT	3	1_3	RPP	Revertant Colony Numbers Per Plate	39	NOT APPLICABLE		39	39	NOT APPLICABLE			INSTRUMENT COUNTED	2015-08-03
4	8325064	Ames	GT	4	1_4	RPP	Revertant Colony Numbers Per Plate	35	NOT APPLICABLE		35	35	NOT APPLICABLE			INSTRUMENT COUNTED	2015-08-03
5	8325064	Ames	GT	5	1_5	RPP	Revertant Colony Numbers Per Plate	30	NOT APPLICABLE		30	30	NOT APPLICABLE			INSTRUMENT COUNTED	2015-08-03

DATA SCIENCE INNOVATION

CDISC Library

- End-to-end standards for tobacco studies
- Inclusion of informative content (e.g., domain assumptions and examples)
- Biomedical Concepts available
- ODM-XML representations of case report forms



HOW YOU CAN BE INVOLVED

Public Review will begin in October with collection of feedback through December.

We invite you to participate in this review!

THANK YOU

- We welcome your questions and feedback!