"FDA-CTP AND CDISC PROJECT TO DEVELOP TOBACCO RELATED STANDARDS TO ACHIEVE EFFICIENCIES FOR ALL STAKEHOLDERS"

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CENTER FOR TOBACCO PRODUCTS

THE TOBACCO CONTROL ACT BECAME LAW ON JUNE 22, 2009

- To protect the public and create a healthier future for all Americans – particularly youth – Congress passed the Tobacco Control Act

- 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 FD&C Act 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 (regulated by other parts of FDA)
- 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

- The Tobacco Control Act does NOT
  - Require prescriptions to purchase tobacco products
  - Require reduction of nicotine yields to zero
  - Ban face to face sales in a particular category of retail outlets
  - Ban certain classes of tobacco products

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

ABOUT CTP

- Vision Statement

  To make tobacco-related death and disease part of America's past, not America's future and, by doing so, ensure a healthier life for every family.

- 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.

- Key Strategic Priorities
  - Product Standards
  - Comprehensive FDA Nicotine Regulatory Policy
  - Pre & Post-Market Controls; Regulations & Product Reviews
  - Compliance and Enforcement
  - Public Education

CTP AND DATA STANDARDS

- CTP Data Standards Strategy 2021-2025
  - Purpose: Strategies for the development and dissemination of data standards to better support the programs of CTP through better, more meaningful data.
  - Areas that are included
    - **Electronic Data Exchange Standards**
    - **Premarket and Postmarket Review**
    - Quality
    - Policy
    - Planning and Governance

CTP AND 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
  - Best Practices
    - Obtain an Industry Account Manager account for CTP Portal
    - Submit applications electronically utilizing eSubmitter and CTP Portal
    - Follow recommendations in the Technical Specification Document
  - Future State
    - Functionality and/or tools to assist submitters in organizing and packaging submissions
    - Validations built into tools to assist submitters in correcting issues prior to submission

CTP AND DATA STANDARDS

- Premarket and Postmarket Review
  - OMB Forms
    - Required forms for Premarket Tobacco Product Application and Substantial Equivalence Applications were released when the rules were published 10/4/2021 and the supporting OMB Forms were published in January 2022.
    - **Form 4057b: Product Application Grouping Spreadsheet** is utilized to standardize product information contained within a submission until such time that a data standard is available.
    - Similar forms are forthcoming for Substantial Equivalence and Exemption applications
  - 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
  - Future State
    - Evaluating development of tools to assist submitters in populating form prior to submission

CTP AND DATA STANDARDS

- 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
    - THE GRANTEE IS THE LEAD
  - Outlines CTP Data Standards Program strategic goals
    - Support open, consensus-based, data standards development
    - Maintain and promote a well-defined data standards governance function,
    - Promote electronic submission of regulatory data using established standards
    - Optimize CTP's regulatory review process to fully leverage data conformed to standards

CTP AND DATA STANDARDS

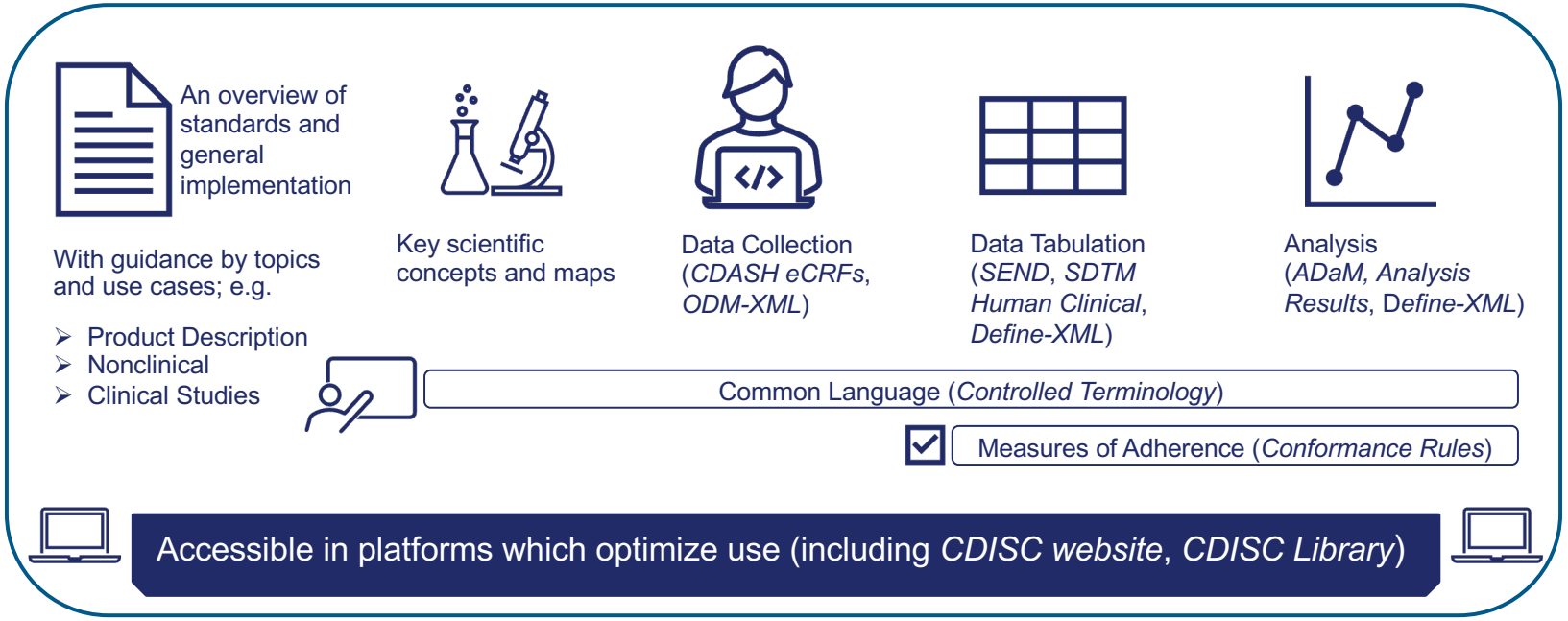
- Benefits to Industry
  - Ensures application is received and processed in a timely manner
  - Reduces time for reviewers to locate and identify required documents
  - Validations can be built into the portal and/or packaging tools to assist Industry in submitting the necessary information required for a particular submission
  - Standardized structured data allows for validation criteria to be built into tools
  - Aligns CTP with FDA Data Standards Catalog in the use of data standards and supporting tools
  - Standardized data helps CTP to streamline the review process by organizing files and data and enabling search and automation capabilities
  - Controlled terminology ensures that the same words mean the same thing to both industry and FDA.
  - Improves collaboration and communication between FDA and Stakeholders
  - FDA leverages form data to obtain administrative information, help determine review types, and populate databases to enable the use of technology for review and analysis

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 studies of tobacco products
  - Will develop a set of standards, collectively referred to as **TIG v1.0**, to be freely available on the CDISC website with publication planned in 2023

TOBACCO IMPLEMENTATION GUIDE (TIG) V1.0

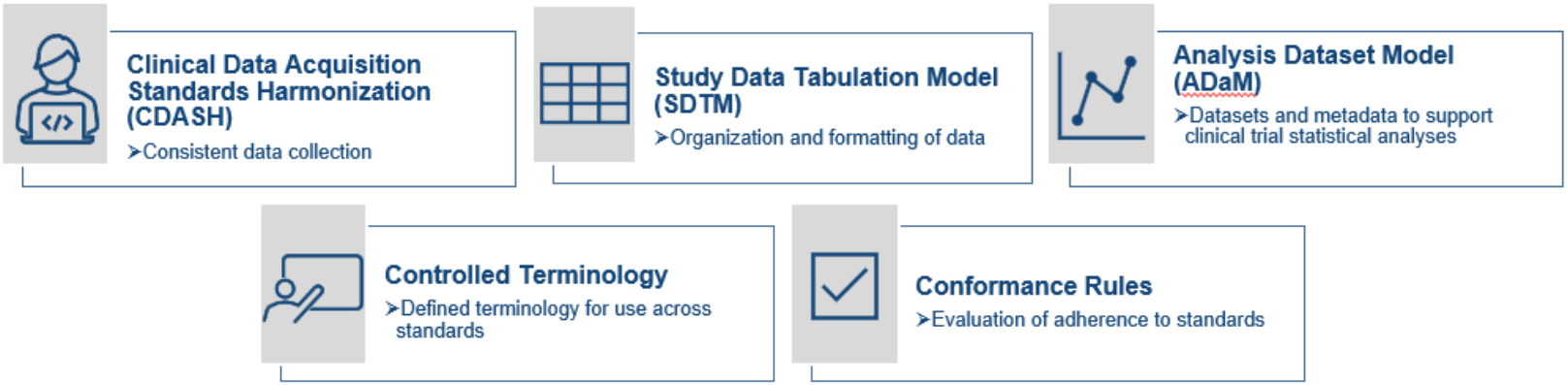
- A single, comprehensive implementation guide designed for use cases unique to tobacco studies



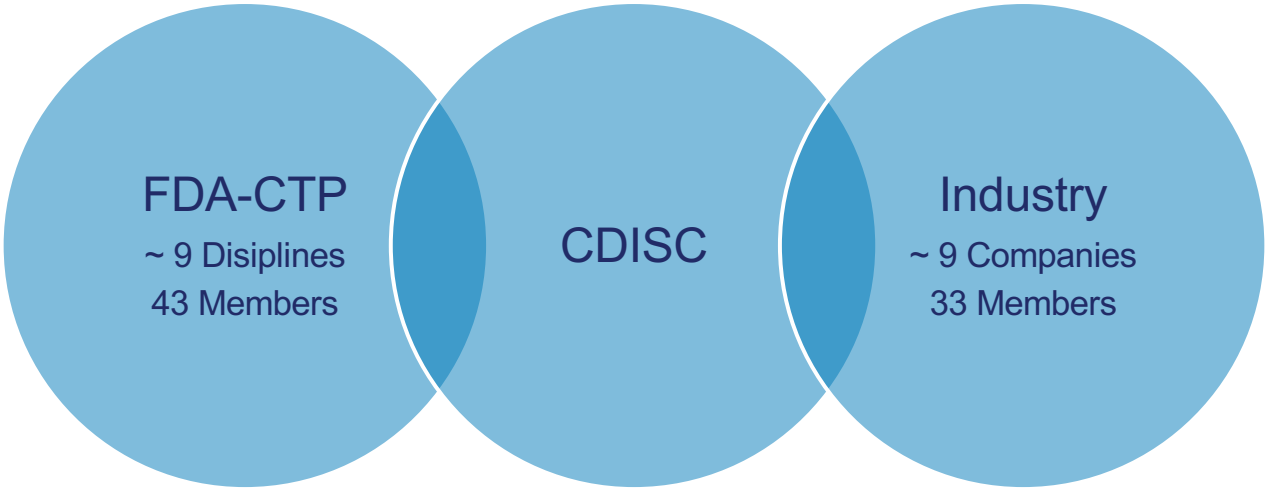
DATA STANDARDS

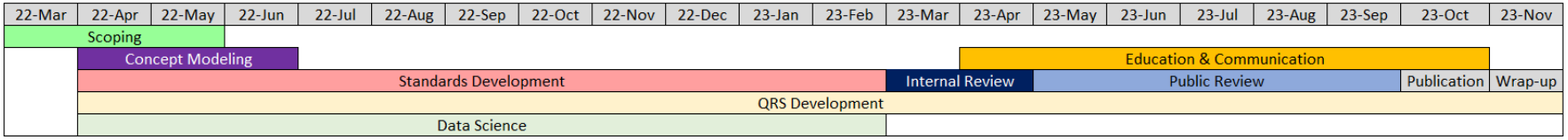
- Address concepts for tobacco studies and translates them into CDISC standards; both:
  - Established CDISC standards
  - New CDISC standards to fill gaps identified by FDA-CTP and Industry SMEs

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



TIG TEAM AND TIMELINES

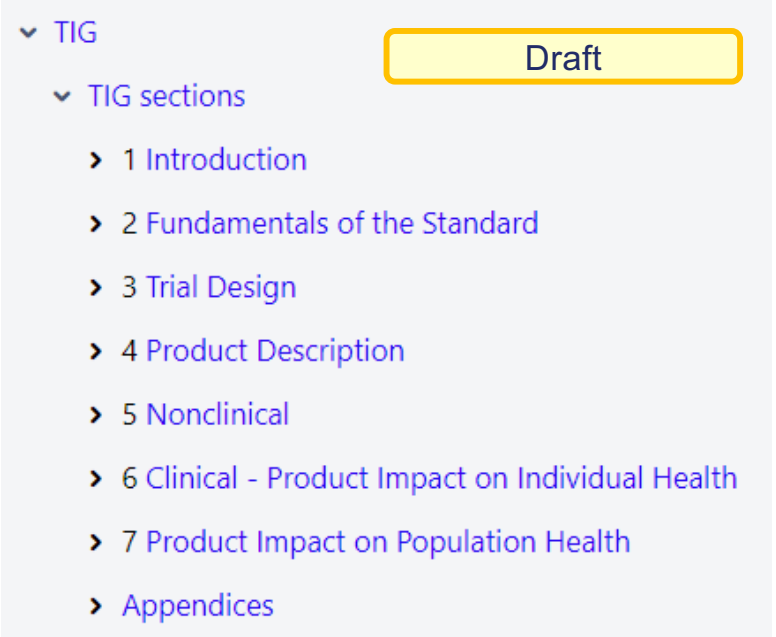




❑ Standards development in progress

PROGRESS

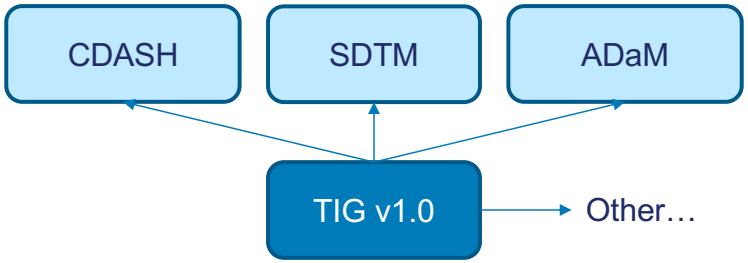
- ✓ Scope and Requirements for TIG v1.0 are complete
- ✓ Key concepts are identified
- ❑ Standards development in progress via four workstreams
- ❑ Data Science exploration of strategy and next steps are in progress
- ❑ Education & Communication started; training development preparation in progress
- ✓ Conference presentations in 2022 to raise awareness



INNOVATION HIGHLIGHTS

- TIG standards support a new stakeholder community; new use cases include:
  - SEND standards for in vitro studies
  - Data for which the “subject” is a product (i.e., not a person, animal, or device)
  - Baseline input parameters for population modeling

- TIG is a hybrid implementation guide
  - Single, comprehensive implementation guide referencing multiple models



INNOVATION HIGHLIGHTS

- TIG will be:
  - The first implementation guide publication with Biomedical Concepts
  - Published with computer executable conformance rules in CORE

- 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

NONCLINICAL IN VITRO STUDIES EXAMPLE

Draft

- Neutral Red Uptake Assay for Mainstream Tobacco Smoke:
  - The neutral red uptake assay provides a quantitative estimation of the number of viable cells in a culture.
  - It is one of the most used cytotoxicity tests with many biomedical and environmental applications. It is based on the ability of viable cells to incorporate and bind the supravital dye neutral red in the lysosomes.

Row	STUDYID	ASSAYID	DOMAIN	TXCD	GTSEQ	GTTESTCD	GTTEST	GTORRES	GTORRESU	GTSTRESC	GTSTRESN	GTSTRESU
1	123	NRU	GT	1-1-A	1	RELABS	Relative Absorbance Reading	100	ug/ml	100	100	ug/ml
2	123	NRU	GT	1-1-B	1	RELABS	Relative Absorbance Reading	107	ug/ml	100	100	ug/ml
3	123	NRU	GT	1-1-C	1	RELABS	Relative Absorbance Reading	98.6	ug/ml	100	100	ug/ml
...				...								
80	123	NRU	GT	1-10-H	1	RELABS	Relative Absorbance Reading	0.791	ug/ml	0.791	0.791	ug/ml
...				...								
160	123	NRU	GT	2-10-H	1	RELABS	Relative Absorbance Reading	0.780	ug/ml	0.780	0.780	ug/ml

Plate 1

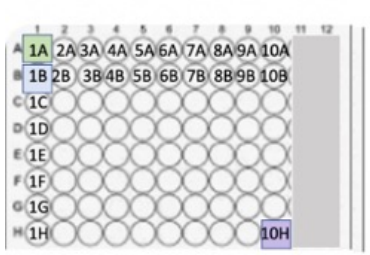
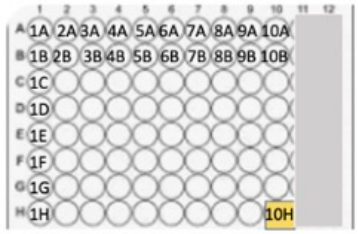


Plate 2



Our sincere thanks to the TIG Nonclinical Workstream lead by Lou Ann Kramer for this work.

HOW YOU CAN BE INVOLVED

- We invite you to contribute to development of TIG standards.
  - Become a Tobacco Implementation Guide (TIG) volunteer
    - www.cdisc.org/volunteer
    - Click link to *Become a Volunteer*
    - Time commitment is generally a one-hour weekly meeting
    - It is never too late to volunteer.
  - Review draft standards as they are released
  - Please reach out with any questions or support you may need.
    - Christine Connolly, CDISC Project Manager: cconnolly@cdisc.org

THANK YOU

- We welcome your questions and feedback!