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

*Presented by*
*Amy Malla*
*Supervisory Regulatory Health Information Specialist*
*DRSI, OS, CTP, FDA*

*Presented by*
*Christine Connolly*
*Head of Standards Projects, CDISC*

September 2022

**CENTER FOR TOBACCO PRODUCTS**

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# 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

# WHAT IS CDISC?

https://www.cdisc.org/

- A Global Standards Development Organization (SDO)
- Founded in 1997 by Volunteers; 501(c)(3) non-profit organization
- 40 employees; 100+ contractors
- >1,000 volunteers
- Education available online and classroom for most standards

# CDISC ALLIANCES AND COLLABORATIONS


- Additional Collaborations
  - Academic Institutions
  - Accumulus Synergy
  - Digital Infuzion
  - BioPharmaceutical Statistics Leaders Consortium
  - Clinical Data Privacy Consortium
  - Learning Health Community
  - Microsoft
  - OpenClinica
  - Pharmaceutical Data Standards Leaders
  - PhUSE
  - RedCap
  - Vivli

# CDISC STANDARDS DEVELOPMENT

- Consensus-based standards development
- Standards for clinical and translational research
- Standards are freely available at www.cdisc.org
- IP Policy ensures open standards
- Ongoing global research support in the Americas, Europe, Japan, China, India, Korea and other regions
- Standards and supporting documents available in English, Japanese, and Chinese

# 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

# TIG V1.0 ADDRESSES UNNECESSARY DATA VARIABILITY

Name for Subject ID is not the same

Name for dataset varies

Gender or Sex - do these mean the same thing!?

Study #1 – demog.xpt

| SUBJID | SEX |
|---|---|
| 0001 | M |
| 0002 | F |
| 0003 | F |
| 0004 | M |
| 0005 | F |

Study #2 – dmg.xpt

| ID | GENDER |
|---|---|
| A1 | Male |
| A2 | Male |
| A3 | Female |
| A4 | Female |
| A5 | Male |

Study #3 – dmgph.xpt

| PTID | GENDER |
|---|---|
| 0001 | 1 |
| 0002 | 1 |
| 0003 | 2 |
| 0004 | 2 |
| 0005 | 1 |

Study #4 – axd222.xpt

| USUBID | SEX |
|---|---|
| 00011 | 0 |
| 00012 | 1 |
| 00013 | 1 |
| 00014 | 0 |
| 00015 | 1 |

Is it Male or Female, M or F, 1 or 2, or 0 or 1?

What do these numeric codes mean?

# DATA STANDARDS

## Tobacco Implementation Guide (TIG) v1.0

An overview of standards and general implementation

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

- Product Description
- Nonclinical
- Clinical Studies

Key scientific concepts and maps

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

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

Analysis (*ADaM, Analysis Results, Define-XML*)

Common Language (*Controlled Terminology*)

Measures of Adherence (*Conformance Rules*)

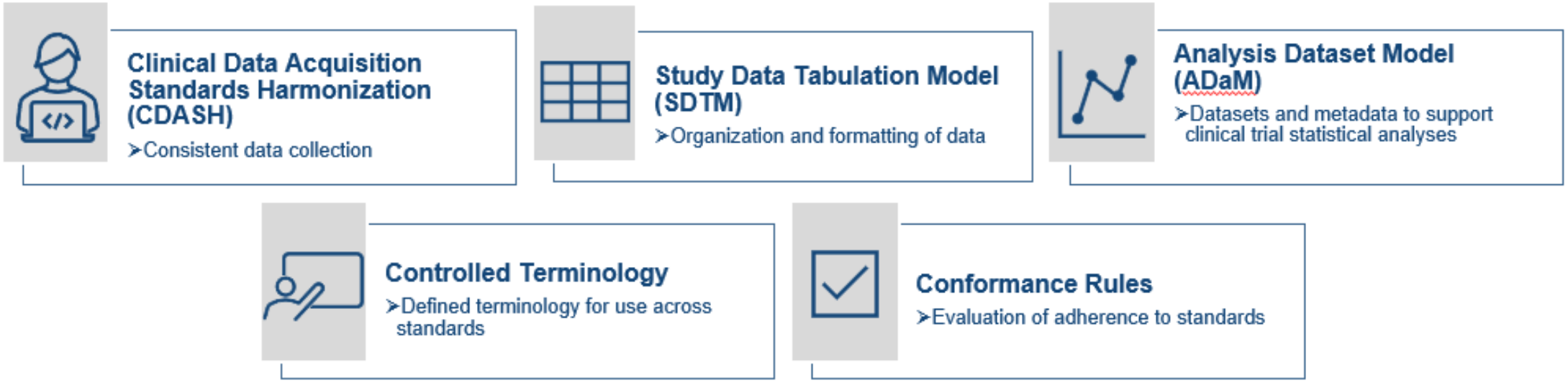
The TIG will describe how to use CDISC standards for tobacco research and is intended to guide the organization, structure, and format of standard data collection, data tabulation, and analysis data submitted to a regulatory authority.

Standards do not define or communicate regulatory positions or requirements. Rather, standards address unnecessary variability to support regulatory review.

# 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:



# DATA STANDARDS IN DEVELOPMENT

| | |
|---|---|
| Product Description | • SDTM, ADaM, Analysis Results Standards (new), Controlled Terminology, Conformance Rules |
| Nonclinical | • SEND, Controlled Terminology, Conformance Rules |
| Clinical – Product Impact on Individual Health | • Biomedical Concepts, CDASH, SDTM (human clinical trials), ADaM, Analysis Results Standards (new), ODM-XML, Define-XML, Controlled Terminology, Conformance Rules |
| Product Impact on Population Health | • New CDISC analysis standards (TBD), Controlled Terminology |

- Standards in development are aligned with hierarchy in Technical Specification Document Appendix A
- Standards are innovative with release to include first hybrid guide, biomedical concepts, Analysis Results Standards, SEND standards for in vitro studies, etc.

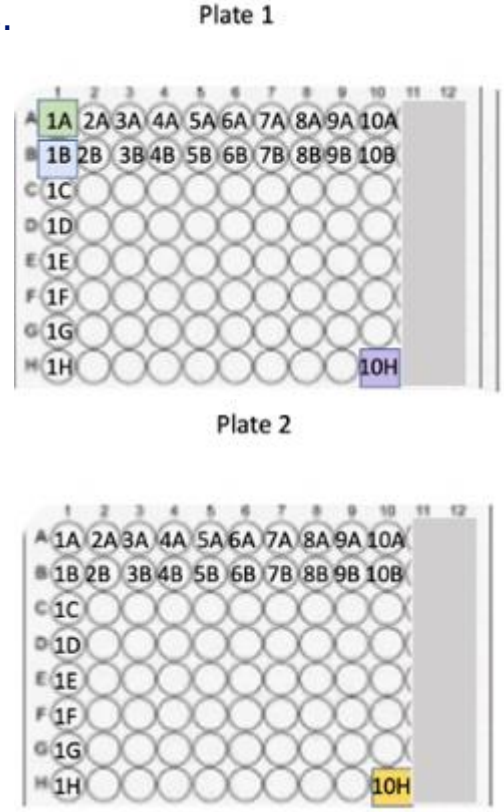
# NONCLINICAL IN VITRO STUDIES EXAMPLE

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 |




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!