Perspectives on CDM from a Tobacco and Nicotine Company

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03 March 2025

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Our refined purpose and vision...

Our purpose is to create A Better Tomorrow™ with a vision to Build a Smokeless world – one where smokers have migrated from cigarettes to smokeless alternatives.

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Tobacco Harm Reduction: Principles[1]

[1] Institute of Medicine (2001): Clearing the smoke
* Based on the weight of evidence and assuming a complete switch from cigarette smoking. These products are not risk free and are addictive.
† Our products as sold in the U.S., including Vuse, Velo, Grizzly, Kodiak, and Camel Snus, are subject to FDA regulation and no reduced-risk claims will be made as to these products without agency clearance.

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BAT's 9-Step Risk Assessment Framework: A weight-of-evidence approach

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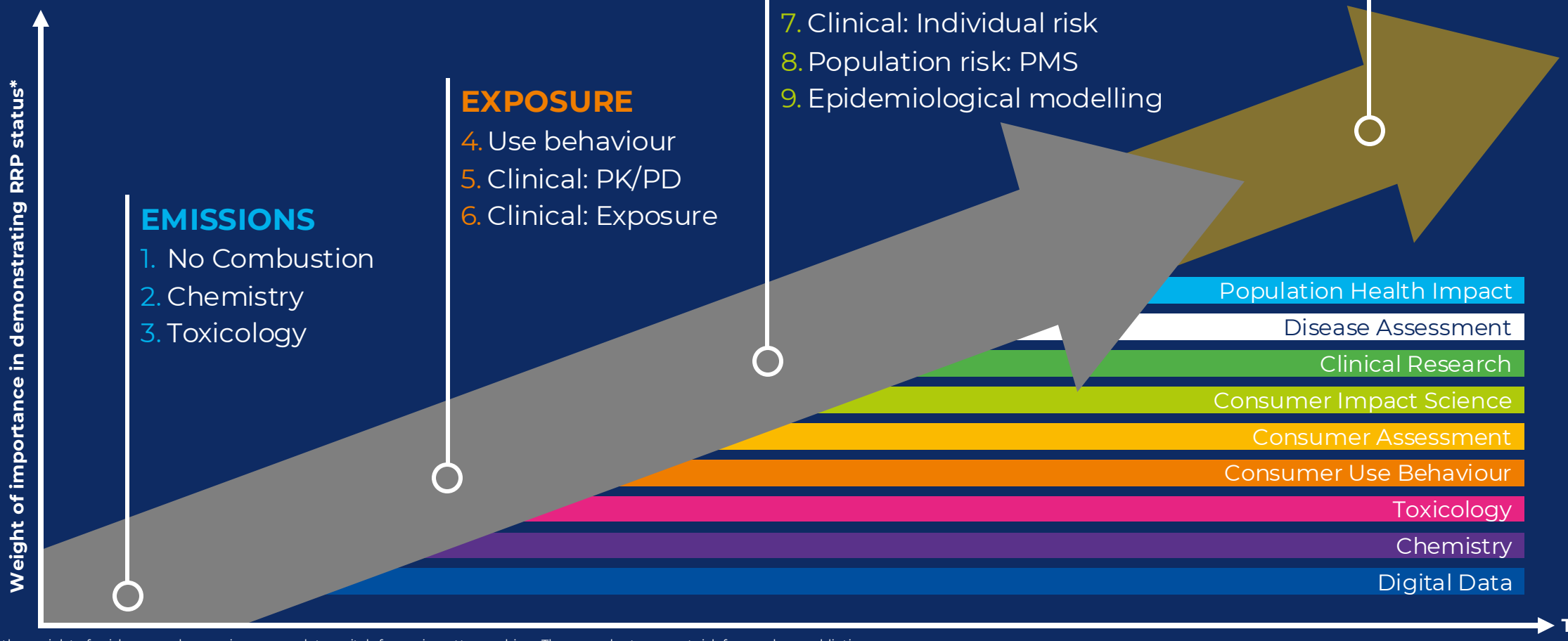
HARM REDUCTION

EMISSIONS
1. No Combustion
2. Chemistry
3. Toxicology

EXPOSURE
4. Use behaviour
5. Clinical: PK/PD
6. Clinical: Exposure

RISK
7. Clinical: Individual risk
8. Population risk: PMS
9. Epidemiological modelling



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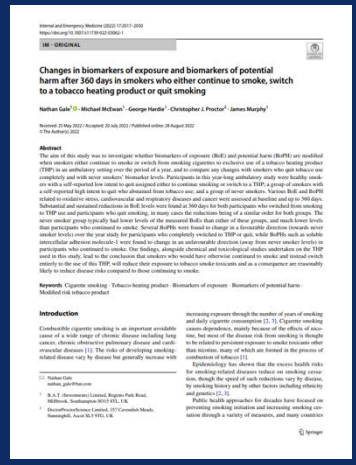
General Overview of Clinical Research

- We outsource the conduct of our studies to CROs and clinicians
- Our clinical studies are approved by independent RECs or IRBs
- We register our clinical studies on registries such as ISRCTN or clinicaltrials.gov
- We prioritise publishing our clinical studies


Changes in biomarkers of exposure and biomarkers of potential harm after 360 days in smokers who either continue to smoke, switch to a tobacco heating product or quit smoking


Assessment of biomarkers of exposure and potential harm, and physiological and subjective health measures in exclusive users of nicotine pouches and current, former and never smokers


Biomarkers of exposure and potential harm in exclusive users of electronic cigarettes and current, former, and never smokers

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Overview of Participants in a Typical Study

Age & Sex	**Male or female smokers, of legal smoking age** Biochemical verification of smoking status at Screening and Admission
Smoking History	**A defined minimum daily cigarette consumption** Established smoking history prior to Screening
Main Exclusion	**Planning to quit smoking in next 12 months** Subjects who are currently trying to stop smoking or considering stopping

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General Overview of CDM in BAT's Tobacco Related Clinical Research

- Data generated is accurate and reliable
- Reduce errors and increase data consistency
- Conducted as per global standards and regulations
- Data has the potential to be part of regulatory submissions

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CDM Role in BAT's Clinical Studies

Data Collection

- Protocol development
- Database design
- QA and UAT
- DMP
- DTAs

Data Cleaning

- Data validation and cleaning (discrepancy management)
- Metrics and performance
- Pre-lock listing review
- Coding consistency

Data Analysis

- Collaborate with CRO/internal Statistician
- aCRF review
- Regulatory package review
- TFL review

Data Reporting

- Final CDM outputs filed in TMF
- Archiving and close out
- CSR accurately represents the data

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CDM Role in BAT's Clinical Studies (continuation)

CDM Build

- Small pool of CROs all using different EDC systems. From proprietary EDC systems to larger systems e.g., RAVE
- We provide guidance on CRF design, code lists and edit checks for study designs
- Variation, data discrepancies and interpretation errors are reduced
- Ensuring compliance with standards, regulatory requirements and change control procedures
- Investing time prevents issues downstream

CDM In-Conduct

- Sponsor CDM access to the CRO EDC system or backend database management system, inclusive of metrics and reporting functionality
- Facilitating direct view of the data, including critical data and endpoint data. Use of status reports
- Open communication between Sponsor and CRO to address issues promptly and prioritise tasks based on impact to timelines
- Risk management and risk based monitoring

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In-conduct Insights

DM metrics

Study endpoints

Clinical Events

Identify patterns and any emerging trends with any clinical events during conduct phase

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Consistency of CDM Close-out Activities

Pre-lock review	Consistency of coded term review by an appointed medical monitor Protocol deviations vs data reconciliation
Final check	Review of data and final checks before approving for DBL
Consistency review	Review of consistency in tabulation across portfolio studies
Data approval	Receipt and approval into the business of data documents ensuring they have been versioned to be representative of state at DBL
Data integrity	Ensuring study records are still accessible and readable as per regulatory and internal policy requirements

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CDISC Tobacco Implementation Guide (TIG)

https://www.cdisc.org/tig

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Foundational Standard

- Non-proprietary, consensus-based, vendor-neutral, platform-independent submission data standards for tobacco related data
- Addresses concepts for tobacco research and translates them into CDISC standards for both:
    - Established CDISC standards
    - New CDISC standards to fill gaps identified by the FDA's Center for Tobacco Products (CTP) and Industry SMEs
- Focuses on implementation for use cases inherent to tobacco related data comprised of concepts identified by one or more stakeholders as important in the context of tobacco product research

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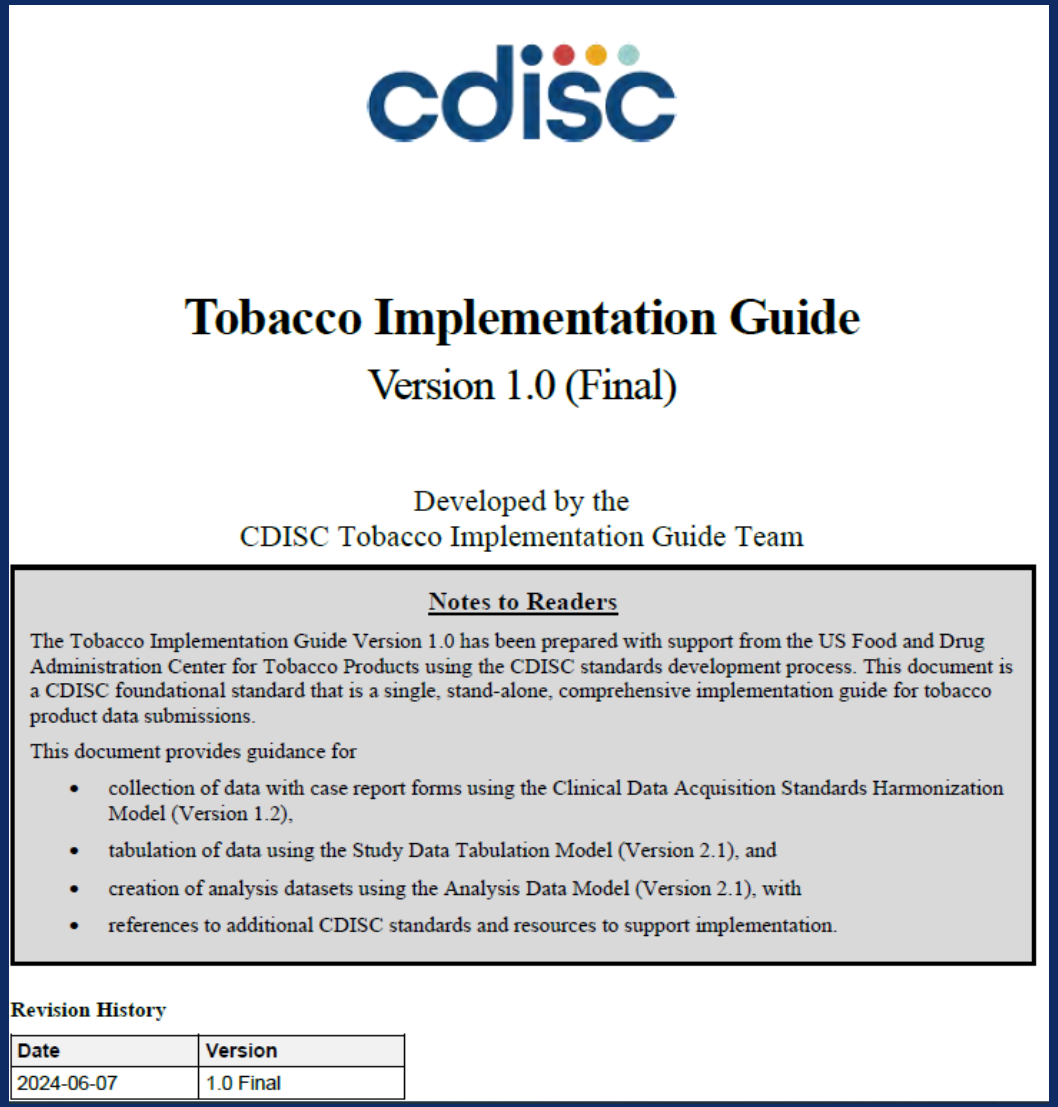
Tobacco Implementation Guide (TIG)

- TIG published in 2024 and available at: https://www.cdisc.org/tig
- All companies remain free to decide whether (and how) they use the standard
- Open to all, on-demand training provides a comprehensive understanding of the CDISC Tobacco-related Standards, focusing on four key use cases



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Tobacco Implementation Guide

Version 1.0 (Final)

Developed by the
CDISC Tobacco Implementation Guide Team

Notes to Readers

The Tobacco Implementation Guide Version 1.0 has been prepared with support from the US Food and Drug Administration Center for Tobacco Products using the CDISC standards development process. This document is a CDISC foundational standard that is a single, stand-alone, comprehensive implementation guide for tobacco product data submissions.

This document provides guidance for

- collection of data with case report forms using the Clinical Data Acquisition Standards Harmonization Model (Version 1.2),
- tabulation of data using the Study Data Tabulation Model (Version 2.1), and
- creation of analysis datasets using the Analysis Data Model (Version 2.1), with
- references to additional CDISC standards and resources to support implementation.

Revision History

Date	Version
2024-06-07	1.0 Final

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Into 2025: TIG v1.0 eSubmission Pilot

- Submit datasets standardized per the TIG v1.0 with related information as part of a simulated eSubmission to FDA CTP
- To build tobacco sector understanding and application of the standards
- To promote the adoption of the standards in the tobacco sector with further feedback to drive and define

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Presentation Wrap-up

Summary

- Overview of BAT's clinical research answering some common questions
- Insights into BATs CDM activities
- Next steps for BATs continued adoption of data standards

Conclusion

- Collaboration between clinical professionals in this setting is key to advancing data management operations

Questions

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