SEND: A New Avenue of Data Standards

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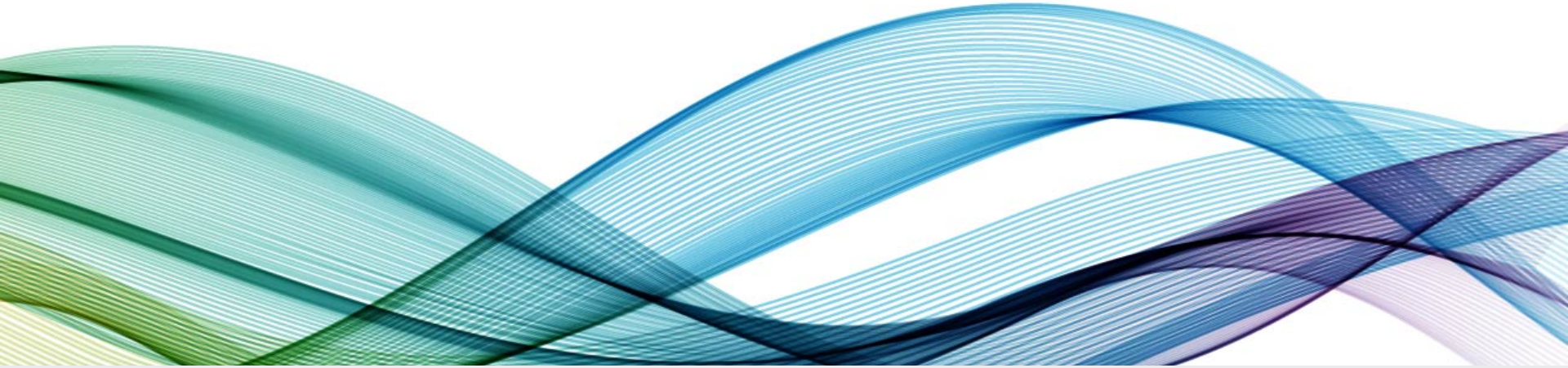


A New Thinking…..

Introduction:
SEND: Standard for Exchange of Non-clinical Data

- SEND is an implementation of the Study Data Tabulation Model (SDTM) for nonclinical toxicology studies and is intended to provide a structured representation of information included in study report appendices.
- SEND terminology will predominately use INHAND (International Harmonization of Nomenclature and Diagnostic).
- SEND Implementation Guide: The implementation guide is a set of instructions and examples of how to structure data into the SEND format.

Who developed SEND?

SEND is a concerted effort of teams from :

- CDISC
- FDA
- Pharmaceutical companies
- Clinical Software Vendors
- CROs

What is the objective?

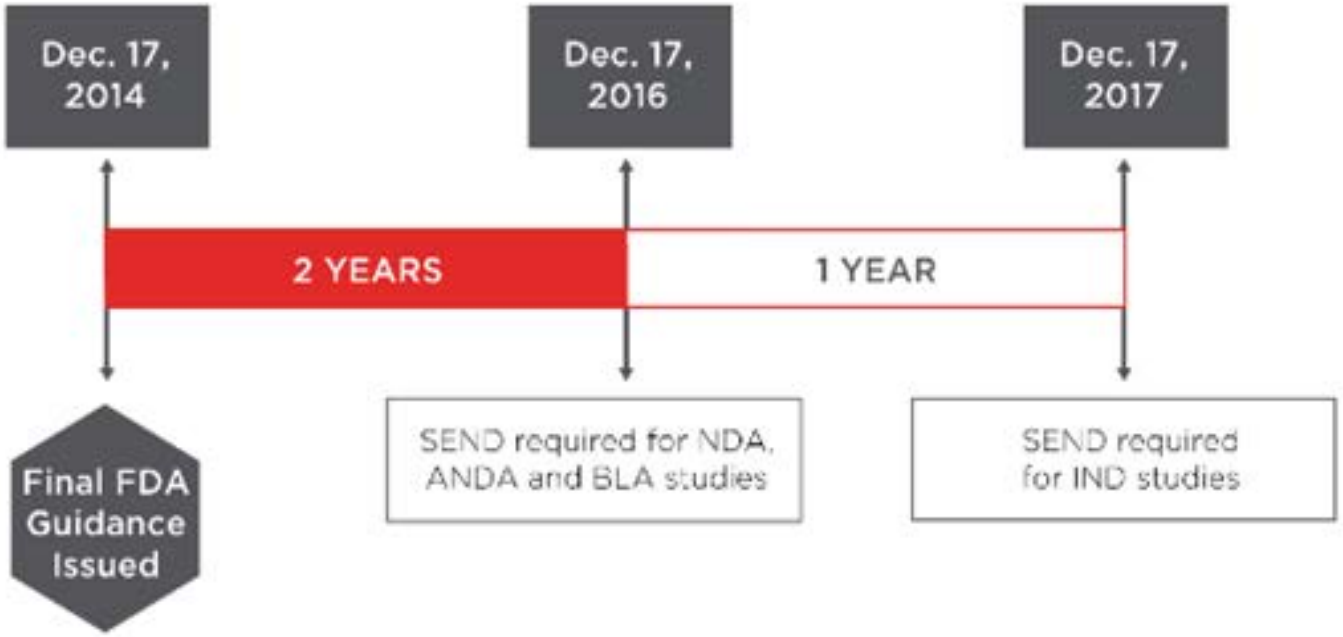
- ❑ A Standardized format for non-clinical data reporting
- ❑ To set controlled terminology
- ❑ Facilitating Data review
- ❑ Enhance data warehouse
- ❑ Better analysis and visualization for predictability

The Mandate

Studies supporting NDA submissions that start (protocol signature date) after December 18, 2016, and studies supporting IND submissions that start after December 18, 2017, must be submitted with electronic data as specified in the electronic data standards catalogue.

(As per Society of Toxicologic Pathology**)**

Timeline for SEND implementation



Before and after SEND-ing….

CURRENT STATE

- Consult several different tables individually
- Search through hundreds of pages of data

SEND STATE

- Use the digital SEND dataset plus a visualization tool
- View data on one screen to organize and analyze data

SEND implementation guide and similarity to SDTM

- The SEND implementation as described in the SENDIG v3.0 has many similarities to the implementation for human clinical trials described in the SDTMIG v3.1.2.

- At a high level, the SENDIG is laid out in the same way as the SDTMIG.

  It is organized to describe:

  - Subject-related special-purpose domains (Section 5)
  - General observation-class domains (Sections 6.1, 6.2 and 6.3)
  - Trial design (Section 7)
  - Relationships (Section 8)

Domain Metadata Model

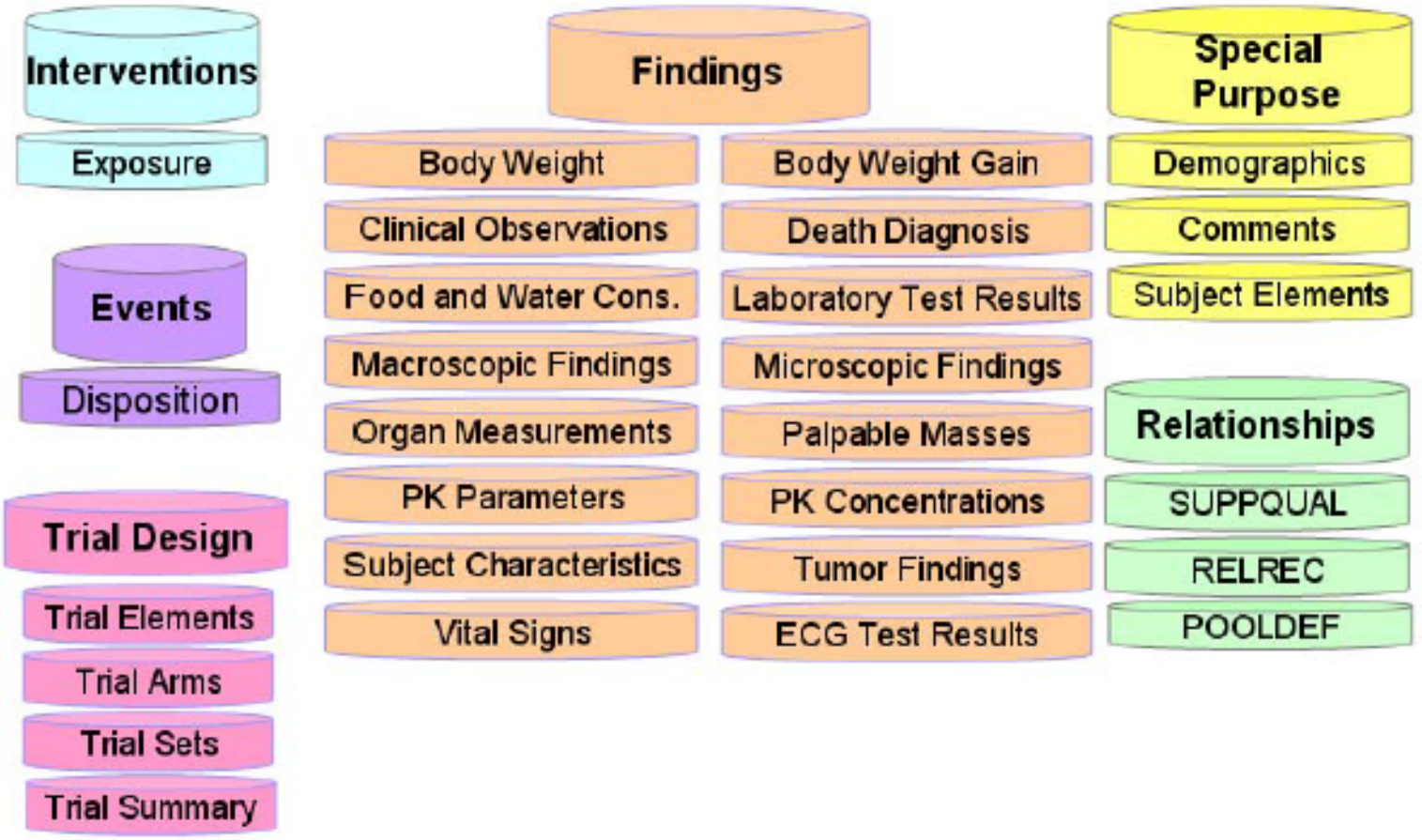
- Domain metadata models are displayed in exactly the same format as SDTM , comprising of columns for :
  - Variable name
  - Variable label
  - Data type
  - Controlled terminology or format
  - Role

- There are the same columns with information to sponsors:
  - CDISC notes
  - Core
  - References

Controlled Terminology

- SEND utilizes an extensive set of controlled terminology that is maintained by CDISC and NCI EVS, and described outside of the implementation guide.
- SEND uses the same controlled terminology lists used for human clinical trials whenever possible.

SENDIG DOMAIN CONTENT



Exclusivity for SEND

DIFFERENCES WITH SDTMIG

Interventions and Events domain

- The Interventions general-observation class has only one modelled domain, Exposure.
  - Concomitant Medications and Substance Use do not apply to toxicology studies, but Concomitant Medications may be relevant as SEND begins to be applied to veterinary-drug studies.
- The Events general-observation class has only one modelled domain, Disposition.
  - The Adverse Events, Medical History, and Protocol Deviations domains have not been modelled in the SENDIG.

DIFFERENCES WITH SDTMIG

Findings domain

The Findings general-observation class contains a number of new domains:

- ✓Body Weights
- ✓ Body Weight Gains
- ✓Clinical Observations
- ✓Death Diagnosis
- ✓Food and Water Consumption
- ✓ Macroscopic Findings
- ✓ Microscopic Findings
- ✓ Organ Measurements
- ✓ Palpable Masses
- ✓ Tumour Findings

Some SEND-specific, non-clinical variable names

❑ **Findings domain**

- LAT ---- Laterality .
- DIR ---- Directionality
- CSTATE ---- Consciousness State
- SPCUFL ---- Specimen Usability for the Test
- ANTREG ---- Anatomical Region

- Example values: LEFT, RIGHT
- Example values: DORSAL, VENTRAL
- Example values: CONSCIOUS, UNCONSCIOUS
- Y, N
- Example values: CORTEX, MEDULLA, MUCOSA

Some SEND-specific, non-clinical variable names (Contd.)

❑ Identifiers

POOLID (Pool Identifier) : Used in place of USUBJID when measurements are collected for a group of animals rather than by Subject

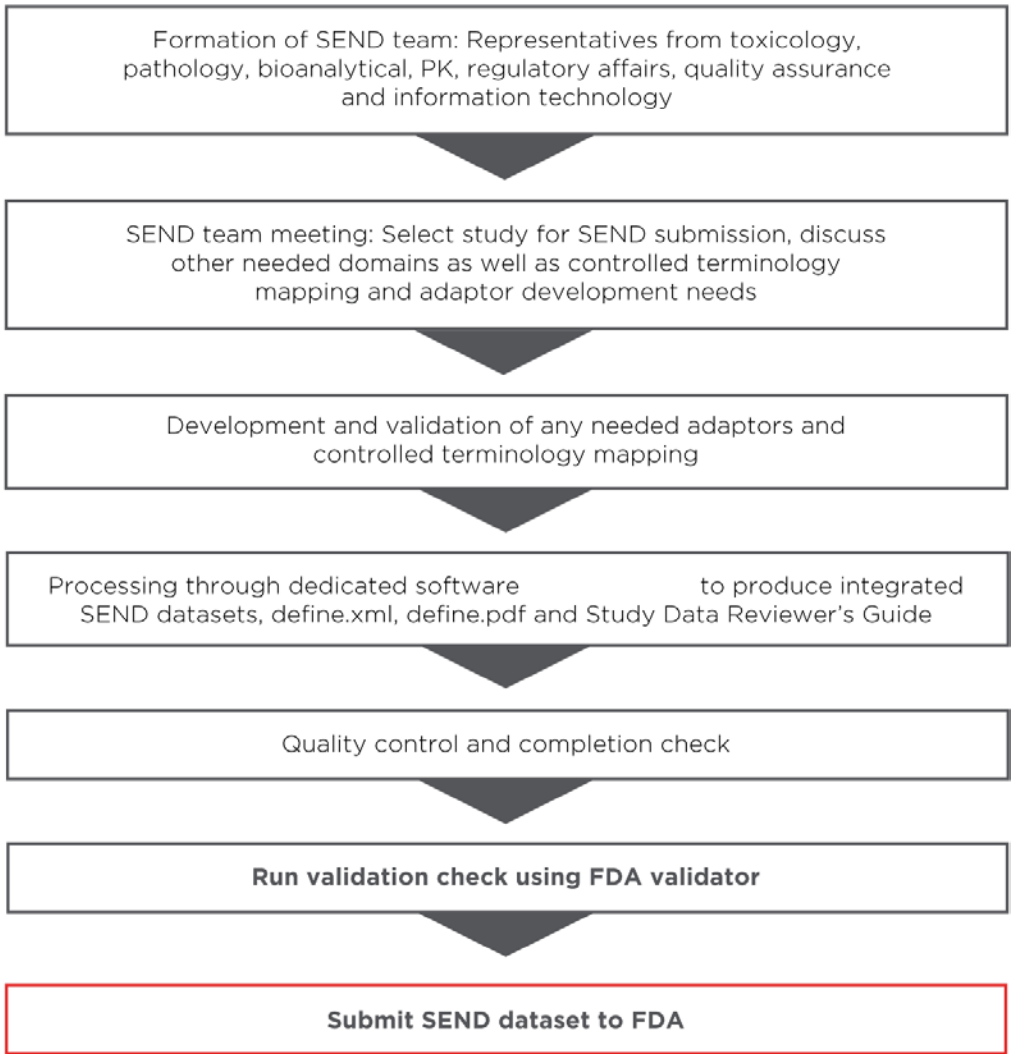
❑ Timing Variables

DETECT (Time in Days to Detection of Tumor) : Needed for the creation of the tumor.xpt file from SEND datasets from carcinogenicity studies

❑ Demographics

- SPECIES (Species) --- Example values: RAT, MOUSE
- STRAIN (Strain/Substrain) ---- Example values: FISCHER 344, B6C3F1
- AGETXT (Age Text) ---- Example value: 4-6 weeks

Standard flow of submitting SEND data to FDA



Benefits of SEND

- More Efficient:

  The SEND format enables more efficient review of nonclinical data, offering improved data quality, accessibility and predictability.

- More Exchangeable :
  - Common format for sharing non-clinical data
  - One format for CROs to meet multiple sponsors need
  - Support smooth data flow through department processes/applications

- More Reusable :
  - Cross-study data mining efficiency
  - Consistent data representation across drug projects
  - Diagnosis analysis of collected data content
  - To better predict future outcomes

Con's for Non-compliance

SEND has major implications for drug development :

Noncompliance will result in a refusal to file from the FDA resulting in submission delays

Pro's for Compliance

- These formats are used by the FDA to analyze pharmaceutical submissions, giving the agency rapid and easy access to complex data
- Utilization of SEND datasets result in faster FDA review and therefore faster time to approval
- Along with analytical and visualization tools for SEND, it will be possible to query data rapidly across species, compounds and clinical and preclinical disciplines in ways that are not currently feasible, both on the part of the FDA and sponsors

SOFTWARE TOOLS AVAILABLE

- Submit (Instem)
- SENDView (Instem)
- Savante (Xybion)
- TransSEND (PDS)

and many more……

- *Disclaimer: Presenter has used the name of software vendor companies and software tools solely for representation purpose and disclaiming any bias for any of the vendors or tools.*

Reference

1. *Guidance for Industry: Providing Regulatory Submissions in Electronic Format — NDAs*. U.S. Department of Health and Human Services, Food and Drug Administration, Center for Drug Evaluation and Research (CDER). IT 3, January 1999.

2. *Wood, F. (2008) The CDISC Study Data Tabulation Model (SDTM):* History, Perspective, and Basics. PharmaSUG Proceedings, June 2008.

3. *Federal Register Notice (2007). Electronic Nonclinical Study Data Submission*; Notice of Pilot Project Vol. 72, No. 191,Wednesday, October 3, 2007.

4. *Wood, F et al.(2011). The Standard for the Exchange of Nonclinical Data (SEND):History and Basics*. PharmaSUG 2011 - Paper CD14

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THANK YOU