What's Different About SDTM for Clinical and Non-Clinical Trials

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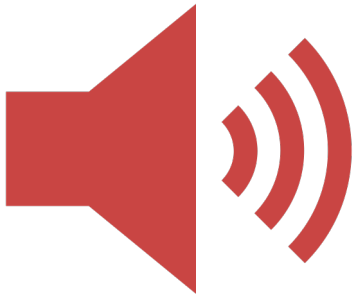
THU 23 FEB
11:00AM-12:30PM ET

Today's Agenda

1. Housekeeping
2. Presenter Introductions
3. Platform Demonstration
4. Question & Answer Session
5. Upcoming Learning Opportunities & Resources

Housekeeping

Housekeeping

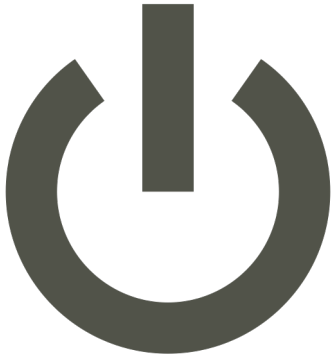


You will remain on **mute**

Housekeeping

There will be a **Q&A**

Housekeeping



Audio issues?

Shut down & restart Zoom

Housekeeping

Webinar slides & recording available
for **CDISC Members**

Our Presenters

- Diane Wold, Sr. Director, Standards Development, CDISC
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THU 18 FEB
11:00AM-12:30PM ET

SDTM for Nonclinical and Human Clinical Trials

February 23, 2021

Agenda

1. Animal Subjects vs Human Subjects
2. Scope of SENDIG vs Scope of SDTMIG
3. Data Handling and Analysis Differences
4. Study Design Differences
5. SDTM Implementation Differences

Animal Subjects vs. Human Subjects

Audrey Walker and Diane Wold

Study Sites

Nonclinical studies

- Specialist nonclinical facilities
- Testing facility (where the animals are housed)
- Testing sites (where certain tests are performed)

Human clinical trials

- Specialist Phase 1 sites
- Clinical sites primarily engaged in patient care
- Often multiple sites, especially for later phase studies

Subject Protections

Nonclinical studies

- Protocols reviewed by QA & sponsor
- Testing facilities are AAALAC accredited
- Rules for ethical treatment of animals incorporated into GLPs and SOPs
- Studies that cannot ethically be conducted in humans are conducted in animals.

Human clinical trials

- Protocols approved by ethics review boards
- Informed consent

Study Subjects

Nonclinical studies

- Animals purchased from a supplier

Human clinical trials

- Subjects recruited over time
- Eligibility assessed
- Informed consent obtained

Subject Participation

Nonclinical studies

- Subjects in a very controlled environment in accordance with protocol and SOPs
- Subjects at study site for entire study
- Subjects can only be observed
- Subjects sacrificed and necropsied
  - Common for rodents
- Protocol deviations documented in study report

Human clinical trials

- Subjects control their own actions
- In many studies, subjects are at the study site only for visits
- Subjects answer questions, describe symptoms
- Subjects may withdraw from a study at any time
- Protocol deviations data collected

SENDIG Scope vs SDTMIG Scope

Audrey Walker and Diane Wold

Studies in Scope

SENDIG

- Single-dose general toxicology
- Repeat-dose general toxicology
- Carcinogenicity studies
- Safety pharmacology subset
  - Respiratory studies
  - Cardiovascular studies

CoDEx describes what endpoints are confidently modeled within the SENDIG

SDTMIG

- All human clinical trials, all phases

Additional Implementation Guides

SENDIG-DART

- Developmental and Reproductive Toxicology subset
  - (Embryofetal development studies)

SENDIG-Animal Rule

- Studies for approval which cannot ethically be conducted in humans
  - Example: lethal or permanently disabling toxic agents such as chemical, biological, radiological or nuclear.

SDTMIG-AP

- Data about associated persons who are not study subjects

SDTMIG-MD

- Data about devices
- Covers devices used in human clinical trials as well as studies in which devices, rather than human or animal subjects, are study subjects.

SDTMIG-PGx

- Genomic data
- To be replaced in next version of the SDTMIG

Data Handling and Analysis

Kit Howard

Reminder!

This is mostly about industry studies supporting regulatory submissions, especially in nonclinical research

Data Handling (1)

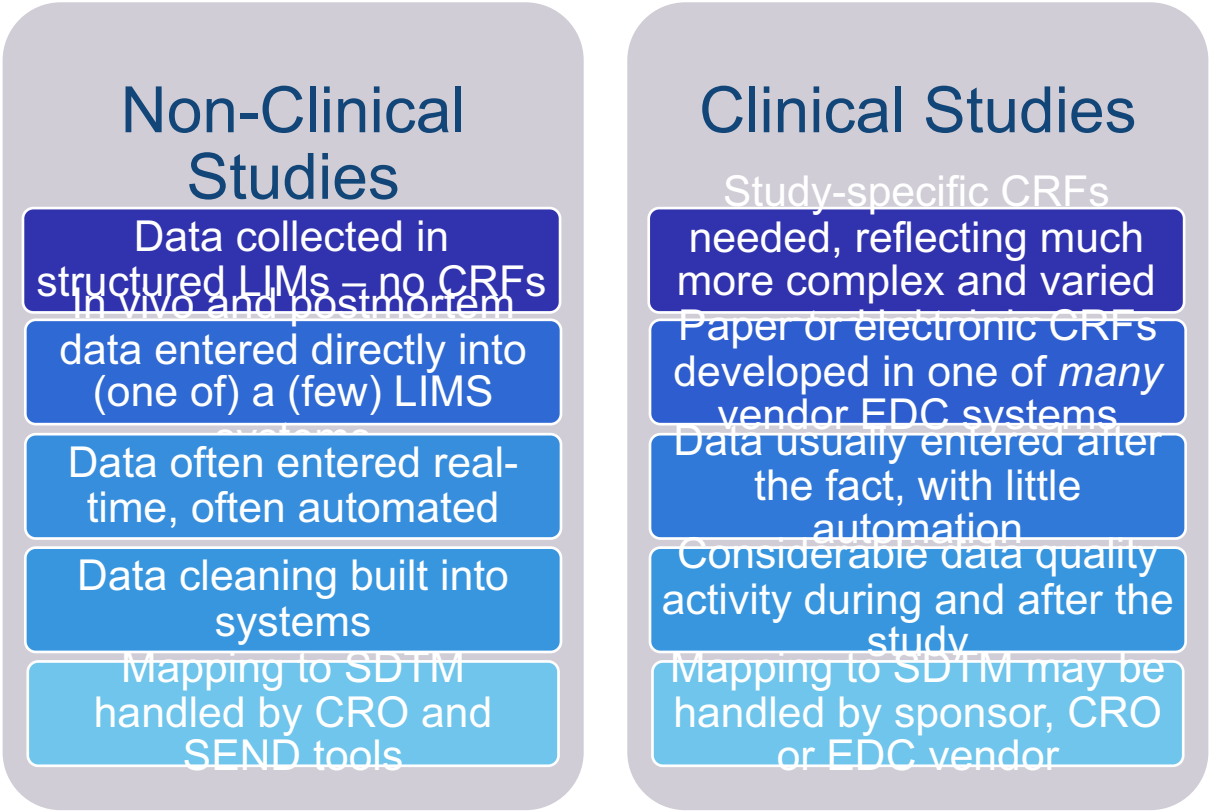
Non-Clinical Studies

- Varied study designs, but structured data collection
- Studies conducted in specialized units
- Studies mostly run by a few CROs, though control studies may be at sponsor
- Minimal data management function, especially at sponsors

Clinical Studies

- Study designs and data collected vary widely
- Usually conducted at clinics and hospitals
- Studies often run by sponsors; many (*many*) CROs also conduct studies
- Substantial data management covering data design, capture, storage, quality, archiving etc

Data Handling (2)



Data Analysis

Non-Clinical Studies

Analyses are generic, generally simpler, based on structured data

Analyses done directly from collected data

Clinical Studies

Analyses are study-specific, with some standard analyses based on study design but often additional analyses driven by data

Analyses usually run from ADaM datasets and metadata, one step away from collected data

Trial Design Differences

Fred Wood

Trial Design Datasets Not in the SENDIG

- Trial Visits (TV)
- Trial Disease Assessments (TD)
- Trial Disease Milestones (TM)

- In nonclinical toxicology studies, animals are often observed twice a day. The most important Timing variables are date/times, study days (represented most often by --NOMDY), and time points.

Trial Design Dataset Not in the SDTMIG

- Trial Sets (TX)

- The Trial Sets (TX) table is in the SDTM and the SENDIG.
- The variable SETCD is required in the SENDIG DM domain.
- Trial Sets Domain Definition:
  - “Provides the list of distinct sets of subjects having different experimental factors, treatment factors, inherent characteristics, or distinct sponsor designations as specified in the trial design.”
- TX represents pre-randomization criteria.
- While there are use cases for TX in human clinical trials, criteria of interest are often analyzed via the ADaM datasets.

Trial Sets Specification

Variable Name	Variable Label	Type	Controlled Terms, Codelist, or Format	Role	CDISC Notes	Core
STUDYID	Study Identifier	Char		Identifier	Unique identifier for a study.	Req
DOMAIN	Domain Abbreviation	Char	TX	Identifier	Two-character abbreviation for the domain.	Req
SETCD	Set Code	Char		Identifier	Short name of the Trial Set.	Req
SET	Set Description	Char		Synonym Qualifier	Long description of a specific Trial Set, as defined by the sponsor.	Req
TXSEQ	Sequence Number	Num		Identifier	Unique number for this record within this dataset.	Req
TXPARMCD	Trial Set Parameter Short Name	Char	(STSPRMCD)	Topic	Short character value for the Trial Set parameter described in TXPARM. Maximum 8 characters.	Req
TXPARM	Trial Set Parameter	Char	(STSPRM)	Synonym Qualifier	Term for the Trial Set parameter. Maximum 40 characters.	Req

Trial Sets Relationship to Trial Arms

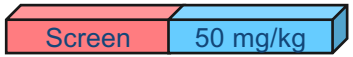
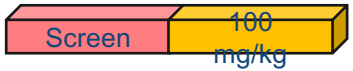
- TX Allows for the subdivision of Arms, using different parameters.
- TX Allows for multiple Arms to be “grouped” together (using the TXPARMCD of SPGRPCD)
- There should be no planned parameters of interest that could further subdivide a Trial Set.
- Each subject must be assigned to one and only one Trial Set in DM.

Example Trial Set Parameters

- Arm Code
- Control Type
- Group Label
- Sponsor-Defined Group Code
- Dose Level
- Dose Units

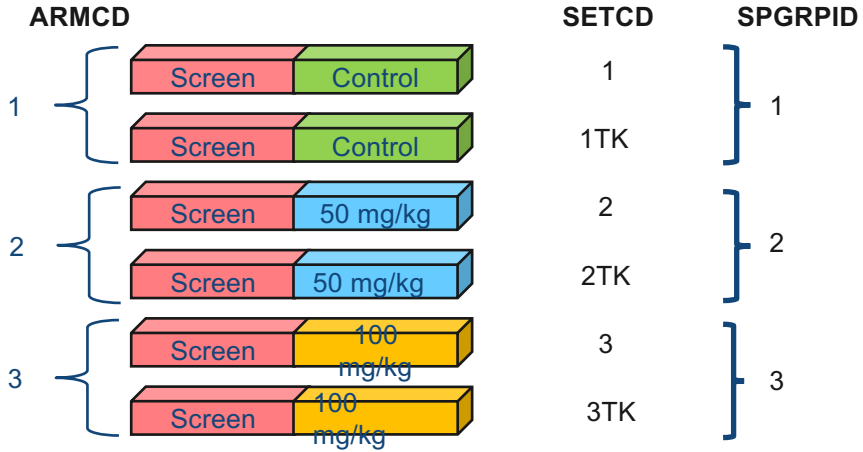
The SENDIG lists a minimum set of parameters that should be included.

Nonclinical TX Example 1: 3 Arms and 3 Sets

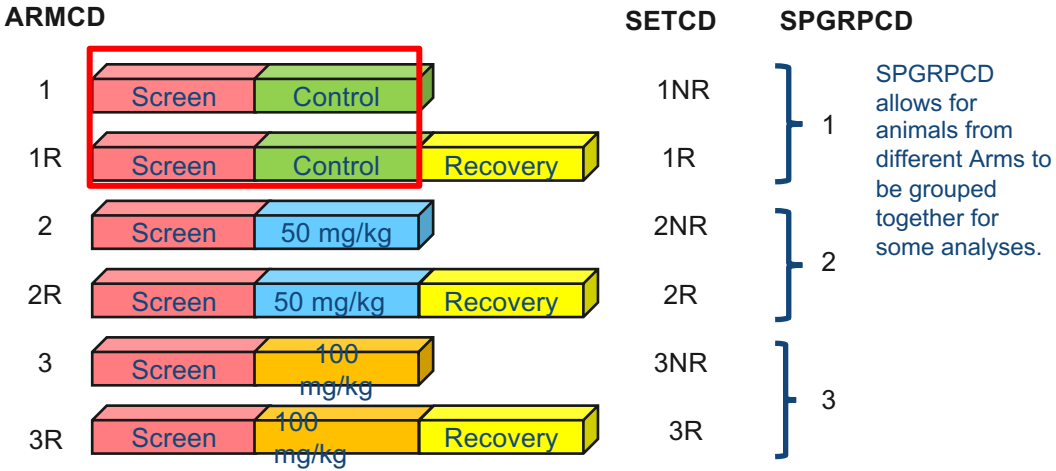
ARMCD		SETCD	SPGRPCD
1		CTRL	1
2		50MGKG	2
3		100MGKG	3

- Even if there is no subdivision of Arms, TX is required, and SETCD in DM is Required

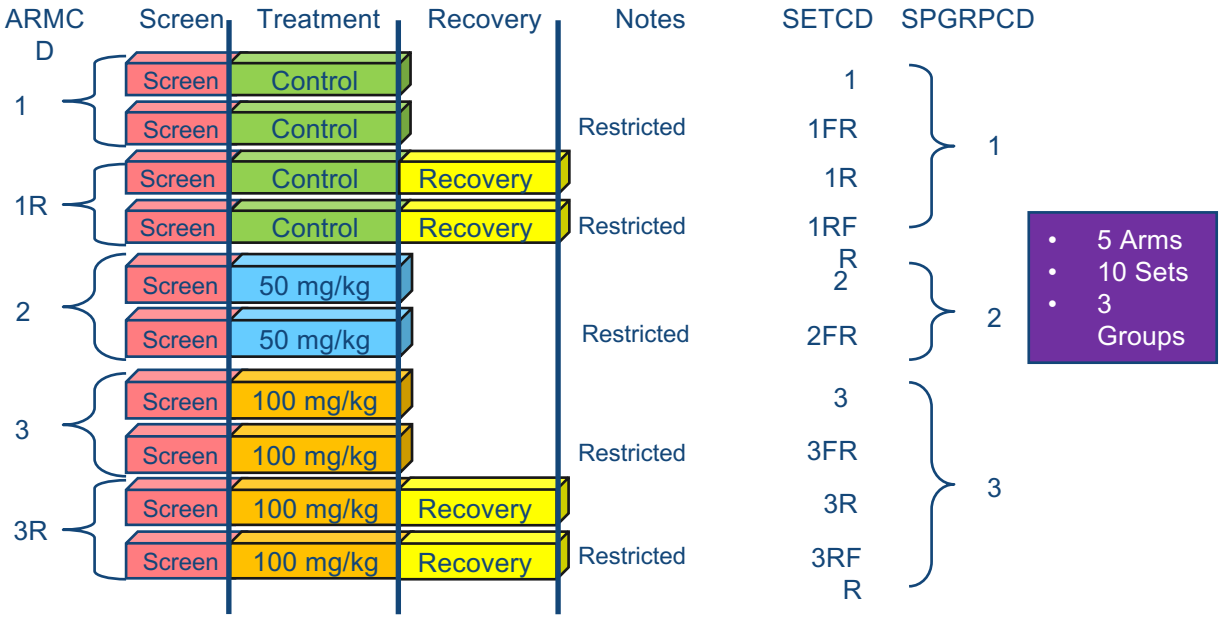
Nonclinical TX Example 2: 3 Arms and 6 Sets Based on Toxicokinetic Groups



Nonclinical TX Example 3:
6 Arms and 6 Sets Based on Recovery (1)Groups



Nonclinical TX Example 4:
Arms Split by Recovery and Food Restriction



SDTM Implementation Differences

Gary Walker

“Shared” domains: SENDIG v3.1 and SDTM-IG v3.3

Interventions
- Exposure

Events
- Disposition

Findings
- Cardiovascular Systems Findings
- ECG Test Results
- Microscopic Findings
- PK Parameters
- Subject Characteristics
- Death (Diagnosis and) Details
- Laboratory Test Results
- PK Concentrations
- Respiratory System Findings
- Vital Signs

Special Purpose
- Demographics
- Comments
- Subject Elements

Trial Design
- Trial Elements
- Trial Arms
- Trial Summary

Relationships
- SUPPQUAL
- RELREC

Unique domains: SENDIG v3.1 and SDTM-IG v3.3

Nonclinical Only (SENDIG v3.1)

Findings
- Body Weights
- Clinical Observations
- Food and Water Consumption
- Macroscopic Findings
- Microscopic Findings
- Palpable Masses
- Organ Measurements
- Tumor Findings

Trial Design
- Trial Sets

Relationships
- POOLDEF

Clinical Only (SDTMIG v3.3)

Interventions
- Concomitant Medications
- Exposure as Collected
- Meal Data
- Procedure Agents
- Procedures
- Substance Use

Events
- Adverse Events
- Clinical Events
- Deviations
- Healthcare Encounters
- Medical History

Findings
- Disease Response and Clin Classification
- Drug Accountability
- Functional Tests
- Immunogenicity Specimen Assessments
- Inclusion/Exclusion Criteria Not Met
- Microbiology Specimen
- Microbiology Susceptibility
- Musculoskeletal System Findings
- Morphology
- Nervous System Findings
- OphthalmicExaminations
- Physical Exam
- Questionnaires
- Reproductive System Findings
- Subject Status
- Skin Response
- Tumor/Lesion Identification
- Tumor/Lesion Results
- Urinary System Findings
- Findings About Subclass

Trial Design
- Trial Visits
- Trial Inclusion/Exclusion
- Trial Disease Milestones

Relationships
- RELSUB

Special Purpose
- Subject Visits
- Subject Disease Milestones

Model Variables reserved for use for SEND

2.7 SDTM Variables Not Allowed in SDTMIG

This section identifies those SDTM variables that either 1) should not be used in SDTM-compliant data tabulations of clinical trials data or 2) have not yet been evaluated for use in human clinical trials.

The following SDTM variables, defined for use in non-clinical studies (SEND), must NEVER be used in the submission of SDTM-based data for human clinical trials:

- --USCHFL (Interventions, Events, Findings)
- --DTHREL (Findings)
- --EXCLFL (Findings)
- --DETECT (Timing Variables)
- --NOMDY (Timing Variables)
- --NOMLBL (Timing Variables)

Model Variables reserved for use for SEND: Demographics Variables

The following variables can be used for non-clinical studies (SEND) but must NEVER be used in the Demographics domain for human clinical trials, where all subjects are human. See Section 9.2, Non-host Organism Identifiers (OI), for information about representing taxonomic information for non-host organisms such as bacteria and viruses.

- SPECIES (Demographics)
- STRAIN (Demographics)
- SBSTRAIN (Demographics)

Model for SEND that MAY BE USED in Clinical SDTM: Variables Not Evaluated for This Purpose

The following variables have not been evaluated for use in human clinical trials and must therefore be used with extreme caution:

- --METHOD (Interventions)
- --ANTREG (Findings)
- --CHRON (Findings)
- --DISTR (Findings) SETCD (Demographics)

The use of SETCD additionally requires the use of the Trials Sets domain.

Model Variables reserved for use for SEND: Demographics Variables

The following identifier variable can be used for non-clinical studies (SEND), and may be used in human clinical trials when appropriate:

- POOLID

> The use of POOLID additionally requires the use of the Pool Definition dataset.

Model Variables Never Used in SEND

- **Appendix E: SDTM Variables to Never Use in SEND**
- The following SDTM variables, defined for use in human clinical trials, do not fit the SEND model and must **NEVER** be used in the submission of non-clinical studies :

Events

BDSYCD	HLT	HLTCD	HLGT	LLT
LLTCD	PARTY	PRTYID	PTCD	SCAN
SCONG	SDISAB	SDTH	SHOSP	SLIFE
SOD	SMIE	SOC	SOCCD	

Demographics

ACTARMCD	ACTARM	COUNTRY	DTHDTC	DTHFL	ETHNIC
INVID	INVNAM	RACE	RFICDTC	RFPENDTC	

Interventions: PRESP

Trial Summary

TSVALCD	TSVCDRF	TSVCDVR

Some differences in assumptions

Most general assumptions (SDTM-IG, Section 4) the same, but some differences

- Handling of multiple variable values
  ("Multiple" convention vs. semi-colon-separated lists)
- Location variables (mentioned in previous slides)
- Records for "non-results"
  (e.g., SENDIG MI has a record for every tissue, whether or not there were any findings)

Thank You!

Questions & Answers

Audience Questions

Is the macroscopic domain that is in only is SEND equivalent to Morphology in SDTMIG? Both appear to have cardiovascular and respiratory.

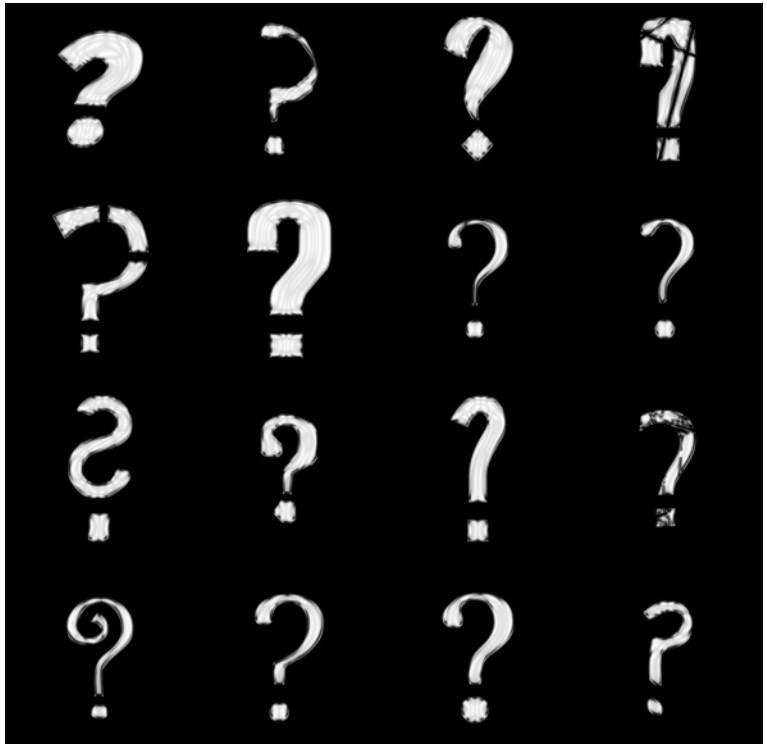
Audience Questions

Does SEND apply to non-GLP studies?

Audience Questions

Is the PCEXCLFL strictly used for excluding samples where there may be an issue with collection of the sample? Or can this be used by PKist to show data excluded from NCA?

Audience Questions



Audience Questions

Audience Questions

Audience Questions

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Audience Questions

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2021 Webinars

Date	Webinar Title
2 MAR	Current and Forthcoming ADaM Publications
16 MAR	QRS "Office Hours"
25 MAR	Public Review Webinar: Pancreatic Cancer Therapeutic Area User Guide
1 APR	Controlled Terminology Updates for Q1 2021
1 JUL	Controlled Terminology Updates for Q2 2021
Coming Soon	CDASH “Office Hours”; ADaM ”Office Hours”; CDISC Library Update
Visit https://www.cdisc.org/education/webinars for information on additional Public Training events.	

Questions

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Thank You!

Questions, comments, concerns? Email bklinke@cdisc.org

Don’t forget to fill out the feedback survey!