

SEND 3.1: GIVING YOUR SUBMISSION A “VITAL” UPGRADE

Megan Bausman
Associate Director
Global Data Management Solutions Team

Mikayla Simons
Nonclinical Data Associate
Global Data Management Solutions

February 27th, 2019

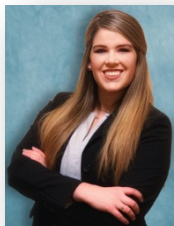
About Us

MEGAN BAUSMAN, MBA



- ▶ Associate Director, Global Data Management Solutions Team
- ▶ Manages all SEND dataset production (inc. software implementation/client relations)
- ▶ Member of the CDISC SEND consortium core team
- ▶ Extensive experience in safety assessment study management and reporting
- ▶ ~20 years at Covance

MIKAYLA SIMONS, BS



- ▶ Nonclinical Data Associate, Global Data Management Solutions
- ▶ Subject Matter Expert in training for the SEND dataset production team
- ▶ Subject Matter Expert for historical control data
- ▶ Leading the effort for Nonclinical Scientific Visualization within Covance
- ▶ Member of PhUSE, focused in visualization
- ▶ ~4 years at Covance

ACKNOWLEDGMENTS

*We would like to thank **John Kremer, PhD** (Covance Cardiac Safety Scientist/Manager) and **Tania Smith, MS** (Covance Nonclinical Data Associate and SEND subject matter expert) for the expert review of the content in this paper.*

Agenda

- ▶ Review of SEND 3.0
- ▶ Review of SEND 3.1
- ▶ Latin Square Design
- ▶ Recommendations

SEND 3.0 & 3.1

Beginning Dec 2016

General Toxicology

- GLP
- Non-GLP
- Single Dose
- Multiple Dose

Carcinogenicity

Beginning Mar 2019

Safety Pharm

- Cardiovascular
- Respiratory

Today's
Focus

1.3 Relationship to Prior CDISC Documents

The most significant changes since the prior version, v3.0, include:

- Realignment with SDTM v1.5.
- Reclassified the use of VISITDY from Expected to Permissible and added three new variables to relevant domains (–USCHFL, –NOMLBL, –NOMDY)
- New FOCID variable added to several domains (EX, CL, MA, and MI). FOCID, described further in Section 4.2.7, is available to all general observation classes to specify a study-specific point of interest.
- Updated Microscopic Findings domain (Section 6.3.8); added three new variables (FOCID, –CHRON, –DISTR).
- Updated Vital Signs domain (Section 6.3.15). With the addition of new domains for nonclinical safety pharmacology study data, CV and RE, the Vital Signs domain was revised, blood pressure measurements were moved to the Cardiovascular (CV) domain, and respiratory rate was moved to the Respiratory (RE) domain. For nonclinical study data, the Vital Signs domain is now intended to hold vital signs measurements, such as body temperature, that are not otherwise covered in domains for respiratory and cardiovascular test data.
- Updated ECG Test Results domain (Section 6.3.16); added two new Timing variables (–STINT and –ENINT).
- New Cardiovascular domain (Section 6.3.17) including blood pressure measurements, which were previously submitted in Vital Signs domain.
- New Respiratory domain (Section 6.3.18) including respiratory rate, which was previously submitted in Vital Signs domain.

Source: Standard for Exchange of Nonclinical Data Implementation Guide: Nonclinical Studies, Version 3.1, 27 June 2016

SEND 3.0 Overview

2.3 THE SENDIG STANDARD DOMAIN MODELS

The following standard domains with their respective domain codes have been defined or referenced by the CDISC SEND Team in this document.

Special-Purpose Domains (Section 5)

- Demographics – DM
- Subject Elements – SE
- Comments – CO

Interventions General Observation Class (Section 6.1)

- Exposure – EX

Events General Observation Class (Section 6.2)

- Disposition – DS

Findings General Observation Class (Section 6.3)

- Body Weights – BW
- Body Weight Gains – BG
- Clinical Observations – CL
- Death Diagnosis – DD
- Food and Water Consumption – FW
- Laboratory Test Results – LB
- Macroscopic Findings – MA
- Microscopic Findings – MI
- Organ Measurements – OM
- Palpable Masses – PM
- Pharmacokinetics Concentrations – PC
- Pharmacokinetics Parameters – PP
- Subject Characteristics – SC
- Tumor Findings – TF
- Vital Signs – VS
- ECG Test Results – EG

Trial Design Domains (Section 7)

- Trial Elements – TE
- Trial Arms – TA
- Trial Sets – TX
- Trial Summary – TS

Relationship Datasets (Section 8)

- Supplemental Qualifiers – SUPP--datasets
- Related Records – RELREC
- Pooling – POOLDEF

Study Types

- General Toxicology (GLP/nonGLP)
- Carcinogenicity

Key Takeaways

- Includes the core data types on tox studies
- VS contains heart rate, body temperature, respiratory rate, blood pressures, oxygen saturation, mean arterial pressure, and pulse pressure, and more
- EG contains ECG mean heart rate, QRS duration, PR interval, QT interval, QTc interval, and RR interval, and more

Source: Standard for Exchange of Nonclinical Data Implementation Guide: Nonclinical Studies, Version 3.0, 19 May 2011

SEND 3.1 Overview – A “Vital” Upgrade

2.3 The SENDIG Standard Domain Models

The following standard domains with their respective domain codes are included in the document.

Special-Purpose Domains (Section [5](#))

- Demographics – DM
- Comments – CO
- Subject Elements – SE

Interventions General Observation Class (Section [6.1](#))

- Exposure – EX

Events General Observation Class (Section [6.2](#))

- Disposition – DS

Findings General Observation Class (Section [6.3](#))

- Body Weight – BW
- Body Weight Gain – BG
- Clinical Observations – CL
- Death Diagnosis and Details – DD
- Food and Water Consumption – FW
- Laboratory Test Results – LB
- Macroscopic Findings – MA
- Microscopic Findings – MI
- Organ Measurements – OM
- Palpable Masses – PM
- Pharmacokinetics Concentrations – PC
- Pharmacokinetics Parameters – PP
- Subject Characteristics – SC
- Tumor Findings – TF
- Vital Signs – VS★
- ECG Test Results – EG★
- Cardiovascular Test Results – CV★
- Respiratory Test Results – RE★

Trial Design Domains (Section [7](#))

- Trial Elements – TE
- Trial Sets – TX
- Trial Arms – TA
- Trial Summary – TS

Relationship Datasets (Section [8](#))

- Related Records – RELREC
- Pool Definition – POOLDEF
- Supplemental Qualifiers – SUPP-- datasets

Source: Standard for Exchange of Nonclinical Data Implementation Guide: Nonclinical Studies, Version 3.1, 27 June 2016

Study Types

- General Toxicology (GLP/nonGLP)
- Carcinogenicity
- Cardiovascular
- Respiratory

Key Takeaways

- Latin Square study design modeled
- VS overhaul
- CV and RE introduced
- EG mostly unchanged

Endpoint Placement: SEND 3.0 vs SEND 3.1

Domain	SEND 3.0	
	EG	VS
Test/Data Type		
ECG Mean Heart Rate	X	
PR Interval	X	
QRS Duration	X	
QT Interval	X	
QTc Interval	X	
RR Interval	X	
Body Temperature		X
Diastolic Blood Pressure		X
Heart Rate		X
Mean Arterial Pressure		X
Minute Volume		X
Oxygen Saturation		X
Pulse Pressure		X
Respiratory Rate		X
Systolic Blood Pressure		X
Tidal Volume		X

Controlled Terminology Considerations

C67153 VS TEST				
NCI Code	CDISC Submission Value	CDISC Synonym	CDISC Definition	NCI Preferred Term
C49679	Mean Arterial Pressure	Mean Arterial Pressure	The mean pressure of the blood within the arterial circulation. The arterial pressure may be directly measured by insertion of an intra-arterial catheter connected to a transducer. The mean arterial pressure (MAP) can be calculated by subsequent analysis of the waveform. MAP can be approximated without an invasive procedure using the following formula: diastolic pressure plus 1/3 of the pulse pressure, where pulse pressure is systolic pressure - diastolic pressure. (NCI)	Mean Arterial Pressure
C49678	Respiratory Rate	Respiratory Rate	The rate of breathing (inhalation and exhalation) measured within in a unit time, usually expressed as breaths per minute. (NCI)	Respiratory Rate

SCVTEST (SEND Cardiovascular Test Name)

NCI Code: C120533, Codelist extensible: Yes

C120533 SCVTEST				
NCI Code	CDISC Submission Value	CDISC Synonym	CDISC Definition	NCI Preferred Term
C49679	Mean Arterial Pressure	Mean Arterial Pressure	The mean pressure of the blood within the arterial circulation. The arterial pressure may be directly measured by insertion of an intra-arterial catheter connected to a transducer. The mean arterial pressure (MAP) can be calculated by subsequent analysis of the waveform. MAP can be approximated without an invasive procedure using the following formula: diastolic pressure plus 1/3 of the pulse pressure, where pulse pressure is systolic pressure - diastolic pressure. (NCI)	Mean Arterial Pressure

SRETEST (SEND Respiratory Test Name)

NCI Code: C120535, Codelist extensible: Yes

C120535 SRETEST				
NCI Code	CDISC Submission Value	CDISC Synonym	CDISC Definition	NCI Preferred Term
C49678	Respiratory Rate	Respiratory Rate	The rate of breathing (inhalation and exhalation) measured within in a unit time, usually expressed as breaths per minute. (NCI)	Respiratory Rate

Source: CDISC Controlled Terminology

Important Note: Controlled Terminology lists are not based on SEND IG version.

Latin Square Study Design/Trial Design

TREATMENT DESIGN AND DOSE LEVEL DESIGNATION					
Animal	Gender	Dose Level Designation on Specified Dosing Days			
		Day 1	Day 8	Day 15	Day 22
1	M	Low	Control	High	Mid
2	M	Mid	High	Control	Low
3	M	High	Low	Mid	Control
4	M	Control	Mid	Low	High

TA

DOMAIN	ARMCD	ARM	TAETORD	ETCD	ELEMENT
TA	1	30-0-300-100		1 T2	30 mg/kg
TA	1	30-0-300-100		2 T1	0 mg/kg
TA	1	30-0-300-100		3 T4	300 mg/kg
TA	1	30-0-300-100		4 T3	100 mg/kg
TA	2	100-300-0-30		1 T3	100 mg/kg
TA	2	100-300-0-30		2 T4	300 mg/kg
TA	2	100-300-0-30		3 T1	0 mg/kg
TA	2	100-300-0-30		4 T2	30 mg/kg

TE

ETCD	ELEMENT
T1	0 mg/kg
T2	30 mg/kg
T3	100 mg/kg
T4	300 mg/kg

TX

DOMAIN	SETCD	SET	TXSEQ	TXPARAMCD	TXPARAM	TXVAL
TX	1	Low, Control, High, Mid		1 ARMCD	Arm Code	1
TX	2	Mid, High, Control, Low		2 ARMCD	Arm Code	2
TX	3	High, Low, Mid, Control		3 ARMCD	Arm Code	3
TX	4	Control, Mid, Low, High		4 ARMCD	Arm Code	4
TX	1	Low, Control, High, Mid		5 TCNTRL	Control Type	Vehicle Control
TX	2	Mid, High, Control, Low		6 TCNTRL	Control Type	Vehicle Control
TX	3	High, Low, Mid, Control		7 TCNTRL	Control Type	Vehicle Control
TX	4	Control, Mid, Low, High		8 TCNTRL	Control Type	Vehicle Control
TX	1	Low, Control, High, Mid		9 TRTDOS	Dose Level	30;0;300;100
TX	2	Mid, High, Control, Low		10 TRTDOS	Dose Level	100;300;0;30
TX	3	High, Low, Mid, Control		11 TRTDOS	Dose Level	300;30;100;0
TX	4	Control, Mid, Low, High		12 TRTDOS	Dose Level	0;100;30;300

Source: Covance training study

8 | SEND 3.1 : A "Vital" Upgrade - February 27th, 2019

Public

Recommendations

1

Confirm that the SEND 3.1 dataset reporting requirement applies.

2

Confirm that trial arms and sets are accurate for the Latin Square design.

3

Confirm the CV and/or RE domains are present.

4

Confirm that the VS has been reduced and does not duplicate data from CV or RE.



Covance Inc., headquartered in Princeton, NJ, USA, is the drug development business of Laboratory Corporation of America Holdings (LabCorp). COVANCE is a registered trademark and the marketing name for Covance Inc. and its subsidiaries around the world.