SEND 3.1: GIVING YOUR SUBMISSION A “VITAL” UPGRADE

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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

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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

## 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

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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

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 – TS

Relationship Datasets (Section 8)
- Related Records – RFLREC
- Pool Definition – POOLDEF

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

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

## Endpoint Placement: SEND 3.0 vs SEND 3.1

<table>
<thead>
<tr>
<th>Test/Data Type</th>
<th>SEND 3.0</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>EG</td>
</tr>
<tr>
<td>ECG Mean Heart Rate</td>
<td>X</td>
</tr>
<tr>
<td>PR Interval</td>
<td>X</td>
</tr>
<tr>
<td>QRS Duration</td>
<td>X</td>
</tr>
<tr>
<td>QT Interval</td>
<td>X</td>
</tr>
<tr>
<td>QTc Interval</td>
<td>X</td>
</tr>
<tr>
<td>RR Interval</td>
<td>X</td>
</tr>
<tr>
<td>Body Temperature</td>
<td></td>
</tr>
<tr>
<td>Diastolic Blood Pressure</td>
<td></td>
</tr>
<tr>
<td>Heart Rate</td>
<td></td>
</tr>
<tr>
<td>Mean Arterial Pressure</td>
<td>X</td>
</tr>
<tr>
<td>Minute Volume</td>
<td></td>
</tr>
<tr>
<td>Oxygen Saturation</td>
<td>X</td>
</tr>
<tr>
<td>Pulse Pressure</td>
<td></td>
</tr>
<tr>
<td>Respiratory Rate</td>
<td></td>
</tr>
<tr>
<td>Systolic Blood Pressure</td>
<td>X</td>
</tr>
<tr>
<td>Tidal Volume</td>
<td></td>
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</tbody>
</table>
Important Note: Controlled Terminology lists are not based on SEND IG version.
Latin Square Study Design/Trial Design

### Treatment Design and Dose Level Designation

<table>
<thead>
<tr>
<th>Animal</th>
<th>Gender</th>
<th>Dose Level Designation on Specified Dosing Days</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>Day 1: Low, Day 8: Control, Day 15: High, Day 22: Mid</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>Day 1: Mid, Day 8: High, Day 15: Control, Day 22: Low</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>Day 1: High, Day 8: Low, Day 15: Mid, Day 22: Control</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>Day 1: Control, Day 8: Mid, Day 15: Low, Day 22: High</td>
</tr>
</tbody>
</table>

### Treatment Levels

<table>
<thead>
<tr>
<th>ETCD</th>
<th>ELEMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>0 mg/kg</td>
</tr>
<tr>
<td>T2</td>
<td>30 mg/kg</td>
</tr>
<tr>
<td>T3</td>
<td>100 mg/kg</td>
</tr>
<tr>
<td>T4</td>
<td>300 mg/kg</td>
</tr>
</tbody>
</table>

### Treatment Assignments

Source: Covance training study
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.
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