FDA / PhUSE Nonclinical
SDRG Working Group

# Template, User Guide, and Examples for Nonclinical Study Data Reviewer's Guide for SEND Submissions

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# Introduction

From the
*Study Data Technical Conformance Guide*:

"The preparation of a Study Data Reviewer's Guide (SDRG) is recommended as an integral part of a standards-compliant study data submission."

*Current version 2.2. June 2015*

# SDRG Table of Contents

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# 1. Introduction

- Study ID information
- SEND data set creation process
- Statement that SEND data sets accurately represent the study report and, if needed, where in SDRG any differences are described.

## 1 Introduction

This document provides context for the SEND tabulation datasets and terminology for Study 54321, in addition to what is provided in the define.xml file, to facilitate the FDA reviewer's and data manager's use of the datasets. It also includes a summary of SEND dataset conformance findings.

### 1.1 Study Protocol Title, Number, and Report Version

| | |
|---|---|
| **Study Title** | A Thirteen-Week Oral Toxicology Study in Dogs with C1234 followed by a Two-Month Recovery Period |
| **Study Number** | 54321 |
| **Report Version** | There have been no report amendments. |

### 1.2 Summary of SEND Dataset Creation Process

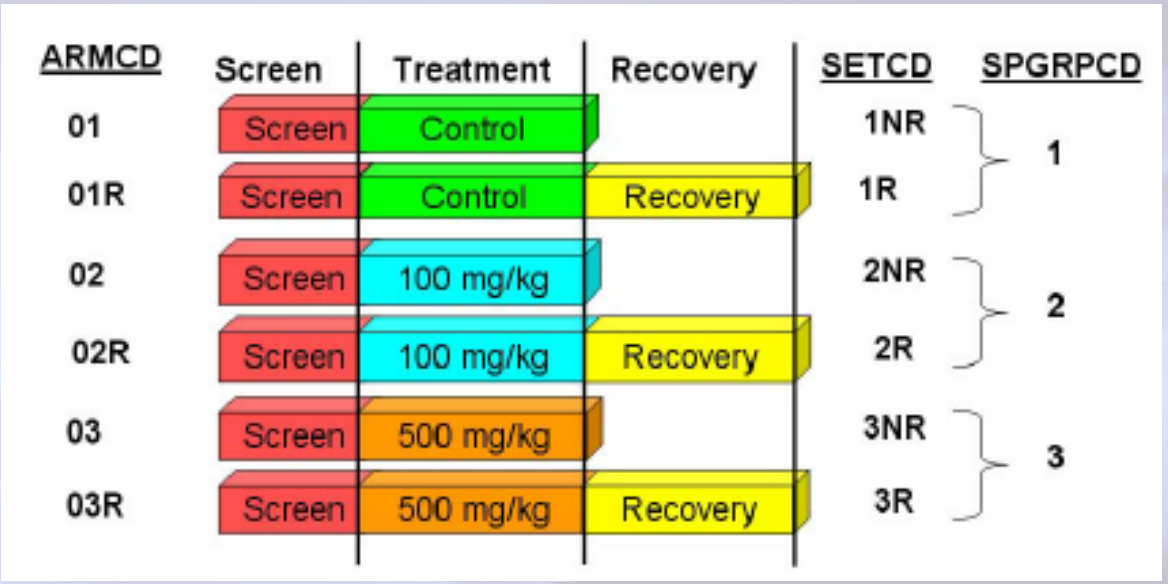
All in-life, clinical pathology, and postmortem data were collected using LIMS 1 (Vendor). Bioanalytical data (plasma drug concentrations) were determined using LIMS 2 (Vendor). Toxicokinetic parameters were calculated using LIMS 3 (LIMS 3). Input from the each of the LIMS via LIMS-specific adaptors was processed by SEND solution XXX (Vendor) to produce one integrated SEND dataset, a define.xml and PDF file, and a validation report. SEND solution XXX and the LIMS-specific adaptors are Part 11 compliant.

### 1.3 SEND Dataset Verification

Data in the SEND datasets are an accurate representation of data in the study report for Study No. 54321. Any differences between the datasets and the report are described in section 6.2.

# 2. Study Design

- Provide text or visual representation of SEND Trial Design to
- Help the Reviewer bridge the study design description in the report with the SEND Trial Design data sets



# 3. Standards, Formats, and Terminologies & their Versions

- Table of standards used in SEND data package
- Explain standards and versions selection
- Explain any Terminology that does not conform to CDISC CT where CDISC CT is required by SENDIG

### 3.1 Standards Used

| Dataset Component | Standard or Dictionary | Version |
|---|---|---|
| Tabulation Datasets | CDISC SEND | 3.0 |
| Data Definition File | CDISC DEFINE.XML | 1.0 |
| Controlled Terminology (CT) | CDISC SEND CT | 2014-12-26 |

### 3.2 Rationale for Standards Selection

The standards and versions selected were the most current ones listed in FDA's Study Data Standards Catalog at the time of dataset creation.

### 3.3 Nonstandard Terminology

Nonstandard terminology was used in the EG domain as shown in the table following.

| Dataset Name | Variable | Codelist | Term Used | Meaning |
|---|---|---|---|---|
| EG | EGTEST | EGTEST | Beat-to-beat QT/TQ ratio | A measure of the ability of the heart to recover from one beat to the next by examining the relationship between action potential duration (QT interval) and diastolic interval (TQ) through the ECG. |

# 4. Description of Study Datasets

- Provide a Dataset Summary list of domains submitted
- Provide explanations of datasets as needed (see following slides)

| Dataset | Dataset Label | Supplemental Qualifiers? | Related Using RELREC? | Observation Class |
|---|---|---|---|---|
| TA | Trial Arms | | | Trial Design |
| TE | Trial Elements | | | Trial Design |
| TS | Trial Summary | | | Trial Design |
| TX | Trial Sets | | | Trial Design |
| CO | Comments | | | Special Purpose |
| DM | Demographics | | | Special Purpose |
| SE | Subject Elements | | | Special Purpose |
| EX | Exposure | | | Interventions |
| DS | Disposition | | | Events |
| BW | Body Weight | | | Findings |
| BG | Body Weight Gain | | | Findings |
| CL | Clinical Observations | | | Findings |
| FW | Food & Water Cons | | | Events |
| LB | Laboratory Test Results | | | Findings |
| MA | Macroscopic Findings | X | X | Findings |
| MI | Microscopic Findings | X | X | Findings |
| OM | Organ Measurements | | | Findings |
| PC | Pharmacokinetic Conc | | | Findings |
| PP | Parmacokinetic Parameters | | | Findings |
| POOLDEF | Pool Definitions | | | Findings |

# 4. Description of Study Datasets (continued)

- For Dataset Explanation, *focus on what is important* on a study-by-study basis, such as:
  - Any agreements with review division on representation of data not specified in SENDIG or other mapping decisions
  - Inclusion of nonstandard variables supporting key analyses in a supplemental qualifier dataset
  - Custom domains

# 4. Description of Study Datasets (continued)

- Questions that may be helpful for Dataset Explanations:
  - Are the submitted data taken from an ongoing study? If so, what was the cut point(s)?
  - Were the SEND datasets used as sources for the analysis?
  - Were any domains planned but not submitted because no data were collected?
  - Are the submitted data a subset of collected data? (The answer will be "yes" if data were collected but not included in the submission.)
- Describe Supplemental Qualifier domains, if included in the dataset

| Dataset Name | Associated Dataset | Qualifiers Used |
|---|---|---|
| **SUPPMA** | MA<br>Macroscopic Findings | Modifiers that were part of MAORRES for which SEND variables have not yet been developed |
| **SUPPMI** | MI<br>Microscopic Findings | Modifiers that were part of MIORRES for which SEND variables have not yet been developed |

# 5. Data Standards Validation Rules, Versions, and Conformance

- Summarize and explain pre-submission validation outcomes
- Recommended to focus on FDA rule conformance even if another validator tool was used
- Explain both Warnings and Errors

**Example: Warnings**

| FDA Rule (2.0) | Message | Domain | Count | Explanation |
|---|---|---|---|---|
| FDAN178 | Missing value for CLORRES, when CLSTAT or CLDRVFL is not populated | CL | 48 | These findings pertain to animals that were not observed for clinical signs during urine collection in accord with the protocol and as indicated in – REASND. |
| FDAN227 | Missing value for CLSTRESC, when CLSTAT is null | CL | 48 | These findings pertain to animals that were not observed for clinical signs during urine collection in accord with the protocol and as indicated in – REASND. |

# 6. Description of Sponsor Decisions Related to Data Standard Implementations

## 6.1 Sponsor-Defined Standardization Descriptions

- Explanation for why certain data elements could not be fully standardized
- Comments on inclusion of any derived values
- Include description of any data that may also be located in another study, such as a shared control group

## 6.2 Differences Between SEND Datasets and Study Report

- Data included in report but not in datasets or vice versa
- Differences in study day numbering
- Explanation for multiple study numbers

## 6.3 Nonstandard Electronic Data Submitted

- Data collected using different terminologies
- Electronic data that do not conform to SDTM format

# Status of the Nonclinical SDRG Package

*DRAFT SDRG template, User Guide, and examples can be found on the PhUSE WIKI:*

*http://www.phusewiki.org/wiki/index.php?title=Nonclinical_SDRG_Template_and_Guide*

- PhUSE Computational Sciences Steering Committee is facilitating internal/informal review by FDA PhUSE participant working group
  - A decision will come from this review whether FDA will formalize review and pursue a process to determine official use of the PhUSE Nonclinical SDRG package. This could involve public review, with announcement in FR.
- The nonclinical SDRG Working Group will continue to meet to update the SDRG template based on feedback and updated guidances from FDA.

*Thank you!*

# Nonclinical SDRG Working Group

| Individual | Affiliation | Individual | Affiliation |
|---|---|---|---|
| Susan DeHaven* | Sanofi | Christy Kubin | MPI Research |
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