

Template and User Guide for Nonclinical Study Data Reviewer's Guide (SDRG)

Nonclinical SDRG Working Group

PP37

Background

According to the recently issued Study Data Technical Conformance Guide (December 2014), "The preparation of a Study Data Reviewer's Guide (SDRG) is recommended as an integral part of a standards-compliant study data submission." An SDRG should describe, for each study, any special considerations that may facilitate an FDA reviewer's and data manager's use of the datasets. These can include clarification of relationships between the study report and the data; highlighting, if appropriate, areas of interest that augment the study report, define file, and datasets; mapping decisions that require explanation; and terminology, standards, and validation rules versions. Preparation of an SDRG needs to have sufficient leeway to focus on what is important on a study-by-study basis. Additionally, the SDRG needs to include a description of how the datasets came together, from data collection to study report to translation to SEND and integration (or not) of the datasets.

The FDA/PhUSE nonclinical SDRG Working Group has developed a template for use as an SDRG with SEND submissions. We evaluated the clinical SDRG template developed by the FDA/PhUSE Clinical Working Group: Optimizing the Use of Data Standards, and adapted it for nonclinical with reference to the recently issued Technical Conformance This poster summarizes our recommended SDRG template and portions of the User Guide. After obtaining input at or after this meeting, the template, user guide, and examples will be posted on the PhUSE Wiki at:

http://www.phusewiki.org/wiki/index.php?title=Study_Data_Reviewer%27s_Guide

Please contact the individuals listed at the bottom of this poster to contribute comments or suggestions. The Nonclinical SDRG Working Group will continue meeting to update the template and associated documents as necessary.

1. SDRG Introduction

1.1 Study Protocol Title, Number, and Version

Any protocol amendments that affected data collection or interpretation should be noted in this recommended section.

Study Title	
Study Number	
Report Version	Include if dataset represents an amended report and indicate what data have been added since earlier submission

1.2 Summary of SEND Dataset Creation Process

This is a high-level summary of the process by which the SEND dataset was created from study data. For example, it might state that all in-life, clinical pathology, postmortem, and TK blood collection data were collected with LIMS 1 by Provider A. Bioanalytical analysis was determined with LIMS 2 by Provider B, with electronic transfer of in-life TK blood collection data from LIMS 1. Toxicokinetic calculations were determined using LIMS 3 by the sponsor. Input (raw data extracts) from each of the LIMS via LIMS-specific adaptors was processed by SEND Solution XX to produce one integrated SEND dataset including define.xml, LIMS terms mapped to controlled terminology, and a validation report.

2. Study Design

2.1 Study Design Summary

This optional section provides a brief two or three sentence textual description and/or table of the protocol design. The table may be taken from the protocol.

2.2 Trial Design Domain Overview

A diagram such as the one following or as shown in the SENDIG should be included here to illustrate the trial design. The following question must be answered:

- Are Trial Design datasets included in the submission?

There should be a subsection for any nonstandard trial design domain(s) that need additional explanation or is sponsor / study specific.

Study Group SPGRPCD	Trial Arms		Element in each Epoch			Trial Set	
	ARMCD	ARM	<EPOCH name 1>	<EPOCH name 2>	<EPOCH name 3>	SETCD	SET
<Sponsors group no.>							<Set name 1>
							<Set name 2>
							<Set name 3>

3. Standards, Formats, Terminologies & Versions

3.1 Standards Used

This section documents standards, versions, and validations used in this study data package.

Dataset Component	Standard or Dictionary	Versions Used
Tabulation Datasets	CDISC SEND	
Data Definition File	CDISC DEFINE.XML	
Controlled Terminology (CT)	CDISC SEND CT	
Tabulation Dataset Validator	FDA SEND Rules	
Other standards (optional)		

3. Standards, Formats, Terminologies & Versions (continued)

3.2 Rationale for Standards Selection

A likely rationale for standards and versions selection is that they were the most current ones listed in FDA's Study Data Standards Catalog at the time of dataset creation. However, this is the place to state if a waiver was granted to use an earlier standard.

3.3 Nonstandard Terminology

Any use of nonstandard terminology should be submitted to NCI for consideration and explained in the SDRG as shown following:

Dataset Name	Variable	Codelist	Term	Meaning

4. Description of Datasets

This section provides additional context for SEND domains that is not adequately addressed in define.xml or SENDIG. Answers to the following questions may be helpful:

- Are the submitted data taken from an ongoing study? If so, what was the cutpoint(s)? What will be coming?
- 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.) See Section 6.2.
- If an extension study is being documented, include description(s) of any data that have been copied from or are located in another study in the submission, such as the use of one control group for multiple studies.

4.1 Dataset Summary

This recommended section provides an overview of all domains included in the SEND dataset. Hyperlinks to additional text should be provided for any domains that require additional explanation. Any custom domains should be included in this section and hyperlinked to Section 6.1. An example of a Dataset Summary table is shown following.

Dataset Name	Dataset Label	Supp Qualifiers?	Related Records?	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			Findings
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	Pharmacokinetic Param			Findings
POOLDEF	Pooled Definition			Relationship

4.2 Dataset Label Explanation

This section is recommended in the event explanation is warranted for any of the datasets.

4.3 Use of Supplemental Qualifiers

This section is recommended in the event supplemental qualifiers are used and can include the following information:

Dataset Name	Associated Dataset	Qualifiers Used

5. Data Standards Validation Rules and Conformance Issues

5.1 Validation Outcome Summary

Conformance issues that relate to FDA SEND validator rules should be documented here along with any explanations for why conformance could not be achieved.

5. Data Standards Validation Rules and Issues (continued)

5.2 Validation Method Used

This section describes in two to three sentences the validation method used to assess SEND conformance. Example: OpenCDISC version 2.0 was used to evaluate SEND compliance of all datasets in this study data package. This version of OpenCDISC maps each OpenCDISC validation rule to the corresponding rule of the FDA SEND validator, version 2.1. Only those errors, warnings, or notices that pertain to FDA SEND validation rules are reported here.

5.3 Errors

This recommended section documents any reported validation errors. The table following should be used to explain any errors.

Rule	Message	Domain(s)	Count	Explanation

5.4 Warnings

Warnings should be summarized in the same fashion and using the same table as errors.

5.5 Notices

Notices should be summarized in the same fashion and using the same table as errors and warnings.

6. Sponsor Decisions Related to Data Standards Implementations

6.1 Sponsor-Defined Standardization Descriptions

This section can be used to describe:

- Custom domains
- Custom endpoints
- Justification for reference start dates that are different from first day of dosing, including any differences across subjects
- Descriptions of notable mapping decisions for legacy data

6.2 Differences between SEND Datasets and Study Report

Any significant differences between the study report and SEND dataset need to be discussed here. These differences could include:

- Differences in study day numbering
 - Dosing start of Day 0 (rather than Day 1)
 - For more complex differences in study days between report and SEND dataset, a mapping diagram may be helpful
- Any data in the study report that is not included in SEND datasets and why
- Any important controlled terminology mapping for that is deemed important for study interpretation

6.3 Nonstandard Electronic Data

Any nonstandard electronic data submitted that cannot be represented in a standard format should be discussed in this section along with rationale for not using standards.

6.4 Legacy Data Conversion Plan

A legacy data conversion plan may be included for studies that do not fit the standards, such as: 1) inability to accurately map to codelists (disposition terms in a carcinogenicity study; 2) collected data missing from SEND datasets; 3) situations where standardization decisions had to be made that could impact the interpretation of the electronic data.

Technical Conformance Guide and SDRG

The nonclinical SDRG Working Group reviewed the recently issued Technical Conformance Guide for inclusion of all SDRG-related recommendations in our template, user guide, and examples. Following are additional items from the Technical Conformance Guide pertaining to sponsor interactions with the Agency and SDRG documentation:

- Section 4.1: There may be instances in which current implementation guides (e.g., SDTMIG, SENDIG) do not provide specific instruction as to how certain study data should be represented. In these instances, sponsors should discuss their proposed solution with the review division in advance of the submission, and then submit supporting documentation that describes their decisions or solutions in the SDRG at the time of submission.
- Section 4.1.3.3: Discussion with the review division should occur if the sponsor intends to include important variables (i.e., that support key analyses) in SUPPQUAL datasets and this should be reflected in the SDRG. Currently, SUPPQUAL should be used to capture some collected information (e.g., pathology modifiers) until the SEND model is further refined to adequately represent such information.

Conclusion

A useful SDRG is not intended to simply repeat information contained in the data or the define file. Rather, it is meant to augment the report, define file, and datasets and highlight for FDA Reviewers and Data Managers what is important in a particular SEND submission.

For comments / input, contact:

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