The Nonclinical Study Data Reviewer’s Guide

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Abstract

According to FDA’s Study Data Technical Conformance Guide v2.2 (June 2015), preparation of a Study Data Reviewer’s Guide (SDRG) is recommended as an integral part of a CDISC standards-compliant study data submission. An SDRG template, completion guidelines, and examples for clinical studies have been available since May 2013. Recently, the PHUSE / FDA Nonclinical SDRG Working Group, with representation from Pharma, CROs, and SEND solution vendors, has developed an SDRG for nonclinical studies with inputs and feedback from FDA. These materials can be found at http://cisweb.cnta.ca/Nonclinical_SDRG_Templateguide.pdf.

The nonclinical SDRG should describe for each study any special considerations that may facilitate review of the dataset by FDA reviewers and data managers. These include clarification of any differences between study report and SEND datasets; identification of SEND standards, controlled terminologies and versions used in the datasets; a summary of included domains; conformance observations relating to FDA SEND validator rules; and decisions related to data standards implementations including deviations and errors where applicable. The SDRG should include a high-level summary of the process by which the SEND datasets were created from study data. Each SDRG should be specific to a particular study to enable effective use by FDA reviewers and data managers. Highlights of recommendations for authoring a nonclinical SDRG are folded into this section of this presentation.

Note: It is critical for an SDRG author to have sufficient flexibility to focus on what is important for a particular study.

SDRG Table of Contents

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1. Introduction

This section should include high-level information for a reviewer to become familiarized with the study submission package:

• Study Information
• SEND dataset creation process
• Statement that SEND datasets accurately represent data in the study report and, if needed, where in the SDRG any differences are noted

Example

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.xmi file, to facilitate the FDA reviewers and data manager’s use of the datasets.

1.1 Study Protocol Title, Number, and Report Version

Example

1.1 Study Protocol Title, Number, and Report Version

<table>
<thead>
<tr>
<th>Study Title</th>
<th>Study Number</th>
<th>Report Version</th>
</tr>
</thead>
<tbody>
<tr>
<td>[Study Name]</td>
<td>[Study ID]</td>
<td>Final</td>
</tr>
</tbody>
</table>

1.2 Summary of SEND Dataset Creation Process

All preclinical, clinical pathology, and postmortem data were collected using LIMS 1 (Vendor). Bioanalytical data were determined using LIMS 2 (Vendor). Toxicokinetic parameters were calculated using LIMS 3 (Vendor), input from the output of the LIMS via LIMS-specific adaptors was processed by SEND solution XYZ (Vendor) to produce one integrated SEND dataset, define.xmi and PDF files, and a validation report, SEND solution XYZ and the LIMS-specific adaptors per Part 1 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 1.2.

2. Study Design

This section provides a brief orientation to the study and additional context about the Trial Design Datasets.

Example

2.1 Study Design Summary

In study 54321, 6 dogs/group were dosed by oral gavage once daily for 13 weeks at doses of 0, 100, and 500 mg/kg C324. At the end of the treatment period, 4 dogs/group underwent terminal sacrifice. The remaining 2 dogs/group were placed on an 8-week recovery period followed by sacrifice.

2.2 Trial Design Domain Overview

This section documents the SEND version, controlled terminology version, validation rule version and dictionary version used in the study and the rationale for the selection.

Example

3. Standards, Formats, Terminologies, & their Versions

This section documents the SEND version, controlled terminology version, validation rule version and dictionary version used in the study and the rationale for the selection.

Example

4. Description of Study Datasets

This section provides an overview of all datasets included in the SEND dataset including the Trial Design datasets. Additional text in section 4.2 should be provided for any domains that require additional explanation.

Example

4.1 Dataset Datasets

Example

5. Data Standards Validation Rules, Versions, & Conformance

All significant conformance findings should be documented in Section 5. It is a detail that will provide a reviewer or data manager a quick and clear overview of any issues with the data package and the rationale for their presence.

Example

6. Sponsor Decisions Related to Data Standards Implementations

6.1 Sponsor-Defined Standardization Descriptions such as:

• Explanation for why certain data elements could not be fully standardized, if applicable
• Comments on inclusion of any derived values

6.2 Differences Between SEND Datasets and Study Report such as:

• Data included in report but not datasets or vice versa
• Differences in study day numbering

6.3 Nonstandard Electronic Data Submitted such as:

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

6.4 Legacy Data Conversion

If data was not collected with a specific standard in mind, this section should outline the legacy data conversion plan for such data.

Status of Nonclinical SDRG Package

• Public review, announced through PHUSE, ended October 30, 2015 - All comments have been addressed
• FDA informal review of Nonclinical SDRG Package was positive - no comments
• A Federal Register announcement is expected for broader public review of the Nonclinical SDRG Package

Note: The opinions expressed in this poster are those of the authors and do not necessarily represent the opinions of their respective companies