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

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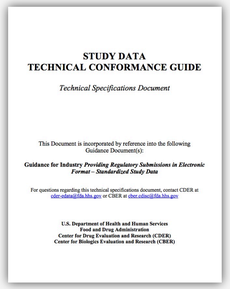
Abstract

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 the FDA. These materials can be found at:
http://phusewiki.org/wiki/index.php?title=Nonclinical_SDRG_Template_and_Guide
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 form the basis of this poster presentation.

SDRG Table of Contents



STUDY DATA
TECHNICAL CONFORMANCE GUIDE

Technical Specifications Document

This Document is incorporated by reference into the following Guidance Document(s):

Guidance for Industry *Providing Regulatory Submissions in Electronic Format – Standardized Study Data*

For questions regarding this technical specifications document, contact CDER at sdre-edata@fda.hhs.gov or CBER at cber.edocs@fda.hhs.gov

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

The SDRG Table of Contents comes from recommendations in FDA's Study Data Technical Conformance Guide (most recent version, October 2015).

1. Introduction

- Study ID 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

1. Introduction (continued)

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.xml file, to facilitate the FDA reviewer's and data manager's use of the datasets.

1.1 Study Protocol Title, Number, and Report Version

Study Title	A 13-week Oral Toxicology Study in Dogs with C1234 followed by an 8-week Recovery Period
Study Number	54321
Report Version	Final. 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 were determined using LIMS 2 (Vendor). Toxicokinetic parameters were calculated using LIMS 3 (Vendor). Input from the each of the LIMS via LIMS-specific adaptors was processed by SEND solution XXX (Vendor) to produce one integrated SEND dataset, define.xml and PDF files, and a validation report. SEND solution XXX and the LIMS-specific adaptors are Part 11 compliant.

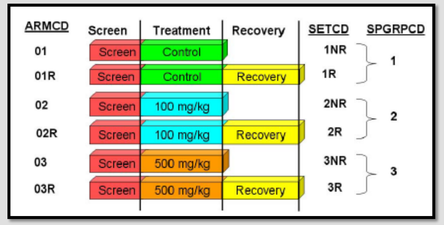
1.3 SEND Dataset Verification
Data in the SEND datasets are an accurate representation of data in the study report for Study No. 54321. Any differences between the datasets and the report are described in section 6.2.

2. Study Design

Example

2.1 Study Design Summary
In study 54321, 6 dogs/sex/group were dosed by oral gavage once daily for 13 weeks at doses of 0, 100, and 500 mg/kg C1234. At the end of the treatment period, 4 dogs/sex/group underwent terminal sacrifice. The remaining 2 dogs/sex/group were placed on an 8-week recovery period followed by sacrifice.

2.2 Trial Design Domain Overview



3. Standards, Formats, Terminologies, & their Versions

Example

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	2015-6-24

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 following:

Dataset Abbreviation	Variable	Term Used	Meaning
EG	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)

4. Description of Study Datasets

Example

4.1 Dataset Summary

Dataset	Dataset Label	Supplemental Qualifiers?	Related using RELREC?	Observation Class
TA	Trial Arm			Trial Design
TE	Trial Elements			Trial Design
TS	Trial Summary			Trial Design
TX	Trial Sets			Trial Design
DS	Disposition			Events
DM	Demographics			Special Purpose
SE	Subject Elements			Special Purpose
EX	Exposure			Interventions
EG	ECG Results			Findings
MA	Macroscopic	X	X	Findings
MI	Microscopic	X	X	Findings

4.2 Dataset Explanations

4.2.1 DS Domain
The DSDECOD of UNPLANNED TERMINAL SACRIFICE was used for animals in the high-dose treatment group that was terminated early by protocol amendment. Other animals in that group were terminated prior to issuance of the protocol amendment and were assigned a DSDECOD of MORIBUND SACRIFICE.

4. Description of Study Datasets (continued)

4.3 Supplemental Qualifiers

Dataset Name	Associated Dataset	Qualifiers Used
SUPPMI	MI (Microscopic Findings)	Modifiers from MIORRES for which SEND 3.0 variables have not yet been developed
SUPPMA	MA (Macroscopic Findings)	Modifiers from MAORRES for which SEND 3.0 variables have not yet been developed

5. Data Standards Validation Rules, Versions, & Conformance

Example

5.1 Validation Method
OpenCDISC Validator version 2.0.1, which includes all FDA SEND validation rules Version 2.0, was used to evaluate conformance to SEND 3.0.

5.2. Validation Outcome Summary
Of a total of 31,682 records, there were 0 errors and 1807 warnings. None of the warnings were relevant to this SEND submission for the reasons provided in Section 5.4.

5.3 Errors
No errors were reported.

5.4 Warnings
The Warnings for Study 54321 resulted from a small number of FDA SEND validation rules as shown in the table following.

FDA Rule	Message	Domain	Count	Explanation
FDAN212	Duplicate Records	FW	1347	The validation rule is incorrectly configured because it does not consider FWORRES.
FDAN164	Missing value for LBSTRESU when LBSTRESC is provided	LB	79	The value for LBSTRESC is albumin / Globulin ratio, which is not associated with units. Accordingly, LBSTRESU should not be populated, and the validation rule is incorrectly configured.

6. Description of 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

Status of Nonclinical SDRG Package

- Public review, announced through PhUSE, ended October 30, 2015
- FDA is currently reviewing Nonclinical SDRG Package
- A Federal Register announcement is expected for broader public review of the Nonclinical SDRG Package

PhUSE Nonclinical SDRG Working Group (in addition to authors)

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