

PhUSE Working
Group 4
developed an
SDTM Study Data
Reviewer’s Guide
(SDRG) template
to supplement the
information found
in define.xml for
drug submissions.

Study Data Reviewer’s Guide

SDRG, Inc.
Study SDRG-001A
Version 2013-02-22

Study SDRG-001A Study Data Reviewer’s Guide

Study Data Reviewer’s Guide

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1. Introduction

1.1 Purpose
This document provides context for tabulation datasets and terminology that benefit from additional explanation beyond the Data Definitions document (define.xml). In addition, this document provides a summary of SDTM conformance findings.

1.2 Study Data Standards and Dictionary Inventory

Standard or Dictionary	Versions Used
SDTM	SDTM v1.2/SDTM IG v3.1.2 including SDTM Amendment 1
Controlled Terminology	2011-07-22
Data Definitions	define.xml v1.0
Medications Dictionary	Proprietary medication dictionary
Medical Events Dictionary	MedDRA v14.1

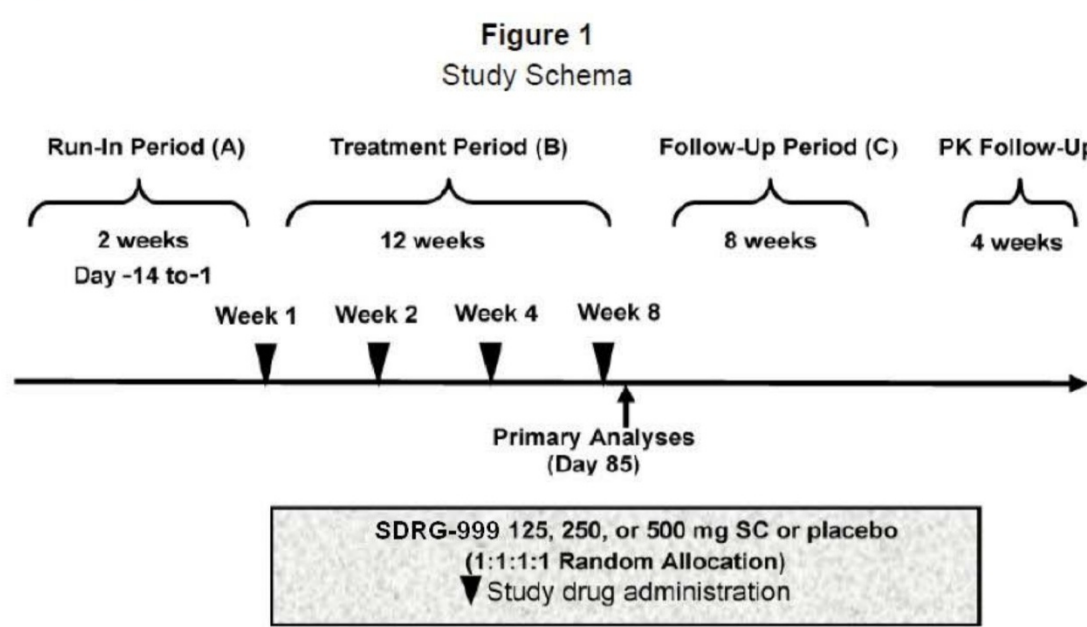
2. Protocol Description

2.1 Protocol Number and Title

Protocol Number: SDRG-001A
Protocol Title: A Phase II, Randomized Double-Blind Placebo-Controlled Dose Ranging Study to Evaluate SDRG-999 in Adults With Asthma
Protocol Versions: SDRG-001A

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2.2 Protocol Design



2.3 Trial Design Datasets

Are Trial Design datasets included in the submission? Yes

Dataset	Dataset Label
TA	Trial Arms
TE	Trial Elements
TV	Trial Visits
TI	Trial Inclusion/Exclusion Criteria
TS	Trial Summary

2.3.1. TI – Trial Inclusion/Exclusion Criteria
The trial inclusion/exclusion criteria are not fully described in the TI domain. Please refer to [Appendix I](#) for the full text of the criteria.
2.3.2. TS – Trial Summary
The TS domain includes the deprecated parameter Adverse Events Dictionary (AEDICT) to support internal processes.
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This sample Study
Data Reviewer's
Guide document
illustrates the
intended use of the
template and
demonstrates what
a finished
document should
look like.

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3. Subject Data Description

3.1 Overview

Are the submitted data taken from an ongoing study? Yes
If yes, describe the data cut or database status:
Per protocol, the primary analyses were planned to occur after all subjects completed their Day 85 visit. This occurred on 2012-07-01; however, the tabulated datasets include all CRF and electronic data as of 2012-09-01. The additional time was allotted for data cleaning.
Were the SDTM datasets used as sources for the analysis datasets? Yes
If no, what were the sources of analysis datasets?
Do the submission datasets include screen failures? Yes
If yes, which datasets include screen failure data?
Screen failure data are found in the DM, IE, DS and AE datasets.
Were any domains planned, but not submitted because no data were collected? No
If yes, list domains not submitted:
Are the submitted data a subset of collected data? No
If yes, describe:
Additional Content of Interest
Key analysis data points include:
• Spirometry endpoints: LB domain where LBCAT = SPIROMETRY and LBNAM = SPIROGRAPH
• Asthma exacerbation endpoints: ZA domain where ZACAT = ASTHMA EXACERBATIONS and QS domain where QSTESTCD = QS12379A
• Safety analysis: AE domain
• Subject deaths: AE domain where AEOUT = FATAL, DS domain where DSSCAT = STUDY DISCONTINUATION and DSDECOD = DEATH
Screening failures are included in the SDTM datasets if the subject experienced an adverse event during the protocol-defined run-in period (see Section 2.2).
Reference start date was assigned as the date of randomization and will be missing for screening failures.
A CRF collected pregnancy event information; however, no pregnancy events were reported.

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3.2 Annotated CRFs

Collected fields that have not been tabulated have been annotated as “Not Mapped”. SDRG Inc. collects certain data elements to facilitate certain operational processes including data cleaning and dynamically creating additional forms in the electronic data capture system. All fields that have been annotated as “Not Mapped” meet these criteria.

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3.3 SDTM Subject Domains

Dataset – Dataset Label	Efficacy	Safety	Other	Supp.	Related Using RELREC	Observation Class
AE – Adverse Events		X			ZA	Events
CM – Concomitant Medications	X	X				Interventions
CO – Comments			X			Special Purpose
DM – Demographics			X			Special Purpose
DS – Disposition			X			Events
EX – Exposure			X			Interventions
LB – Laboratory Test Results	X	X		X		Findings
MH – Medical History			X			Events
QS – Questionnaires	X	X				Findings
SE – Subject Elements			X			Special Purpose
SV – Subject Visits			X			Special Purpose
VS – Vital Signs		X				Findings
ZA – Clinical Assessments	X				AE	Findings

3.3.1. CM – Concomitant Medications
The start date for historical corticosteroids was not reported for 37 subjects. As a result, validation rule errors are to be expected.
3.3.2. DS – Disposition
After a subject completes the trial, two observations with DSCAT equal to DISPOSITION EVENT are expected. DSCAT equal to TREATMENT DISCONTINUATION indicates the subject’s completion status relative to Day 85. DSCAT equal to STUDY DISCONTINUATION indicates the subject’s completion status at study exit. As the submitted data only include data at the time the last subject completed Day 85, not all subjects will have the aforementioned two observations.

- This template was produced with FDA participation.
- A reviewer’s guide is not required for SDTM submissions yet, but could be in the future.
- This template is open-ended. It supports many possible study data scenarios.
- The questionnaire format gives the finished SDRG a consistent look and feel, to help reviewers find the information they need.
- We’ve started the document for you, you just have to fill it out!

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3.3.3. EX – Exposure

Four SDRG-999/Placebo injections were planned at each visit. Each injection is recorded as a separate observation in the EX domain. The total dose received at each visit can be calculated by summing the individual doses at each visit. If SDRG-999/Placebo was not administered at a visit, an observation has been recorded in EX for that visit and EXOCCUR assigned to N.

3.3.4. LB – Laboratory Test Results

QNAM	Description
LBCVRESC	Character result in conventional units
LBCVRESU	Conventional unit
LBCVNRLO	Reference range lower limit in conventional units
LBCVNRHI	Reference ranges upper limit in conventional units

3.3.5. VS – Vital Signs
Temperature was not collected prior to randomization; therefore, BLFL will be missing for all observations where VSTESTCD equals TEMP.

3.3.6. ZA – Clinical Assessments
ZA is a sponsor-defined domain that tabulates the investigator’s assessment of the interventions and asthma-related symptoms indicative of an exacerbation event. The considerations for this assessment are defined in the protocol. If the investigator believes an asthma exacerbation event has occurred, the investigator will record this as an adverse event. An explicit link has been collected between the assessment and the corresponding adverse event. This relationship between ZA and AE is defined in RELREC.

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4. Data Conformance Summary

4.1 Conformance Inputs

Was OpenCDISC used to evaluate conformance? Yes
If yes, specify the version of the OpenCDISC validation rules:
OpenCDISC SDTM v3.1.2 Amendment 1 rules
Were sponsor-defined validation rules used to evaluate conformance? No
If yes, describe any significant sponsor-defined validation rules:
Were the SDTM datasets evaluated in relation to define.xml? No
Was define.xml evaluated? No
Provide any additional compliance evaluation information:

4.2 Issues Summary

Dataset	Diagnostic Message	Severity	Count	Explanation
CM	Start Date/Time of Observation (~STDTC) or Start Relative to Reference Period (~STRF) should not be NULL, when End Date/Time of Observation (~ENDTC) or End Relative to Reference Period (~ENRF) is not NULL	Warning	37	The start date for historical corticosteroids was not reported for 37 subjects.

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Appendix I: Inclusion/Exclusion Criteria

Protocol/Amendment Version	Category	TESTCD	Full Text of Criterion
SDRG-001A	INCLUSION	INCL01	Signed Informed Consent
SDRG-001A	INCLUSION	INCL02	Age >= 18 years and <= 65 years at Screening Visit
SDRG-001A	INCLUSION	INCL03	Body Weight >=50 kg and <=150 kg at Screening Visit
SDRG-001A	INCLUSION	INCL04	Stable asthma defined by the following criteria. 1. Diagnosis of asthma >= 12 months prior to Screening Visit 2. Bronchodilator response of a minimum of 15% relative increase in the volume of FEV1 after bronchodilator at Visit 1 or Visit 2 3. Prebronchodilator FEV1 >=60% and <=85% predicted at Visit 2.
SDRG-001A	EXCLUSION	EXCL01	Basal or squamous cell carcinoma
SDRG-001A	EXCLUSION	EXCL02	Known immunodeficiency including but not limited to HIV infection
SDRG-001A	EXCLUSION	EXCL03	Noncompliance or inability to participate in all assessments

- This reviewer’s guide fills in gaps in current submission documentation.
- The design and testing of this package may inform future documentation standards.
- Include your SDRG in Module 5 of the eCTD with the study’s SDTM datasets.