

Clinical Study Data Reviewer's Guide

SDRG, Inc.

Study SDRG-001A

cSDRG Template Version 2018-11-01

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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 Acronyms

Acronym	Translation
aCRF	Annotated Case Report Form
eCRF	Electronic Case Report Form
eDT	Electronic Data Transfer (e.g. central lab data, ECG vendor data, PK data, etc.)

1.3 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 Added 'WASHOUT PERIOD 1' 'WASHOUT PERIOD 2' to EPOCH extensible codelist as the study design includes two washout periods.
Data Definitions	define.xml v1.0
Medications Dictionary	Proprietary medication dictionary
Medical Events Dictionary	MedDRA v14.1

2. Protocol Description

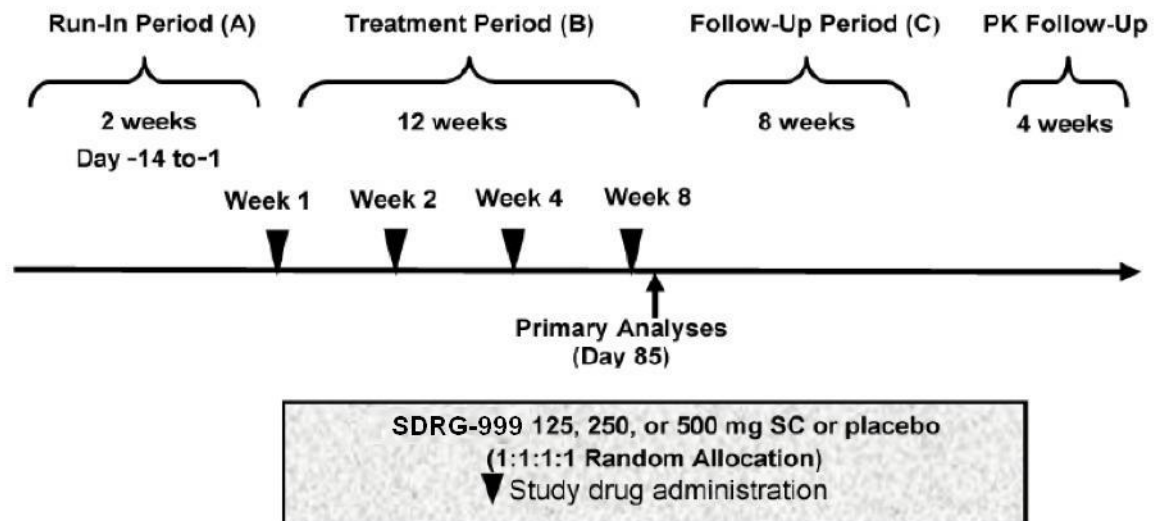
2.1 Protocol Number and Title

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

Figure 1
Study Schema



2.3 Trial Design Datasets

Are Trial Design datasets included in the submission? Yes

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.

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

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

Are the submitted data a subset of collected data? No

Is adjudication data present? Yes

If yes, describe the implementation approach and location of the adjudication data:

Primary cause of death was adjudicated by the subject's primary care physician. Death details are located in the Death Details domain.

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).

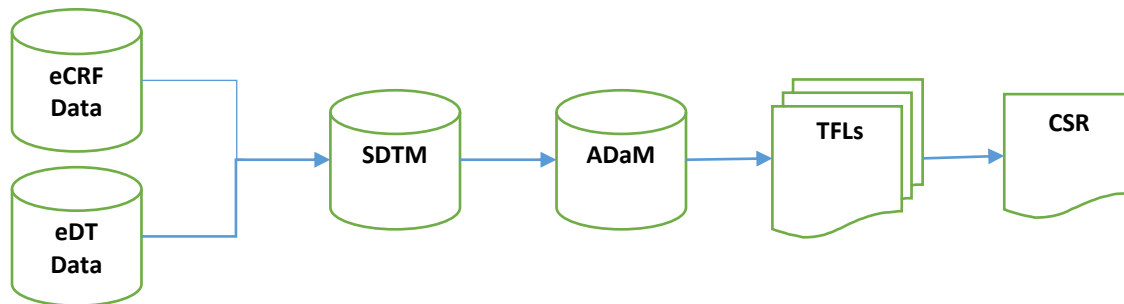
Reference start date was assigned as the date of randomization and will be missing for screening failures.

A CRF collected pregnancy event information; however, no pregnancy events were reported.

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3.2 Traceability Flow Diagram

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3.3 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.

Explanation of data fields [Not Submitted]

aCRF page Number(s)	Data Collection Field	Explanation of why [NOT SUBMITTED]
5	Were there any product complaints?	For internal use only.
30	PI Signature Date	Not needed for analysis.

3.4 SDTM Subject Domains

Dataset – Dataset Label	Efficacy	Safety	Other	Custom	SUPP-	Related Using RELREC
AE – Adverse Events		X				ZA
CM – Concomitant Medications	X	X				
CO – Comments			X			
DD – Death Details			X			
DM – Demographics			X			
DS – Disposition			X			
EX – Exposure			X			

Dataset – Dataset Label	Efficacy	Safety	Other	Custom	SUPP.	Related Using RELREC
LB – Laboratory Test Results	X	X			X	
MH – Medical History			X			
QS – Questionnaires	X	X				
SE – Subject Elements			X			
SV – Subject Visits			X			
VS – Vital Signs		X				
XL – Laboratory Test Results CN				X	X	
ZA – Clinical Assessments		X				AE

3.4.1. 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.

3.4.2. DS – Disposition

After a subject completes the trial, two observations with DSCAT equal to DISPOSITION EVENT are expected. DSSCAT 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.

3.4.3. 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.

3.4.4. 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

3.4.5. VS – Vital Signs

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

3.4.6. XL – Laboratory Test Results CN

XL is a custom domain that contains laboratory test results. The data is a mirror image of the LB domain data except the standard variables are represented in conventional units rather than SI units.

3.4.7. 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.

4. Data Conformance Summary

4.1 Conformance Inputs

Was a validator used to evaluate conformance? Yes

If yes, specify the version(s) of the validation rules:

Pinnacle 21 Enterprise 3.4 (FDA), SDTM v3.1.3 rules

Were sponsor-defined validation rules used to evaluate conformance? No

Were the SDTM datasets evaluated in relation to define.xml? No

Was define.xml evaluated? No

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.

4.3 Additional Conformance Details

There are no additional details to be documented.

Appendix I: Inclusion/Exclusion Criteria

Protocol/ Amendment Version	Category	IETESTCD	Full Text of Criterion
SDRG-001A	INCLUSION	INCL01	Signed Informed Consent
SDRG-001A	INCLUSION	INCL02	Age \geq 18 years and \leq 65 years at Screening Visit
SDRG-001A	INCLUSION	INCL03	Body Weight \geq 50 kg and \leq 150 kg at Screening Visit
SDRG-001A	INCLUSION	INCL04	Stable asthma defined by the following criteria. 1. Diagnosis of asthma \geq 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 \geq 60% and \leq 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