

Clinical Study Data Reviewer's Guide

LDCP, Inc.

Study LDCP-0242-005

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 compliance findings as well as details regarding legacy data tabulation conversion to SDTM.

1.2 Acronyms

Acronym	Translation
aCRF	Annotated Case Report Form
CRU	Clinical Research Unit
ECG	Electrocardiography
eCRF	Electronic Case Report Form
eDT	Electronic Data Transfer
PK	Pharmacokinetics

1.3 Study Data Standards and Dictionary Inventory

Standard or Dictionary	Versions Used
SDTM	SDTM v1.3/SDTM IG 3.1.3
Controlled Terminology	2016-03-25
Data Definitions	define.xml v2.0
Medications Dictionary	Proprietary medication dictionary
Medical Events Dictionary	MedDRA v14.1

2. Protocol Description

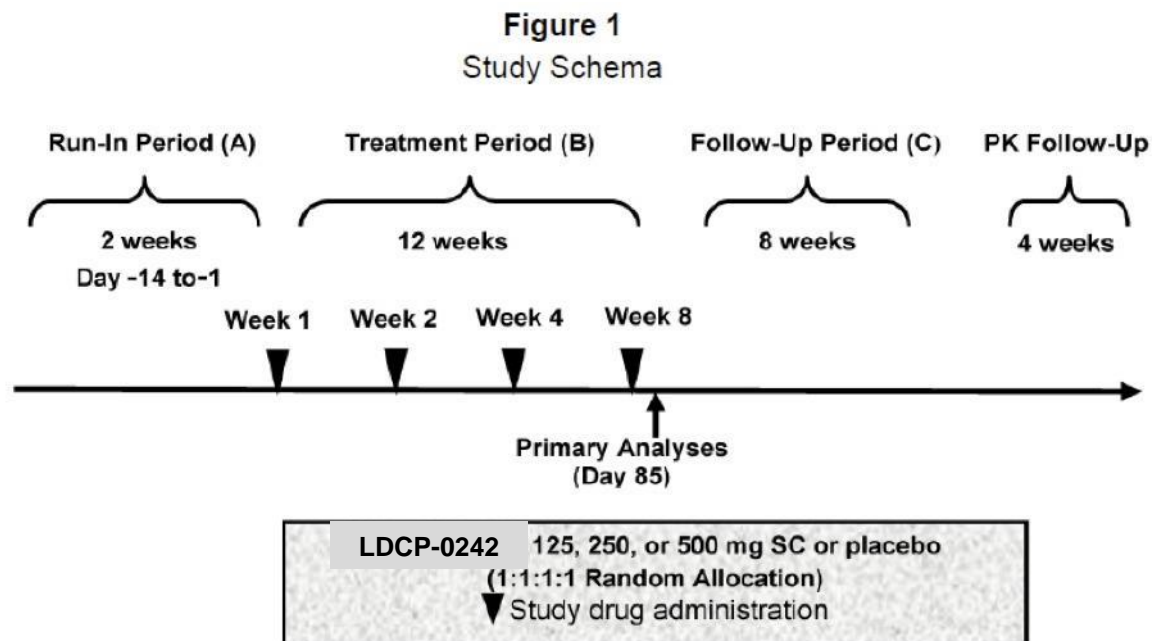
2.1 Protocol Number and Title

Protocol Number: LDCP-0242-005

Protocol Title: A Phase II, Randomized Double-Blind Placebo-Controlled Dose Ranging Study to Evaluate LDCP-0242 in Adults with Asthma

Protocol Versions: LDCP-0242-005 v1.0

2.2 Protocol Design



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. Subject Data Description

3.1 Overview

Are the submitted data taken from an ongoing study? No

Were the SDTM datasets used as sources for the analysis datasets? No

If no, what were the sources of analysis datasets? Legacy tabulation data

Please refer to 'Legacy Data Conversion Plan and Report Appendix' for details.

Do the submission datasets include screen failures? Yes

If yes, which datasets include screen failure data?

Screen failure data is 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? No

Additional Content of Interest

Key analysis data points include:

- Spirometry endpoints: RE domain where RECAT = SPIROMETRY and RENAM = SPIROGRAPH
- Asthma exacerbation endpoints: RE domain where RECAT = 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

Reference start date was assigned as the date of first dose of study medication and will be missing for screening failures as well as subjects that were randomized but not treated.

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

3.2 Traceability Flow Diagram

Please refer to 'Legacy Data Conversion Plan and Report Appendix' for the diagram.

3.3 Annotated CRFs

Collected fields that have not been tabulated have been annotated as "NOT SUBMITTED". LDCP, Inc. collects certain data elements (e.g. prompt questions) to facilitate certain operational processes including data cleaning and dynamically creating additional forms in the electronic data capture (eDC) system. All fields that have been annotated as "NOT SUBMITTED" 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				RE
CM – Concomitant Medications	X	X				
CO – Comments			X			
DM – Demographics			X			
DS – Disposition			X			
EX – Exposure			X			
LB – Laboratory Test Results	X	X			X	
MH – Medical History			X			
QS – Questionnaires	X	X				
RE – Respiratory System Findings	X	X		X	X	AE
SE – Subject Elements			X			
SV – Subject Visits			X			
VS – Vital Signs		X				

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 = 'TREATMENT DISCONTINUATION' indicates the subject's completion

status relative to Day 85. DSSCAT = 'STUDY DISCONTINUATION' indicates the subject's completion status at study exit.

3.4.3. EX – Exposure

Four LDCP-0242/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 LDCP-0242/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. RE – Respiratory System Findings

RE is a CDISC draft body-system domain that is not yet finalized and will be considered a custom domain until such time. It contains data pertaining to 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 RE and AE is defined in RELREC.

RE also contains data collected in relation to spirometry assessments.

3.4.6. VS – Vital Signs

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

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:

Pinnacle21 Community v2.2.0, SDTM 3.1.3 (FDA)

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

Were the SDTM datasets evaluated in relation to define.xml? Yes

Was define.xml evaluated? Yes

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

Legacy Data Conversion Plan and Report Appendix

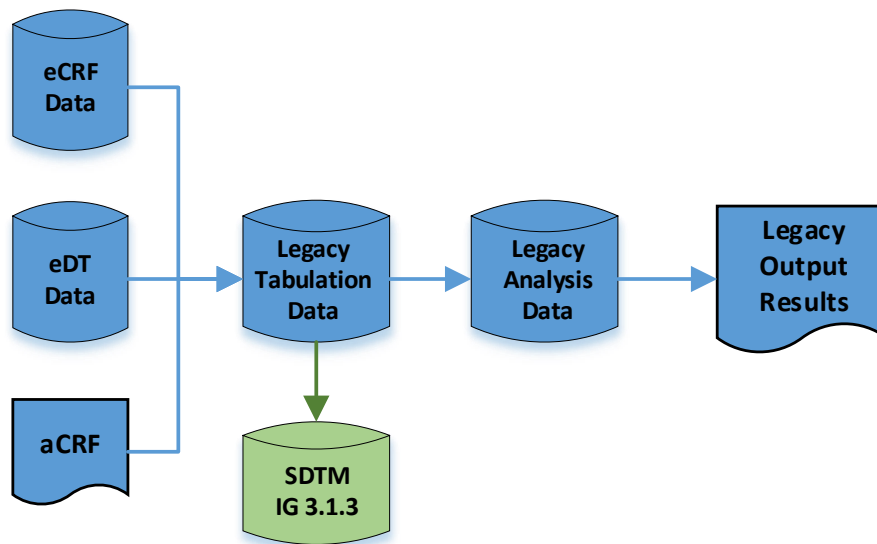
1. Purpose

The purpose of this appendix is to document the conversion of legacy tabulation data to SDTM.

Because of transformations required during SDTM conversion, some of the terms, categories and data formats used in the tabulation data have been translated into CDISC standard formats in the SDTM data. This appendix identifies differences between the legacy tabulation and SDTM data, and explains how SDTM represents the equivalent data.

2. Conversion Data Flow

The legacy data was converted to SDTM as described in the following data flow diagram.



The legacy data was converted to SDTM v1.3/SDTM IG 3.1.3 without creating ADaM datasets since the study started before December 17, 2016. The rationale for only converting to SDTM was to support pooling activities for the ISS and ISE. The tabulation data was pooled at the SDTM level and ADaM datasets were created to be used as input for the ISS/ISE.

3. Converted Data Summary

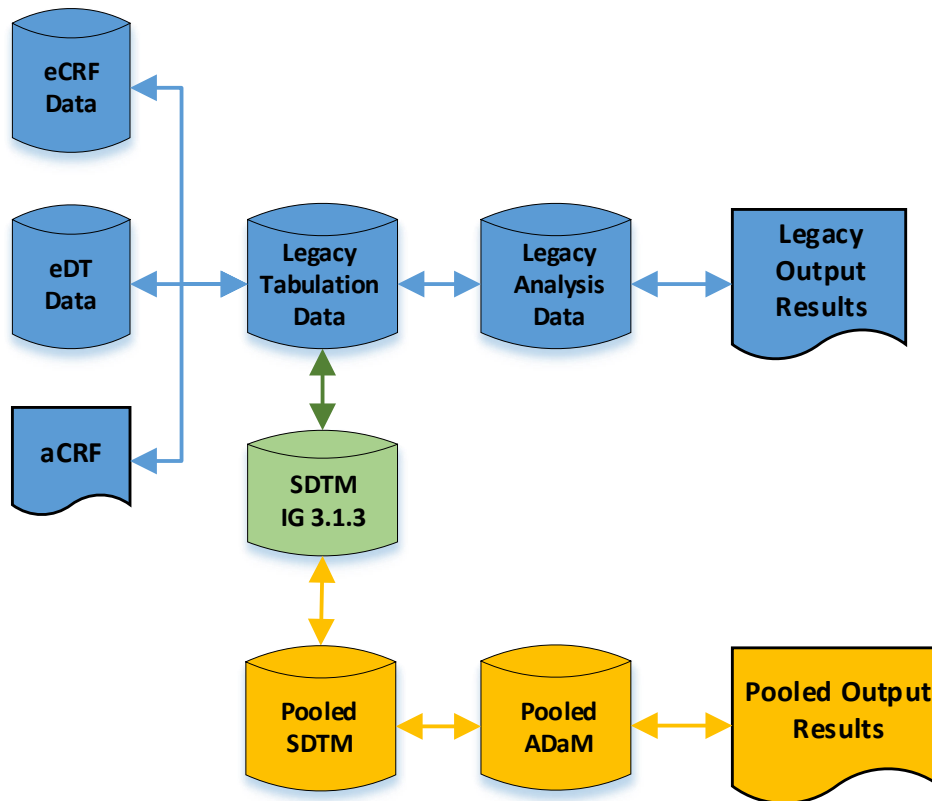
The legacy data was available in SAS format (.sas7bdat). A formats catalog was applied to the datasets prior to conversion to SDTM in order to aid in source-to-target mapping (e.g. straight map or minimal conditional statements needed). During authoring of the mapping specification from legacy data to SDTM, CDISC Controlled Terminology was applied where applicable. After authoring of a mapping specification and programming of the SDTM SAS datasets, the Pinnacle21 validator was run to check compliance to SDTM IG 3.1.3. Any checks that signified a programming issue were addressed and the relevant SDTM datasets were updated.

After resolution of all validation issues that could be fixed, a QC step was performed where the datasets were double-programmed by a separate QC programmer using the mapping spec as a reference. Any fallouts were recorded per the sponsor's SOPs and returned to the SDTM programmer for updates. After confirmation that updates were applied properly, the SDTM data was considered complete and sent to a publishing programmer for creation of the SDTM annotated CRF as well as the define.xml. Each of these tasks included QC steps as well.

3.1 Issues Encountered and Resolved

- MedDRA v14.1 was used to encode adverse events in the legacy data for this study. This version was retained when mapped to the SDTM AE domain to maintain traceability to the CSR. Terms will be re-coded to MedDRA v20.0 at the pooled SDTM level per advice in the Technical Conformance Guide to encode to one version of the dictionary. A lookup table from source to target terms will be provided with pooled SDTM datasets for the ISS.
- A proprietary drug dictionary was used to encode data for prior/concomitant medications in the legacy data for this study. This dictionary was retained when mapped to the SDTM CM domain to maintain traceability to the CSR. Medications will be re-coded to WHODrug March 2017 at the pooled SDTM level per advice in the Technical Conformance Guide to encode to one version of the dictionary. A lookup table from source to target terms will be provided with pooled SDTM datasets for the ISS.
- Lab normal ranges were not in the same legacy dataset as the lab tests and results. Normal ranges had to be merged with the lab dataset. QC steps were performed to ensure that ranges were applied appropriately.

4. Traceability Data Flow



The legacy datasets, legacy aCRF, and legacy define.pdf have been provided in the 'legacy' folder.

5. Outstanding Issues

- SDTM DM.RACE: Eight race values were collected on the CRF for this study and mapped to only 5 races in SDTM since the CDISC CT RACE codelist is non-extensible. Not all DM Race values will be traceable to the CSR. A lookup table is provided below to convey the mapping done for race from legacy values to SDTM. For values of race that do not directly map to a standardized race value (e.g. 'Japanese' to 'ASIAN'), the original race value was also retained in SUPPDM.QVAL where QNAM = 'RACEOR'.

CRF Collected Race	Count	SDTM RACE	Count
White/Caucasian	145	WHITE	145
Black or African American	112	BLACK OR AFRICAN AMERICAN	112
Asian Indian	50	ASIAN	135
Japanese	30		
Chinese	40		
Korean	15		
Native Hawaiian	57	NATIVE HAWAIIAN OR OTHER PACIFIC ISLANDER	83
Other Pacific Islander	26		
Alaskan Native or American Indian	34	AMERICAN INDIAN OR ALASKA NATIVE	34

- SDTM DS.DSDECOD: Eleven disposition terms were collected on the eCRF but all did not map directly to DS.DSDECOD from the CDISC CT NCOMPLT codelist. Not all terms will be traceable to the CSR. A lookup table is provided below to convey the mapping done for subject disposition from legacy values to SDTM DSDECOD in the DS domain. For values that do not map directly, the original term captured will be retained in the DSTERM variable.

CRF Collected Disposition	Count	SDTM DSDECOD	Count
Completed	325	COMPLETED	325
Need for Excluded Medication	42	OTHER	82
Treatment Unblinded	2		
Non-Compliance With Protocol	33		
Lack of Qualifying Event	5		
Subject Withdrew Consent	15	WITHDRAWAL BY SUBJECT	15
Physician Discontinued Subject	8	PHYSICIAN DECISION	8
Treatment Failure	22	LACK OF EFFICACY	22
Adverse Event	53	ADVERSE EVENT	53
Lost to Follow-Up	3	LOST TO FOLLOW-UP	3
Death	1	DEATH	1

- Legacy lab test names and units will match names in CSR listings but will not match the lab test names and units in the SDTM LB dataset. In SDTM LB, CDISC Controlled Terminology was

applied. This was done in order to easily pool the data with other studies included in the ISS. The LBTESTCD/LBTESTs present in the SDTM data are listed in the define.xml. Please see Appendix II for Lab lookup table that maps legacy test names to SDTM CT to provide traceability from legacy to SDTM.

Appendix II: Lab test Look-up Table

Source Test Code	Source Test Name	SDTM_LBTESTCD	SDTM_LBTEST	SDTM_LBSPEC
BILITOT	Total Bilirubin	BILI	Bilirubin	SERUM
BRALCOHL	Alcohol Breath Test	ETHANOL	Ethanol	BREATH
BASO_P	Basophils (Percent)	BASOLE	Basophils/Leukocytes	BLOOD
EOS_P	Eosinophils (Percent)	EOSLE	Eosinophils/Leukocytes	BLOOD
HEPCAB	Hepatitis C Antibody	HCAB	Hepatitis C Virus Antibody	SERUM
MONO_P	Monocytes (Percent)	MONOLE	Monocytes/Leukocytes	BLOOD
NA	Sodium	SODIUM	Sodium	SERUM
NEUT_P	Neutrophils (Percent)	NEUTLE	Neutrophils/Leukocytes	BLOOD
PROTOT	Total Protein	PROT	Protein	SERUM
PTINR	Prothrombin Time INR	INR	Prothrombin Intl. Normalized Ratio	BLOOD
BILICY	Bilirubin Crystals	CYBILI	Bilirubin Crystals	URINE
PROT	Urine Protein	PROT	Protein	URINE
UGLUC	Urine Glucose	GLUC	Glucose	URINE