

Introduction to Analysis Data Reviewer Guide from PhUSE

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- ADaM Define
- Overview of ADRG
- ADRG Template
- Completion Guidelines
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ADaM Define (1)

- Datasets in XPT format
- Metadata: Analysis Results Level, Dataset Level, Variable Level, and Value Level.
 - [Traceable hyperlinks](#)
- **Analysis Data Reviewer Guide (ADRG)**

ADaM Define (2)

Name	Date modified	Type	Size
 adae.xpt	2013/11/20 21:54	SAS Xport Transport File	697 KB
 adqsadas.xpt	2013/11/20 21:55	SAS Xport Transport File	5,058 KB
 adsl.xpt	2013/11/20 21:52	SAS Xport Transport File	112 KB
 analysis-data-reviewers-guide.pdf	2014/7/10 21:56	Adobe Acrobat Document	405 KB
 define2-0-0.xsl	2014/9/3 12:20	XSLT Stylesheet	126 KB
 define2-0-0-example-adam-results.html	2014/9/3 12:57	HTML Document	201 KB
 define2-0-0-example-adam-results.xml	2014/9/3 12:56	XML Document	145 KB

Open <AResM\adam folder>

ADaM Define (3)

Analysis Results Metadata (Summary) for Study CDISC-Sample

Table 14-3.01 Primary Endpoint Analysis: ADAS-Cog - Summary at Week 24 - LOCF (Efficacy Population) Dose response analysis for ADAS-Cog changes from baseline Pairwise comparisons to placebo for ADAS-Cog changes from baseline
Table 14-5.02 Incidence of Treatment Emergent Serious Adverse Events by Treatment Group Incidence of Treatment Emergent Serious Adverse Events by Treatment Group

Analysis Results Metadata (Detail) for Study CDISC-Sample

Table 14-3.01

Display	Table 14-3.01 Primary Endpoint Analysis: ADAS-Cog - Summary at Week 24 - LOCF (Efficacy Population)
Analysis Result	Dose response analysis for ADAS-Cog changes from baseline
Analysis Parameter(s)	ACTOT = Adas-Cog(11) Subscore
Analysis Variable(s)	CHG (Change from Baseline)
Analysis Reason	SPECIFIED IN SAP
Analysis Purpose	PRIMARY OUTCOME MEASURE
Data References (incl. Selection Criteria)	ADQSADAS [PARAMCD = "ACTOT" and AVISIT = "Week 24" and EFFFL = "Y" and ANL01FL = "Y"]
Documentation	Linear model analysis of CHG for dose response; using randomized dose (0 for placebo; 54 for low dose; 81 for high dose) and site group in model. Used PROC GLM in SAS to produce p-value (from Type III SS for treatment dose). SAP Section 10.1.1
Programming Statements	[SAS version 9.2] proc glm data = ADQSADAS; where EFFFL='Y' and ANL01FL='Y' and AVISIT='Week 24' and PARAMCD="ACTOT"; class SITEGR1; model CHG = TRTFN SITEGR1; run;
Analysis Result	Pairwise comparisons to placebo for ADAS-Cog changes from baseline
Analysis Parameter(s)	ACTOT = Adas-Cog(11) Subscore

ADaM Define (4)

Analysis Datasets for Study CDISC-Sample (ADaM-IG 1.0)

Dataset	Description	Class	Structure	Purpose	Keys	Location	Documentation
ADSL	Subject-Level Analysis	SUBJECT LEVEL ANALYSIS DATASET	one record per subject	Analysis	STUDYID, USUBJID	adsl.xpt	Screen Failures are excluded since they are not needed for this study analysis. See Analysis Data Reviewer's Guide, page 6. Analysis Data Reviewer's Guide
ADQSADAS	ADAS-Cog Analysis	BASIC DATA STRUCTURE	One record per subject per parameter per analysis visit per analysis date	Analysis	STUDYID, USUBJID, PARAMCD, AVISIT, ADT	adqsadas.xpt	See referenced dataset creation program and Analysis Data Reviewer's Guide, Section 2.1 adqsadas.sas Analysis Data Reviewer's Guide
ADAE	Adverse Events Analysis Dataset	ADAM OTHER	one record per subject per adverse event	Analysis	STUDYID, USUBJID, AETERM, ASTDT, AESEQ	adae.xpt	See SAS program adae.sas

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Subject-Level Analysis (ADSL) [Location: [adsl.xpt](#)]

Variable	Label	Key	Type	Length / Display Format	Controlled Terms or Format	Source/Derivation/Comment
STUDYID	Study Identifier	1	text	12		Predecessor: DM.STUDYID
USUBJID	Unique Subject Identifier	2	text	11		Predecessor: DM.USUBJID
SUBJID	Subject Identifier for the Study		text	4		Predecessor: DM.SUBJID
SITEID	Study Site Identifier		text	3		Predecessor: DM.SITEID
SITEGR1	Pooled Site Group 1		text	3		Derived: refer to SAP, Section 7.1 - if not pooled then SITEGR1=SITEID. If pooled, SITEGR1 will be 900
ARM	Description of Planned Arm		text	20	["Placebo", "Xanomeline Low Dose", "Xanomeline High Dose"] <Actual Treatment>	Predecessor: DM.ARM
TRT01P	Planned Treatment for Period 01		text	20	["Placebo", "Xanomeline Low Dose", "Xanomeline High Dose"] <Actual Treatment>	Predecessor: DM.ARM
TRT01PN	Planned Treatment for Period 01 (N)		integer	8	[0 = "Placebo", 54 = "Xanomeline Low Dose", 81 = "Xanomeline High Dose"] <Actual Treatment (N)>	Assigned: Numeric code for TRT01P which corresponds to the randomized dose

From Draft Analysis Results Metadata Specs v1 for Define-XML V2 released on 10Sep2014

ADaM Define (5)

Analysis Data Reviewer's Guide

<Sponsor Name>

Study <Protocol Number>

Study <Protocol Number>

Analysis Data Reviewer's Guide

Analysis Data Reviewer's Guide

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Overview of ADRG (1)



Project Overview

- Overview
 - ADaM provides a framework that enables analysis of the data, while at the same time allowing reviewers and other recipients of the data to have a clear understanding of the data's lineage from collection to analysis to results
 - Although ADaM provides a robust metadata framework, FDA Reviewers benefit from additional, human-readable, documentation of analysis methods, datasets, and programs that cannot be fully explained within the ADaM metadata
 - Development of an Analysis Data Reviewer's Guide (ADRG) template will ensure this documentation is provided to the FDA in consistent and usable format
- Project Leadership Team
 - Susan Kenny, Amgen & Gail Stoner, J&J
- FDA Observers
 - Ben Vali & Mina Hohlen, FDA

Borrowed from "CSS_Working_Group_Slides_-_ADRG.pdf"

Overview of ADRG (2)

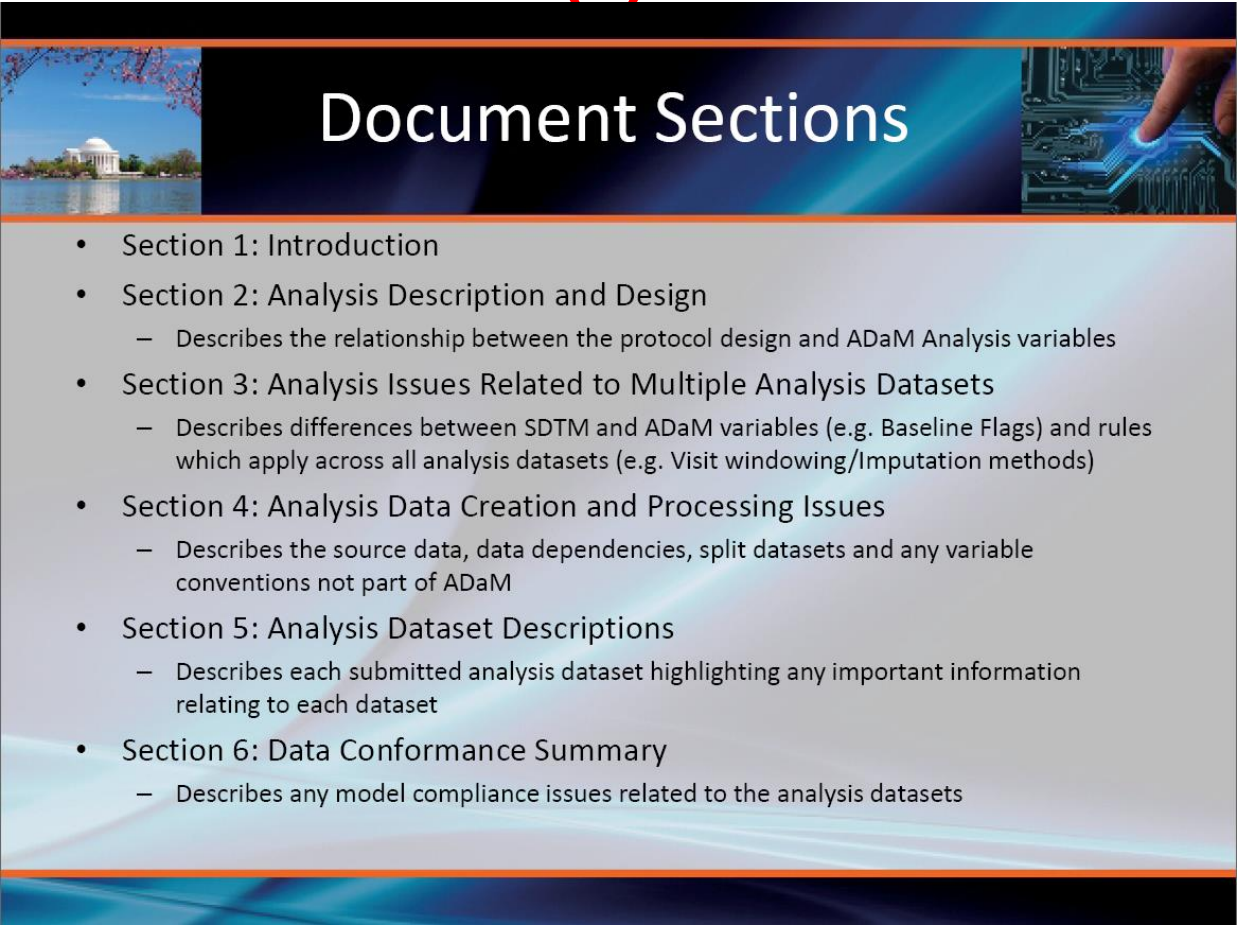


Project Overview

- This template is being produced with FDA participation
- A reviewer's guide is not required for ADaM submissions yet, but could be in the future.
- The template will be open ended but is designed with SDTM and ADaM in mind. It will supports many possible analysis data scenarios.
- The questionnaire format will give the finished ADRG a consistent look and feel, to help reviewers find the information they need.
- Include your ADRG in Module 5 of the eCTD with the study's ADaM datasets.

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Overview of ADRG (3)



Document Sections

- Section 1: Introduction
- Section 2: Analysis Description and Design
 - Describes the relationship between the protocol design and ADaM Analysis variables
- Section 3: Analysis Issues Related to Multiple Analysis Datasets
 - Describes differences between SDTM and ADaM variables (e.g. Baseline Flags) and rules which apply across all analysis datasets (e.g. Visit windowing/Imputation methods)
- Section 4: Analysis Data Creation and Processing Issues
 - Describes the source data, data dependencies, split datasets and any variable conventions not part of ADaM
- Section 5: Analysis Dataset Descriptions
 - Describes each submitted analysis dataset highlighting any important information relating to each dataset
- Section 6: Data Conformance Summary
 - Describes any model compliance issues related to the analysis datasets

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ADRG website



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Analysis Data Reviewer's Guide

The final ADaM Data Reviewer's Guide zip file is available for download at this link: '[Final ADRG Package \(V1.01\) 2014-05-13](#)'

Project Overview

ADaM "provides a framework that enables analysis of the data, while at the same time allowing reviewers and other recipients of the data to have a clear understanding of the data's lineage from collection to analysis to results. Although ADaM provides a robust metadata framework, FDA Reviewers benefit from additional, human-readable, documentation of analysis methods, datasets, and programs that cannot be fully explained within the ADaM metadata. The development of an Analysis Data Reviewer's Guide (ADRG) template will ensure this documentation is provided to the agency in consistent and usable format.

Project Leads

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Mina Hohlen	FDA Liaison	FDA	mina.hohlen (at) fda.hhs.gov 

Project Updates

The Final ADRG package contains a template to be used in submissions with completion guidelines and examples. The ADRG template provides an orientation to the submitted data in a consistent and usable format.

The ADaM Data Reviewer's Guide zip file is available for download at this link: [Final ADRG Package 2014-05-13](#)

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Documents library	
ADRG_V1.01_2014-05-20	
Name	Date modified
 ADRG_Template_2014-05-04.doc	2014/5/13 13:03
 ADRG_Completion_Guidelines_2014-05-04.pdf	2014/5/13 12:35
 ADRG CDISC pilot project sample 2014-05-13.pdf	2014/5/13 12:34
 analysis-data-reviewers-guide SAMPLE 9999 2014-05-13.pdf	2014/5/13 11:39

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ADRG Template

Analysis Data Reviewer's Guide

<Sponsor Name>

Study <Protocol Number>

Study <Protocol Number>

Analysis Data Reviewer's Guide

Analysis Data Reviewer's Guide

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Data Conformance

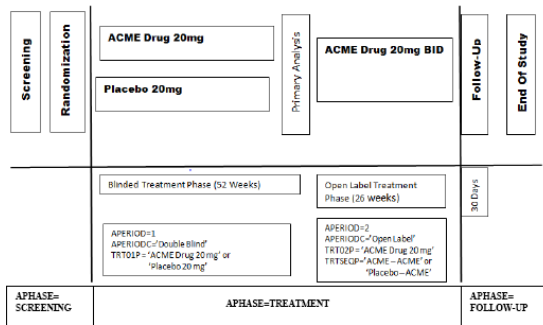
- OpenCDISC
- SAS CST
- Sponsor-defined
- Other

Completion Guidelines

Text Example:

This is a two arm randomized double-blind to open-label study. APERIOD is used to describe the double-blind period (APERIOD=1) and the open label period (APERIOD=2). TRT01P represents the treatment to which a subject was randomized at the start of the double-blind period and TRT02P represents the open label treatment. The variable TRTSEQP provides a description of the sequence of planned treatments from double-blind to open-label. Records collected prior to randomization are considered to be APHASE=Screening, all records collected during double-blind or open label have APHASE= 'Treatment' and records collected during the 30 day follow-up have APHASE= 'Follow-up'

Pictorial Example:



3. Analysis Considerations Related to Multiple Analysis Datasets

3.1 Comparison of SDTM and ADaM Content

The following questions must be answered:

- Are data for screen failures, including data for run-in screening (for example, SDTM values of ARMCD= 'SCRNFAIL', or 'NOTASSGN') included in ADaM datasets?
If yes, then refer reader to the appropriate Section 5.2.x below for individual datasets that contain screen failure and/or run-in failure data.
If no, if screen failure/run-in data are in SDTM but not included in ADaM, then briefly explain why these data are not needed for ADaM.

- Are data taken from an ongoing study?
If yes then describe the data cut and any issues that might influence record selection from SDTM to ADaM and refer to Section 4.1 for more information as appropriate.
Additional content may include, but is not limited to the following:
Discussion of any differences between SDTM and ADaM in the definitions of derived variable concepts (for example, baseline (xxBLFL versus ABLFL), actual study day (xxDY versus ADY), population flags (SAFETY versus SAFFL))? If yes, refer reader to the appropriate section 5.2.x below as necessary.

3.2 Core Variables

Core variables are those that are represented across all/most analysis datasets. The designation of 'core' is given to a variable that is useful for nearly all analyses (such as age group, sex, race, treatment arm) and/or serves as an important reference variable (such as studyid). If core variables are defined, then a table with the core variable name and a brief description is required.

Since both USUBJID and STUDYID are required by the ADaM model, then at a minimum, this table would contain these two variables.

Example:

Variable Name	Variable Description
USUBJID	Unique subject identifier
STUDYID	Study identifier used for this protocol
SITEID	Unique site identifier for the investigator site
COUNTRY	Country code using ISO
ARM	Planned treatment arm from SDTM
TRT01P	Randomized treatment description
SEX	Sex
AGEGRP1	Age group (<65 and >=65)
RACE	Race description
ITFL	Flag to indicate inclusion ('Y') or exclusion ('N') from the intent to treat population
HBA1CBL	Baseline value of HbA1C which is used as a covariate in all efficacy analyses

Pilot Project Sample

CDISCPilot01

Analysis Data Reviewer's Guide

1. Introduction

1.1 Purpose

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

1.2 Acronyms

Acronym	Translation
CRF	Case Report Form
IG	Implementation Guide

1.3 Study Data Standards and Dictionary Inventory

Standard or Dictionary	Versions Used
SDTM	SDTM v1.2/SDTM IG v3.1.2 (with amendment 1)
ADaM	ADaM Model Document 2.0 ADaM Implementation Guide v1.0 ADaM Data Structure for Adverse Event Analysis v1.0 ADaM Basic Data Structure for Time-to-Event Analysis v1.0
Data Definitions	define.xml v1.0

1.4 Source Data Used for Analysis Dataset Creation

The analysis files for this study were derived from the submitted SDTM files. SDTM files were prepared from CRF data according to version 3.1.2 of the SDTM IG (with amendment 1). No non-CRF or non-SDTM data were used to create the ADaM data.

2. Protocol Description

2.1 Protocol Number and Title

Protocol Number: CDISCPilot01

Protocol Title: Safety and Efficacy of the Xanomeline Transdermal Therapeutic System (TTS) in Patients with Mild to Moderate Alzheimer's Disease

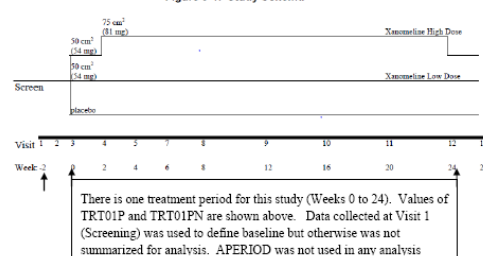
PDF created 2014-05-13

CDISCPilot01

Analysis Data Reviewer's Guide

2.2 Protocol Design in Relation to ADaM Concepts

Figure 9-1. Study Schema



3. Analysis Considerations Related to Multiple Analysis Datasets

3.1 Comparison of SDTM and ADaM Content

- Are data for screen failures, including data for run-in screening (for example, SDTM values of ARMCD= 'SCRNFAL', or 'NOTASSGN') included in ADaM datasets?

No data for screen failures are used for analysis. Therefore, there are no records for screen failures in any analysis dataset.

- Are data taken from an ongoing study?

Data are not taken from an ongoing study.

Additional Content of Interest

- Values of baseline are identical between SDTM domains (xxSTRESN where xxBLFL='Y') and ADaM datasets (AVAL where ABLFL='Y').
- Population flags are included in both SDTM (SUPPDM) and in ADaM (ADSL) and have identical values.

3.2 Core Variables

Core variables are those that are represented across all analysis datasets.

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Summary

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- Overview of ADRG
- ADRG Template
- Completion Guidelines
- Pilot Project Sample

SDTM Data Review Guide (SDRG)



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Study Data Reviewer's Guide

The Study Data Reviewer's Guide zip file is available for download at this link: [Final SDRG Package 2013-05-13](#)

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Overview & Scope

CGD-010: define.XML does not adequately document SDTM mapping decisions, sponsor-defined domains, sponsor-defined controlled terminology, and sponsor extensions to CDISC controlled terminology. A standardized Data Guide would help to address this documentation gap. The content of the Data Guide should be standardized and developed jointly between CDER, Industry, and CDISC.

Scope: The Study Data Reviewer's Guide (SDRG) will be proposed as a component of the eCTD's Module 5 SDTM data documentation. This document will be defined for SDTM data descriptions only. An Analysis Data Reviewer's Guide will be handled in a future project.

SDRG Core Team

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