Introduction to Analysis Data Reviewer Guide from PhUSE

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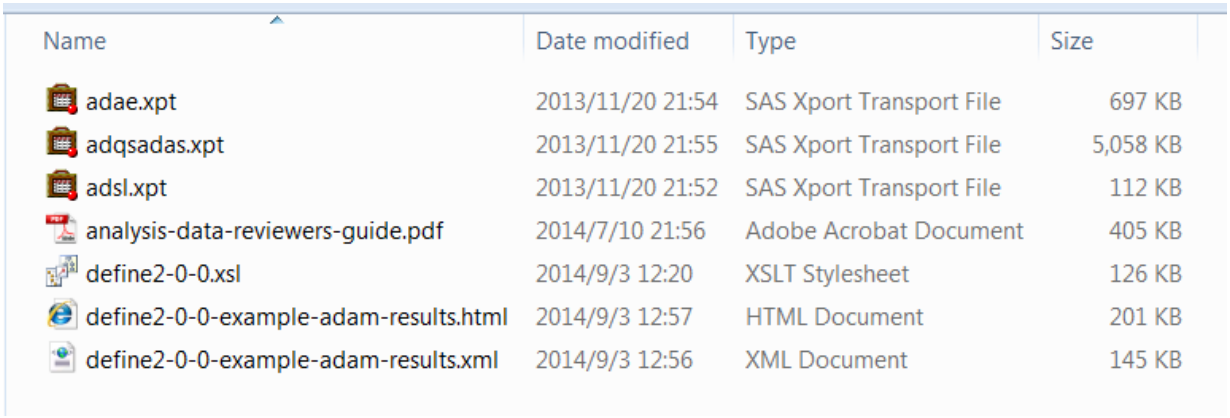
- Overview of ADRG
- ADRG Template
- Completion Guidelines
- Pilot Project Sample

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)



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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>

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

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 = TRTPN SITEGR1;`
	`run;`

Analysis Result	**Pairwise comparisons to placebo for ADAS-Cog changes from baseline**
Analysis Parameter(s)	ACTOT = Adas-Cog(11) Subscore

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

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

Go to the top of the define.xml

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

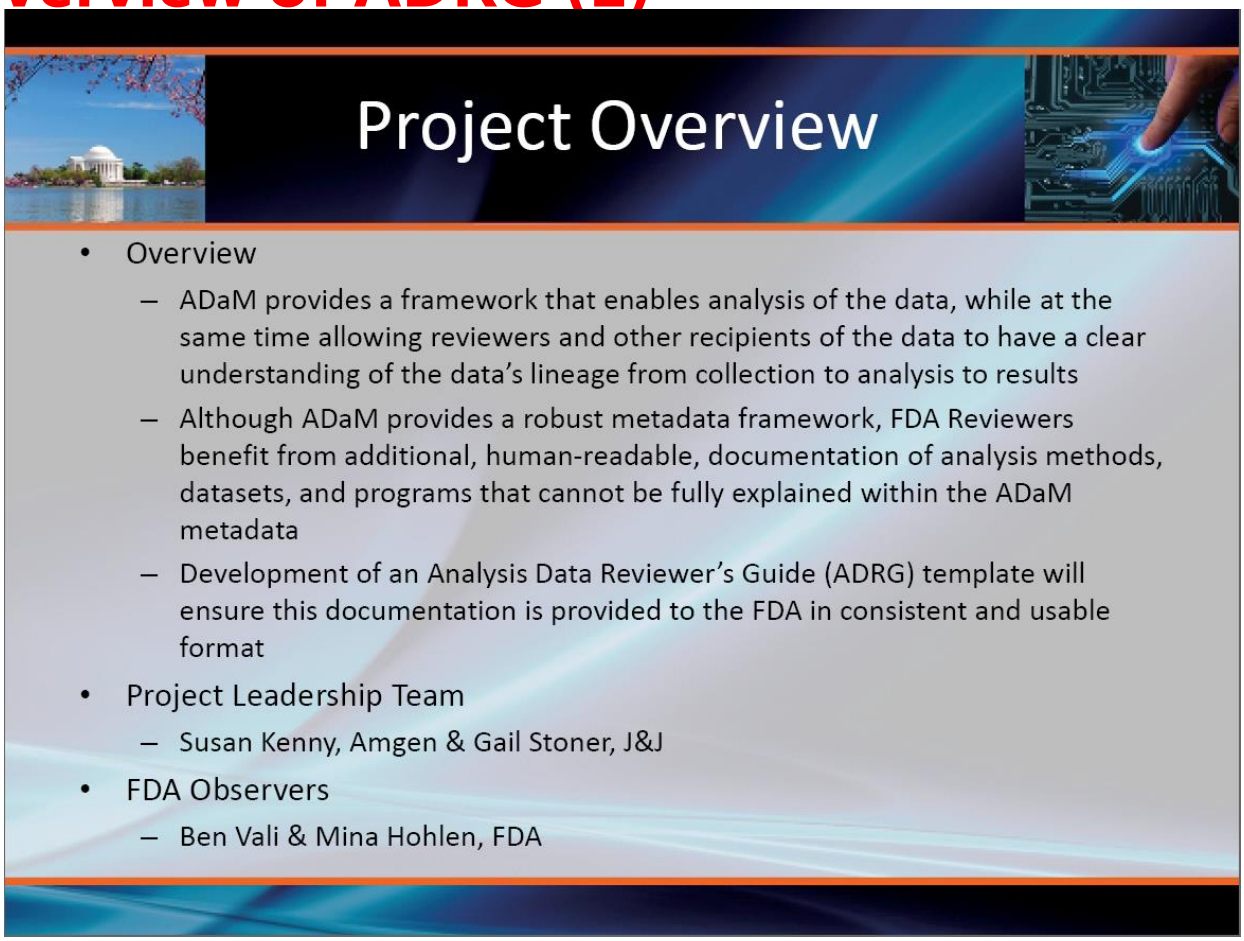
<Sponsor Name>

Study <Protocol Number>

Analysis Data Reviewer's Guide

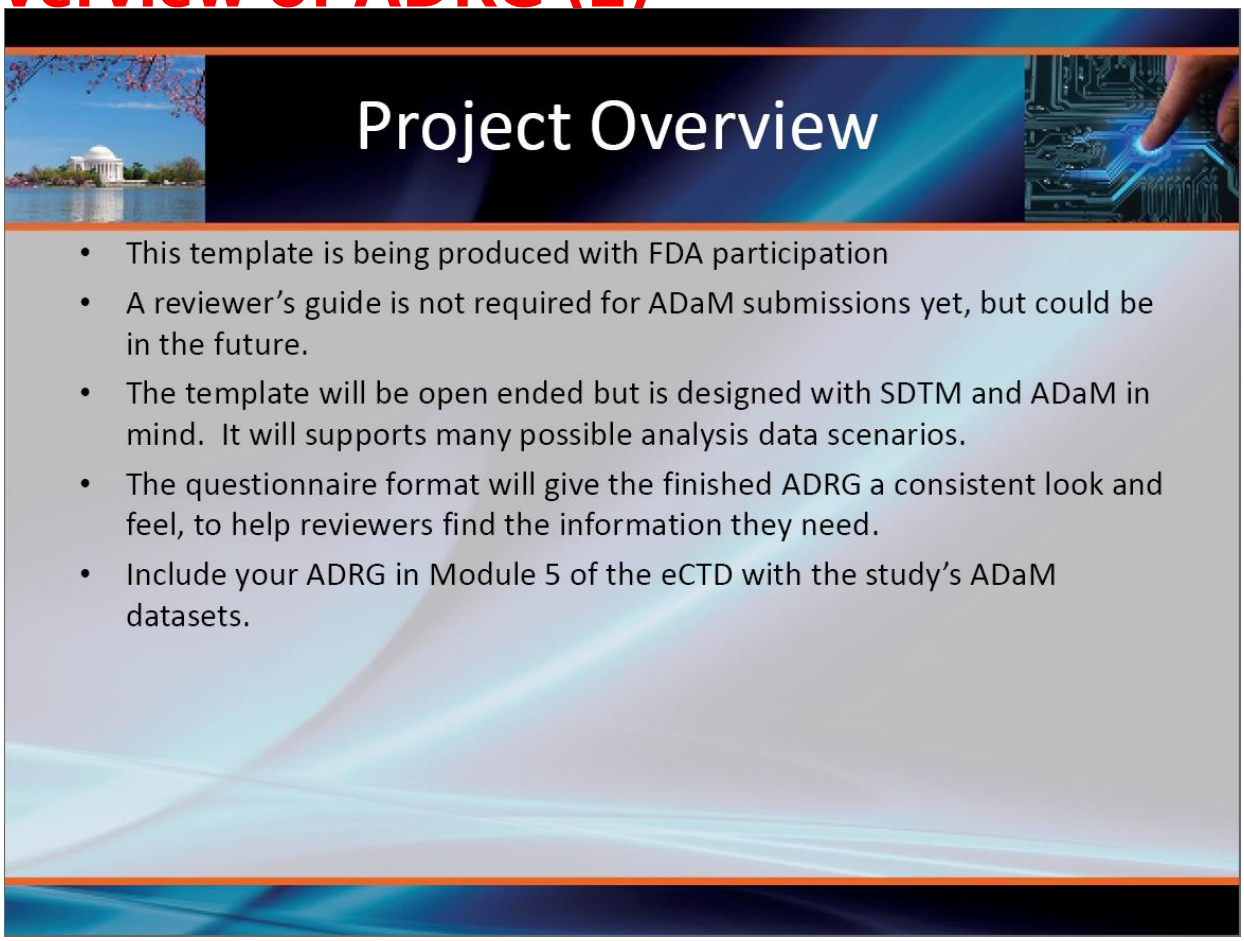
Contents

Overview of ADRG (1)



Borrowed from "CSS_Working_Group_Slides_-_ADRG.pdf"

Overview of ADRG (2)



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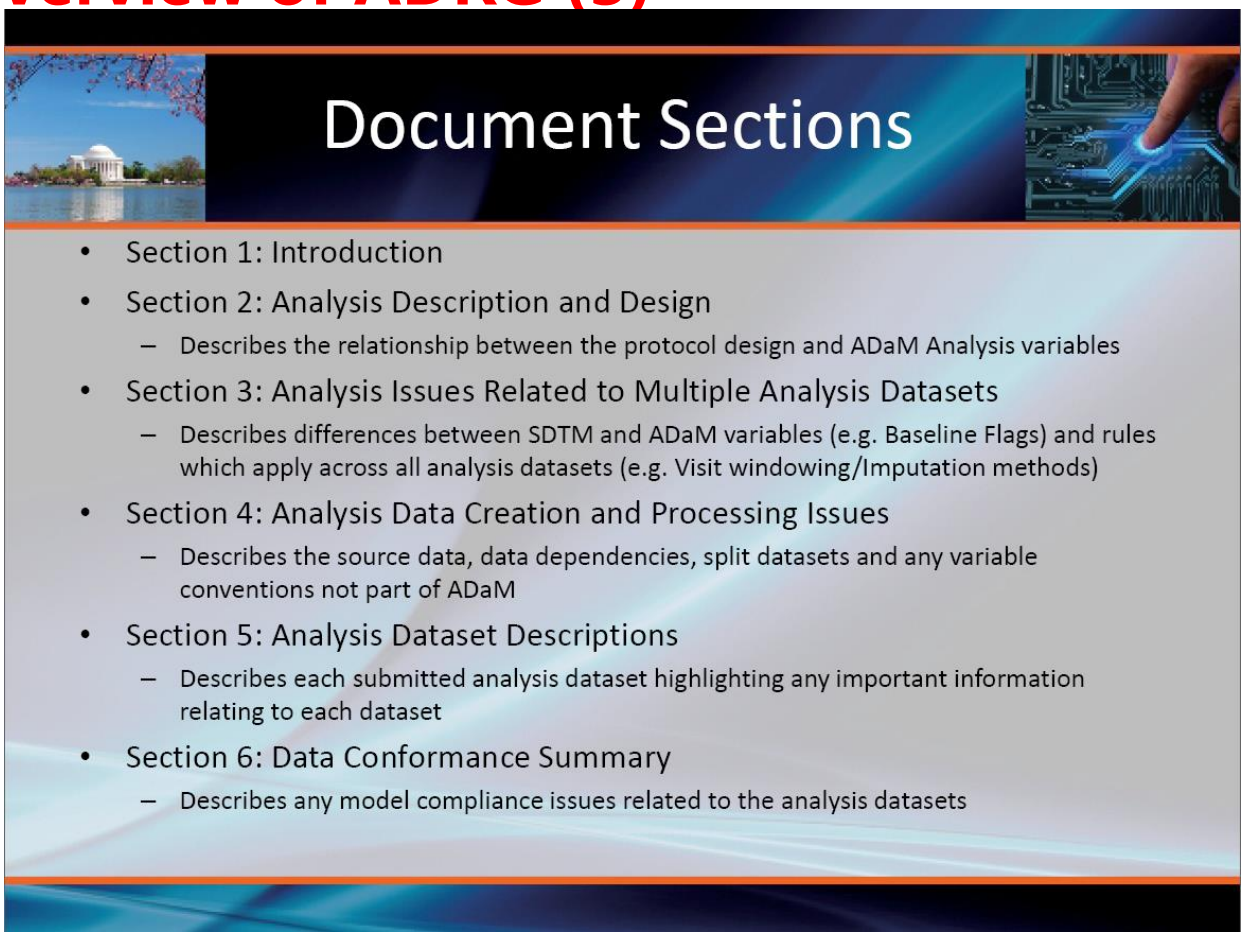
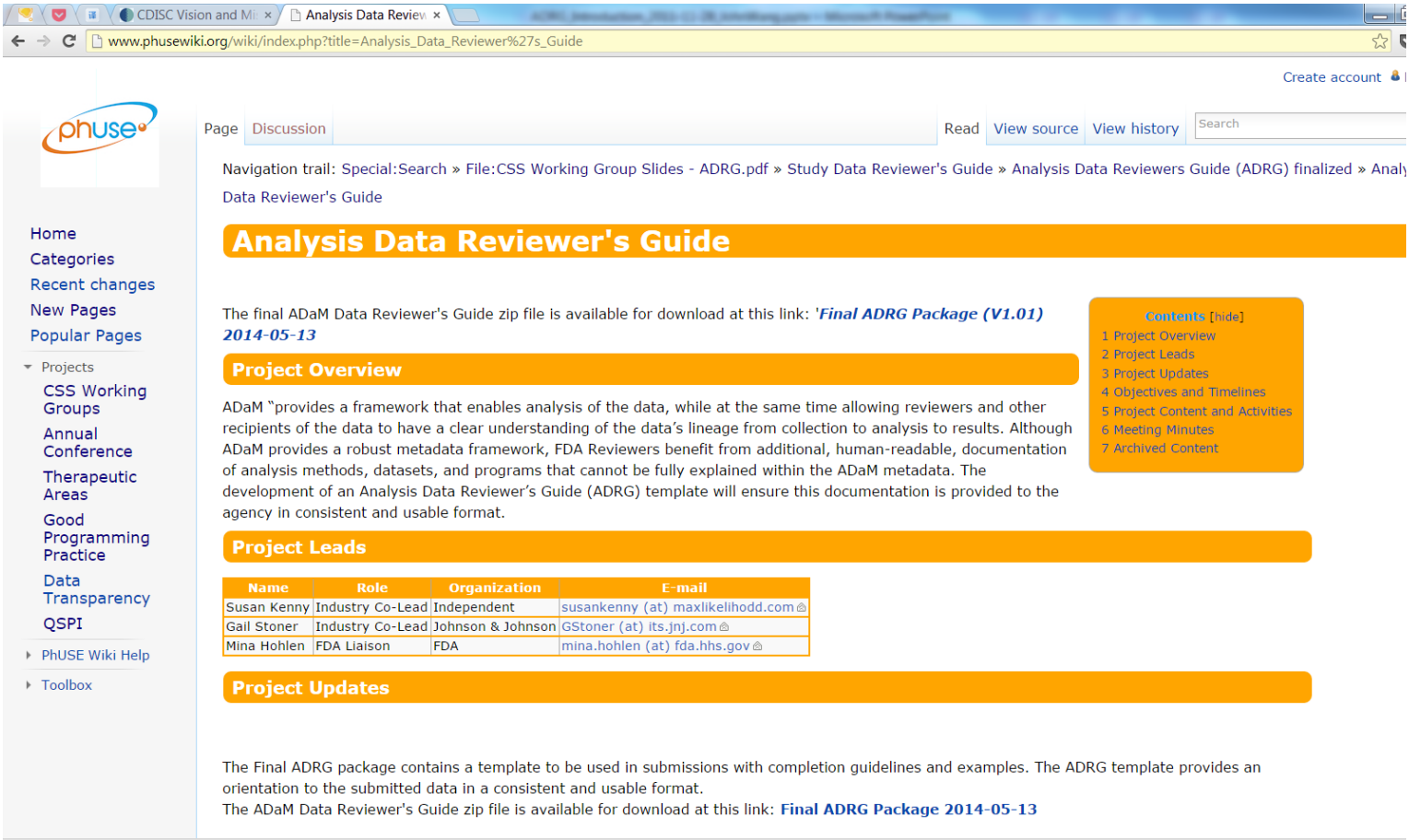
Overview of ADRG (3)



Borrowed from "CSS_Working_Group_Slides_-_ADRG.pdf"

ADRG website



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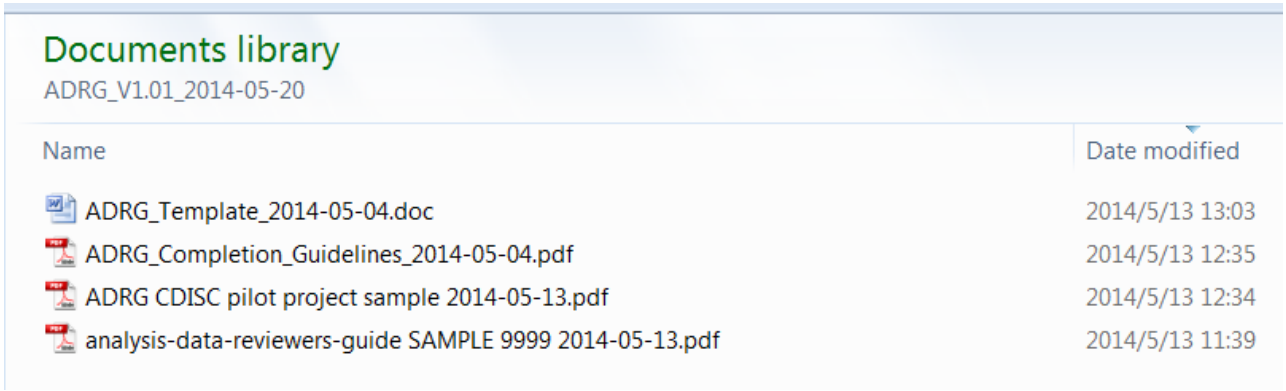


Open <ADRG folder>

ADRG Template

Analysis Data Reviewer's Guide

<Sponsor Name>

Study <Protocol Number>

Analysis Data Reviewer's Guide

Contents

Data Conformance

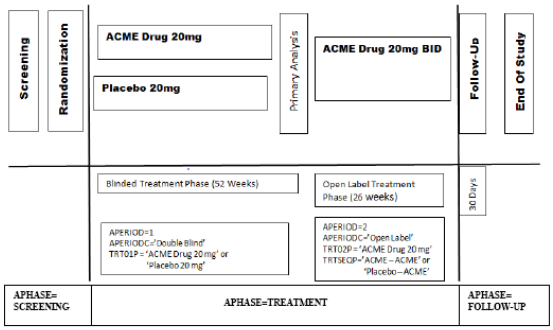
- OpenCDISC
- SAS CST
- Sponsor-defined
- Other

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.

If screen failure/run-in data are not in SDTM either, then state this.

- 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
ITTFL	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

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

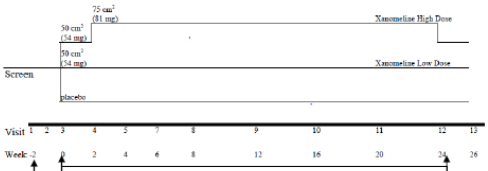
Protocol Number: CDISCPILOT01

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

CDISCPilot01 Analysis Data Reviewer's Guide

2.2 Protocol Design in Relation to ADaM Concepts

Figure 9-1. Study Schema



There is one treatment period for this study (Weeks 0 to 24). Values of TRT01P and TRT01PN are shown above. Data collected at Visit 1 (Screening) was used to define baseline but otherwise was not summarized for analysis. APERIOD was not used in any analysis

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='SCRNFAIL', 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.

PDF created 2014-05-13

Summary

- ADaM Define
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SDTM Data Review Guide (SDRG)