Analysis Data Reviewer's Guide

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WHAT IS A ADRG? WHAT IS ITS PURPOSE?

- Analysis Data Reviewers Guide (ADRG) is a document included in Module 5 of the eCTD with the study's define.xml and ADaM datasets.
- It's a pdf document that has a link in the define.xml
- The ADRG provides FDA reviewers with context for analysis datasets and terminology, received as part of a regulatory product submission, additional to what is presented within the data definition file (i.e., define.xml).
- Currently ADRG is not a requirement for ADaM submission, but the preparation of an Analysis Data Reviewer's Guide (ADRG) is recommended as an important part of a standards-compliant analysis data submission for clinical trials

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Phuse Template for ADRG

- Template produced with FDA participation
- Open ended with a questionnaire format
- Template gives ADRG a consistent look and feel, to help reviewers find the information they need
- Current version : v1.1, release date: 26Jan2015
- Excellent sample ADRG along with examples are available

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Sections in ADRG

Sections 1:

- Introduction
- Information about IG versions
- Dictionary version and CT versions used.
- Information regarding source data used in creating ADAMs. Example: SDTM, lookup tables, WinNonLin outputs.

Section 2:

- Protocol Description
- Protocol design in relation to ADAM creation

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1. Introduction

1.1 Purpose

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

1.2 Acronyms

Acronym	Translation

1.3 Study Data Standards and Dictionary Inventory

Standard or Dictionary	Versions Used
SDTM	
ADaM	
Controlled Terminology	
Data Definitions	
Other standards (optional)	

1.4 Source Data Used for Analysis Dataset Creation

(insert your text here)

2. Protocol Description

2.1 Protocol Number and Title

Protocol Number:

Protocol Title:

Protocol Versions:

(Note changes in protocol amendments that affected data analysis)

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Section 3 :

- Subject Issues that require special analysis rule
- Use of visit windowing, unscheduled visits and record selection.
- Imputation/Derivation Methods

Section 4 : Data creation and processing issues.

- Data Dependencies
- Intermediate datasets
- Variable conventions used when creating subgroup analysis variables

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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?

  <insert text here>

- Are data taken from an ongoing study?

  <insert text here>

Additional Content of Interest

<See ADRG Completion Guidelines for additional content of interest, and include text here or remove this text >.

3.2 Core Variables

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

Variable Name	Variable Description
USUBJID	Unique subject identifier
STUDYID	Study identifier used for this protocol

3.3 Treatment Variables

ARM versus TRTxxP

- Are the values of ARM equivalent in meaning to values of TRTxxP?

ACTARM versus TRTxxA

- If TRTxxA is used, then are the values of ACTARM equivalent in meaning to values of TRTxxA?

Use of ADaM Treatment Variables in Analysis

- Are both planned and actual treatment variables used in analyses?

3.4 Subject Issues that Require Special Analysis Rules

(insert your text here)

3.5 Use of Visit Windowing, Unscheduled Visits, and Record Selection

- Was windowing used in one or more analysis datasets?
- Were unscheduled visits used in any analyses?

Additional Content of Interest

<See ADRG Completion Guidelines for additional content of interest, and include text here or remove this text >.

3.6 Imputation/Derivation Methods

- If date imputation was performed, were there rules that were used in multiple analysis datasets?

  (insert your text here)

Additional Content of Interest

<See ADRG Completion Guidelines for additional content of interest, and include text here or remove this text >.

4. Analysis Data Creation and Processing Issues

4.1 Split Datasets

(insert your text here)

4.2 Data Dependencies

(insert your text here)

4.3 Intermediate Datasets

(insert your text here)

4.4 Variable Conventions

(insert your text here)

Section 5 : Analysis Dataset Descriptions

- Derivations in each dataset will be explained in detailed
- Sections from the SAP along with more detailed explanation will be given in this section

Section 6: Data conformance summary

- Give proper explanation to the CDISC ADaM compliance check for errors and warnings

Example: please don't put an explanation: *"as per sponsor standards"*

Section 7: List of programs that will be submitted

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5. Analysis Dataset Descriptions

5.1 Overview

- Do the analysis datasets support all protocol- and statistical analysis plan-specified objectives?

  Include all objectives listed in the protocol or SAP which are not supported in the analysis datasets and the reason for their absence.

Additional Content of Interest

(See ADRG Completion Guidelines for additional content of interest, and include text here or remove this text).

5.2 Analysis Datasets

Dataset Dataset Label	Class	Efficacy	Safety	Baseline or other subject characteristics	PK/PD	Primary Objective	Structure
ADSL Subject Level Analysis Dataset	ADSL			X			One observation per subject

5.2.1 ADSL – Subject Level Analysis Dataset

(insert your text here)

5.2.x Dataset – Dataset Label

(A new section is required for each dataset that is hyperlinked in the inventory table. This section should be copied to create a new section for each dataset. The text in the section header above must be edited to match the dataset name and label.

Note that the header numbering in this section is NOT automatic. The header number for each dataset must be manually edited.)

6. Data Conformance Summary

6.1 Conformance Inputs

- Were the analysis datasets evaluated for conformance with CDISC ADaM Validation Checks?

  If yes:

  - Version of CDISC ADaM Validation Checks:
  - Specify software used:
    - OpenCDISC
    - Sponsor-defined
    - Other (describe)
- Were the ADaM datasets evaluated in relation to define.xml?
- Was define.xml evaluated?

6.2 Issues Summary

(insert your text here and/or use following table)

Dataset(s)	Diagnostic Message and/or Check ID	Severity	Count/ Issue Rate	Explanation

7. Submission of Programs

(insert your text here)

8. Appendix

(insert text here or remove this section)

Advantages of a well written ADRG

- Will help if faster review of submission
- Minimize the request for information after submission from authorities
- ADRG is programmer's chance to explain how SAP was implemented in the ADaMs.
- Explain derivations in detail
- The ADRG purposefully duplicates limited information found in other submission documentation:

Like the *protocol, statistical analysis plan (SAP), clinical study report, define.xml*.

This is in order to provide FDA reviewers with a single point of orientation to the analysis datasets.

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Inputs from the reviewers

- ADRG is your chance to explain the analysis data in detail.
- Include details.
- Reviewers like it if they don't have to refer multiple documents while reviewing the analysis
- Use the ADRG to your advantage, explain the data imputations, derived data and complex derivations
- Show data dependencies clearly

When is ADRG generally created?

- All SDTMs , ADAMs and TLFs are final
- CSR is being written and reviewed
- Define is created and being QCed
- Big rush to finally get the ADRG done

  - so in this time crunch ADRG is treated as a requirement

  - due to less time spent in writing the ADRG, some important details can be forgotten to be put in

  - quality of the document will suffer

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A New Approach

- Start with creating a draft ADRG as the study progresses.
- Write down all the different decisions made along the way regarding derivations; meeting minutes and email conversations organized by datasets.
- If CRO/external partner is creating ARDG, then pass the draft ADRG along to the external partner programming team, at the time when ADRG is being written.
- Will be helpful in a long duration studies.
- This approach will help if a new study lead is assigned.
- Request the study statistician to review the ADRG.

THANK YOU

QUESTIONS?