THINK THEOREM

Who, What, When, Where and How: Basics of Analysis Data Reviewer's Guide (ADRG)

Presented by: Theorem Clinical Research

Cathy Michalsky and Mark Gummel

WHO?

- Who should submit an ADRG?
  - Any submission to Regulatory which are utilizing analysis data sets
- Who should create an ADRG?
  - Typically this is built by the statistician and/ or programmer who is responsible for creating the data set specifications
- Who should review an ADRG?
  - Regulatory authorities
  - Statisticians
  - Programmers

WHAT?

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- What is ADRG?
  - ADRG = Analysis Data Reviewers Guide

- What is the purpose ADRG?
  - Provides a single point of orientation to the analysis datasets.
  - Provides a context for analysis datasets and terminology
  - Provides a summary of ADaM conformance findings.

WHEN?

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- **WHEN SHOULD THE ADRG BE BUILT AND SUBMITTED?**

BUILT

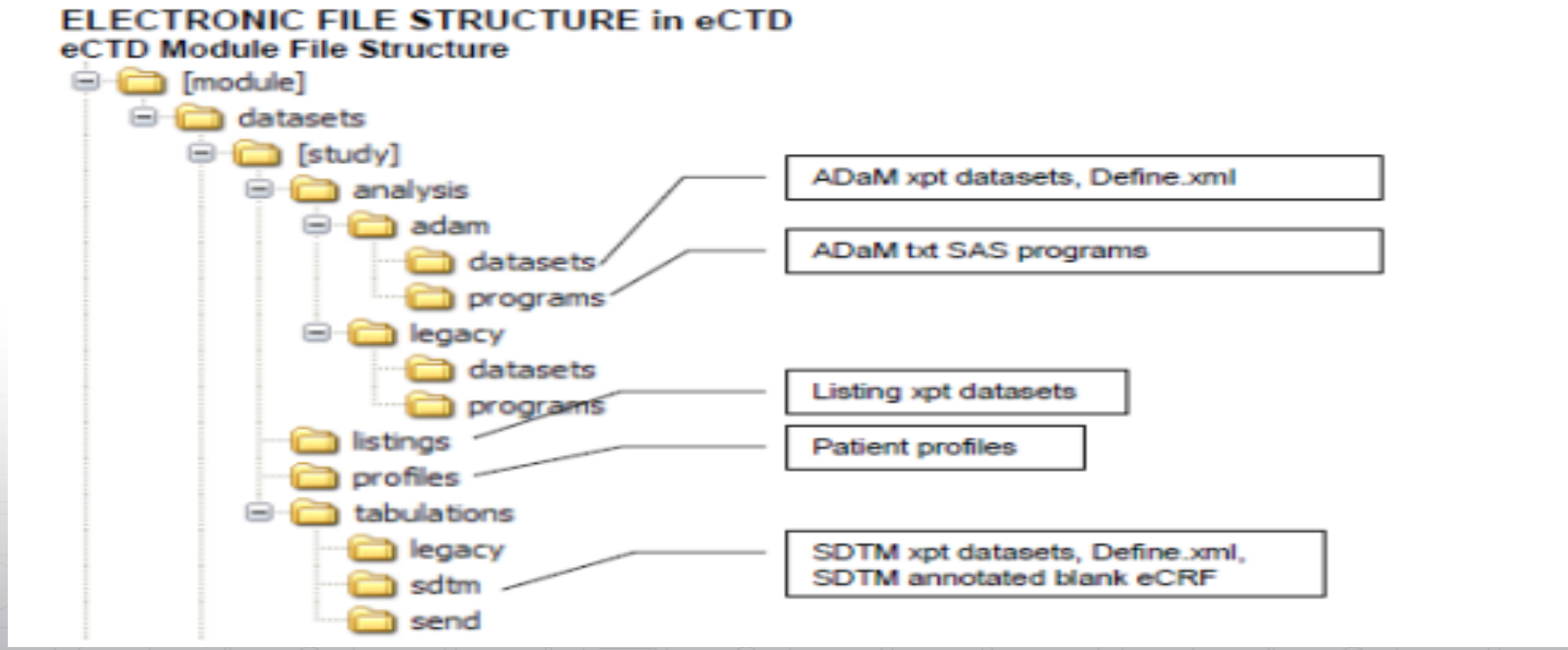
- Reviewer's guide should be built after the analysis data sets have been defined and programmed

SUBMITTED

- Typically it will be included with the Regulatory Submission Package which includes XPTs, define.xml and programs.

WHERE?

- The *ADRG* for a clinical study should be placed with the analysis data in Module 5 of the Electronic Common Technical Document (eCTD)
- It is often a hyperlink in the define.xml



HOW?

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- Key components of the ADRG are:
  - Overview of Where to find key data
  - Description of ADaM data set included in the submission including classification of the ADaM data set (i.e. efficacy vs safety), structure, and source
  - Core variables were identified
  - Descriptions of key information regarding if subjects appeared in SDTM but not the analysis data set
  - Separate documents submitted along with the ADRG included computational methods and a Program Guide which can now be found within the PhUSE ADRG template

HOW?

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Guide to ADaM Analysis Data

This document gives an introduction to the ADaM analysis datasets, providing additional information beyond what is available in the Data Definitions (define.xml) document.

Contents

Computational Methods

This document provides extended descriptions of computational methods for ADaM analysis Definitions (define.xml) document.

Contents

HOW?

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- PRESENT: ADRG TEMPLATE

Comprises of seven components:

- Introduction
- Protocol Description
- Analysis Considerations related to Multiple Analysis
- Analysis Data Creation and Processing Issues
- Analysis Dataset Descriptions
- Data Conformance Summary
- Submission of Programs

INTRODUCTION

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- Includes:
  - Overview of the Purpose of the Document
  - Acronyms
  - Data Standard Versions used including Dictionary Versions
  - Source Data used to create Analysis datasets

PROTOCOL DESCRIPTION

- Protocol Number and Title – if an amendment occurred note any significant changes which impacted data interpretation or analysis
- Protocol Design
  - Treatment Assignments
  - Phases including periods and/or cycles

ANALYSIS CONSIDERATIONS: MULTIPLE ANALYSIS DATA SETS

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Describe overarching concepts such as:

- When and where screen failure and/or run-in patients are kept in the analysis data sets
- Is there data that appears in SDTM but not an analysis data set
- Do any definitions defer in the SDTM vs. ADaM
- Describe if the data is final or considered interim (such as primary endpoint lock); for interim locks describe how the subset of data was determined (i.e. cut-off algorithms)
- Core Variables – include name and brief description
- Treatment Variables
- Special Analysis Rules
- Visit Windowing and/or Record Selection
- Imputation Rules

ANALYSIS DATA CREATION AND PROCESSING ISSUES

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- Any Technical Issues – did data sets need to be split due to size constraints
- Data Dependencies
- Intermediate Data Sets – optional section
- Variable Conventions: ANLzzFL, AVISIT, AVISITN, PARAM, PARAMCD

ANALYSIS DATA SET DESCRIPTIONS

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- Overview of analysis data sets including flagging algorithms that were not described in the conventions, location of the key or special interest data, any adjudication process and how it was implemented into the analysis data sets, algorithms for timing variables (i.e. ADY)
- Inventory Analysis Data sets Created in alphabetical order and include the data set name and label, class (such as Efficacy, Safety, Baseline or Other Subject Characteristics, PK/PD) and structure
- Dataset Name – Label
  - Describe what is included in the data set
  - Key information beyond what is included in the define.xml
  - Identify study objective if key or secondary

DATA CONFORMANCE SUMMARY

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- Describe what conformance checks were completed
- If industry standard validation tools were used then include version and description of the tool and what items were checked
- Describe any errors that appear in the data provided

SUBMISSION OF PROGRAMS

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- Inventory of programs provided in submission including inputs and outputs of the program
- What platform will the programs execute on (i.e. PC SAS version x)
- Discuss whether the programs need to be executable with FDA reviewer for submissions

ANSWERS TO BASIC QUESTIONS OF THE ADRG

- Now you know the basics of the ADRG:
  - Who needs it
  - Who creates it
  - What is it
  - When should it be created
  - Where does it belong
  - How to build it both past and present formats