

The Strategy of eSUB Package Delivery in a Programming Perspective



FMD

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Well-Prepared Package

Benefit from **Well-Prepared Package**

- ❑ Reduce Agency Review Questions
- ❑ Accelerate the Approval
- ❑ Success in Business



Well-Prepared Package

The Feature of **Well-Prepared Package**

▣ Traceability

- Dependency: Data/Program/Document
EX: CRF > SDTM > ADaM > TLGs

Traceability is a major issue in FDA submission

▣ Compliance

- Follow Agency Guidance
 - Electronic Common Technical Document
- Hierarchy: Folder Structure/File Contents

Well-Prepared Package

Contents (programmer part only)

- ▣ ISE/ISS Reports
- ▣ Patient Profile
- ▣ SDTM Define Package (CRT)
 - (SDTM Dataset, Annotated CRF, SDTM Data Review Guide and Define XML)
- ▣ ADaM Define Package
 - (ADaM Dataset, ADaM Data Review Guide and Define XML)

Well-Prepared Package

Contents (programmer part only)

- BIMO(Bioresearch Monitoring) Package/OSI (Office of Scientific Investigation)
 - Part 1 Tabular Listings of Site Information
 - Tabular information for all sites in the study (Data listings, by study, PDF)
 - Protocols and Annotated CRFs for each study (Sample annotated case report form, by study, PDF)
 - Part 2 Line Listings by Site
 - Subject data listings organized by site for each study (Data listings, by study, line listings by site, PDF)
 - Part 3 Site-Level Data set
 - Site-level datasets, across studies (XPT)
 - Define file (PDF)

Timeline Control

Strategy: Proactive

▣ Legacy Non-CDISC Data

- Data Standard Conversion?
- Hierarchy: Folder Structure/File Contents

▣ Legacy SDTM Version

- Seek for Waiver

Reference is made to Docket No. FDA-2012-N-0710 posted on January, 28, 2013 indicating that CBER, CDER, and CDRH would be ending support for SDTM IG v3.1.1 effective January 28, 2015. In this notice, the FDA indicated that submitters seeking a special arrangement to provide data using SDTM IG v3.1.1 beyond the established support end date for SDTM IG v3.1.1 of January 28, 2015 should submit a waiver request.

Timeline Control

Strategy: Negotiate

- ▣ Simultaneous

- Closed Collaboration



- ▣ Priority Driven

- Using PERT(Program Evaluation and Review Technique) to define the order

Package Preparation

Strategy: Auto Handle by Code

■ Data Size should be < 1 GB

- Split by Category, not by site/subject
- Resize the dataset to the maximum length used for each character variable prior to splitting
- Define.xml and ADRG.pdf should clearly document and specify how the dataset is split
 - %splitvar – split variables when text is more than 200 characters
 - %splitsize – control ADaM dataset size by input parameters
 - %lengthadj – reduce value length as to be needed

Package Preparation

Strategy: The Same Source

▣ SDTM/ADaM Define

- Use the same dataset specification (**source**)
- Auto add Dataset Attributes from spec
 - Read Excel Content into SAS
 - Add Attributes by Programming
- Using spec as source file to create define xml by macro

Package Preparation

Strategy: Simplicity over Comprehension

▣ ADaM Programming

- Questionnaire Domains (too many parameters, SF36)
 - ▣ Need many derived scores for analysis
 - ▣ Create a separate analysis dataset ADSF including analysis records only
- Variable Derivation Logic is complicated
 - ▣ Add an appendix page in the spec or define file. Ensure the hyper link works well.

Package Preparation

Strategy: Traceability

▣ ADaM Programming

- LB only has the LBORRES result, to ensure the 1-1 mapping between AVAL and AVALC, usually add AVALORI to record the LBORRES for traceability.
- AVAL will be derived from AVALORI and AVALC will be derived from AVAL.

Package Preparation

Strategy: Auto File Management

▣ Folder Hierarchy

- Follow Agency Requirements
 - ▣ STUDY DATA TECHNICAL CONFORMANCE GUIDE
- Multiple Level, Many Files across studies
- Using SAS to do the file management
 - ▣ Create/Delete Folder Structure
 - ▣ Move/Copy/Delete/Rename Files
 - ▣ SAS File Functions

Package Preparation

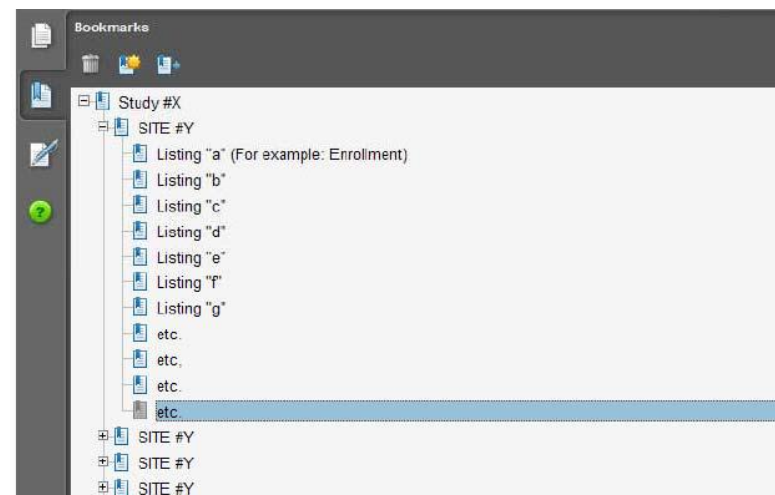
Strategy: Beyond SAS

❑ OSI Package Structure

- Difficult/Time Consuming Part
- **Content Hierarchy**

❑ Solution

- SAS: Combine RTF then RTF to PDF (File Size Limitation)
- SAS: HTML Index to PDF
- Adobe Add-On: ISIToolBox
- Latex?



Quality Review

Strategy: Reviewed by Machine

▣ SDTM Data Review

- OpenCDISC Validator
- Improved Toolkits
 - Controlling OpenCDISC Validator using R
 - Running OpenCDISC from SAS®
 - Corroborate OpenCDISC Error Messages by SAS

▣ ADaM Data Review

- OpenCDISC Validator
- Utility Codes
 - %chkSource – check data source are correctly listed
 - %chkKeyVar – check if key variables can uniquely identify single record
 - %chkTrunc – check if there is potential truncation

Quality Review

Strategy: Reviewed by Machine

- Key Results and other Documents (SRA, SDRG, ADRG and etc.) Review
 - Multiple Versions
 - Version Control
 - Tracking/Accept Function (Microsoft Office Software)
 - Version Compare:
 - Single File (Word, Adobe)
 - Multiple Files/Folder (Beyond Compare, Compare it!)

Quality Review

Strategy: Reviewed by Human (Traceability)

■ The Whole Package

- Verbatim Review
- Random Check
 - Trial Design Domains
 - Key Parameters: compare the SDTM data points against the corresponding listing provided in CSR
- Source CSR Page

Strategy

- Traceability
- Programming Thoughts
- Beyond SAS

Thanks for your attention!



Questions and Comments?