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Proactive Role of a Lead Programmer Could Help Prevent Potential Delay in Submission

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ABSTRACT

In general you see data issues as data is collected after database go live, but if you can think proactively about the potential data issues that could happen based on the Study design, CRF design, and the way DM collects the raw data, you could avoid major data issues which could delay submission. Also as a lead programmer if you get familiarize yourself with eSub components and their preparation, and your company specific process and SOPs you will save time.

INTRODUCTION

As a Lead Programmer you get the opportunity to attend study team meetings and also get an opportunity to review CRFs before the database go live. It is best if you can use this opportunity to think proactively about the potential data issues that could happen based on the Study design, CRF design, and the way DM collects the raw data before the database go live, by doing so you could avoid major data issues in the study which could potentially delay overall submission timelines.

This paper will discuss about the data collection issues we faced from a real example of an OLE safety study which almost delayed the draft timelines for SCS/ISS summaries, and also proposes solutions which could help prevent these delays.

This paper will also discuss about preparing for electronic submission (eSub) components and following/completing processes and sop's for submission.

DESIGN OF OLE SAFETY STUDY

OLE Safety study has subjects coming in from 5 different feeder studies. The subjects who complete the feeder study will enroll into OLE safety study.

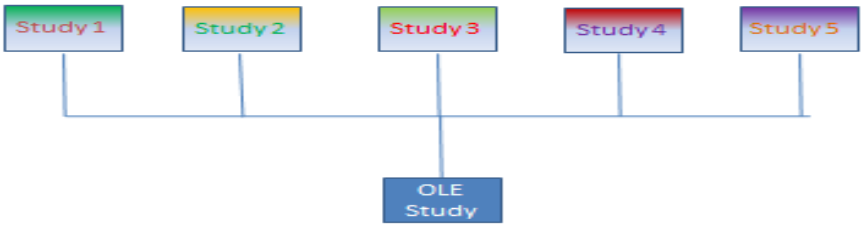


Figure 1. OLE Safety Study Design

ISSUES, SOLUTIONS AND RISKS

GENERAL ISSUES:

Demographics:

Issue: Demographics information was not collected in the OLE study, programmer has to get it from feeder studies.

Solution: May be better to collect Demographics information in OLE studies as well, otherwise it will be very difficult to program the DM domain in SDTM as you need to get the info from so many other feeder studies, and all the feeder studies collected information differently.

Risk: The risk involved is Data Management (DM) may need to reconcile the OLE data against feeder studies.

Last dose date:

Issue: Last dose date of feeder study was not collected in OLE study.

Solution: Better to collect last dose date of feeder study in OLE study, this will help in doing some integrated SCS/ISS analysis.

Risk: The risk involved is DM may need to reconcile the OLE data against feeder studies, also some sites may not be able to share data between studies, it is better to discuss with the study team at the beginning of the study.

Death Date:

Issue: Deriving Death info from AE CRF page.

Solution: In general review the CRFs and make sure all the required dates needed for analyses are collected. For example, sometimes death date is not collected separately, but is derived from AE stop date when the outcome is Fatal.

LAB DATA ISSUES:

Normal Ranges:

Issue: Merging lab data with normal range spreadsheet from vendors.

Solution: If possible, make sure the lab normal ranges for local labs are collected within the database itself, don't get a separate excel spreadsheet from the local labs, because there will always be issues with missing ranges, incorrect lab names, units etc and this will be very difficult to merge it back with raw lab dataset.

Collection of Absolute/Differential Labs:

Issue: Collecting Absolute/Differential labs with the same test name and/or units.

Solution: Make sure both the absolute and differential labs are required per protocol, and if required collect them separately with different lab test names and units, otherwise you have to derive them programmatically. If both are not required per protocol then collect only what is needed with correct unit.

Collection of Lab Visits:

Issue: Not collecting follow-up visits with actual visit name/number.

Solution: Make Generally, the follow-up visits in protocol are mentioned as 'Every 2 Weeks', 'Every 4 Weeks' etc, it is ok for DM to use repeating visits in the raw database, but DM still needs to collect actual visit name/number with the repeating visits DOV form

PREPARING FOR SUBMISSION

DATASETS:

You can only submit datasets in SAS XPT file format for electronic submission. So, convert individual SAS datasets to SAS v5 XPT files using PROC COPY and make sure no data and formats are lost during the conversion. Also make sure that the size of the datasets being submitted is less than or equal to 5 GB. If you have datasets greater than 5 GB then you should split the datasets; refer to Display 1 below for an example.

PROGRAMS:

You need to submit the programs as ASCII text (*.txt) files; refer to Display 1 below for an example.

DEFINE FILES:

If you are submitting define.XML then you should also submit the XSL stylesheet along with the XML file, otherwise the reviewers cannot open the XML file in readable format; refer to Display 1 below for an example. If possible try to submit define.PDF as well along with the define.XML, just in case if the reviewer wants to print the define file.

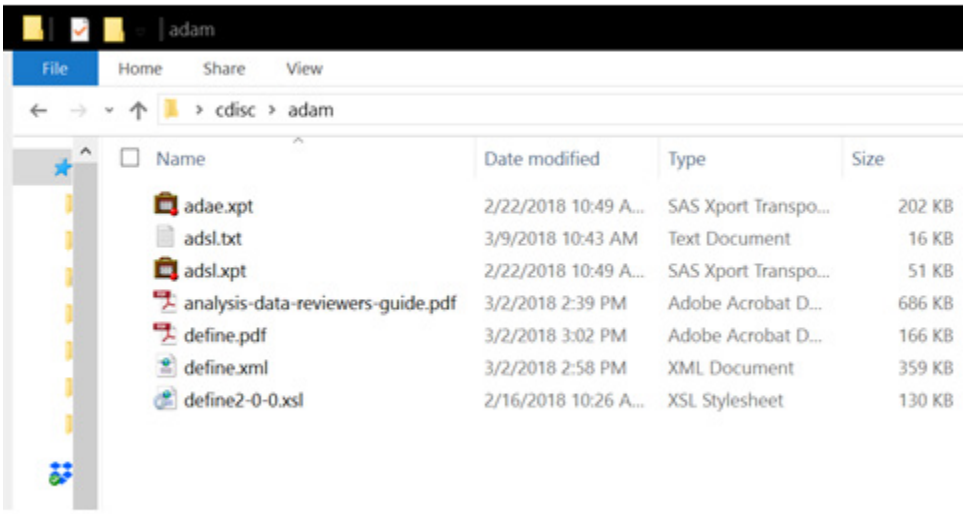
SDRG/ADRG:

It is recommended to provide SDRG/ADRG along with the other submission components. It provides the reviewers the detailed explanation about algorithms used in datasets.

You should make sure that you update all the PDF document properties as per the reviewers-guide completion guidelines.

FOLDER:

Put all the eSub components such as, datasets (.xpt files), programs (.txt files), define files, stylesheet, reviewers-guide in the same folder. Make separate folders for SDTMs and ADaMs. Display 1 below is an example of a folder with all the ADaM eSub components.



Display 1. Example for an ADaM eSub folder

PROCESSES/SOP'S

Companies have their own processes and sop's. Be aware of all your companies SOPs related to programming deliverables and make sure you follow all of them. Make sure that you have the QC SOP documentation ready and signed for all the submission related components. This will help you getting prepared for audit readiness.

CONCLUSION

As a Lead Programmer if you can think proactively and identify data issues and discuss with Study team at the beginning of the study, this will help us prevent many issues at the later stage of the study especially during the critical submission timelines. Most of these data issues could happen in any study, not just OLE studies. Also as a lead programmer it is best if you get yourself prepared and trained with all the requirements for submission components and have all the QC and SOP documentation ready.

CONTACT INFORMATION

Your comments and questions are valued and encouraged. Contact the author at:

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