INTRODUCTION

Acquisitions have increased in the biopharmaceutical world and, as a result, so have the need for legacy data conversions, which is always a challenge. We recently had a successful eSubmission with a very complicated regulatory submission strategy including many legacy studies. This poster will discuss the following:

- How we quickly assembled supplemental teams to distribute risk and workload
- Prioritized rigorous efforts on SDTM to minimize rework and prevent multiple rounds of changes downstream
- Created an innovative way of managing SUPPQUAL data during many interim data transfers that helped save time and resources
- Communicated with FDA reviewers efficiently and effectively about our complicated data submission strategy ensuring fewer questions

BACKGROUND AND CHALLENGES

- Key CRO was unable to meet its commitment in the middle of the submission, then withdrew from the contract and left the team very vulnerable
- Nine individual legacy clinical studies plus integrated summaries of safety and efficacy (ISS/ISE)
- Multiple data cuts and 3 EDC systems: many external non-SDA datasets
- Complicated regulatory submission strategy

SCOPE OF WORK

Figure 1 – Submission Strategy

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WHY AND HOW DID WE SUCCEED

- Diversified vendor network: initial strategy was to streamline the outsourced multiple functional areas by working with a single vendor. After the original CRO announced they couldn’t meet their commitment, we quickly assembled supplemental teams of highly skilled and very professional individuals selected from multiple organizations. Most of them came pre-vetted as we had successfully worked with them previously
- Adopted original vendor’s process/metadata into our own system: our original vendor used their own metadata system to create .pdf specifications for SDTM and ADaM as well as .sas7bdubit metadata. We converted the .sas7bdubit metadata into excel so that we could have editdble SDTM/ADaM specifications instead of starting from scratch
- Efficiently managed many non-SDA external data in one central location for each protocol (as shown in Figure 2)
- Prioritized rigorous efforts on SDTM
  1. Due to the 3 different EDC systems, the source data looked very different for the same data in different studies. We standardized the individual SDTMs from different databases, different studies, including controlled terms, to prepare for the integrated analysis
  2. We also realized any change in SDTM will potentially impact ADaM/TLF programming. We put in rigorous efforts/resource in finalizing SDTM as early as possible
- We worked closely with the biostat reviewers and the data manager to develop an early SDTM passed validation, and in frequent intervals after each database update. Although there were a lot of findings in the OpenCDISC report because of data issues, we focused on rectifying any data structure findings before ADaM got started. This way we avoided making changes all the way from SDTM/ADaM/TLF after database lock
- We implemented an innovative way of managing SUPPQUAL data by developing a new process and macro. SUPPQUAL variables were mapped and programmed as if they were additional variables in the parent domain (as shown in Figure 3). Then we implemented a “QNAME” row in the SUPPQUAL. All SUPPQUAL variables are programmed even if the source data were not present (e.g. not all comment fields populated). The macro would automatically structure the parent and SUPPQUAL domain using metadata created from the specifications, and removed any null records from the SUPP domain. If there were no data to populate SUPPQUAL then it would not be produced. Using this process and macro, we did not need to re-check the source data at each data transfer. This saved us so much time/resource, especially for multiple databases working with a single protocol

CONCLUSIONS

- The more detailed plan (i.e. submission strategy, CRO selection, timeline) you have, the easier the project will go, the better result you will have in the end
- SDTM is NOT easy, nor is it trivial
- Specifications are NOT just for programmers; specifications will turn into define/SDRG/ADRG
- So programs and specifications need to be consistent and synchronized
- Documentation is VERY important. Documentation = communication with FDA reviewers
- FDA reviewers are not unreasonable. Don’t be afraid to ask questions and speak up

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