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Sharing and Building Sponsor-Specific CRFs – No Paper Required

Scott Bahlavooni, Biogen-Idec, Cambridge, USA
Retha Gerber, Quintiles, Melbourne, Australia

ABSTRACT

As development of the CDASH data collection standard has trailed SDTM tabulation standard, pharmaceutical and biotechnology companies continue to define and maintain sponsor-specific standard case report forms (CRFs). Sponsors instantiate their internal data management system (DMS) with their standards. This expedites study-specific DMS builds and ensures consistent data collection across studies. Unfortunately, these benefits are limited to studies conducted using the sponsor's DMS. How can sponsors effectively extend the use of their sponsor-specific standards to studies conducted on systems managed by strategic partners or Contract Research Organizations (CRO)? Well-defined metadata.

INTRODUCTION

Biogen Idec and Quintiles entered a strategic clinical development collaboration focused on efficiency through quality, transparency, and innovation. A Quintiles-managed Medidata Rave ® instance was selected as the primary data management system (DMS) for strategic partnership. Rave provides library functionality via a Global Volume (GV). A GV enables the storage and re-use of CRFs and their extended attributes, derivation and validation procedures, and custom functions. The development of a GV comprised of Biogen Idec data collection standards serves as the foundation for consistent, quality data capture and efficient study-specific DMS builds for studies conducted within the partnership. This paper provides the unique perspective and opinions from both the sponsor and strategic partner on the value of well-defined metadata in the GV development.

BIOGEN IDEC DATA COLLECTION STANDARDS

Biogen Idec, akin to other sponsors, has a storied history developing data collection standards. These standards began as legacy constructs to support efficient data capture and analyses. They evolved and continue to evolve as the science changes, the pipeline expands, and industry standards gain acceptance. Institutional knowledge is a constant in this evolution be it the rationale for collecting a certain data element or instituting a specific validation procedure.

Again, similar to other sponsors, Biogen Idec manually maintained its data collection standards as human-readable documents – mock CRF PDFs annotated with DMS attributes, mock CRF PDFs annotated with raw DMS extract attributes, mock CRF PDFs annotated with SDTM attributes, an Excel spreadsheet with DMS-specific data validation rules, etc. As Biogen Idec initiated a search for a strategic partner to assist with its clinical development and study conduct, the team, Data Standards Team (DST), responsible for the development and maintenance of Biogen Idec's data collection standards launched an initiative to translate the standards into a machine-processable format. The business drivers for this initiative included (a) improving consistency across the data collection standard suites, (b) expediting data collection standards development, (c) reducing manual overhead inherent in manually designing, annotating, and maintaining PDF documents, and (d) providing its future strategic partner or partners with a DMS-agnostic representation of its data collection standards embedded with institutional knowledge. The future partner or partners could then consume this content and develop a library of Biogen Idec data collection standards on their DMS of choice.

DEVELOPING SPONSOR-SPECIFIC CRF LIBRARIES ON CRO'S DMS

Sponsors typically have proprietary data collection standards and libraries of their proprietary standards built on the internal DMS. As employing well-defined standards expedite a study-specific DMS build, Quintiles is able to take a sponsor's data collection standards and build a library on Quintiles DMS. Although Quintiles supports multiple DMS platforms, this paper will focus on Medidata Rave.

During the DMS build, Quintiles employs their own Standard Operating Procedures (SOPs) or, depending on the contract, Sponsor SOPs or a combination thereof to ensure quality and compliance. CRF design is by far the most time-consuming step for any DMS build and that can be especially true for a CRF library. Team members must be

familiar with both the requirements of the data elements being collected and the DMS in which the data elements will be designed. As sponsors usually provide their data collection standards as an annotated Word or PDF document or extracts downloaded from the sponsor's DMS, a Quintiles Technical Designer (TD) needs to account for how the sponsor's data collection standards will be translated into Rave including: Form Layout, Fields, Codelists, etc.

After initial CRF development, a number of review meetings including online screen reviews occur to ensure requirements are met. Additional reviews ensure the front-end design does not adversely impact back-end programming activities such as data cleaning, transforming the data to SDTM, or data analysis. After the CRF design has been completed and finalized, edit check specification programming and internal validation activities occur and upon completion, the database is released for sponsor User Acceptance Testing (UAT). A library is typically moved to production within a few days of completion of sponsor UAT. Timelines vary based on the complexity of a sponsor's data collection standards and the amount of translation required for both the CRFs and edit checks, the engagement of the sponsor, and other business requirements.

Alternatively, Quintiles assists sponsors in the development of data collection standards and will develop those standards on Quintiles DMS. For example, Quintiles assisted a sponsor in the rapid development and deployment of a suite of data collection standards. The sponsor and Quintiles assembled key team members at their office for a number of weeks. This approach ensured a rapid library build as issues were discussed and resolved quickly. For this sponsor, the travel costs and resource demand were outweighed by the need to complete the library build in a very short timeframe.

BIOGEN IDEC/QUINTILES STRATEGIC PARTNERSHIP RAVE GLOBAL VOLUME BUILD

Biogen Idec and Quintiles entered a strategic partnership focused on efficiency through quality, transparency and innovation. The partners embarked on a project to develop a GV of Biogen Idec's data collection standards on Quintiles instance of Rave. This GV would provide a foundation for consistent, quality data capture and efficient study-specific DMS builds.

CRF DESIGN AND BUILD, A BIOGEN IDEC PERSPECTIVE

Biogen Idec had nearly completed the machine-processable representation of its standard CRFs when the GV Build Project launched. This representation included a system-agnostic representation of CRF constructs such as form attributes, field attributes, and codelist values. As Rave provides a medium to instantiate a build via formatted spreadsheet known as the Architect Loader Spreadsheet (ALS), Biogen Idec extended its machine-processable representation to include certain Rave-specific attributes such as Form OIDs, Field OIDs, and Field Compliance Requirements.

The addition of Rave-specific attributes enabled Biogen Idec to provide Quintiles with a "starter" ALS embedded with institutional knowledge. This presumably would eliminate translate-review-rework cycles inherent in sponsor/CRO relationships and enable the partners' GV Teams to focus on CRF designs from Biogen Idec's standards suite that have historically been troublesome. For example, providing Quintiles with metadata that indicated Biogen Idec requires sites to complete the Concomitant Medication Start Date, but will allow the site to provide a partial date eliminates the need for Quintiles to either (a) review Biogen Idec documents for this (buried) piece of institutional knowledge, (b) explicitly request Biogen Idec provide this institutional knowledge or (c) make assumptions and required Biogen Idec review the assumptions. Providing metadata such as this, in part, allowed Quintiles to quickly provide prototypes for problematic disease history CRFs. The final design eliminated nearly half of the edit checks historically associated with these CRFs.

In my opinion, the ability to provide Quintiles with a "starter" ALS significantly expedited the initial CRF build. Representing our standard CRFs in a machine-processable format required the DST to address inconsistencies that while mostly trivial slipped through years of human review, but were easily identified by a machine. Further, I believe providing Quintiles with a "starter" ALS enabled the Biogen Idec GV Team, a team with differing levels of Rave experience, to focus on problematic CRF designs rather than fret about minutia. Finally, this did indeed eliminate typical sponsor/CRO translate-review-rework cycles. Issues identified by the Biogen Idec GV Team were usually problems with our own metadata! In my opinion, this exemplifies the partnership maxim – efficiency through quality, transparency, and innovation.

CRF DESIGN AND BUILD, A QUINTILES PERSPECTIVE

Instead of following the traditional approach of providing Quintiles with an annotated Word or PDF document of standard CRFs, Biogen Idec created an ALS and provided it to Quintiles for upload into Rave. Once initial upload errors were resolved, this ensured rapid progress on the initial design steps since minimal discussion on form layout and field formats were needed.

Quintiles and Biogen Idec worked closely together on finding preeminent options to standardize certain complicated CRFs whilst allowing for compulsory modifications based on study protocols. Inexperience of most end-users in the use of electronic data capture systems creates a need for uncomplicated design and functionality. Quintiles developed a few prototypes for certain CRFs and discussed the advantages and disadvantages of each prototype with Biogen Idec before selecting the final design.

EDIT SPECIFICATION AND PROGRAMMING, A BIOGEN IDEC PERSPECTIVE

Unfortunately, data validation rules had not been incorporated into Biogen Idec's machine-processable representation of its data collection standards when the GV Build Project launched. As a result, Biogen Idec provided Quintiles with data validation rule or "edit check" specifications based on both an earlier version of its standard CRFs **and** a different DMS. Quintiles provided an exemplary translation of these specifications into a Rave-specific implementation; however, the inconsistencies and institutional knowledge gaps within Biogen Idec's specification became apparent when translated. Further, implementation of Rave-specific configurations required additional changes quite late in the specification and programming development cycle.

In my opinion, the absence of well-defined data validation rule metadata caused Biogen Idec to regress into the typical sponsor/CRO paradigm of "sponsor knows best". Although Quintiles provided an exemplary translation, Biogen Idec significantly revised Quintiles specification - harmonizing inconsistencies in our original specification provided to Quintiles and ensuring none of our data validation rules were missed during the translation. If Biogen Idec had been able to provide the same level of detail with its data validation rules as with its CRFs, a significant translation-review-rework cycle would have been avoided. Biogen Idec is remediating this deficiency and retrospectively incorporating data validation rules into its machine-processable representation.

EDIT SPECIFICATION AND PROGRAMMING, QUINTILES PERSPECTIVE

As Biogen Idec's standard Data Review Guidelines were initially developed for their legacy DMS, Quintiles was tasked to transfer the specifications into Quintiles TopTeam Net Client. Following Biogen Idec's review of the Quintiles Data Validation Specification (DVS) document, extra columns were added to the DVS document at Biogen Idec's request.

Unfortunately, these additional information in these columns were not adequately captured the in TopTeam due to system limitations. The lack of well-defined specifications in TopTeam led to uncertainty and a difference in interpretation of approximately 50% of checks by the Quintiles programming and validation teams. Implementation of new functionality at URL level created the need for updates to multiple edit checks at a crucial time during the validation process of the GV, as well as other studies that were fast approaching their planned go-live dates. Both matters had a significant impact on timelines for completing validation and release for sponsor User Acceptance Testing (UAT) and beyond.

CONCLUSION

A BIOGEN IDEC PERSPECTIVE

In my opinion, the Biogen Idec/Quintiles strategic partnership Rave GV build exemplifies not only the value of well-defined metadata, but also that the sponsor/CRO paradigm shifts when the partners share rather than assume or translate institutional knowledge. Well-defined metadata expedited the GV CRF design and build and its absence hindered edit check specification and programming. Biogen Idec has definitely learned this lesson and as its standards continue to evolve will ensure it can provide Quintiles with a more robust package such that both partners can focus on innovation rather than translate-review-rework.

A QUINTILES PERSPECTIVE

Through this project, we have confirmed the importance of adapting methods and ways of working to find ways in which both parties can cooperate to reach the common goal of creating standardised data collection specifications. On the one hand we had a steady framework, and on the other hand a degree of flexibility to allow for necessary (and often immediate) changes. In addition, there was strong communication, leading to maximum transparency and a mutual trust between partners.

Based on this, we now have a better understanding of Biogen Idecs's institutional knowledge which would lead to expedited timelines for study start up processes and delivery of quality data to ensure speedy database locks.

The gained efficiencies are undoubtedly be to the benefit of both organizations.

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CONTACT INFORMATION

Author Name: Scott Bahlavooni
Company: Biogen Idec
Address: 14 Cambridge Center
City / Postcode: Cambridge, MA 02142
Work Phone: 617.914.4082
Email: scott.bahlavooni@biogenidec.com

Author Name: Retha Gerber
Company: Quintiles
Address: 10/606 St Kilda Rd
City / Postcode: Melbourne VIC 3004, Australia
Work Phone: +61 3 9519 6800
Email: retha.gerber@quintiles.com