Sharing and Building Sponsor-Specific CRFs – No Paper Required

PhUSE 2014 – TT02

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Agenda

- Biogen Idec – Quintiles Partnership
- Historical Perspectives
  - Biogen Idec Data Collection Standards
  - Developing Sponsor-Specific CRF Libraries on Quintiles Data Management Systems
- Partnership Medidata Rave Global Library Build
- Summary
Biogen Idec – Quintiles Partnership
The Partnership

• Five year strategic clinical development collaboration focused on efficiency through quality, transparency, and innovation

• Partnership Principles
  • Set clear definition of roles, accountabilities, and responsibilities
  • Allow both organizations to focus on their core competencies
  • Biogen Idec provides robust oversight without micro-management; Quintiles takes more responsibility and accountability
  • Reduce duplication of effort to enable greater resource efficiency
  • Align on a streamlined set of processes to drive efficiency and productivity

• Key partnership benefits
  • Increased predictability and productivity creating sustainable relationships and capturing lessons learned across studies
  • Increased standardization and efficiency due to streamlined and cross-portfolio standardized processes
  • Reduced duplication and clarity of roles and responsibilities such that each organization can focus on core competencies
  • Increased customer site focus through effective communications, streamlined interactions, and enhanced training to improve study execution and customer experience
Historical Perspectives:
Biogen Idec Data Collection Standards
Biogen Idec Data Collection Standards

• V1 finalized in 2006 to support efficient data collection and data analyses
  • V1 included core CRFs and data validation rules

• V6 finalized in 2009 included the first therapeutic area data collection standards

• Data collection standards continued to evolve as science changes and industry standards (i.e. CDASH and SDTM) gained acceptance

• Data collection standards maintained as human-readable documents
  • Mock CRF PDFs annotated with Data Management System (DMS) attributes
  • Mock CRF PDFs annotated with raw DMS SAS extract attributes
  • Mock CRF PDFs annotated with SDTM attributes
  • DMS-specific data validation rules maintained in Excel

• 2013 initiative launched to represent Biogen Idec’s data collection standards in a machine-processable format
  • Rationale:
    • Improve consistency within data collection standards
    • Expedite data standards development
    • Reduce resources required to maintain multiple PDF documents
    • Provide partners with a DMS-agnostic representation of Biogen Idec’s data collection standards embedded with institutional knowledge
Translating Institutional Knowledge to Metadata

Data Collection Standards Metadata

### Demography

<table>
<thead>
<tr>
<th>Sex</th>
<th>Race</th>
<th>Ethnicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>White</td>
<td>Other</td>
</tr>
<tr>
<td>Female</td>
<td>Black</td>
<td>Native American</td>
</tr>
<tr>
<td>Other</td>
<td>Hispanic</td>
<td>Asian</td>
</tr>
<tr>
<td>Other</td>
<td>Other</td>
<td>Other</td>
</tr>
</tbody>
</table>

**Rules:**
- Sex must be present. Sex is blank. Please provide.
- Race must be present. Race is blank. Please provide.
- Ethnicity must be present. Ethnicity is blank. Please provide.

**Notes:**
- For Race, if Other has been marked, then specify must be present.
- For Ethnicity, if Other has been marked, then specify must be present.

**Data Collection Standards:**

- **Site Check Name:** Demo Check Number
- **Data as Found:** Demo Data Found
- **Data as Input:** Demo Data Input
- **Data Validation Rules:**
  - No blank or blanked out fields allowed.
  - Sex must be present.
  - Race must be present.
  - Ethnicity must be present.

**Data Collection Standards Metadata:**

- **Item Name:** Demo
- **Data Category:** Demo Data Category
- **Data Type:** Demo Data Type
- **Data Element:** Demo Data Element
- **Data Validation:**
  - No blank or blanked out fields allowed.
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**Data Validation Rules:**

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Historical Perspectives:
Developing Sponsor-Specific CRF Libraries on Quintiles DMS
Steps to Develop a Sponsor-Specific CRF Library

- Sponsors often supply their CRF standards as annotated Word or PDF documents or as extracts downloaded from the sponsor’s DMS.

- A Technical Designer translates the sponsor’s data collection standards into constructs required by DMS platform of choice.
  - Quintiles supports multiple DMS platforms; therefore, multiple translations may be required based upon sponsor requirements.

- After the sponsor’s standard CRFs are built in the DMS, Quintiles hosts online screen review meetings to ensure build meets the sponsor’s expectations.

- Edit check specification, development, and validation occurs after the CRF build has been finalized and signed-off by the sponsor.

- After edit check validation completes, the library is released to the sponsor for user acceptance testing (UAT).

- Upon completion of UAT, the library is pushed to production and made available for expediting study-specific DMS builds.

- Timelines may vary based on the complexity of a sponsor’s data collection standards, sponsor engagement in the development process, and other business requirements.
Partnership Medidata Rave Global Volume Build
Project Overview

• A Quintiles-managed Medidata Rave instance was selected as the primary DMS
  • Rave provides library functionality via a Global Volume (GV) for the storage and re-use of CRFs and their extended attributes, derivation and validation procedures, and custom functions
  • Rave provides functionality to instantiate a build by uploading formatted spreadsheet, the Architect Loader Spreadsheet (ALS)

• Partnership GV build of Biogen Idec data collection standards followed Quintiles business processes

• Biogen Idec extended its data collection standards metadata to include certain Rave-specific attributes
  • The extension applied to CRF standards only
  • Enabled Biogen Idec to create a “starter” ALS of its CRF standards

• Biogen Idec provided Quintiles with a “starter” ALS of its CRF standards and a data validation rule specification based on a different DMS

• Quintiles instantiated the GV using the ALS and provided design expertise for challenging CRF designs
Project Overview Continued

- Quintiles developed a Rave-specific data validation rule specification based on the specification provided by Biogen Idec
  - Biogen Idec revised the specification to harmonize inconsistencies within the original document provided to Quintiles

- Quintiles programmed and validated edit checks

- Biogen Idec performed sponsor UAT

- The GV was pushed to production and made available to Study Management Teams developing study-specific DMS builds
CRF Design and Build: A Biogen Idec Perspective

• Biogen Idec GV Team’s exposure to Rave varied and resulted in concerns regarding implementing Biogen Idec standard CRFs in a new DMS

• Extending Biogen Idec’s data collection standards metadata with Rave-specific attributes to facilitate the creation of a “starter” ALS significantly expedited the initial CRF build
  • Eliminated the requirement for Quintiles to translate Biogen Idec standard CRFs into a Rave-specific format
  • Enabled Biogen Idec GV Team to focus on historically troublesome CRF designs
    • Enabled Quintiles to quickly prototype designs for these CRFs
    • Example: Quintiles developed two designs for a troublesome disease history CRF and provided the Biogen Idec GV team with the requisite information to select a design
      – Final design eliminated 50% of the edit checks relative Biogen Idec’s legacy DMS
  • Eliminated “translate-review- rework” cycles inherent in sponsor/CRO relationships
    • Majority of issues identified by Biogen Idec GV Team were due to our metadata!

• Exemplified partnership maxim of efficiency through quality, transparency, and innovation
CRF Design and Build: A Quintiles Perspective

• Although Quintiles resolved a few initial upload errors, Biogen Idec’s ability to provide an ALS for upload into Rave ensured rapid progress on the CRF build

• Minimal discussion of form layout, field format, and field attributes was needed

• Quintiles and Biogen Idec were able to collaborate to standardize certain complicated CRF designs
  • Quintiles developed prototypes and presented the advantages and disadvantages to both the front end user at the site and data extract user transforming the data to SDTM
Edit Check Specification and Programming: A Biogen Idec Perspective

• Data validation rules were not incorporated into Biogen Idec’s machine-processable representation of its data collection standards at the start of the GV build project.

• Biogen Idec provided Quintiles with an edit check specification based on both an earlier version of its standard CRFs and a different DMS.
  • Quintiles provided an exemplary translation of the specification into Rave; however, inconsistencies in Biogen Idec’s specification were apparent after the translation.
  • Biogen Idec revised the Quintiles specification resolving our inconsistencies and adding institutional knowledge.
    • Biogen Idec regressed into the typical sponsor/CRO paradigm of “sponsor knows best”.

• Implementation of Rave-specific configurations resulted in additional changes late in the specification programming development cycle.

• 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 Check Specification and Programming: A Quintiles Perspective

- Biogen Idec provided Quintiles with an edit check specification based on its legacy DMS.

- Quintiles translated the Biogen Idec’s specification into Quintiles TopTeam Net Client.

- After Biogen Idec’s review of the translation, additional columns were added to the document at Biogen Idec’s request.
  - The additional information was not adequately captured 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.

- Implementation of new Rave configuration created the need for updates to multiple edit checks at a crucial time during the validation process.
Summary
A Partnership Global Volume Built With and Without Well-Defined Metadata

Biogen Idec Perspective:
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.

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 Idec’s institutional knowledge which would lead to expedited timelines for study start up processes and delivery of quality data to ensure speedy database locks.
Acknowledgements

**Biogen Idec:**
Todd Bazin, Laura Putnam, and Kevin Stephenson and Retha Gerber and the Quintiles GV Team

**Quintiles:**
Quintiles Programming and Validation team, special thanks to Sabrina Steffen, Kevin Coughlin, Mita Valera, Aruna Ravi and Biogen’s Scott Bahlavooni.