APPLICATION NOTE

BioFortis
Empowering Researchers Through Innovative Software

MERCK BBMS: A CLINICAL TRIALS SPECIMEN MANAGEMENT SYSTEM

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INTRODUCTION

Clinical trials in the last decade have become more complex due to increases in protocol procedures, trial lengths, number of participating partners and sites, changing regulations, and resulting data types. These challenges have placed greater operational burdens on the management of biospecimens from trials. The variations in biospecimen types, collection sites, permissions, and data formats from different business partners all contribute to the complexity of running clinical trials today. Furthermore, there are challenges in linking the "future use" specimens collected from clinical trials to other important data such as consent, demographics, clinical data, and test results. The ability to link to important specimen and subject metadata while managing appropriate restricted access is critical to enable future biomedical research from these specimens. Merck's Biospecimen & Biorepository Management System (BBMS) is a transformational informatics project that improves operational visibility, increases efficiency, and maintains biospecimen traceability for clinical trial stakeholders; it is essentially a "Biospecimen CTMS" for trial specimens, in addition to functioning as a life cycle inventory management system for future use specimens.

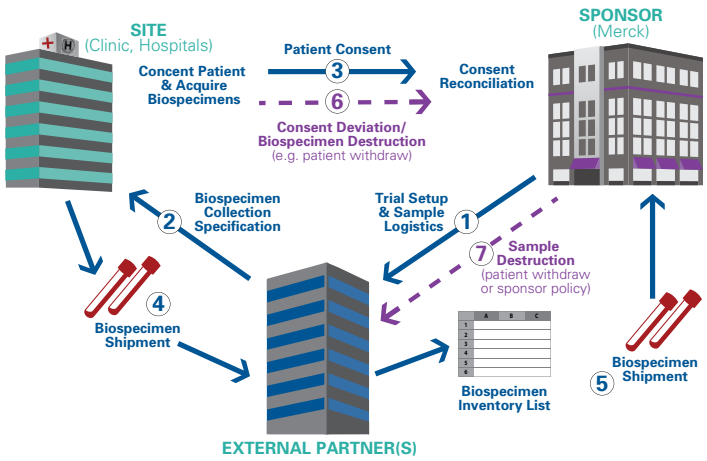

Figure 1: Distributed Clinical Trial Specimen Management Process. The numbers represent the sequence of events taking place among clinical trial stakeholders.

DISCUSSION

Existing CTMS software solutions are well-understood in supporting today's clinical trial logistics from site & subject perspectives. However, there is a lack of a cohesive informatics infrastructure for managing clinical trial samples in a distributed environment that can involve multiple clinical trial partners, where operational workflows occur asynchronously.

The primary challenge faced by Merck in managing millions of valuable biospecimens collected from past and current clinical trials is "How do we organize

and provide an interface to clinical biospecimen data?" The Clinical Pharmacogenomics and Clinical Specimen Management team is burdened with variable data spread over many different systems (both internal and external to Merck) which causes lengthy data reconciliation and verification processes.

Future use specimens (specimens collected in a trial that can be used for exploratory purposes beyond the study timeline) are becoming increasingly valuable. These specimens can be used to help develop molecular biomarkers that can guide treatment decisions and selection of appropriate patient populations for maximum therapeutic benefit. Management of future use specimens involves special tracking, reconciliation and privacy considerations that were incorporated into the system design.

The key considerations for the BBMS system, to support a the complex Inventory Lifecycle of in-life and future use specimens (Figure 2) are detailed below.

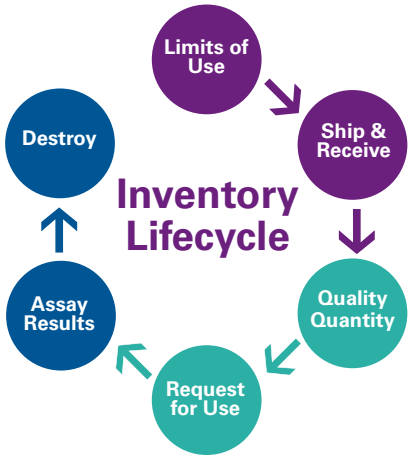

Figure 2: BBMS Future Use specimen lifecycle management.

Inventory Management Goals

- Track permissions for specimen use import shipment and receipt records to track specimen location.
- Provide field level restricted access control for sensitive information and PHI
- Associate specimen QC information to inventory. (e.g., DNA quality and quantity)
- Enable associated clinical and demographic data to be related to specimens to facilitate searches and requests supporting biomarker research.
- Link assay results. (e.g., genotyping to specimens in inventory
- Allow curation of inventory, including specimen destruction.

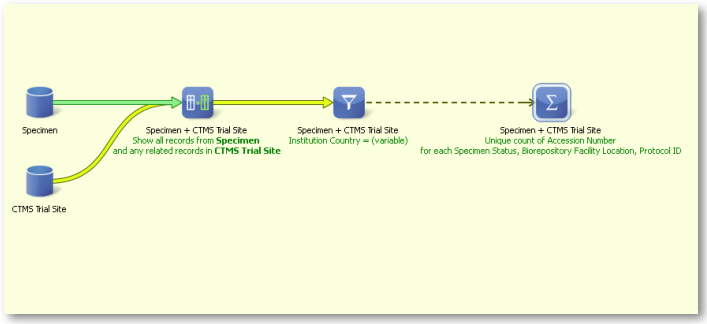

Figure 3: Diagrammatic query with Labmatrix's Qiagram search engine: count of unique subject specimens for each specimen status, protocol, and biorepository, given the variable "Country" where the clinical sites reside.

RESULTS

With the implementation of BBMS, for the first time, users involved in curation of trial biospecimens can see all related data side-by-side and get a holistic view of all specimens. In addition users benefited from;

Improved Consent Management Strategy:

- Centralizes specimen permissions with inventory.
- Provides clear, explicit limits on specimen handling and use.
- Reduces time & effort to reconcile specimens.

Improved Data Utilization:

- Centralized inventory and consent data creates the opportunity for users to interrogate the specimen inventory for myriad reasons ranging from monitoring ongoing studies to exploring various scientific lines of thought.
- Cycle times for specimen release dropped significantly due to increased data accessibility and the system's support of improved processes.

Reduced IT Maintenance:

- Automated integrations and data migrations reduced IT resource needs.
- Reduction in the need for business and IT experts to generate custom reports (e.g. for DNA specimen collection rates).
- Reduced reliance on Access databases and XLS data sets.

Improved Search Capability:

- No need for IT support to create queries for users, instead the diagrammatic query tool Qiagram, allows users to search data in real time. (Figure. 3)
- Users can create "widgets" to show real time data visualizations on their BBMS desktop. (Figure. 4)
- Allows creation of calculations and iterative result sets to enable complex questions to be asked and answered. (e.g., filters, joins, calculations)

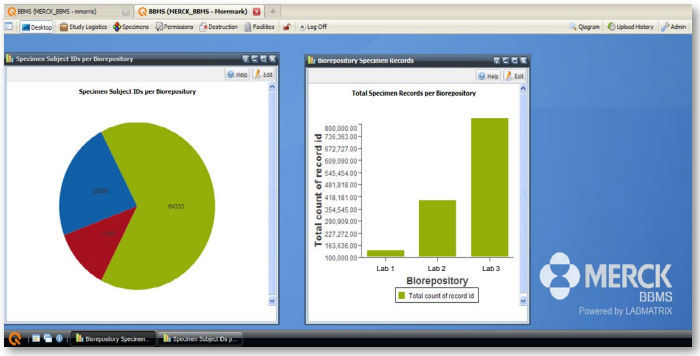

Figure 4: Merck BBMS user landing page, where widgets can be placed, after being configured in Qiagram, that produce visual displays reflecting real time data within the system. Note: Data displayed is not representative of production data.

CONCLUSIONS

Merck recognized the need to manage clinical biospecimen information in a validated, integrated application to ensure compliance and meet business goals for managing and leveraging biospecimens effectively. The Labmatrix software platform was quickly configured in a 10 month agile development project in 2011 to meet the utmost-pressing needs, enabling consistent workflow management, standardizing and normalizing data, providing a "one-stop shop" for viewing and querying information, and maintaining appropriate data access permission and regulatory compliance. Additional BBMS development in 2012 further enhanced this foundational platform for clinical biospecimen management to better support novel clinical research goals at Merck.

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