

Challenges and Opportunities for Real Time Learning & Decision Making (RTLDM) Clinical Data Review-A Case Study

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Introduction

- Protocol design includes 2 parts in the study. Part 1 requires Weekly or Biweekly unblinded review by an Operations Committee (OC) to monitor safety and also make dose escalation decisions. OC should be reviewing as close to 'real time' data as possible. All clinical events are adjudicated by an external party.

Challenges and Proposed Solution

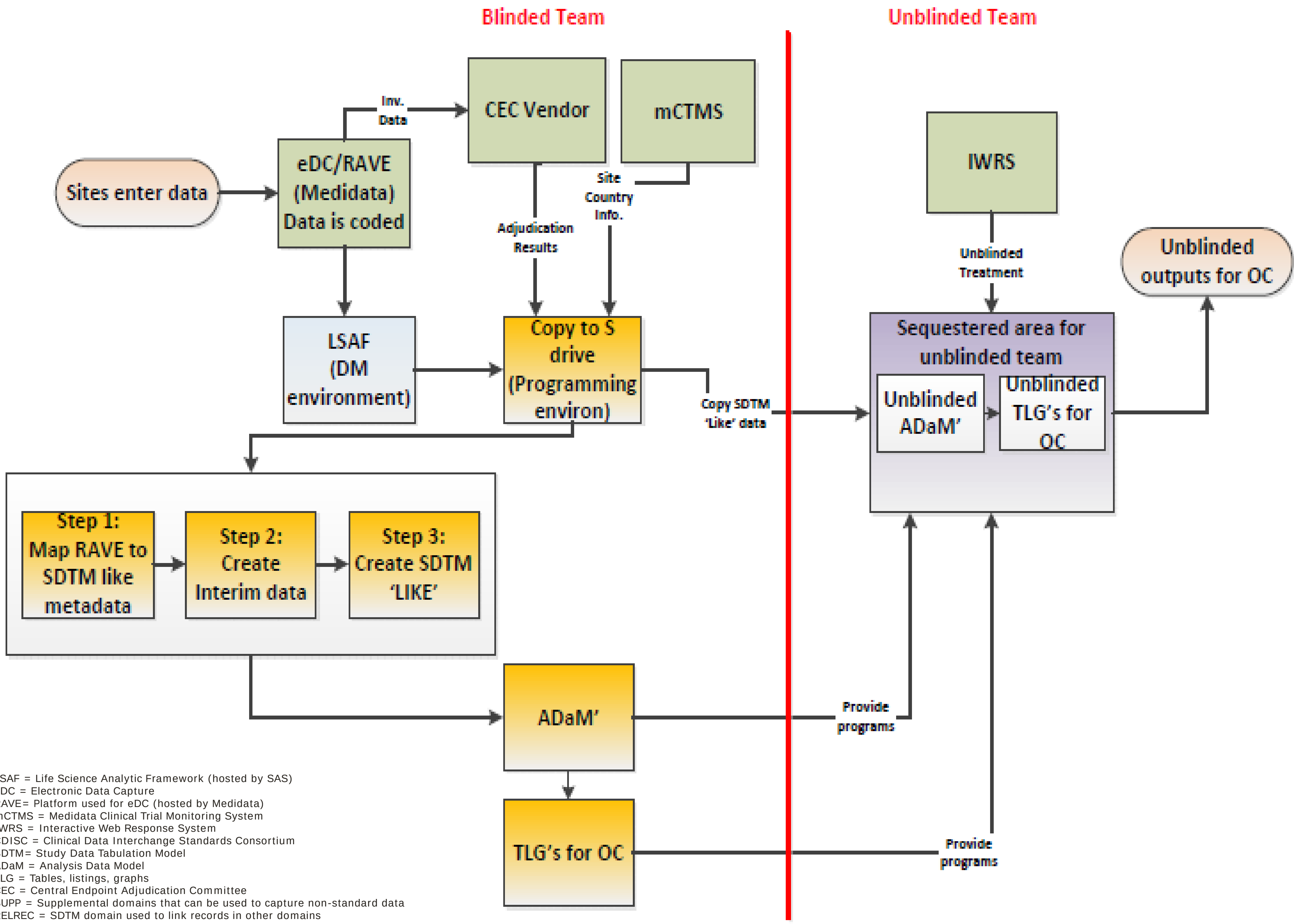
Challenges to RTLDM

- Availability of investigator reported subject data 'quickly'
- Availability of data in a format that follows standard conventions
- Some source data files could be SAS or XLS
- Frequent changes in requirements/specifications for outputs
- Internal and external functions and hand offs

Enabling RTLDM

- Open access to programming team to Data Management (DM) Staging environment where RAVE data stored
- Extract data from earlier up stream-RAVE
- Conduct mapping from RAVE to a Data Review Model (DRM) in SDTM (CDISC Standard) 'Like' format within programming team
 - Streamlined approach, only map domains required for RTLDM
 - Reduce complexity-avoid SUPP domains, RELREC
 - Add flags in parent domains to handle linking (e.g. between AE and DS or AE and CE)
 - Ensure critical aspects such as linking between domains and between INV and adjudication records is implemented accurately and matches 'true' SDTM
- QC against submission-ready SDTM to confirm accuracy of mapping
- Smooth collaborations of all stake holders involved (DM, Biostatistics, Clinical and Programming)

High Level Data Flow Process for Operations Committee (OC)



Operational Challenges

- Leverage mapping programs from Consumer and adapt to Pharma environment. Customization needed for Pharma specific domains related to Clinical Events such as Bleeding, DVT, MI etc.
- Complexity related to linking of event data records captured in Clinical Events (CE) and Findings About (FA) domains
- Site ID and country information extracted from mCTMS not in RAVE
- CEC vendor entered data into custom platform, data extracted from platform and transferred to Janssen. Programming team incorporates these data into SDTM 'like' domains for analysis
- inconsistencies in CEC and Investigator eCRF
- Global team supporting trial in different time zones, team meetings scheduled in evenings or early mornings
- Time difference facilitated deliverables since round the clock coverage and ability to accommodate last minute requests
- Folder naming conventions and process to use existing folder structures to store data and metadata at each step

Domain	Complexities
DM (Demographics)	Collapsing RACE, adding Reference date and ARM variables
DS (Disposition)	Combining data from 3 different RAVE datasets
VS (Vital Statistics)	Changing structure from horizontal to vertical, adding baseline flag
CE (Clinical Events) and FA (Findings About)	Combining data from 5-6 RAVE datasets and linking across datasets
CE (Clinical Events) and FA (Findings About)	Combining data for event details from 5-6 RAVE datasets
PR (Procedures)	Combine data from surgery and study specific procedure pages
SV (Subject Visit)	Adding visit number, not included in RAVE dataset
ZR (Randomization)	Creating a dummy randomization dataset using DS domain

Lessons learned

- Concept applied in Consumer division which cross sector collaboration allowed us to quickly get familiar with concept
- Collaborations within cross functional team to 'think out of the box', anticipate issues and find solutions
- This study can serve as a pilot and knowledge sharing for ongoing larger Data Review Model (DRM) for RTLDM initiatives

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