SCDM India
Single Day Event

THEME
CDM — Revisiting fundamentals in an evolving clinical research landscape

August 26, 2023, Mumbai
Agenda

• Lab/external data
• various types of data
• Challenges
• Mitigations
• Case Study
• Key Takeaways
• Q & A

Disclaimer: The views and opinions shared in this presentation are solely of mine and do not necessarily reflect the views of my organization. Information presented here is for informational purposes only and not to be considered as professional advice. Before making any decisions based on the information provided here, it is recommended that you seek professional advice. Please use at your own risk.
Lab/External Data

• Labs are where biologic samples, diagnostic images or data such as electrocardiograms or Holter monitors are evaluated or interpreted.

• CDM personnel are responsible for data integrity throughout all lab data transfer and cleaning activities.

• CDM personnel may also be involved with setting up standards and processes for their organization to help ensure the integrity of all data.
Various types of Lab/External Data

- Central Labs
- PK/PD Data
- Safety Data
- Biomarkers Data
- Local Labs
- Specialty Labs
- Genomics Data
- Bioanalytical Data
Challenges

- Data volume & complexity
- Instrumentation Limitations
- Human Error
- Sample Contamination
- Data Validation & quality control
- CDISC & Regulatory authorities requirements
Mitigations

• Data Management & Monitoring Tools
  o **Real-Time Analytics:** which helps to monitor key metrics.
  o **Intuitive Visualizations:** Quickly interpret complex data and make informed decisions.
  o **Data Integration:** Access and analyze all data from one centralized platform.
  o **Scalability:** Handle large datasets and increasing analytics demands.

• Regulated standard operating procedures
  o Establishing robust steps, including Edit checks, Standard eCRF specs ensuring the reliability & integrity of the collected data.
Mitigations

• Calibration & Maintenance
  ○ Regular calibration and maintenance of lab instruments can reduce limitations and enhance the accuracy and reliability of measurements.

• Contamination control measures
  ○ Implementing stringent protocols for sample handling, storage and laboratory hygiene can minimize contamination risks and maintain sample integrity.
### International System of Units (SI) Unit

<table>
<thead>
<tr>
<th>Lab Test</th>
<th>Merck Manual</th>
<th>Sponsor</th>
<th>Lab A</th>
<th>Lab B</th>
<th>Lab C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ferritin</td>
<td>mcg/L (ug/L)</td>
<td>ug/L</td>
<td>ug/L</td>
<td>pmol/L</td>
<td>mcg/L</td>
</tr>
<tr>
<td>Troponin T</td>
<td>mcg/L (ug/L)</td>
<td>ug/L</td>
<td>ng/L</td>
<td>ng/L</td>
<td>mcg/L</td>
</tr>
<tr>
<td>Thyroxine</td>
<td>nmol/L</td>
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<tr>
<td>Aldosteron</td>
<td>pmol/L</td>
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- Sponsor X has defined SI units based on Merck Manual and uses it for Local Labs.
- Sponsor X SI units sometimes does not match with Central Labs.
- SI units are not consistent even among Central Labs.
- No single source of truth to verify SI units.
International System of Units (SI Unit)...Challenge

- Pinnacle 21 generates warnings if SI unit is not unique for a combination of Category, Test, Specimen and Method
- Summarizing tests with multiple SI units for analysis is a challenge
- Central Labs does not provide unrounded results hence apply conversion by Sponsors leads to double rounding
  - No single source of truth for Conversion Factors and Precisions lead to additional challenges
FDA’s ask for Additional Lab Dataset

Technical Conformance Guide June 2023

For clinical studies, please submit two separate domains for lab results. The LB domain should contain SI units in LBSTRESU for the SI results in the LBSTRESC and LBSTRESN fields. An additional custom domain structured identically to LB should contain conventional units in --STRESU for the results in conventional units in the --STRESC and --STRESN variables. It is ideal if both conventional and SI units come directly from the lab vendor.

<table>
<thead>
<tr>
<th>LBTESTCD</th>
<th>LBTEST</th>
<th>LBORRES</th>
<th>LBORRESU</th>
<th>LBORNRLLO</th>
<th>LBORNRIHI</th>
<th>LBSTRESC</th>
<th>LBSTRESN</th>
<th>LBSTRESU</th>
<th>LBSTNRLO</th>
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<tr>
<td>K</td>
<td>Potassium</td>
<td>4.3 mEq/L</td>
<td>3.3</td>
<td>5.1</td>
<td>4.3</td>
<td>4.3 mmol/L</td>
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<td>NORMAL</td>
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<td></td>
</tr>
<tr>
<td>ALB</td>
<td>Albumin</td>
<td>4.5 g/dL</td>
<td>3.5</td>
<td>5.2</td>
<td>45</td>
<td>45 g/L</td>
<td>35</td>
<td>52</td>
<td>NORMAL</td>
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</tr>
<tr>
<td>CA</td>
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<td>9.4 mg/dL</td>
<td>8.8</td>
<td>10.2</td>
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<tr>
<td>WBC</td>
<td>Leukocytes</td>
<td>7.3 10E9/L</td>
<td>4.1</td>
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FDA’s ask for Additional Lab Dataset...Challenge

• No single source of truth for Conventional Units may lead to differences in units
• Challenge maintaining (generating, validating, etc.) two datasets with almost same information
• Increase in size of submission package
• High chances of errors/inconsistencies
• Additional explanation effort in cSDRG
Mitigation

Sponsor Level Mitigation (Short Term)

- Align on requirements with all applicable line functions
- Engage early with Central Labs to get aligned on usage of Sponsor defined SI and Conventional units, minimize double rounding by converting inhouse
- Get single dataset from Central Lab with SI and Conventional data in separate set of variables
- Perform all the required derivations and finally create two separate datasets keeping required variables
Solution

Global Solution (Long Term)

• Sponsors, Labs and Health Authorities to come together and define a single source of truth for SI and Conventional units

• Apart from units, it is also important that Conversion Factors and Precisions are defined globally to avoid inconsistencies
Case Study

Challenges:
- Multiple Sponsors with different standards
- Various OIDs, Lengths, formats, Types
- Multiple vendors/EDC systems
- Vendor Reconciliations

Solution:
- Template vendor data plan with most used data points
- Auto load vendor & EDC data
- Automated vendor reconciliations

Benefits:
- Automated data process from data availability to issue tracking
- Data driven metrics and KPIs
- Reduce risk to improve quality and confidence
- Time & resource savings which turns into budget savings
Key Takeaways

• Address initial challenges with Lab data management.
• Have better understanding of the vendor data plan and focus on patient centricity to have effective outcomes.
• Align with applicable functions and set clear expectations for vendor.
• Collaborate with Sponsors, CDISC, NCI and Health Authorities.
• Request NCI, CDISC and Health Authorities to publish the aligned approach.
• Align with standards and adhere to re-usability.
• Leverage technologies in line with regulatory compliance.
• Define Textbook reference range?

• Is it possible to have a Local lab and Central lab for one single study?

• Mention a visualization tool used in lab data trend analysis?

• Which document specifies the frequency for lab data transfers?

• What is the meaning of calibration date?