ADaM or SDTM?
A Comparison of Pooling Strategies for Integrated Analyses in the Age of CDISC

Joerg Guettner, Lead Statistical Analyst, Bayer Pharma, Wuppertal, Germany

Alexandru Cuza, Project Statistical Programmer, UCB Biosciences, Monheim, Germany
Introduction
Strategy based on SDTM (UCB)
Strategy based on ADaM (Bayer)
Comparison of Advantages/Disadvantages of both Strategies
Conclusion
Introduction

• The past:
  • Sponsor defined standards (on whatever level)
  • Very few ADS (if at all - derivations often done just during analysis), not taken care of traceability

• Today:
  • Two CDISC standards: SDTM and ADaM
  • But: still studies in legacy standards, i.e. non-CDISC standards

• The problem:
  How to build integrated databases?
  Start with the SDTM or the ADaM data sets?
  (Going back to legacy standards should be no option)
UCB Submission

- Task: create integrated database for ISS

- Data to integrate:
  - 13 phase III studies parallel design with extensions
  - 1 phase IV study
  - 3 different legacy standards in place

- Decision to integrate SDTM
UCB Data Flow

Study 1
- CRF
- Lab data
- Device data
- Legacy or ONE
- SDTM
- ADS (ADaM)

Study 2
- CRF
- Lab data
- Device data
- Legacy or ONE
- SDTM
- ADS (ADaM)

Study n
- CRF
- Lab data
- Device data
- Legacy or ONE
- SDTM
- ADS (ADaM)

Integrated Database
ADaM

ADaM or SDTM? A Comparison of Pooling Strategies for Integrated Analyses in the Age of CDISC • October 17, 2012
Bayer Submission

- Project was cooperation with external partner
- Task: create integrated database for ISE/ISS
- Data to integrate:
  - 6 phase I (in patients)/ II studies (incl. one extension study)
  - 2 pivotal trials
  - Data collected in legacy standards

- Decision to integrate ADaM
  (first indication for submission, all newer indications use already SDTM/ADaM)
Bayer Planned Data Flow

Study 1
- EDC
- Lab data
- Device data
- OAD (SDTM plus)
  - ADS (ADaM)
  - SDTM

Study 2
- EDC
- Lab data
- Device data
- OAD (SDTM plus)
  - ADS (ADaM)
  - SDTM

Study n
- EDC
- Lab data
- Device data
- OAD (SDTM plus)
  - ADS (ADaM)
  - SDTM

Integrated Database (ADaM)
Experiences

UCB:
- Increased amount of time when creating SDTM out of 3 different raw data structures
- Reconciliation of CDISC controlled terminology over all study SDTM due to different ages of SDTM panels
- Integration of SDTM into ADaM easier than expected

Bayer:
- Huge amount of time and resources needed for pooling of legacy studies
- Pooling of pivotal trials surprisingly easy one exception: for one analysis parameter the single studies used different tests (found during validation)
- Extra effort: reconciliation ADS against SDTM
Traceability

- Traceability to single study data
  - In SDTM approach the variables (flags) and derivations (e.g. new records) defined in CDISC guides are used.

- Traceability to single study analysis
  - Two additional variables in integrated database in each data set (one for record used by study, one for record used by integrated analysis)
  - Additional record, if record used in integrated analysis record differs from the one used by study
## Comparison of Both Strategies (1)

<table>
<thead>
<tr>
<th></th>
<th>SDTM (UCB)</th>
<th>ADaM (Bayer)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Requirements</td>
<td>ONE database a plus, but not required.</td>
<td>Standards for data, metadata, derivations and analysis</td>
</tr>
<tr>
<td>Time/Resources</td>
<td>Increased amount if raw data not standardized (ONE)</td>
<td>Amount high for legacy studies, low for ADaM</td>
</tr>
<tr>
<td>Traceability to single study data</td>
<td>Very easy from ADaM to SDTM being within CDISC standards</td>
<td>Sometimes difficult, e.g. change from horizontal to vertical structure</td>
</tr>
<tr>
<td>Traceability to single study analysis</td>
<td>Sometimes difficult if derivations in the integrated ADaM differs from study-level ones</td>
<td>Possible for pivotal trials (ADaM)</td>
</tr>
</tbody>
</table>
## Comparison of Both Strategies

<table>
<thead>
<tr>
<th></th>
<th>SDTM (UCB)</th>
<th>ADaM (Bayer)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Additional tasks</td>
<td>Reconciliation needed for controlled terminology due to different ages of SDTM being integrated</td>
<td>Additional reconciliation needed</td>
</tr>
<tr>
<td>Complexity of transfer programs (validation)</td>
<td>Low increase during mapping several legacy to SDTM. Easy when integrating into ADaM</td>
<td>Quite complex for legacy, easy for ADaM</td>
</tr>
<tr>
<td>Harmonization of algorithms/derivations</td>
<td>Not applicable as integrated ADaM done from SDTM directly</td>
<td>For legacy partially solved by macros; ADaM by standard derivations (in study)</td>
</tr>
</tbody>
</table>
Conclusion

- Both strategies are acceptable pooling strategies
- Both have their own prerequisites, advantages and disadvantages

Recommendation:
- In highly standardized environments: ADaM
  (but lot of time and work needed to integrate legacy standards, especially if you have more than one legacy standard and difficulty in keeping traceability to SDTM)
- In less standardized environments: SDTM
  (but difficulty in keeping traceability to study level analysis)
Thank you!
**SDTM**
- Start point for all ADaM the same and CDISC conform
- Raw data structure has lower impact as SDTM does the reconciliation
- Keeps traceability from each analysis back to the raw data
- High level of freedom to drive several kind of different analyses based on same data easily
- No reconciliation needed between SDTM and ADaM
- Easier way to ADaM being already CDISC style (lot of just copying variables from SDTM, controlled terminology, etc.)
- Fewer controlled terminology to consolidate as almost all lists are the same.

**ADaM**
- Required high level standardization of AD leads to stable and robust AD over studies and analyses
- Keeps traceability between integrated and study level analysis
- Keeps traceability to SDTM, if OAD (SDTM plus) standard used

**Different raw data structures in place lead to more work when mapping to SDTM. (CRF standardization and ONE database is solving this.)**
**Difficult traceability between integrated and study level analysis**

**Requires high level of standardization (data, derivations, analysis)**
**Legacy structures increase difficulty and amount of work**
**Traceability between CRF, SDTM and ADaM makes reconciliation necessary for legacy studies**