

Science For A Better Life

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



Agenda/ Content

- 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?

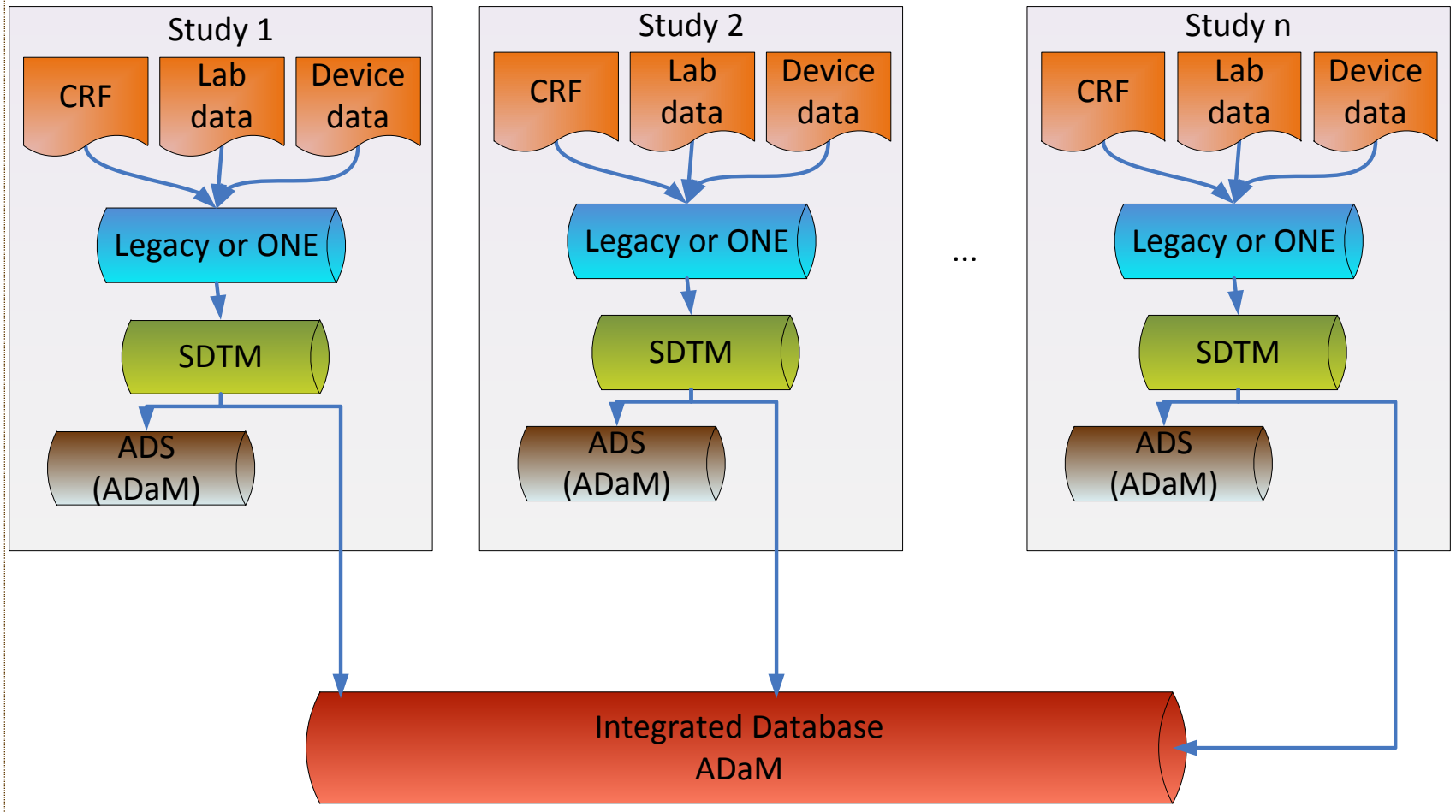
  Start with the SDTM or the ADaM data sets?

  (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

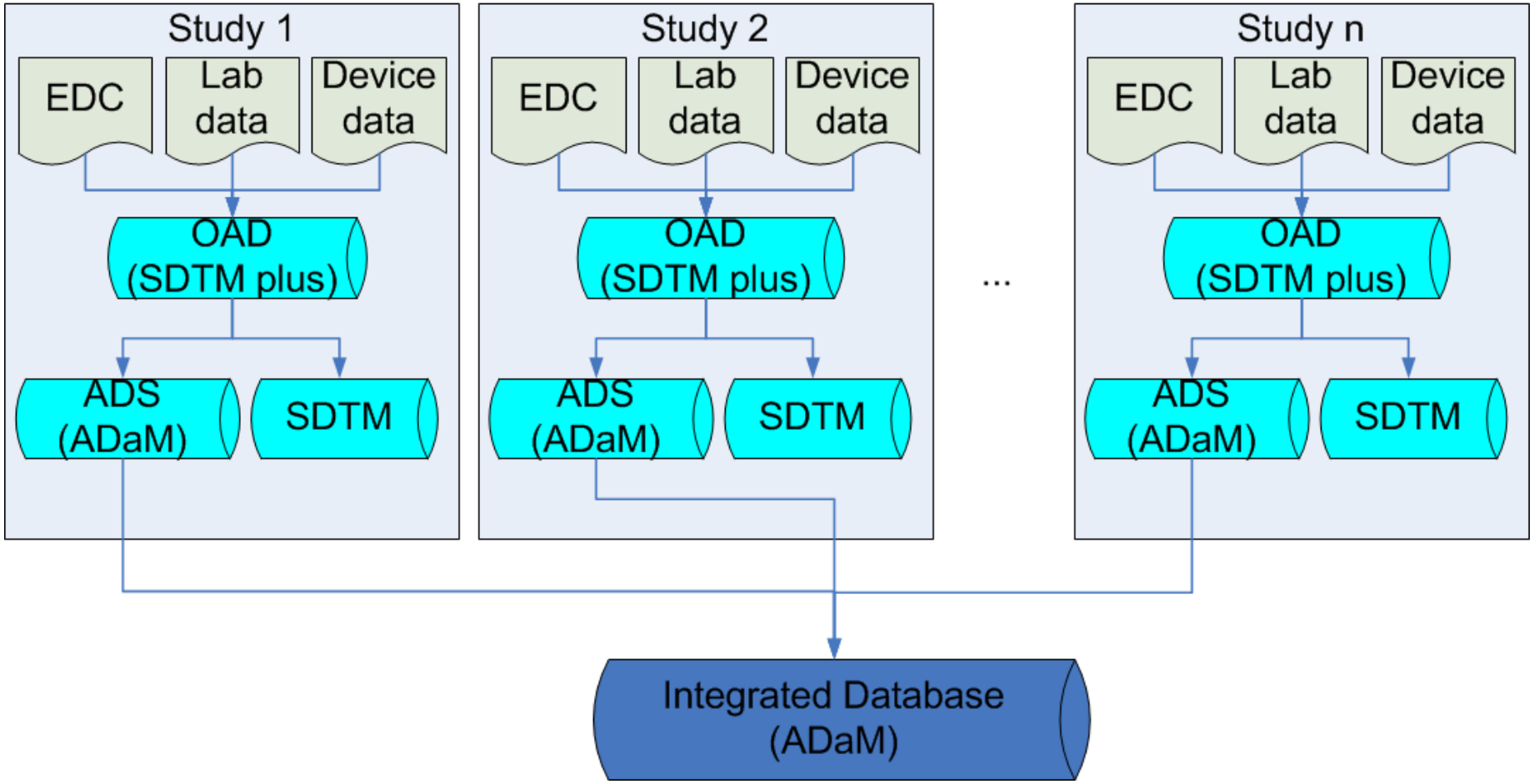


Bayer Submission

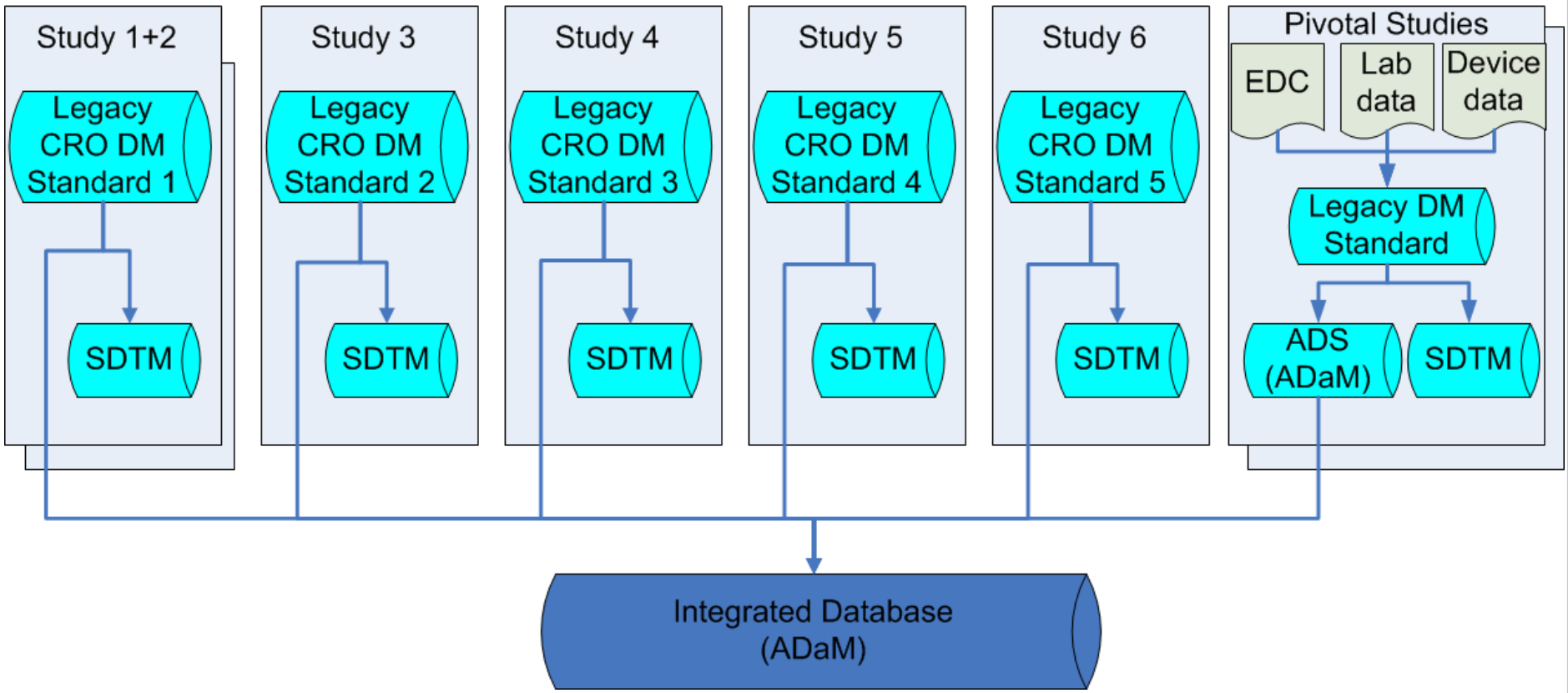
- Project was cooperation with external partner
- Task: create integrated database for ISE/ISS
- Data to integrate:
  - 6 phase I (in patients)/ II studies (incl. one extension study)
  - 2 pivotal trials
  - Data collected in legacy standards

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

Bayer Planned Data Flow



Bayer Actual Data Flow for Submission



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)

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

Comparison of Both Strategies

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

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)



Science For A Better Life

Thank you!

Appendix: One page overview

SDTM

- Start point for all ADaM the same and CDISC conform
- Raw data structure has lower impact as SDTM does the reconcilation
- 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.

- 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

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

- 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