Rethinking ADaM Specs: Efficient Creation of High-Quality ADaM Datasets and Metadata Without Predefined Specifications

Presented by Jeroen Den Herder and Wouter Milis,
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SGS Pharma – Clinical Research

Meet the Speakers

Jeroen Den Herder

Title: Senior Biostatistical Analyst

Organization: SGS Pharma – Clinical Research

Jeroen joined the Biostatistics and Pharmacokinetics department 12 years ago after having worked for 5 years as a Medical Writer at SGS. He took an additional role as CDISC standards expert as of 2015, with a focus on ADaM and define.xml to ensure proper implementation of these standards across studies and clients.

Wouter Milis

Title: Senior Biostatistical Analyst

Organization: SGS Pharma – Clinical Research

Wouter has been with SGS for 20 years and has taken on various roles in Biometrics before transitioning to Biostatistical Analyst in 2014. Nowadays, he specializes in analysis metadata and supports the Biostatistics and Pharmacokinetics department by providing training and guidance on submission requirements.

SGS

Disclaimer and Disclosures

- *The views and opinions expressed in this presentation are those of the authors and do not necessarily reflect the official policy or position of CDISC or SGS.*

- *The authors have no real or apparent conflicts of interest to report.*

Agenda

- About Us
- What Are ADaM Specs?
- Past: With ADaM Specs
- Present: Without ADaM Specs
- Testimonial
- Key Takeaways

About Us

About Us

CRO

- Multiple sponsors: different requirements
- Wide range of therapeutic areas and indications
- Portfolio: high volume of complex studies

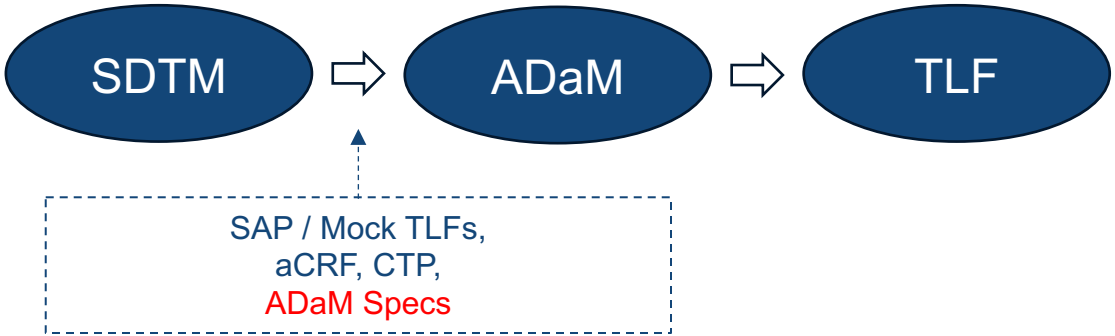
Biostatistics

- Source data variability (across studies)
- Early onset of programming activities (within a study)
- Not always involved from beginning of clinical development program

What Are ADaM Specs?

ADaM Specs: Definition

A **study-specific** data model definition, outlining how **analysis datasets** in CDISC ADaM are derived from CDISC SDTM, detailing dataset **structure**, **content** and **derivation logic**

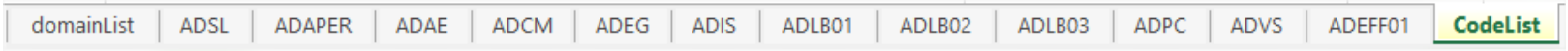


ADaM Specs: Format

Dataset Name	Dataset Description	Dataset Structure	Key Variables of Dataset	Class of Dataset
ADSL	Subject-Level Analysis Dataset	One record per subject	STUDYID, USUBJID	SUBJECT LEVEL ANALYSIS DATASET
ADVS	Analysis of Vital Signs Test Results	One record per vital sign measurement per analysis visit per subject	STUDYID, USUBJID, PARAM, AVISITN, VSDTC	BASIC DATA STRUCTURE
ADEFF01	Analysis of Efficacy Assessments	One record per efficacy assessment per analysis visit per subject	STUDYID, USUBJID, PARAM, AVISITN, VSDTC	BASIC DATA STRUCTURE

Dataset name	Variable sequence	Variable name	Variable label	Variable type	Variable length	Display format	Codelist	Source / Derivation
ADSL	6	AGE	[sdtm]	[sdtm]	[sdtm]			DM.AGE
ADSL	7	AGEU	[sdtm]	[sdtm]	[sdtm]			DM.AGEU
ADSL	8	AGEGR1	Pooled Age Group 1	Char	40		{AGEGR}	Derived: '< 65 years (REFERENCE)' when DM.AGE < 65, '>= 65 years' when DM.AGE >= 65.
ADSL	9	SEX	[sdtm]	[sdtm]	[sdtm]			DM.SEX
ADSL	10	CHILDPOT	[testcd]	[testcd]	[testcd]			RP.RPORRES where RPTESTCD='CHILDPOT'

CodeList Name	CodeList Value	CodeList Label
AGEGR	< 65 years (REFERENCE)	
AGEGR	>= 65 years	

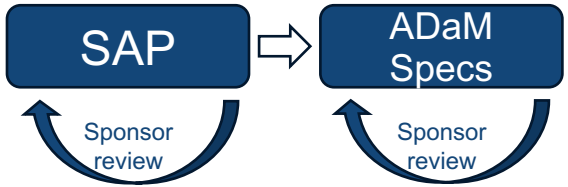


Past: With ADaM Specs

With ADaM Specs: Process

- Create stable SAP (Statistical Analysis Plan)
  - Sponsor review of first draft

With ADaM Specs: Process



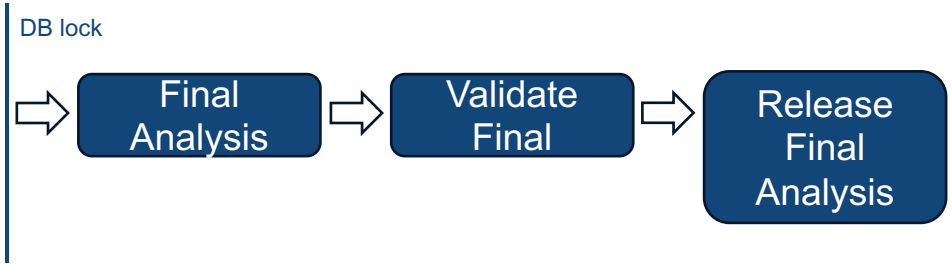
- Create study-specific ADaM specs
  - Based on SAP, mock TLFs, (a)CRF, SDTM structure
  - Specify domains, variables, values

- Sponsor review of ADaM specs
  - Implement sponsor comments prior to onset of programming activities

With ADaM Specs: Process

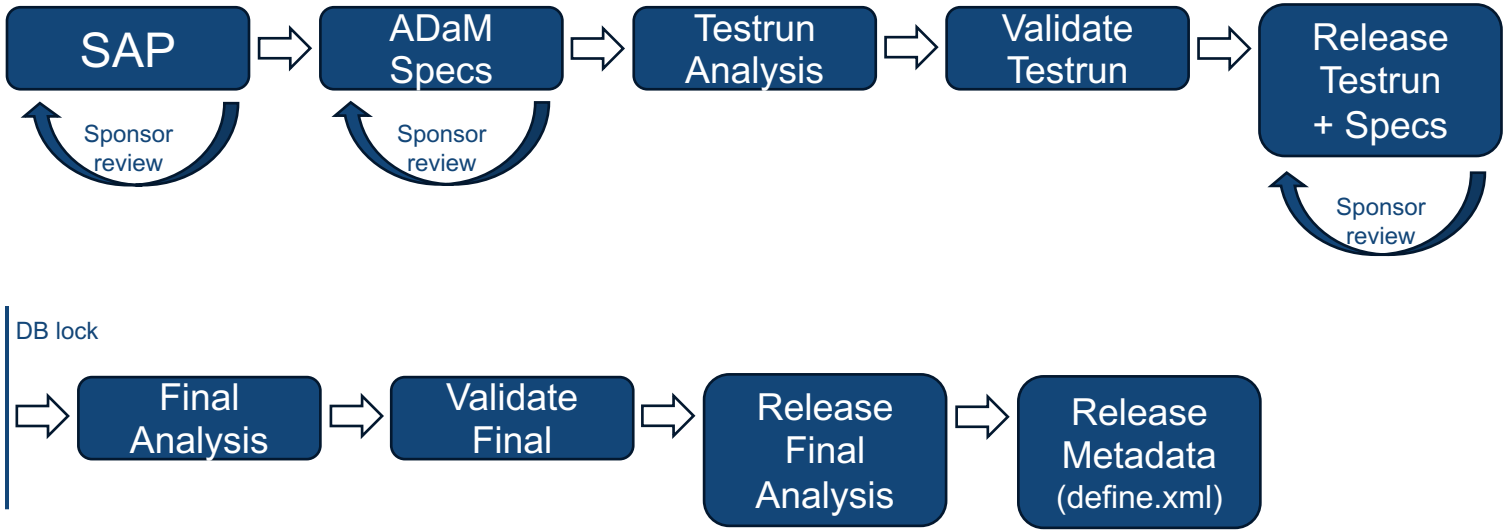
- Develop testrun analysis (ADaMs + TLFs)
  - Based on ADaM specs, SAP, mock TLFs, (a)CRF, CTP, …
- Validate testrun analysis
  - Same info as developer (SAP + ADaM specs)
- Release testrun analysis + ADaM specs to sponsor
  - Sponsor review of testrun analysis

With ADaM Specs: Process



- After DB lock:
  - Develop, validate and release final analysis

With ADaM Specs: Process



- Metadata (define.xml):
  - Created after the final analysis using ADaM specs as input

With ADaM Specs: Challenges

1) Initial creation: time consuming

- Theoretical thinking about the ADaM dataset design
- Study data not yet or partly available

2) During programming: maintenance

- Changes in SDTM domains, variables, values
- Changes due to SAP updates
- Derivation algorithms

3) Limited reusability

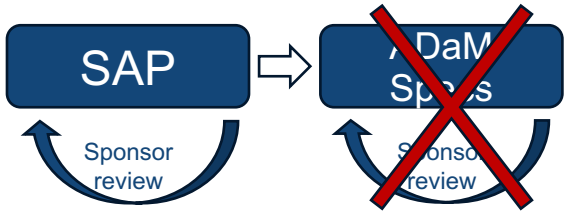
- Snapshot of certain CDISC standard and terminology
- Not up-to-date with updated standards or terminology

Present: Without ADaM Specs

Without ADaM Specs: Process

- Create stable SAP (statistical analysis plan)
  - Sponsor review of first draft

Without ADaM Specs: Process

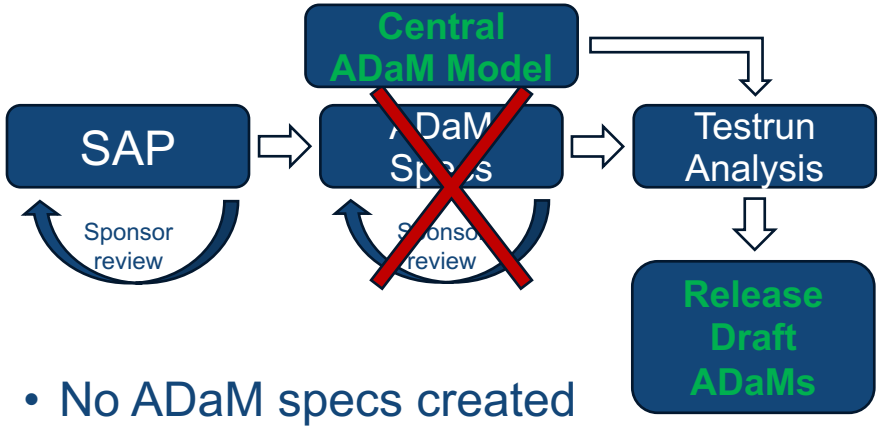


- No ADaM specs created

Without ADaM Specs: Process

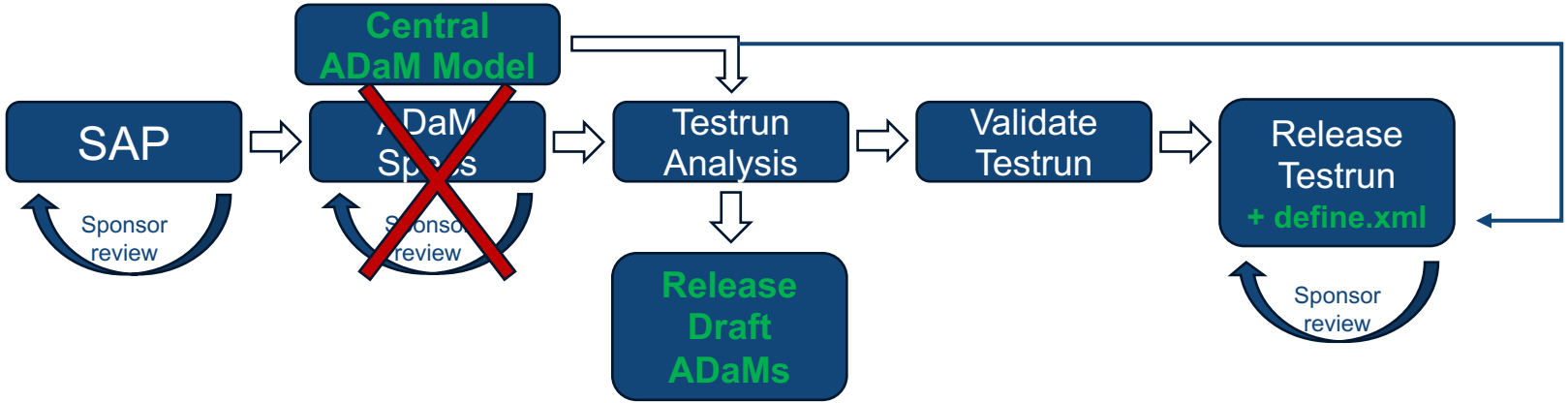
- No ADaM specs created
- Develop testrun analysis (ADaMs + TLFs)
  - Based on ~~ADaM specs~~, SAP, mock TLFs, (a)CRF, CTP, …

Without ADaM Specs: Process



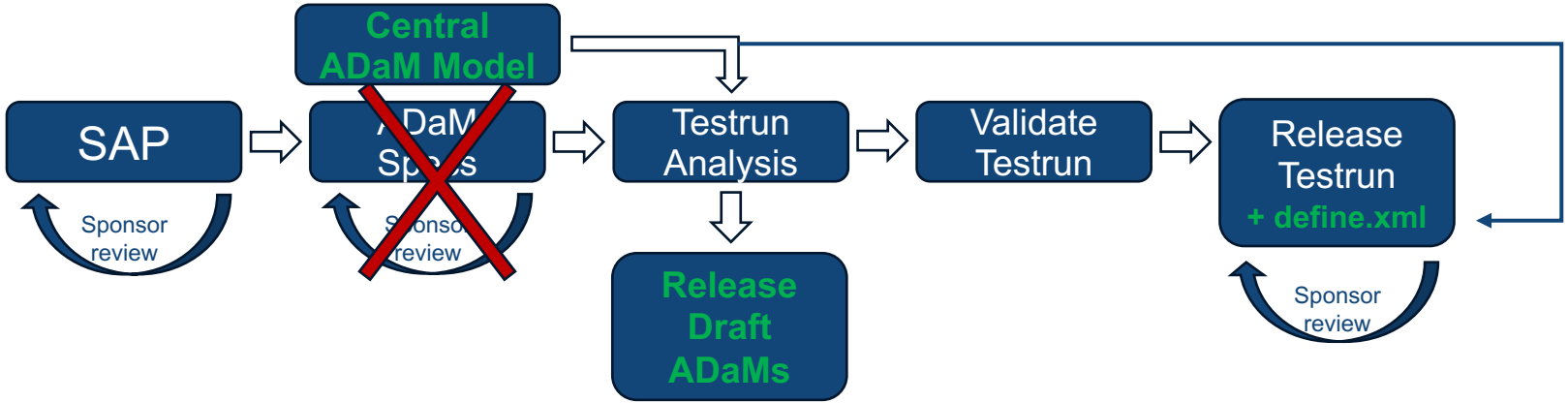
- No ADaM specs created
- Develop testrun analysis (ADaMs + TLFs)
  - Based on **central ADaM model**, SAP, mock TLFs, (a)CRF, CTP, …
- Release draft ADaM datasets to sponsor

Without ADaM Specs: Process



- Validate testrun analysis
  - Same info as developer (SAP) → derivation algorithms defined independently
- Release testrun analysis + define.xml to sponsor
  - Metadata as define.xml including derivation algorithms
  - Sponsor review of testrun analysis and define.xml

Without ADaM Specs: Process



- After DB lock:
  - Develop, validate and release final analysis
  - Re-run define.xml

Without ADaM Specs: Advantages

1) High-quality ADaM datasets

- Programming on actual (vs. expected) data
- Derivation algorithms independently by developer and validator
- Automated checks via central model

2) Increased efficiency

- No ADaM specs creation or maintenance
- Earlier programming onset
- Define.xml directly from central model and analysis datasets

Without ADaM Specs: Advantages

3) Engaging for programmers

- Skilled programmers translate source documentation into ADaM
- Derivations based on SAP and actual study data
- Developer-validator discussions optimize approaches

4) Early accurate metadata to sponsor

- Timely validation preparation using draft ADaM datasets
- Full validation of testrun, including complete define.xml

Testimonial

Our Experience + Sponsor Feedback

Our Experience

- Sponsors initially request to create ADaM specs
  - Explain our alternative process
  - 100% acceptance

- Process in place for several years for all our current sponsors
  - Efficient process for internal as well as sponsor validation
  - High-quality ADaM datasets
  - Reduced timelines during testrun and final analysis

Sponsor Feedback

*"Their commitment to open communication between sponsor and CRO programmers, treating us as one team, ensures **clarity** and efficient **problem-solving** during ADaM creation. By developing specifications dynamically alongside the code, we gain **early visibility** into draft deliverables, allowing for **proactive** feedback and continuous improvement, a far more **effective** process than static upfront specifications."*

- Head of Statistical Programming at argenx

Key Takeaways

Summary

Summary

- The traditional process using pre-defined, study-specific ADaM specs posed challenges, especially for complex studies
- We developed an alternative approach without ADaM specs, offering greater flexibility and efficiency
- This process evolved through years of hands-on experience and has been well received by our sponsors

Thank You!

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