An Evaluation of ADaM
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An Evaluation of ADaM
Agenda

- Why standardize?
- ADaM's key principles - are they useful?
- Shouldn't CDISC standards be consistent?
- Does one size really fit all?
- Traceability – how much is required?
- Are Criteria flags the best way forward?
- Analysis Flags and Derivation Types
- Conclusions

Introduction

- ADaM IG v1.0 and ADaM v2.1 were released for public comment in June 2008
- Roche set up a team was set up to evaluate the possible implementation of ADaM
- A project team has implemented ADaM using SDTM as a source

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Why standardize?

- Benefits of standardization apply to everyone
- Benefits of any standard:
  - Standard code for analysis datasets
  - Standard code for creating outputs
- Benefits of an industry wide standard:
  - Health authority reviewers receive analysis data in a consistent format
  - Sharing analysis data between collaborative partners
- We must not to let the analysis dataset structure drive the analysis

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ADaM's key principles - are they useful?

- High level principles are very good
  - BUT there is nothing particularly new
- The key principles are:
  - Clear and unambiguous communication of the contents of analysis datasets
  - Provide a level of traceability back to the input data
  - Identify when and how data has been imputed
  - Analysis data should be linked to machine readable metadata
  - Analysis data should be 'analysis ready'
- ADaM sometime violates it's key principles

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Shouldn't CDISC standards be consistent?

- Some variables can be derived in both SDTM and ADaM
- Sometimes these may differ due to valid reasons
  - BUT, deriving the same variable twice is inadvisable
- Traditionally population and baseline flags are derived in analysis datasets
  - BUT, these are expected in SDTM
- Provide variables with the same meaning with different values to health authorities could be confusing
- The is no definitive guidance in ADaM for maintaining consistency

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Does one size really fit all?

- For basic summary statistics and analysis of variance ADaM is adequate
  - BUT, we do other types of analysis
- Insufficient guidance is provided for other types of analysis
- Too much is left open for sponsor interpretation
- How should time to event analysis data be structured?
- How do we produce listings with derived variables?

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Does one size really fit all?

- A single structure does not fit all types of analysis
- SDTM has a clearly defined hierarchal structure
  - Individual domains inherit structure and variables from the domain class
- ADaM could/should follow the same model
  - ADSL
  - Summary Statistics and ANOVA
  - Time to Event
  - Etc...

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Traceability – how much is required?

- Implementing traceability for the simplest cases is ok
- For complex scenarios it leads to massive duplication
  - Multiple SDTM domains and --SEQ variables
  - Including all possible source parameters
  - Derived parameters lose traceability
- Better to focus on specifications
- Does not help in providing clear and unambiguous communication of data

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Traceability – how much is required?

USUBJID	AVISITN	PARAMCD	ZJSEQ	AVAL	AVALC
AB12345-6789-09876	1	RSPIP5	198	0	N
AB12345-6789-09876	1	RSSHLD	150	0	N
AB12345-6789-09876	1	RSSJ	142	0	N
AB12345-6789-09876	1	RST	182	0	N
AB12345-6789-09876	1	RSTARS	230	1	Y
AB12345-6789-09876	1	RSTJ	138	0	N
AB12345-6789-09876	1	RSWRST	158	1	Y
AB12345-6789-09876	1	SJC	.	15	
AB12345-6789-09876	1	SJC28	.	9	

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Are Criteria flags the best way forward?

- Removes the link between variable names and labels and the content
- When merging multiple ADaM datasets together there are potential conflicts
- Potential issues with pooling across multiple studies
- An attempt to over-standardize
- Guidance to store information about analysis values horizontally would aid a clearer standard

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Are Criteria flags the best way forward?

	USUBJID	AVAL	CRIT1	CRIT1FL
1	AB12345-6789-00001	25	ACRn >= 20	Y
2	AB12345-6789-00002	-20	ACRn >= 20	N
3	AB12345-6789-00003	37	ACRn >= 20	Y
4	AB12345-6789-00004	5	ACRn >= 20	N

	USUBJID	AVAL	CRIT2	CRIT2FL
1	AB54321-6789-00001	57	ACRn >= 20	Y
2	AB54321-6789-00002	13	ACRn >= 20	N
3	AB1543216789-00003	49	ACRn >= 20	Y
4	AB54321-6789-00004	-7	ACRn >= 20	N

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Analysis Flags and Derivation Types

- Analysis flags will often be used in conjunction with DTYPE
  - BUT in many cases this will make DTYPE redundant
- Analysis flags may form part of the primary key
- Controlled terminology for ANLxFL is “Y” and null
  - Violates primary key principles
  - Not good programming practice – there is a difference between “N” and null
- Naming convention can cause problems
  - Pooling across studies
  - Joining multiple analysis datasets

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Analysis Flags and Derivation Types

	USUBJID	AVAL	AVISITN	ANL1FL	DTYPE
1	AB12345-6789-01234	12	2	Y	
2	AB12345-6789-01234	28	3	Y	
3	AB12345-6789-01234	12	.	Y	
4	AB12345-6789-01234	28	4	Y	LOCF
5	AB12345-6789-01234	37	5	Y	
6	AB12345-6789-01234	29	6	Y	

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Conclusions

- After adopting SDTM an industry analysis dataset standard is a logical step
- ADaM is currently an immature standard
- A sponsor introducing it would be taking a big risk
- There are too many grey areas
- Current documentation is insufficient for full scale implementation
- Datasets using the standard can become increasingly complex very quickly
- It is worthwhile piloting the standard and providing feedback
- Providing feedback will allow the standard to improve to the point where it can be adopted

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