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The Role of the Clinical Statistician in Understanding and Using ADaM Data Standards: Perspectives from a CRO Statistician

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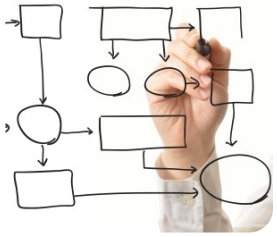
The CRO Statistician: Before



Simple workflow

(FDA guidance "Providing Regulatory Submissions in Electronic Format – NDAs" [1999])

Minimal guidance requirements regarding documentation

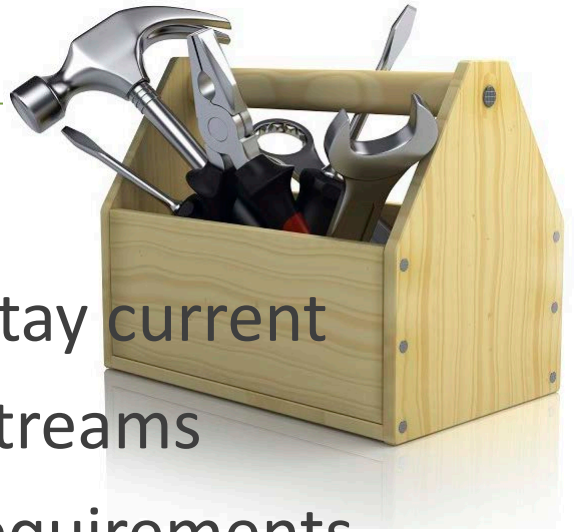
Skill set of the CRO statistician primarily SAS related

Abolafia, J., DiIorio, F. Brave New World: How to Adapt to the CDISC Statistical Computing Environment. PharmaSUG 2011.

Evolving Data Standards and Regulatory Environment

- Move to ADaM and CDISC Standards
  - December 2014 Binding Guidance documents
  - Heightened guidance-based requirements:
    - Dataset format and content
    - Traceability
    - Consistency
    - Documentation
    - Metadata

What does this mean for the CRO statistician?



- Skill set expansion …
  - Understand standards, apply, and stay current
  - Manage new work and new work streams
  - Understand additional validation requirements
  - Prepare documentation (ADRG)
  - Knowledge of regulatory landscape
  - Be a software development contributor
  - Well beyond SAS now …

Guidelines for the CRO Statistician: Using ADaM Standards

1. Know ADaM key concepts
    a) ADaM is a set of guidelines rather than just a schema
    b) End in mind – required analyses, not all analyses
    c) Include variables necessary to support analyses

Guidelines for the CRO Statistician : Using ADaM Standards

2. Engage early with sponsors: understand preferences, be prepared to offer opinions and advice.

Guidelines for the CRO Statistician : Using ADaM Standards

3. Make use of CDASH and SDTM.

Guidelines for the CRO Statistician : Using ADaM Standards

4. Develop a data standardization plan as early as possible in the clinical development program.

Guidelines for the CRO Statistician : Using ADaM Standards

5. Document (more rather than less):

a) Using the Analysis Data Reviewer Guide template (found on PHUSE wiki)
b) Analysis database-related decisions
c) Analysis database-related exceptions
d) Exceptions to standards
e) As you go

Guidelines for the CRO Statistician : Using ADaM Standards

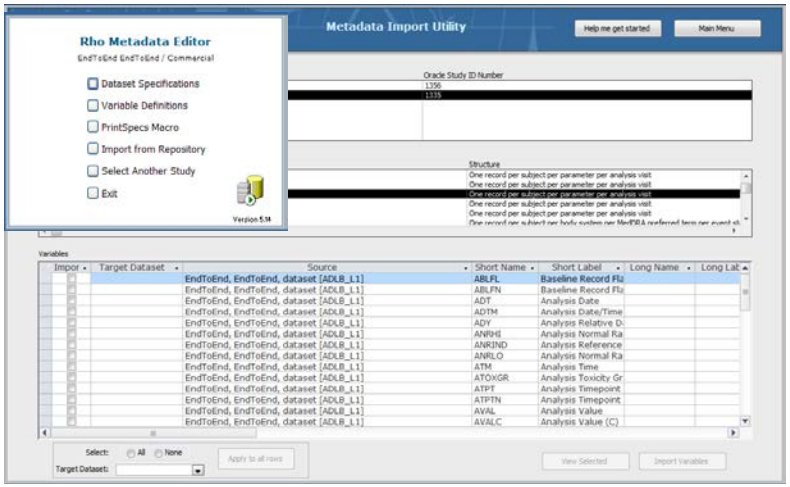
6. There is a short-term burden that comes with standardization – reduce as much as possible. Leverage the positives and develop systems.

Guidelines for the CRO Statistician : Using ADaM Standards

7. Build an ADaM Tool Kit – should include:

a) Multi-purpose metadata – supports programmer communication, reviewer communication, and define file creation
b) Gold standard metadata
c) 'Single entry information'
d) Repository capabilities
e) Compliance and functionality checks
f) ADRG completion

Rho ADaM Tool Kit



BDS Variable Label Check per ADaM IG 1.0

Dataset	Variable	Label	IG Label	Descrption
ADEF	PARAMN	Parameter Number	Parameter (N)	Label does not match IG Label
ADEF	AVAL	Analysis value	Analysis Value	Label does not match IG Label
ADEF	AVALC	Analysis Value (C)	Analysis Value	Label does not match IG Label
ADMB				
ADMB				
ADMS				
ADMS				

Variable Format Consistency by Variable Type

Dataset	Variable	Format	Description	Recommended Action
ADSL	COMPLDT		Format for variables ending in *DT are not consistent.	Date variable incorrectly presented in character format. Update to numeric with DATE9. format for consistency.
ADSL	DISCDT		Format for variables ending in *DT are not consistent.	Date variable incorrectly presented in character format. Update to numeric with DATE9. format for consistency.
ADSL				
ADSL				

Variable Value Consistency for SDTM.DM and ADAM.ADSL

Dataset	Description	Recommended Action
		DM.BRTHDTC ^=ADSL.BRTHDTC on all records (same nuemric value, different character presentation). Required to be same. Update.
DERIVE.ADSL	Values are not consistent: Obs No.=_ALL_ in DERIVE.ADSL and SDTM.DM (BRTHDTC, COUNTRY)	DM.COUNTRY^=ADSL.COUNTRY on all records. Required to be same. Update.

DatasetName	Name	Label	Programming Definition	Type	Length	Code List
ADPE	PARAM	Parameter	=PE.PETEST	C	18	Abdomen Cardiovascular General Appearance HEENT Musculoskeletal Neurological Other Respiratory Skin
ADPE	AVAL	Analysis Value	=1 if AVALC="NORMAL" =2 if AVALC="ABNORMAL"	N	8	1=NORMAL 2=ABNORMAL
ADPE	AVALC	Analysis Value (C)	=PE.PESTRESC	C	8	NORMAL ABNORMAL
ADPE	BASE	Baseline Value	=AVAL on record where ABLFL='Y' merged onto records by USUBJID PARAMCD	C	18	Baseline, Day 7, Day 28, Day 35
ADPE	SHIFT1N	Shift 1 (N)	=1 if ADPE.SHIFT1="ABNORMAL-ABNORMAL" =2 if ADPE.SHIFT1="ABNORMAL-NORMAL" =3 if ADPE.SHIFT1="NORMAL-ABNORMAL" =4 if ADPE.SHIFT1="NORMAL-NORMAL"	N	8	1=ABNORMAL-ABNORMAL, 2=ABNORMAL-NORMAL,3= NORMAL-ABNORMAL, 4=NORMAL-NORMAL

Utility of the ADaM: the CRO perspective

- Standards bring a common language to analysis datasets – leverage this
- A few examples implemented at Rho …

Utility of the ADaM Standard: the CRO perspective

- 'End-to-end' clinical database and analysis development:
  - Within an individual clinical study
  - Across a clinical development program

Table PE_TXC_01
Shift in Physical Examination Findings from Baseline to Each Visit by Treatment Group
Population: Safety

Parameter / Visit	Baseline							
	Treatment A N=xx		Treatment B N=xx		Treatment C N=xx		Treatment D N=xx	
	Normal n (%)	Abnormal n (%)	Normal n (%)	Abnormal n (%)	Normal n (%)	Abnormal n (%)	Normal n (%)	Abnormal n (%)
Parameter 1								
Visit 1								
Normal	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
Abnormal	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
Visit 2								
Normal	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
Abnormal	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
Etc.								

PHYSICAL EXAM DOMAIN=PE

PETEST PESTAT Date: / / PEDN

Category	Result	If Abnormal, specify
General Appearance	Normal / Abnormal	PEORRES
Abdomen	Normal / Abnormal	
Skin	Normal / Abnormal	
Respiratory	Normal / Abnormal	

DatasetName	Name	Label	Programming Definition	Type	Length	Code List
			=PE.PETEST	C	18	Abdomen Cardiovascular General Appearance HEENT Musculoskeletal Neurological Other Respiratory Skin
			=1 if AVALC="NORMAL" =2 if AVALC="ABNORMAL"	N	8	1=NORMAL 2=ABNORMAL
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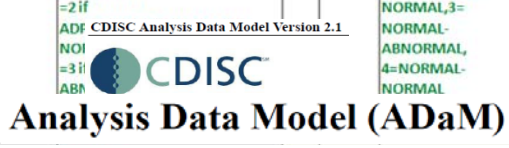

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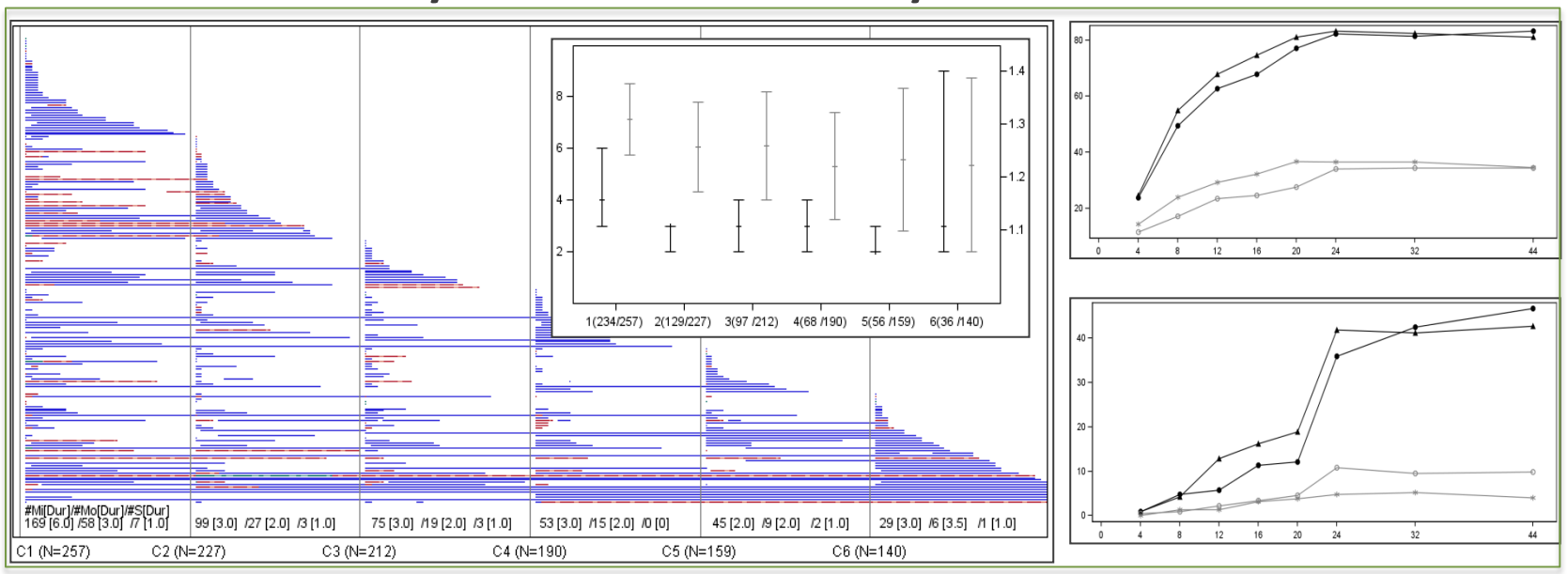
Utility of the ADaM Standard: the CRO perspective

- Data exploration systems: tools for data exploration and key decision point support
- Risk Based Monitoring: tools require data commonly found in analysis databases



Summary

- Expanded skill set of the CRO statistician
- Focus on data analysis rather than data management
- Leverage the positives
- Active role in system design

Special thanks to …

- Jeff Abolafia and Ryan Burns of Rho, Inc. and Frank DiIorio of CodeCrafters, Inc. and their numerous publications and presentations on preparing for and implementing CDISC standards.

Thank You

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