

PRAHEALTHSCIENCES

**ADaM Compliance – Starts with
Your Specifications**

PharmaSUG Single Day Event

Chicago, November 1, 2017

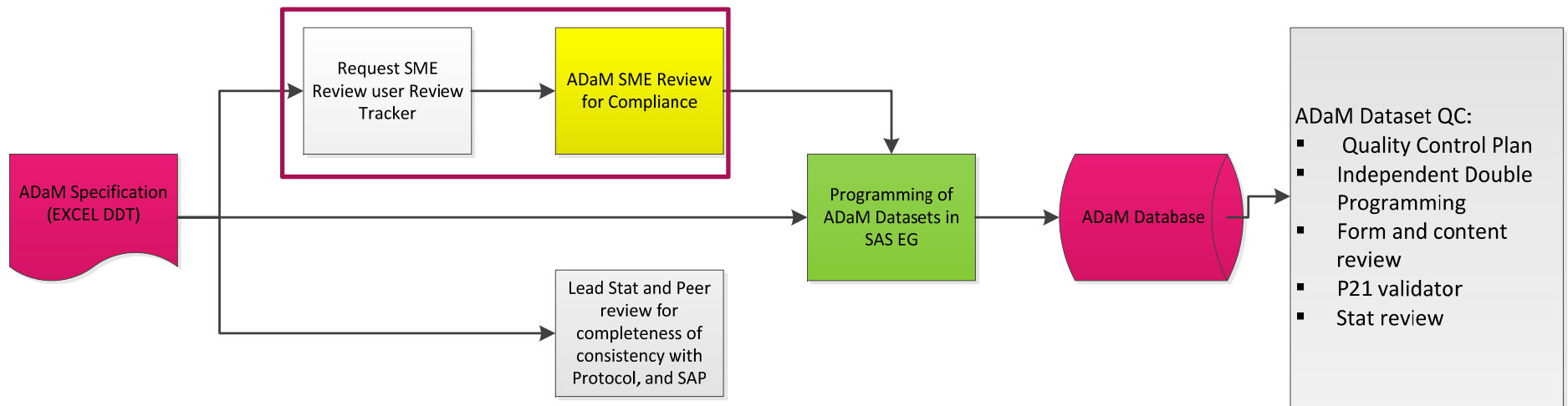


Agenda

- High Level View of PRA ADaM Development Process
- Overview of ADaM Compliance Checks
- Detailed Discussion on ADaM Specification Compliance Review Process
- Conclusions



ADaM Process Including QC Steps





- Automated Checks where possible
 - Based upon CDISC ADaM team checks
 - Could add sponsor specific checks as needed
- SME Reviews
 - For things that cannot be checked programmatically
 - Also include review that specs will lead to high quality define.xml creation from specifications.



- 308 Validation Checks have been define by CDISC
 - These are organized by:
 - ADaM Structure Groups (ALL, ADSL, ALL:SDTM, BDS, etc.)
 - Functional Groups (controlled terminology, metadata, present/populated, etc.)
 - ADaM Variable Groups (General, ADSL, ADAE, flag variables, etc.)
- Some of these checks are looking at the values within the ADaM dataset but many are only looking at the structural metadata.

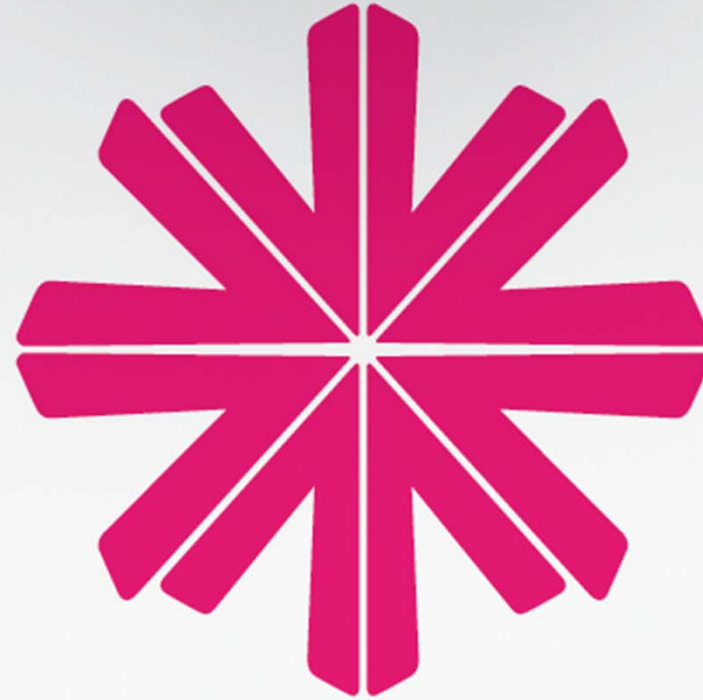


- Chose a subset of the ADaM v1.3 checks that could be programmed against metadata only
 - 139 checks are based on metadata only
- Develop a report formatted similarly to industry available compliance reporting for ease of understanding
- Programs written in SAS that access that ADaM spec metadata.



Why Review Specs for Compliance with ADaM Rules

- Finding issues after you have programmed dataset leads to re-work and is inefficient.
- SME reviews of specs can identify gaps in training of the lead statistical programmers (i.e. ADaM concepts that are not understood well)
- High quality specs lead to:
 - more efficient programming,
 - higher quality datasets,
 - define.xml deliverables.



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Trevor Mankus
Senior Principal Data Standards
Consultant






- Process Outline

- Lead submits a request via custom SharePoint app
- ADaM SME assigned to do the review
- Review consists of:
 - Run automated tool and review output
 - Compliance checklist
- Summary of findings is communicated with lead
- ADaM SME consults with project team to ensure ADaM compliance



ADaM SME Specification Review Request

- Request Form
 - SharePoint
 - Alerts
 - Validation
 - Customizable

PART 1 Request Your Review <i>(Completed by PRA data standards users)</i>	
Study ID:	<input type="text"/> *
Study Phase:	<input type="text"/> ▼
Study Indication:	<input type="text"/>
Databasics Time Code:	<input type="text"/> * Time spent reviewing ADaM specifications will be billed to your project.
Requested By:	<input type="text"/>  Enter your PRA username
ADaMIG Version:	<input type="text"/> * ▼
Spec Name and Location:	<input type="text"/> * Name and network location to ADaM specification (e.g., \\NA1SASFILE1\...)
SDTM Data Location:	<input type="text"/> Network location of the study SDTM data, if available (e.g., \\NA1SASFILE1\...) <input type="checkbox"/> Unblinded / Restricted Additional user access may be required
Date Available:	<input type="text"/> *  Enter the date that the ADaM specification will be available for review
Date Completed By:	<input type="text"/> *  Enter the date you need to have feedback returned



ADaM SME Specification Review Request

- Alert e-mail contains all important information

[Global Data Standards](#)

Item ID4 has been added

[Modify my alert settings](#) | [View Item ID4](#) | [View ADaM Specification Review Tracker](#) | [Mobile View](#)

Study ID:	PRA-TEST-001
Requested By:	Mankus, Trevor
ADaMIG Version:	1.1
Spec Location:	\\na1sasfile1\PRA\PRA-TEST-001\ADaM\Specs\DDT.xlsm
Date Available:	8/4/2016
Date Completed By:	8/9/2016
Additional Comments:	Review can start earlier than 8/4 as the specs are stable, but there are a few things still outstanding in the DDT.
SDTM Data Location:	\\na1sasfile1\PRA\PRA-TEST-001\SDTM\Data\
Study Phase:	Phase I Trial
Study Indication:	Oncology
Unblinded/Restricted:	No



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Spec Location:	\\na1sasfile1\PRA\PRA-TEST-001\ADaM\Specs\DDT.xlsm
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SDTM Data Location:	\\na1sasfile1\PRA\PRA-TEST-001\SDTM\Data\
Study Phase:	Phase I Trial
Study Indication:	Oncology
Unblinded/Restricted:	No

ADaMIG version allows us to customize which compliance checks fire in tool



ADaM SME Specification Review Request

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[Global Data Standards](#)

Item ID4 has been added

Modify my alert settings	View Item ID4	View ADaM Specification Review Tracker	Mobile View
Study ID:	PRA-TEST-001	Dates help us assign a resource to do the review based on who is available	
Requested By:	Mankus, Trevor		
ADaMIG Version:	1.1		
Spec Location:	\\na1sasfile1\PRA\PRA-TEST-001\ADaM\Specs\DDT.xlsm		
Date Available:	8/4/2016		
Date Completed By:	8/9/2016		
Additional Comments:	Review can start earlier than 8/4 as the specs are stable, but there are a few things still outstanding in the DDT.		
SDTM Data Location:	\\na1sasfile1\PRA\PRA-TEST-001\SDTM\Data\		
Study Phase:	Phase I Trial		
Study Indication:	Oncology		
Unblinded/Restricted:	No		



ADaM SME Specification Review Request

- Alert e-mail contains all important information

[Global Data Standards](#)

Item ID4 has been added

Modify my alert settings View Item ID4 View ADaM Specification Review Tracker Mobile View	
Study ID:	PRA-TEST-001
Requested By:	Mankus, Trevor
ADaMIG Version:	1.1
Spec Location:	\\na1sasfile1\PRA\PRA-TEST-001\ADaM\Specs\DDT.xlsm
Date Available:	8/4/2016
Date Completed By:	8/9/2016
Additional Comments:	Review can start earlier than 8/4 as the specs are stable, but there are a few things still outstanding in the DDT.
SDTM Data Location:	\\na1sasfile1\PRA\PRA-TEST-001\SDTM\Data\
Study Phase:	Phase I Trial
Study Indication:	Oncology
Unblinded/Restricted:	No

Compliance checks can fire based on SDTM : ADaM relationships



ADaM SME Specification Review Request

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[Global Data Standards](#)

Item ID4 has been added

Modify my alert settings View Item ID4 View ADaM Specification Review Tracker Mobile View	
Study ID:	PRA-TEST-001
Requested By:	Mankus, Trevor
ADaMIG Version:	1.1
Spec Location:	\\na1sasfile1\PRA\PRA-TEST-001\ADaM\Specs\DDT.xlsm
Date Available:	8/4/2016
Date Completed By:	8/9/2016
Additional Comments:	Review can start earlier than 8/4 as the specs are stable, but there are a few things still outstanding in the DDT.
SDTM Data Location:	\\na1sasfile1\PRA\PRA-TEST-001\SDTM\Data\
Study Phase:	Phase I Trial
Study Indication:	Oncology
Unblinded/Restricted:	No

Additional information about study phase & indication help assign a resource



Sample Code Snippet

```
%g_sADaM_DDTValidator(projid    = PRA-TEST-001,  
                        admslib   = \\nalsasfile1\PRA\PRA-TEST-001\ADaM\Data,  
                        admsnm    = adms,  
                        template  = %str(\\Applications\ADaM DDT Review\ADMS-DDT.xlsx),  
                        adsl      = ADSL,  
                        occds     = ADAE ADCM ADMH,  
                        bds       = ADEG ADLB ADVS,  
                        sdtmlib   = %str(\\nalsasfile1\PRA\PRA-TEST-001\SDTM\Data\),  
                        out       = \\Applications\ADaM DDT Review);
```




Sample Code Snippet

```
%g_sADaM_DDTValidator projid = PRA-TEST-001,  
admslib = \\nalsasfile1\PRA\PRA-TEST-001\ADaM\Data,  
admsnm = adms,  
template = %str(\\Applications\ADaM DDT Review\ADMS-DDT.xlsx),  
adsl = ADSL,  
occds = ADAE ADCM ADMH,  
bds = ADEG ADLB ADVS,  
sdtmlib = %str(\\nalsasfile1\PRA\PRA-TEST-001\SDTM\Data\),  
out = \\Applications\ADaM DDT Review);
```

PRA Project Identifier
Used for naming of report file and header/footer information



Sample Code Snippet

```
%g_sADaM_DDTValidator(projid = PRA-TEST-001,  
admslib = \\nalsasfile1\PRA\PRA-TEST-001\ADaM\Data,  
admsnm = adms,  
template = %str(\\Applications\ADaM DDT Review\ADMS-DDT.xlsx),  
adsl = ADSL,  
occds = ADAE ADCM ADMH,  
bds = ADEG ADLB ADVS,  
sdtmlib = %str(\\nalsasfile1\PRA\PRA-TEST-001\SDTM\Data\),  
out = \\Applications\ADaM DDT Review);
```

ADMS.sas7bdat Metadata Information
Path and name of ADMS.sas7bdat file (generated from ADaM specs)



Sample Code Snippet

```
%g_sADaM_DDTValidator(projid = PRA-TEST-001,  
  admslib = \\nalsasfile1\PRA\PRA-TEST-001\ADaM\Data,  
  admsnm = adms,  
  template = %str(\\Applications\ADaM DDT Review\ADMS-DDT.xlsx),  
  adsl = ADSL,  
  occds = ADAE ADCM ADMH,  
  bds = ADEG ADLB ADVS,  
  sdtmLib = %str(\\nalsasfile1\PRA\PRA-TEST-001\SDTM\Data\),  
  out = \\Applications\ADaM DDT Review);
```

Template
Path and name of PRA's ADaM metadata library



Sample Code Snippet

```
%g_sADaM_DDTValidator(projid = PRA-TEST-001,  
  admslib = \\nalsasfile1\PRA\PRA-TEST-001\ADaM\Data,  
  admsnm = adms,  
  template = %str(\\Applications\ADaM DDT Review\ADMS-DDT.xlsx),  
  adsl = ADSL,  
  occds = ADAE ADCM ADMH,  
  bds = ADEG ADLB ADVS,  
  sdtmlib = %str(\\nalsasfile1\PRA\PRA-TEST-001\SDTM\Data\),  
  out = \\Applications\ADaM DDT Review);
```

ADaM Dataset Class
Space separated list of ADaM datasets by class



Sample Code Snippet

```
%g_sADaM_DDTValidator(projid = PRA-TEST-001,  
  admslib = \\nalsasfile1\PRA\PRA-TEST-001\ADaM\Data,  
  admsnm = adms,  
  template = %str(\\Applications\ADaM DDT Review\ADMS-DDT.xlsx),  
  adsl = ADSL,  
  occds = ADAE ADCM ADMH,  
  bds = ADEG ADLB ADVS,  
  sdtmlib = %str(\\nalsasfile1\PRA\PRA-TEST-001\SDTM\Data\),  
  out = \\Applications\ADaM DDT Review);
```

SDTM Library

Path of SDTM data (if available) so checks can fire based on SDTM:ADaM



Sample Code Snippet

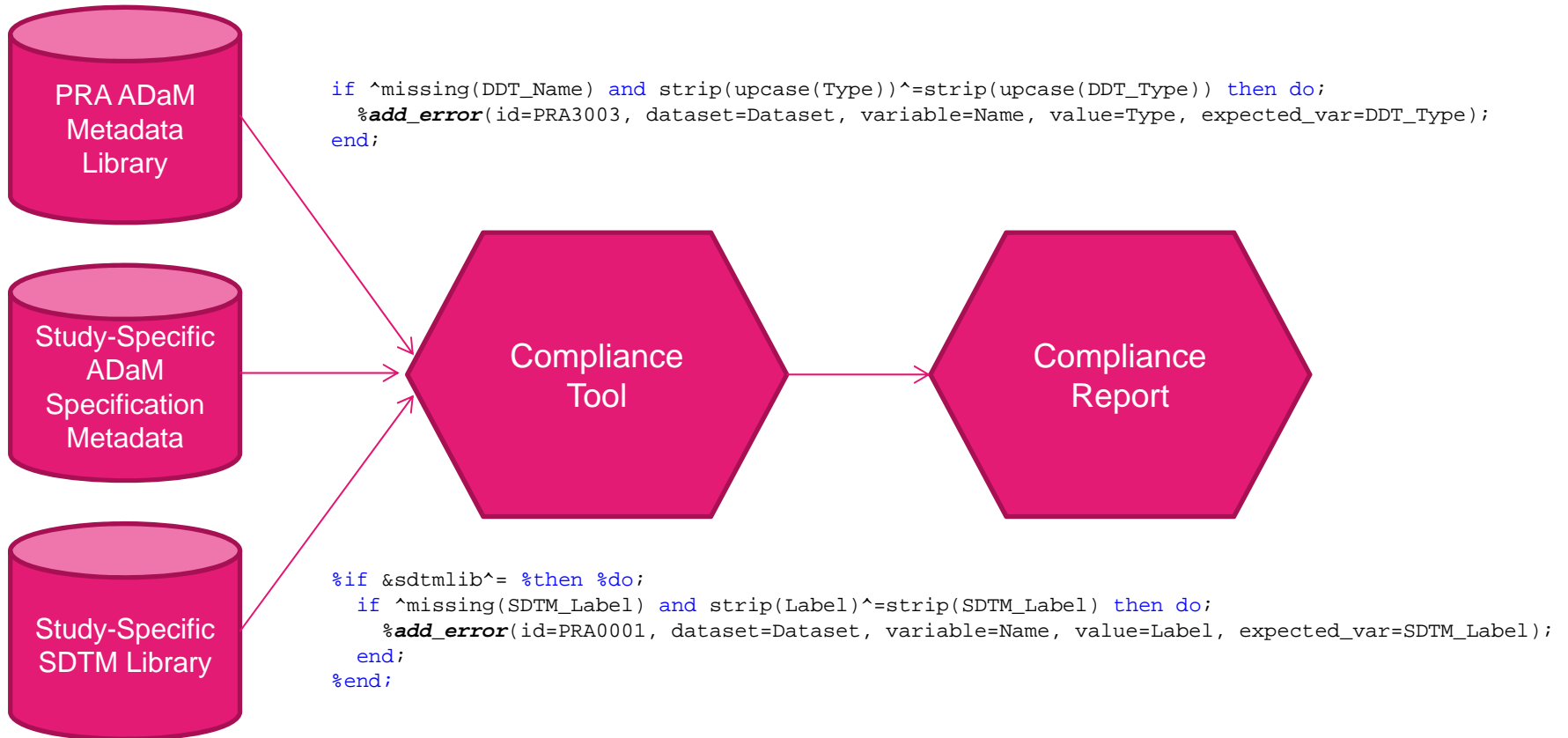
```
%g_sADaM_DDTValidator(projid = PRA-TEST-001,  
    admslib = \\nalsasfile1\PRA\PRA-TEST-001\ADaM\Data,  
    admsnm = adms,  
    template = %str(\\Applications\ADaM DDT Review\ADMS-DDT.xlsx),  
    adsl = ADSL,  
    occds = ADAE ADCM ADMH,  
    bds = ADEG ADLB ADVS,  
    sdtmlib = %str(\\nalsasfile1\PRA\PRA-TEST-001\SDTM\Data\),  
    out = \\Applications\ADaM DDT Review);
```

Output Path

Path of where output file (compliance report) will be saved



Compliance Tool Process Flow





Compliance Report

Summary Tab

	A	B	C	D
1	PRA Health Sciences			
2	PRA Project ID: PRA-TEST-001			
3	Global Data Standards ADaM Specification QC Report v1.0			
4	ADSL: ADSL OCCDS: ADAE ADCM ADMH BDS: ADEG ADLB ADVS			
5	Generated by MankusTrevor on 28SEP2016 at 12:23 (EST)			
6	Report File: \\Applications\ADaM DDT Review\PRA-TEST-001_GDS_ADaM_Spec_Validation_Report_28SEP2016.xlsx			
7	Configuration File: GDS_ADaM_Validation_Checks_v1.3.xlsx			
8				
9	Summary of Findings			
10				
11	Rule Information			
12	ID	Description	Category	Issues Found
13	PRA0001	A variable is present in ADaM with the same name as a variable present in SDTM but the variables do not have identical labels	Metadata	5
14	PRA0003	A variable is present in ADaM with the same name as a variable present in SDTM but the variables do not have identical lengths	Metadata	14
15	PRA0009	Labels for ADaM variables do not match the standard labels for ADaM variables listed in the implementation guide that cannot be modified (with the exception of 1) variables whose names contain indexes y, xx, or zz and (2) variable labels with asterisks (*) and ellipses (...) indicated for sponsor appropriate text)	Metadata	83
16	PRA0022	A variable is present with the same name as a variable present in ADSL but the variables do not have identical labels	Metadata	1
17	PRA0023	A variable is present with the same name as a variable present in ADSL but the variables do not have identical formats	Metadata	4
18	PRA0024	A variable is present with the same name as a variable present in ADSL but the variables do not have identical lengths	Metadata	1
19	PRA1001	A variable with a suffix of FL has a value that is not Y, N or null	Controlled Terminology	434
20	PRA1003	COMPLFL is present and has a value that is not Y or N	Controlled Terminology	1
21	PRA1007	SAFFL is present and has a value that is not Y or N	Controlled Terminology	1
22	PRA1017	A variable with a suffix of RFL has a value that is not Y or null	Controlled Terminology	22
23	PRA1018	A variable with a suffix of PFL has a value that is not Y or null	Controlled Terminology	22
24	PRA2003	SITEID is not present within ADSL	Presence	1



Compliance Report

Details Tab

PRA Health Sciences						
PRA Project ID: PRA-TEST-001						
Global Data Standards ADaM Specification QC Report v1.0						
ADSL: ADSL OCCDS: ADAE ADCM ADMH BDS: ADEG ADLB ADVS						
Generated by MankusTrevor on 28SEP2016 at 12:23 (EST)						
Report File: \\Applications\ADaM DDT Review\PRA-TEST-001_GDS_ADaM_Spec_Validation_Report_28SEP2016.xlsx						
Configuration File: GDS_ADaM_Validation_Checks_v1.3.xlsx						
Details of Findings						
Rule Information						
ID	Description	Category	Dataset(s)	Variable(s)	Value	Expected
13 PRA0001	A variable is present in ADaM with the same name as a variable present in SDTM but the variables do not have identical labels	Metadata	ADAE	AECAT	Category of Adverse Event	Category for Adverse Event
14 PRA0001	A variable is present in ADaM with the same name as a variable present in SDTM but the variables do not have identical labels	Metadata	ADAE	AEENDTC	Analysis End Date/Time	End Date/Time of Adverse Event
19 PRA0001	A variable is present in ADaM with the same name as a variable present in SDTM but the variables do not have identical labels	Metadata	ADAEMQ	AECAT	Category of Adverse Event	Category for Adverse Event
20 PRA0001	A variable is present in ADaM with the same name as a variable present in SDTM but the variables do not have identical labels	Metadata	ADAEMQ	AEENDTC	Analysis End Date/Time	End Date/Time of Adverse Event
25 PRA0009	Labels for ADaM variables do not match the standard labels for ADaM variables listed in the implementation guide that cannot be modified (with the exception of 1) variables whose names contain indexes y, xx, or zz and (2) variable labels with asterisks (*) and ellipses (...) indicated for sponsor appropriate text	Metadata	ADCM	ANL01FL	Analysis Flag - Original Data Structure	Analysis Flag 01 <insert text>
26 PRA0009	Labels for ADaM variables do not match the standard labels for ADaM variables listed in the implementation guide that cannot be modified (with the exception of 1) variables whose names contain indexes y, xx, or zz and (2) variable labels with asterisks (*) and ellipses (...) indicated for sponsor appropriate text	Metadata	ADCM	ONTRFL	On-Treatment Flag	On Treatment Record Flag
27 PRA0009	Labels for ADaM variables do not match the standard labels for ADaM variables listed in the implementation guide that cannot be modified (with the exception of 1) variables whose names contain indexes y, xx, or zz and (2) variable labels with asterisks (*) and ellipses (...) indicated for sponsor appropriate text	Metadata	ADCM	PREFL	Pre-Treatment Flag	Pre-treatment Flag
28 PRA0009	Labels for ADaM variables do not match the standard labels for ADaM variables listed in the implementation guide that cannot be modified (with the exception of 1) variables whose names contain indexes y, xx, or zz and (2) variable labels with asterisks (*) and ellipses (...) indicated for sponsor appropriate text	Metadata	ADEG	ADTM	Analysis Date/Time	Analysis Datetime



Compliance Report

Non-Standard Metadata Tab

1	PRA Health Sciences			
2	PRA Project ID: PRA-TEST-001			
3	Global Data Standards ADaM Specification QC Report v1.0			
4	ADSL: ADSL OCCDS: ADAE ADCM ADMH BDS: ADEG ADLB ADVS			
5	Generated by MankusTrevor on 28SEP2016 at 12:23 (EST)			
6	Report File: \\Applications\ADaM DDT Review\PRA-TEST-001_GDS_ADaM_Spec_Validation_Report_28SEP2016.xlsx			
7	Configuration File: GDS_ADaM_Validation_Checks_v1.3.xlsx			
8				
9	Non-Standard Metadata			
10				
11	Dataset Class	Dataset	Variable	Label
40	OCCURRENCE DATA STRUCTURE	ADAE	ANTHYPFL	Antihypertensive Flag
78	OCCURRENCE DATA STRUCTURE	ADAE	MENIMPFL	Pre-existing Mental Impairment Flag
101	OCCURRENCE DATA STRUCTURE	ADAE	TRNPRFL	Treated but no Procedure Flag
218	OCCURRENCE DATA STRUCTURE	ADCM	ANTHYPFL	Antihypertensive Flag
263	OCCURRENCE DATA STRUCTURE	ADCM	HYPERFL	Arterial Hypertension Flag
265	OCCURRENCE DATA STRUCTURE	ADCM	MENIMPFL	Pre-existing Mental Impairment Flag
272	OCCURRENCE DATA STRUCTURE	ADCM	PRSPTRFL	Protocol Specified Treatment Flag
289	OCCURRENCE DATA STRUCTURE	ADCM	TRNPRFL	Treated but no Procedure Flag
298	BASIC DATA STRUCTURE	ADEG	ANTHYPFL	Antihypertensive Flag
333	BASIC DATA STRUCTURE	ADEG	HYPERFL	Arterial Hypertension Flag
335	BASIC DATA STRUCTURE	ADEG	MENIMPFL	Pre-existing Mental Impairment Flag
357	BASIC DATA STRUCTURE	ADEG	TRNPRFL	Treated but no Procedure Flag
770	OCCURRENCE DATA STRUCTURE	ADMH	ANTHYPFL	Antihypertensive Flag
802	OCCURRENCE DATA STRUCTURE	ADMH	HYPERFL	Arterial Hypertension Flag
804	OCCURRENCE DATA STRUCTURE	ADMH	MENIMPFL	Pre-existing Mental Impairment Flag
832	OCCURRENCE DATA STRUCTURE	ADMH	TRNPRFL	Treated but no Procedure Flag
903	SUBJECT LEVEL ANALYSIS DATASET	ADSL	ANTHYPFL	Antihypertensive Flag
945	SUBJECT LEVEL ANALYSIS DATASET	ADSL	HYPERFL	Arterial Hypertension Flag
947	SUBJECT LEVEL ANALYSIS DATASET	ADSL	MENIMPFL	Pre-existing Mental Impairment Flag
968	SUBJECT LEVEL ANALYSIS DATASET	ADSL	TRNPRFL	Treated but no Procedure Flag



SharePoint QC Checklist

3. Manual Review: Variable Level Metadata		
3.01	Each defined ADaM dataset has variable level definitions.	<input type="checkbox"/>
3.02	Variable derivations/comments are formatted properly for the Define-XML standard. <i>Note: Derivations and comments should be in a consistent tense (past or present, not future) and avoid using SAS code or references to specific SAS functions or procedures.</i>	<input type="checkbox"/>
3.03	Variables which contain complex or long derivations have a reference to a simpler variable in the derivation.	<input type="checkbox"/>
3.08	ADaM datasets which use the SRCSEQ variable have a SRCSEQ variable. SRCSEQ is present to support datapoint traceability.	<input type="checkbox"/>
3.09	For BDS datasets, if the dataset contains records from more than one source, then SRCDOM/SRCVAR/SRCSEQ should be present to support datapoint traceability.	<input type="checkbox"/>
3.10	If the CHG variable is defined, the derivation must be AVAL – BASE.	<input type="checkbox"/>
3.11	If the PCHG variable is defined, the derivation must be ((AVAL – BASE)/BASE)*100.	<input type="checkbox"/>
3.12	If the R2BASE variable is defined, the derivation must be AVAL / BASE.	<input type="checkbox"/>



- Benefits of using e-checklist
 - Can be pooled to look for common trends of findings
 - Further training may be needed in certain areas
 - Centralized location for all checklists
 - Electronic format, no paper to maintain
 - Customizable, easy to update



- Long term goals

- Metrics should show an increase in ADaM compliance
 - Measured in a reduction of compliance findings from tool and checklist review
- Amount of time spend programming each ADaM dataset should be reduced (less re-work)
- Commonly used validation tools should show less findings when run on data which passes through this process

- Conclusions

- ADaM compliance is more than just machine testable logic. It requires expertise and manual review.
- Start checking compliance early in the process!



Acknowledgements

- Special Thanks to our colleagues:
 - Deb Goodfellow
 - Paul Burmenko
 - Jessica Lehman

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