Step Up Your ADaM Compliance Game

Ramesh Ayyappath & Graham Oakley
Agenda

- Regulatory Requirement
- Current Situation
- iACE-Toolbox
- 3 Step Process
- Macros
- Types of Issues
- Assumptions & Limitations
- Benefits
Introduction

Regulatory Requirement:

- Required standards for data submissions to FDA (US) and PMDA (Japan).

- Timely and efficient review as the reviewers could utilize standardized tools.

- Fewer questions and faster approval.
Current Situation

- Compliance check tools require datasets as an input and therefore checked at later stage.

- Rework resulting in timeline and cost implication.

- Certain validation checks not covered by P21C (V2.2.0).
iACE (ICON ADaM Capabilities and Expertise) – Toolbox
3 Step Process

1. In-house macro (**specs2xpt**) converts ADaM dataset specifications to empty SAS datasets and xpt files.

2. The xpt files are subjected to Pinnacle 21 Validator (Community V2.2.0) checks.

3. In-house ADaM compliance check macro (based on ADaM Validation Checks v1.3) is run on the empty SAS datasets generated by specs2xpt.
ADaM Compliance Checks (Start)

Populated ADaM XPT Files (Input) - Produced from ADaM Datasets

Populated ADaM Datasets (Input)

Run ADaM Other Checks Macro (Assumes SDTM datasets available)

ADaM Other Checks Report Created (Output)

Report Clean?

Yes

ADaM Compliance Checks Complete (End)

No

Run P21 Checks (Assumes SDTM xpt files available)
P21 Report Created (Output)

Report Clean?

Yes

Run ADaM Other Checks Macro (Assumes SDTM datasets available)

No

Explain in ADRG/report if issues/warnings cannot be fixed.
SPECS2XPT and ADaM Compliance Checks (Start)

ADaM Specifications (input)

Run specs2xpt macro

Successful run?

Yes

SAS Dataset Shells Created (Output)

Run ADaM Other Checks macro (Assumes SDTM datasets available)

ADaM Other Checks Report Created (output)

Reports Clean?

Yes

SPECS2XPT and ADaM Compliance Checks Complete (end)

No

No

Fix Issues?

No

Yes

SAS XPT files Created (Output)

Run P21 Checks (Assumes SDTM xpt files available)

P21 Report Created (output)

Reports Clean?

Yes

Explain in ADRG/report if issues/warnings cannot be fixed.

No
Macros

SPECS2XPT

- Work with ICON ADaM Specs template.
- Structural checks before creating output files.

Input

- ADaM Specs – XL file, including metadata sheet.

Output

- Empty datasets and XPT files.

Errors and Warnings printed in log if

- Metadata sheet and ADaM specs not in sync wrt to dataset name.
- Variable attributes not as expected or missing.

WARNING: For variable UTIME label mentioned in the ADSL is greater than 40 characters.

NOTE: Line generated by the macro variable "FORMS".

1 time5.

-----

48

ERROR 48-59: The format $TIME was not found or could not be loaded.

NOTE: The SAS System stopped processing this step because of errors.

WARNING: The data set SHELL_OUT.ADSL may be incomplete. When this step was stopped there were 0 observations and 72 variables.

WARNING: Data set SHELL_OUT.ADSL was not replaced because this step was stopped.
**ADaM Compliance Check Macro**

- Used with empty or populated datasets.

**Input**

- Analysis datasets following ADaM standards.

**Output**

- Temporary work dataset and a report showing status.

<table>
<thead>
<tr>
<th>Check Number</th>
<th>ADaM IG 1.0 Section Number</th>
<th>Text from ADaM IG</th>
<th>ADaM Structure Group</th>
<th>Functional Group</th>
<th>ADaM Variable Group</th>
<th>Machine-Testable Failure Criteria</th>
<th>Pass/Fail</th>
<th>Reason</th>
<th>Additional Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>S3</td>
<td>The names of all other character flag (or indicator) variables end in FL</td>
<td>ALL</td>
<td>Controlled Terminology</td>
<td>Flag Variables</td>
<td>A variable with a suffix of FL has a value that is not Y, N or null</td>
<td>Failed</td>
<td></td>
<td>null</td>
</tr>
<tr>
<td>6</td>
<td>S3</td>
<td>The names of the corresponding numeric flag (or indicator) variables end in FN</td>
<td>ALL</td>
<td>Controlled Terminology</td>
<td>Flag Variables</td>
<td>A variable with a suffix of FN has a value that is not 0, 1 or null</td>
<td>Passed</td>
<td></td>
<td>null</td>
</tr>
<tr>
<td>7</td>
<td>S3</td>
<td>If the numeric flag is used, the character version (FL) is required</td>
<td>ALL</td>
<td>Present/Populated</td>
<td>Flag Variables</td>
<td>A variable with a suffix of FN is present but a variable with the same root and a suffix of FL is not present</td>
<td>Passed</td>
<td></td>
<td>null</td>
</tr>
</tbody>
</table>
Types of Issues

- Many of these findings are not easily identifiable by manual checks.
- ICON’s in-house macros identify potential structural issues in specs early on.
  - Missing metadata
  - Incorrect variable data type/format
  - Inconsistency in attributes
  - Variable name and label mismatches
  - Variables labels or names over allowed lengths
  - Missing required variables
Assumptions & Limitations

SPECS2XPT

- Assumes ICON ADaM Specs template as input.

ADaM Compliance Check Macro

- Programmed utilizing the SASHELP tables VTABLE and VCOLUMN in conjunction with ADaM datasets.
- Checks are based on ADaM Validation Checks v1.3, as released by CDISC.
- Will need to be updated when CDISC releases a new version of Validation Checks depending on whether or not all checks in that version will be covered by Pinnacle 21 Validator (Community).
Benefits

- Reduced reliance on manual compliance checks.
- Ability to check metadata compliance prior to sending ADaM specification for internal or external review.
- Reduction in time in the reporting process by capturing metadata issues as early as possible instead of later in the study.
- Collection of metrics to identify common findings across studies.
Thank You

iconplc.com

© 2017 ICON. All rights reserved. Internal use only.