FERRING PHARMACEUTICALS

STREAM (PP08)

TATA CONSULTANCY SERVICES

STandardized REporting using ADaM

Introduction

ADaM was implemented in Ferring in 2008 and over the years the model has become more mature and stable.

The datasets used for reporting in Ferring are of basically 3 different types: Subject level (ADSL), occurrence data structure (e.g. ADAE) and base data structure (e.g. ADLB).

This means that these 3 data structures are same across domains but with different content which is perfectly suited for standardization of output.

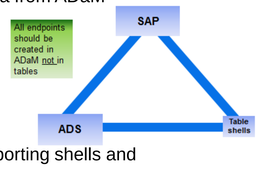
By designing ADaM datasets to include all the metadata used in production of tables 2-3 standard macros can be built to produce > 90% of the summary tables for a clinical trial or integrated summary.

Objective

- Standardize and automatize the reporting of clinical data for regulatory documents
  - CTR, ISS/ISE, IB, DSUR, RMP etc.
- Minimize risk associated with:
  - manual work, copy/paste, validation
- Reduce cost and time
  - workload, resources
- Optimize resourcing
  - focus on science

Concept

- Define SAP in a more structured way to include reporting metadata
- Design ADaM datasets to include all the metadata using ADaMIG principles
- Automatically extract reporting metadata from ADaM specification (ADS) and link it to ADaM
- Design standard mock-ups
- Design standard reporting programs to create these tables
- Push all the derivation back to ADaM
- Reduce the documentation effort on reporting shells and specifications



Implementation of Concept

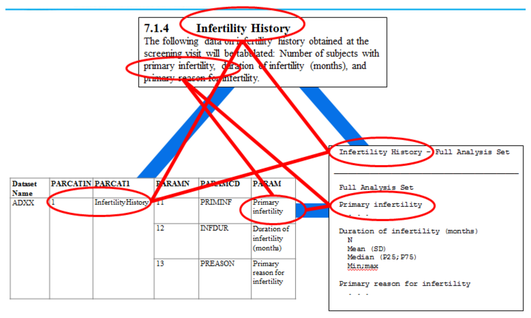
1. Consistency through Metadata

ADaM – Metadata linked from SAP

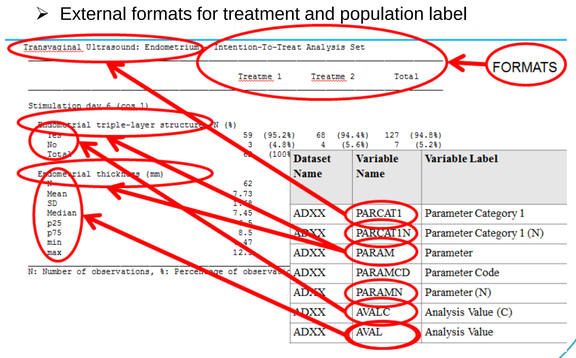
- Define the parameters concisely in SAP (along with the intended order of reporting)
- Use BDS data structure to design the ADaM
- Create variables with values directly coming from SAP e.g. PARCAT1, PARAM
- Use numeric sorting variables to control the display order e.g. PARCAT1N, PARAMN

Reporting – Metadata linked from ADaM

- Put the exact values in the ADaM that needs to be reported
  - Title in PARCAT1
  - Parameter description in PARAM
  - Parameter sorting in PARAMN
  - Parameter response in AVALC
  - Response sorting / Numeric response in AVAL
- External formats for treatment and population label



Dataset Name	PARCAT1N	PARCAT1	PARAMN	PARAMCD	PARAM
ADXX	1	Infertility History	11	PRIMINF	Primary infertility
			12	INFDUR	Duration of infertility (months)
			13	PREASON	Primary reason for infertility



Dataset Name	Variable Name	Variable Label
ADXX	PARCAT1	Parameter Category 1
ADXX	PARCAT1N	Parameter Category 1 (N)
ADXX	PARAM	Parameter
ADXX	PARAMCD	Parameter Code
ADXX	PARAMN	Parameter (N)
ADXX	AVALC	Analysis Value (C)
ADXX	AVAL	Analysis Value

2. ADaM – Metadata linked from SAP

STEP 1:

Define the ADaM Specification (ADS) as per the SAP defination and create a SAS dataset to store this metadata from ADS.

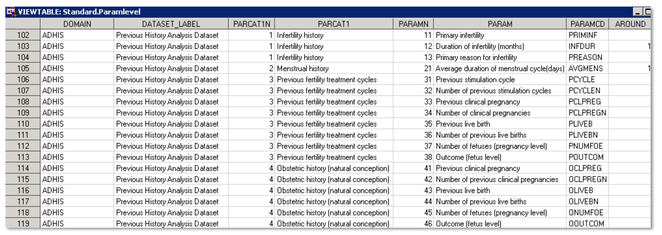
Dataset Name	PARCAT1N	PARCAT1	PARAMN	PARAMCD	PARAM	Variable Name	Codelist/Controlled Terms
ADHIS	1	Infertility history	11	PRIMINF	Primary infertility	AVALC	Yes No
ADHIS	1	Infertility history	11	PRIMINF	Primary infertility	AVAL	1, 2
ADHIS	1	Infertility history	12	INFDUR	Duration of infertility (months)	AVAL	

DataSetName	PARCAT1N	parcat1	PARAMN	param	paramcd
ADHIS	1	Infertility history	11	Primary infertility	PRIMINF
ADHIS	1	Infertility history	12	Duration of infertility (months)	INFDUR
ADHIS	1	Infertility history	13	Primary reason for infertility	PREASON

STEP 2:

Derive only PARAMCD, AVAL & AVALC in temporary ADaM and link reporting metadata created in STEP 1 with this data to get the final ADaM.

	SUBJID	PARAMCD	AVALC
1	0202-10	PRIMINF	Y
2	0202-10	INFDUR	99
3	0202-10	PREASON	UNEXPLAINED INFERTILITY
4	0202-10	PRIMINF	Y
5	0202-10	INFDUR	39
6	0202-10	PREASON	ENDOMETRIOSIS I/II
7	0202-10	PRIMINF	Y
8	0202-10	INFDUR	39
9	0202-10	PREASON	ENDOMETRIOSIS I/II
10	0202-10	PRIMINF	Y
11	0202-10	INFDUR	46
12	0202-10	PREASON	UNEXPLAINED INFERTILITY
13	0202-10	PRIMINF	Y
14	0202-10	INFDUR	24
15	0202-10	PREASON	UNEXPLAINED INFERTILITY
16	0202-10	PRIMINF	N
17	0202-10	INFDUR	48
18	0202-10	PREASON	TUBAL INFERTILITY
19	0202-10	PRIMINF	N
20	0202-10	INFDUR	48
21	0202-10	PREASON	TUBAL INFERTILITY
22	0202-10	PRIMINF	N
23	0202-10	INFDUR	48
24	0202-10	PREASON	TUBAL INFERTILITY
25	0202-10	PRIMINF	Y
26	0202-10	INFDUR	24
27	0202-10	PREASON	ENDOMETRIOSIS I/II
28	0202-10	PRIMINF	Y
29	0202-10	INFDUR	24
30	0202-10	PREASON	ENDOMETRIOSIS I/II
31	0202-10	PRIMINF	Y
32	0202-10	INFDUR	24
33	0202-10	PREASON	ENDOMETRIOSIS I/II
34	0202-10	PRIMINF	Y
35	0202-10	INFDUR	24
36	0202-10	PREASON	ENDOMETRIOSIS I/II
37	0202-10	PRIMINF	N



VIEWTABLE: Standard.Paramlevel

	DOMAIN	DATASET_LABEL	PARCAT1N	PARCAT1	PARAMN	PARAM	PARAMCD	AROUND
102	ADHIS	Previous History Analysis Dataset	1	Infertility history	11	Primary infertility	PRIMINF	
103	ADHIS	Previous History Analysis Dataset	1	Infertility history	12	Duration of infertility (months)	INFDUR	1
104	ADHIS	Previous History Analysis Dataset	1	Infertility history	13	Primary reason for infertility	PREASON	
105	ADHIS	Previous History Analysis Dataset	2	Menstrual history	21	Average duration of menstrual cycle(days)	AVGMENS	1
106	ADHIS	Previous History Analysis Dataset	3	Previous fertility treatment cycles	31	Previous stimulation cycle	PCYCLE	
107	ADHIS	Previous History Analysis Dataset	3	Previous fertility treatment cycles	32	Number of previous stimulation cycles	PCYCLEN	
108	ADHIS	Previous History Analysis Dataset	3	Previous fertility treatment cycles	33	Previous clinical pregnancy	PCLPREG	
109	ADHIS	Previous History Analysis Dataset	3	Previous fertility treatment cycles	34	Number of clinical pregnancies	PCLPREGN	
110	ADHIS	Previous History Analysis Dataset	3	Previous fertility treatment cycles	35	Previous live birth	PLIVEB	
111	ADHIS	Previous History Analysis Dataset	3	Previous fertility treatment cycles	36	Number of previous live births	PLIVEBN	
112	ADHIS	Previous History Analysis Dataset	3	Previous fertility treatment cycles	37	Number of fetuses (pregnancy level)	PNUMFOE	
113	ADHIS	Previous History Analysis Dataset	3	Previous fertility treatment cycles	38	Outcome (fetus level)	POUTCOM	
114	ADHIS	Previous History Analysis Dataset	4	Obstetric history (natural conception)	41	Previous clinical pregnancy	OCLPREG	
115	ADHIS	Previous History Analysis Dataset	4	Obstetric history (natural conception)	42	Number of previous clinical pregnancies	OCLPREGN	
116	ADHIS	Previous History Analysis Dataset	4	Obstetric history (natural conception)	43	Previous live birth	OLIVEB	
117	ADHIS	Previous History Analysis Dataset	4	Obstetric history (natural conception)	44	Number of previous live births	OLIVEBN	
118	ADHIS	Previous History Analysis Dataset	4	Obstetric history (natural conception)	45	Number of fetuses (pregnancy level)	ONUMFOE	
119	ADHIS	Previous History Analysis Dataset	4	Obstetric history (natural conception)	46	Outcome (fetus level)	OOUTCOM	

3. Generate Standard Tables

Standardized Mockups can be created to cater various layouts.

Below example shows an example of BDS data's layout for a summary table with both numeric and character parameters.

```
Template for BDS Dataset - <population text>

                                  Treat 1        Treat 2        Total
                                  (N=xxx)        (N=xxx)        (N=xxx)

Param 1
   n                              xxx            xxx            xxx
   Mean (SD)                      x.x (x.xx)     x.x (x.xx)     x.x (x.xx)
   Median (P25;P75)               x.x (x.x;x.x)  x.x (x.x;x.x)  x.x (x.x;x.x)
   Min;max                        x;x            x;x            x;x

Param 2, n (%)
   Category 1                      xx   (xx.x)     xx   (xx.x)     xx   (xx.x)
   Category 2                      xx   (xx.x)     xx   (xx.x)     xx   (xx.x)
   Category 3                      xx   (xx.x)     xx   (xx.x)     xx   (xx.x)
   Category 4                      xx   (xx.x)     xx   (xx.x)     xx   (xx.x)
   All                            xxx  (100.0)    xxx  (100.0)    xxx  (100.0)

N = Number of subjects
n = Number of subjects with observation
% = Percentage of subjects with observation
```

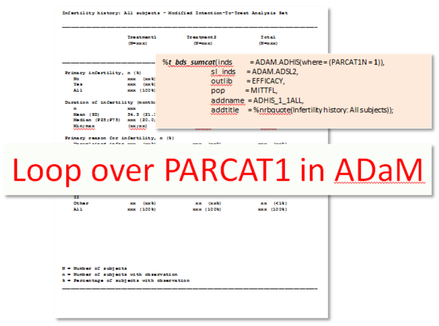
Standardized programs can then be created based on the standard layouts to generate the summary tables.

Next figure shows how looping through various PARCAT1 values in a BDS ADaM will create summary table of similar layout.

Number of values in PARCAT1 controls the number of tables and any number of parameters can be added within an PARCAT1. All parameters within a same PARCAT1 will be reported in the same table.

If new tables are needed then we add new values in PARCAT1 in ADaM and if new parameters are needed in an existing PARCAT then we only have to update our ADaM program and this change will flow directly to the table output.

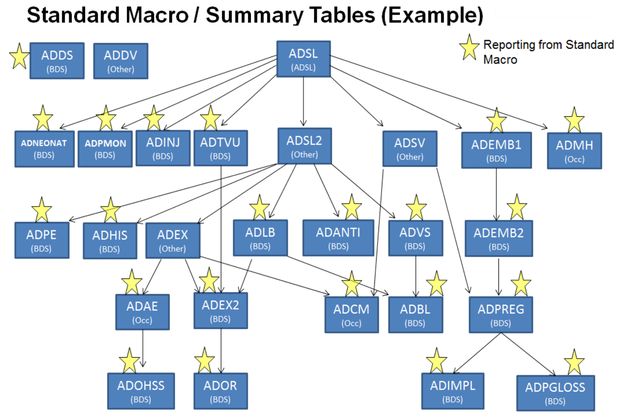
Summary statistics on BDS data



Pilot Implementation Results

- We implemented the STREAM concept in a pilot study
- Designed SAP and ADaM specification with close link to each other
- Designed most of the ADaMs as BDS
- Created standardized reporting mockups & standardized reporting macros
- We were able to generate 99% of all the summary tables using this approach
- Below figure show the different ADaMs that we are able to use directly from this approach

Standard Macro / Summary Tables (Example)



Conclusion

- Reduces programming efforts
- Ensures consistency
- No need for Table specifications
- Produces > 90% of summary tables
- Very few standard macros are needed
- Reduces validation effort

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