

Digitization of Specifications

Brave new world of Analysis Definitions

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Digitizing Analysis Definitions

Digitizing of Analysis Definitions Entails:

- Constructing machine and human readable analysis instructions – Analysis Definitions
- Making information machine readable → parameterizing the information
- Programmatically ingesting the parameterized information to generate analyses

Standardizing Digitized Analysis Definitions Entails:

- Defining standard metadata structures of the digitized information
- Applying standard controlled terminology to the metadata
- Enabling automation requires expected structures and terminology





Definition of a Single Analysis Definition

How many analyses? 4

Analysis Variable

System Organ Class Preferred Term	Control		Low		High		Total	
	N = xxx		N = yyy		N = zzz		N = ttt	
	n	(%)	n	(%)	n	(%)	n	(%)
1 Subject's with at least 1 AF	xx	(xx.x)	xx	(xx.x)	xx	(xx.x)	xx	(xx.x)
3 SOC1	xx	(xx.x)	xx	(xx.x)	xx	(xx.x)	xx	(xx.x)
4 PT1-1	xx	(xx.x)	xx	(xx.x)	xx	(xx.x)	xx	(xx.x)
PT1-2	xx	(xx.x)	xx	(xx.x)	xx	(xx.x)	xx	(xx.x)
PT1-3	xx	(xx.x)	xx	(xx.x)	xx	(xx.x)	xx	(xx.x)
3 SOC2	xx	(xx.x)	xx	(xx.x)	xx	(xx.x)	xx	(xx.x)
4 PT2-1	xx	(xx.x)	xx	(xx.x)	xx	(xx.x)	xx	(xx.x)
PT2-2	xx	(xx.x)	xx	(xx.x)	xx	(xx.x)	xx	(xx.x)
PT2-3	xx	(xx.x)	xx	(xx.x)	xx	(xx.x)	xx	(xx.x)

ADSL.SAFFL

ADAE.AOCCFL

ADAE.AOCCSFL

ADAE.AOCCPFL



Parameterization of an Analysis Definitions



Analysis Description

Analysis Description Parameters

Name

Label

Description

Endpoint

Reason

Example Values

ADAE_TEAE_SOC

Summary of TEAEs at SOC level

Descriptive statistics at the SOC level for subjects with at least 1 TEAE

Adverse Events across the trial

Primary safety endpoint

Data Requirements

Analysis Role Parameters

Dataset

Analysis Variable

Comparator Variable

Selection Variables

By Variables

Example Values

ADAE

ADAE.AOCCSFL

TRTA

TRTEMFL, ANL01FL

AESOC

Statistical Methods





Parameterization of Statistical Methods

Types of Statistical Parameters:

Statistical Methods	Defines how to perform the statistical analysis
Statistical Tests	Defines statistical tests to be performed
Statistical Outputs	Defines what statistics are wanted for the analysis

Example: SAS® Mixed Procedure

```
proc mixed method=TYPE2 <data=dataset>;  
  <where clause>;  
  <by statement>;  
class TRTP;  
model aval = AGE TRTP;  
repeated / type=UN subject=USUBJID;  
lsmeans TRTP / alpha=.05 adjust=DUNNETT CL PDIF;  
run;
```





Statistical Method Parameters

Statistical Method Parameter	Statistical Method Parameter Value
Type Error	TYPE2
Fixed Effect	TRTP
Covariate	AGE
Covariance Structure	Unstructured
Repeated Variable	USUBJID

```
proc mixed method=TYPE2;  
class TRTP;  
model aval = AGE TRTP;  
repeated / type=UN subject=USUBJID;  
lsmeans TRTP/ alpha=.05 adjust=DUNNETT  
CL PDIF;  
run;
```

Key point 1: Statistical method parameters change as need and should be code agnostic

Key point 2: If parameters values are not tied to a dataset,
the stats method can be used for multiple analysis definitions

Key point 3: Standards to define parameter names and possibly values





Statistical Test Parameters

Statistical Test	Apha Level	Sided-ness	Adjustment
T-test	0.05	2-sided	Dunnett

```
proc mixed method=TYPE2;  
class TRTP;  
model aval = AGE TRTP;  
repeated / type=UN subject=USUBJID;  
lsmeans TRTP/ alpha=.05 adjust=DUNNETT  
CL PDIFF;  
run;
```

Key point 1: Can add as many stat test as needed

Key point 2: Standards to define parameter names and possibly values





Statistical Output Parameters

Statistical Output Parameters
Dunnett p-values
LS Means
95% Lower Confidence Limit for LS Means
95% Upper Confidence Limit for LS Means
LS Mean Difference
95% Lower Confidence Limit for LS Mean Differences
95% Upper Confidence Limit for LS Mean Differences

```
proc mixed method=TYPE2;  
class TRTP;  
model aval = AGE TRTP;  
repeated / type=UN subject=USUBJID;  
lsmeans TRTP/ alpha=.05 adjust=DUNNETT  
CL PDIF;  
run;
```

Key point 1: Statistical output parameters change as needed

Key point 2: Standards to define parameter values



Conclusions



- Need to define what defines AN analysis definition
- Parameterization is what defines digitization
- Need to standardize the structure of the parameterization
- Define where controlled terminology could benefit the process
- Standardized structure and values are precursors to automation



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