

PhUSE CSS White Paper on Analyses and Displays Associated to Pharmacokinetics – With a Focus on Clinical Trials

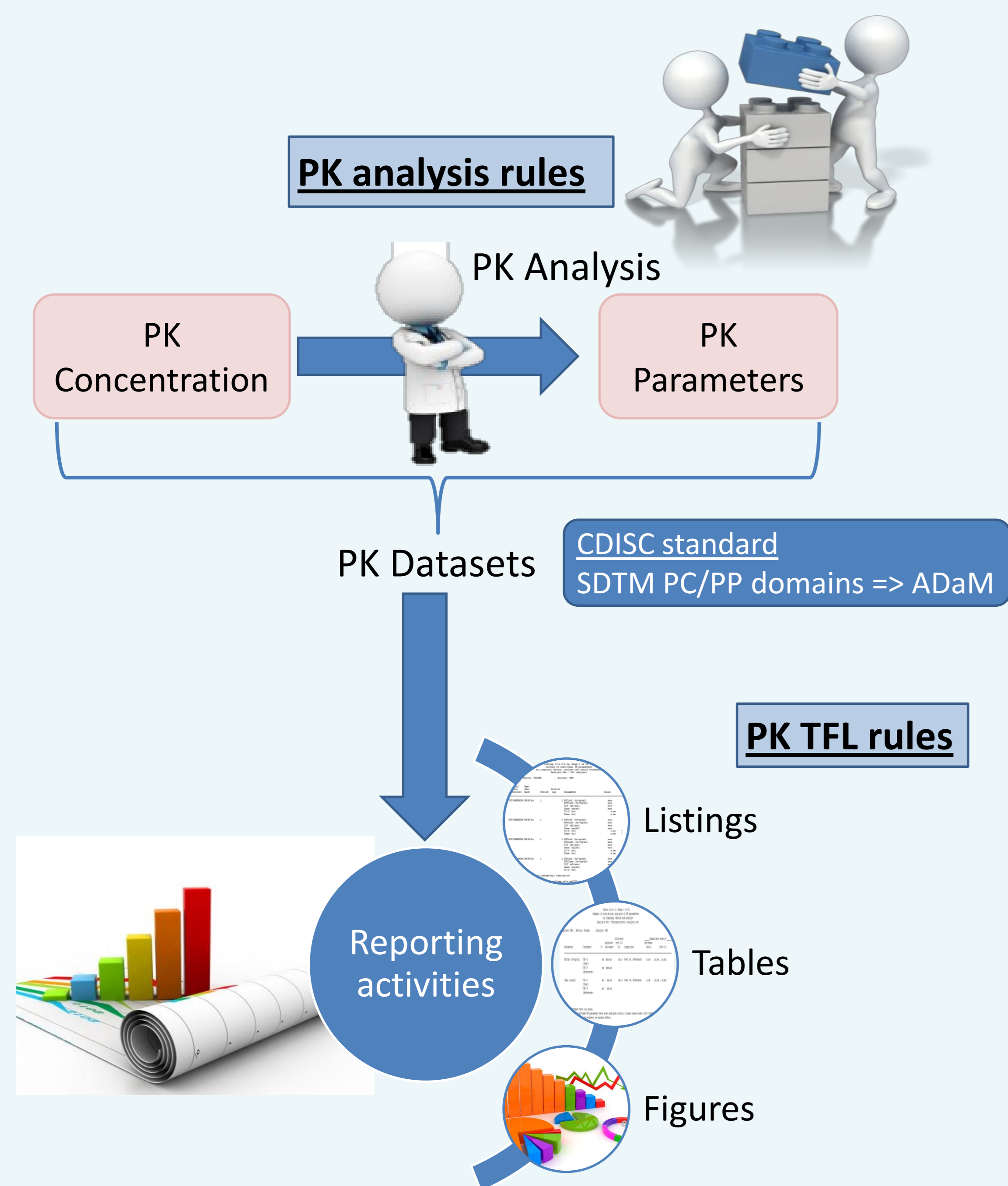
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Introduction

- ✓ As part of the FDA/PhUSE CSS Working Group 5, our goal is to develop **Standard Scripts** for Analysis and Programming of **Pharmacokinetics**.
- ✓ We have issued a **white paper** to define the reporting flow, dataset mapping process, rules for non-compartmental analysis (NCA), standard labels and TFL shells for PK concentrations and parameters.
- ✓ This poster presents the general project framework in order to **stimulate voluntary support for the programming of the PK datasets and TFLs**.

Deliverable #1: PK reporting workflow



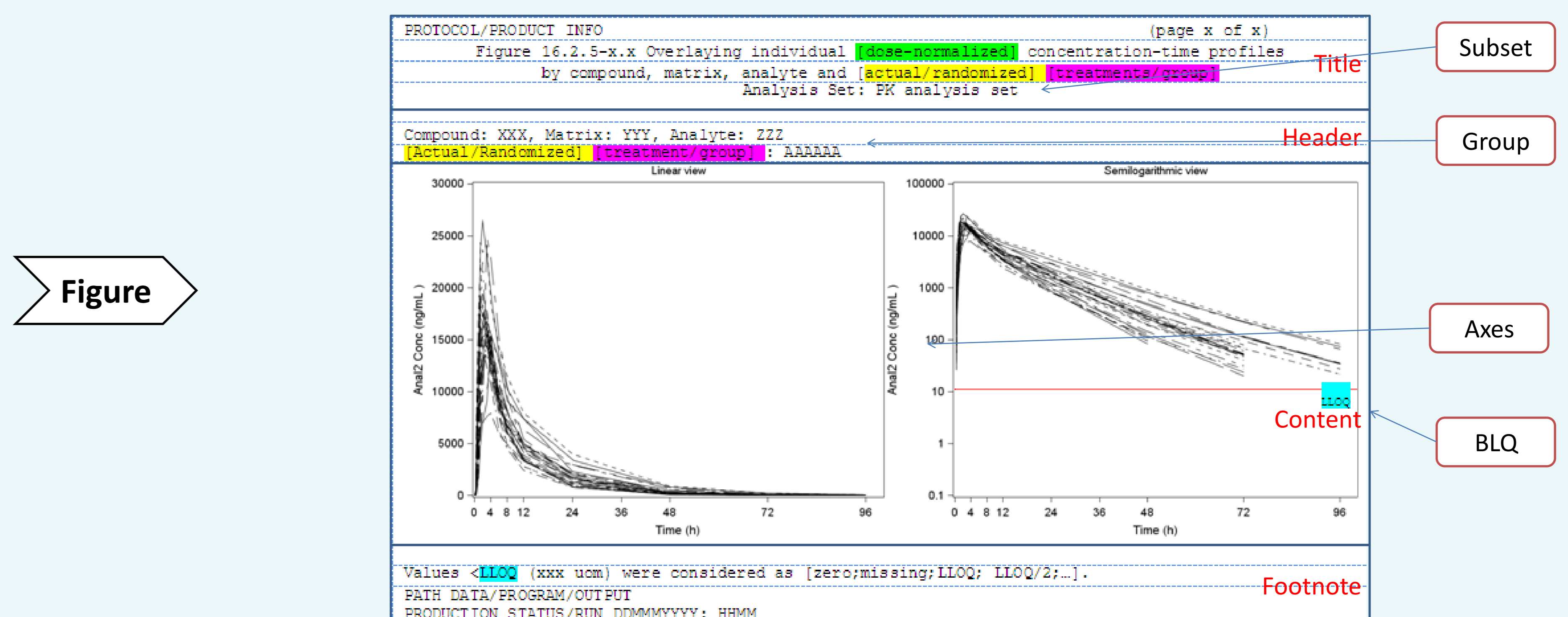
Deliverable #4: Annotated PK TFLs

The WG has established a standard list of PK TFLs. They were annotated and assembled by modules. See 3 illustrative examples below:

Table

PROTOCOL/PRODUCT INFO (page x of x)					
Table 14.2-x.x Summary statistics for PK parameters					
by compound, matrix, analyte and [actual/randomized] [treatments/group]					
Analysis Set : PK analysis set					
Compound: XXX, Matrix: YYY, Analyte: ZZZ					
Actual treatment	Period day	Statistic	<Parameter 1> <unit>	<Parameter 2> <unit>	<Parameter 3> <unit>
TRTA	1	N	xx	xx	xxx (xxx)
		Mean (SD)	xxx (xxx)	xxx (xxx)	xxx (xxx)
		CV% mean	xx.x	xx.x	xx.x
		Geo-mean	xxx	xxx	xxx
		CV% geo-mean	xx.x	xx.x	xxx
		Median	xxx	xxx	xxx
		[Min; Max]	[xxx;xxx]	[xxx;xxx]	[xxx;xxx]

CV% = coefficient of variation (%)=sd/mean*100;
CV% geo-mean=(sqrt (exp (variance for log transformed data)-1))*100
Geo-mean: Geometric mean.
Geo-mean and CV% geo-mean not presented when the minimum value for a parameter is zero.
PATH DATA/PROGRAM/OUTPUT
PRODUCTION STATUS/RUN DDDMMYYYY: HHMM

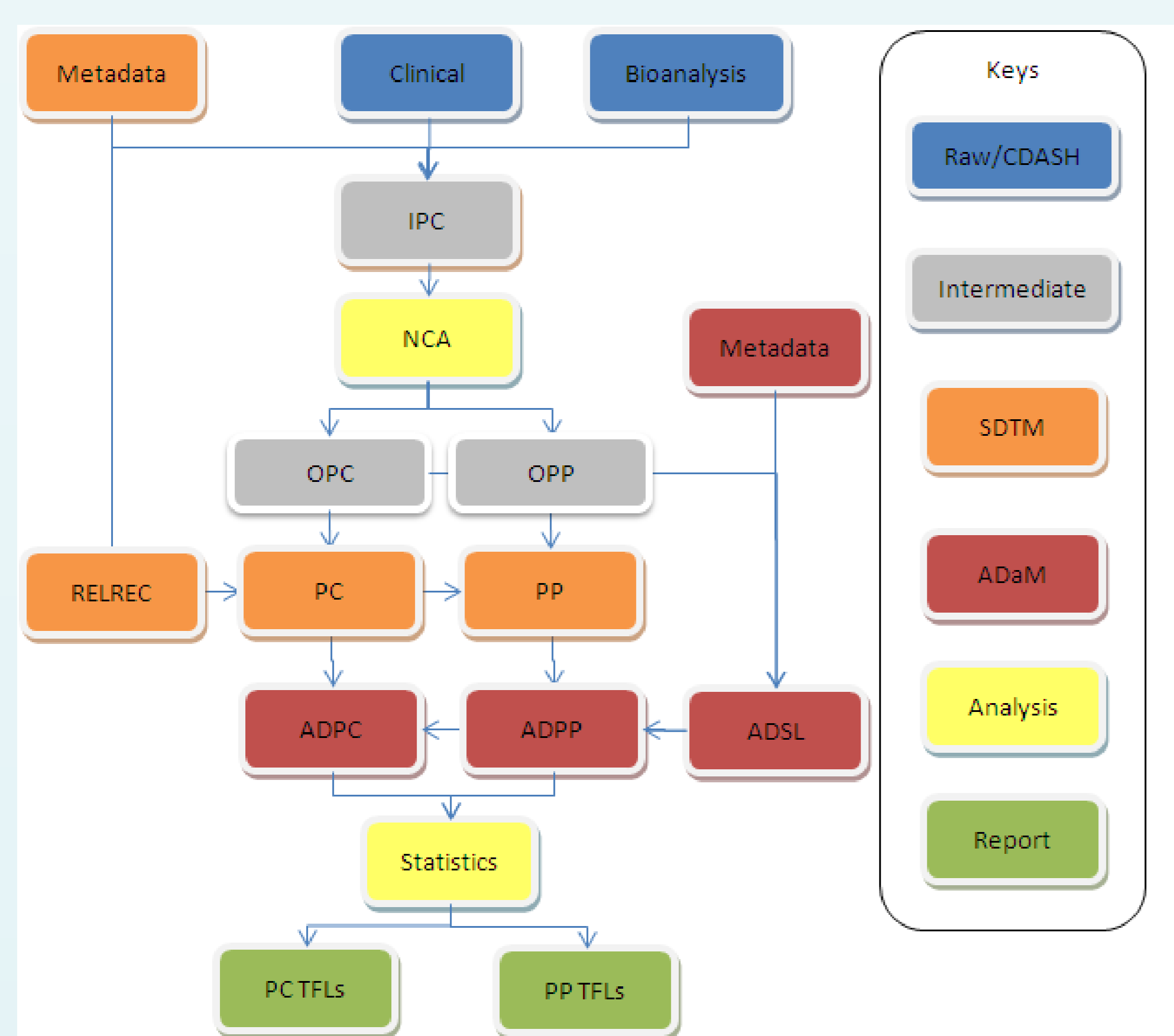


Listing

PROTOCOL/PRODUCT INFO (page x of x)									
Listing 16.2.5-x.x Individual pharmacokinetic concentrations									
by compound, matrix, analyte and [actual/randomized] [treatments/group]									
Analysis Set : PK analysis set									
Compound: XXX, Matrix: YYY, Analyte: ZZZ									
[Actual/Randomized] [treatment/group] [sequence] AAAAAA									
Treatment									
Country/ Site/ Subject	Age/ Sex/ Race	Dose (uom)	Date/Time of dosing	Profile day	Scheduled Sampling Time (uom)	Date/Time of collection	Actual Time (uom)	Concentration (uom)	Exclusion Comment
CNTR/ ST1/ XXXXX	YY/ M/ Ca	xx mg	2000-02-12Txx:xx	1	0.0	2000-02-12Txx:xx	- xx.x	xxx.xx +*	Pre-dose >0
					1.0	2000-02-12Txx:xx	xx.x	xxx.xx +	Outlier
					1.5	2000-02-12Txx:xx	xx.x	0 (<1)	
					2.0	2000-02-12Txx:xx	xx.x	NV	

Age/Sex/Race: M=Male, F=Female, Ca=Caucasian, ...
NV : No Value collected.
Value * was not considered for summary and inferential procedures.
Value + was excluded from estimation of PK parameters.
For values <LLOQ, the reported (<LLOQ) values are presented.
PATH DATA/PROGRAM/OUTPUT
PRODUCTION STATUS/RUN DDDMMYYYY: HHMM

Deliverable #2 : CDISC Datasets workflow



- Process map for the creation of SDTM (PC, PP) and ADaM (ADPC, ADPP) datasets
- List of standard PK parameters, labels and formula for NCA
- Mapping between SDTM terminology and output labels

Deliverable #3: Rules for PK parameters

- Imputation of missing data
- Management of BLQ values
- Exclusion of outliers
- Actual vs. planned timepoints
- Non-reported values

Deliverable #5: Rules for PK TFLs

- Summary statistics
- Non-reported statistics
- Excluded data
- BLQ values
- Significant digits/Rounding
- Figures: Error bars, Scale, Axis Range, Timepoints

Conclusion

- ✓ FDA/PhUSE CSS WG5 project 8 will be an important contribution to the standardization of PK analysis reports.
- ✓ The white paper presents standards for the reporting flow, the derived datasets, and the output shells.
- ✓ Its review was extensive. It involved PK scientists, pharmacologists, statisticians, programmers and data experts from many companies.
- ✓ This will be the basis for the creation of automated and validated reporting programs for PK analyses.
- ✓ Sample datasets (ADPP and ADPC) and annotated shells are available and programming can start.
- ✓ These programs will be published on the PhUSE Standards Script repository.