

Pharmacokinetics standardization: patients' healthcare is becoming central

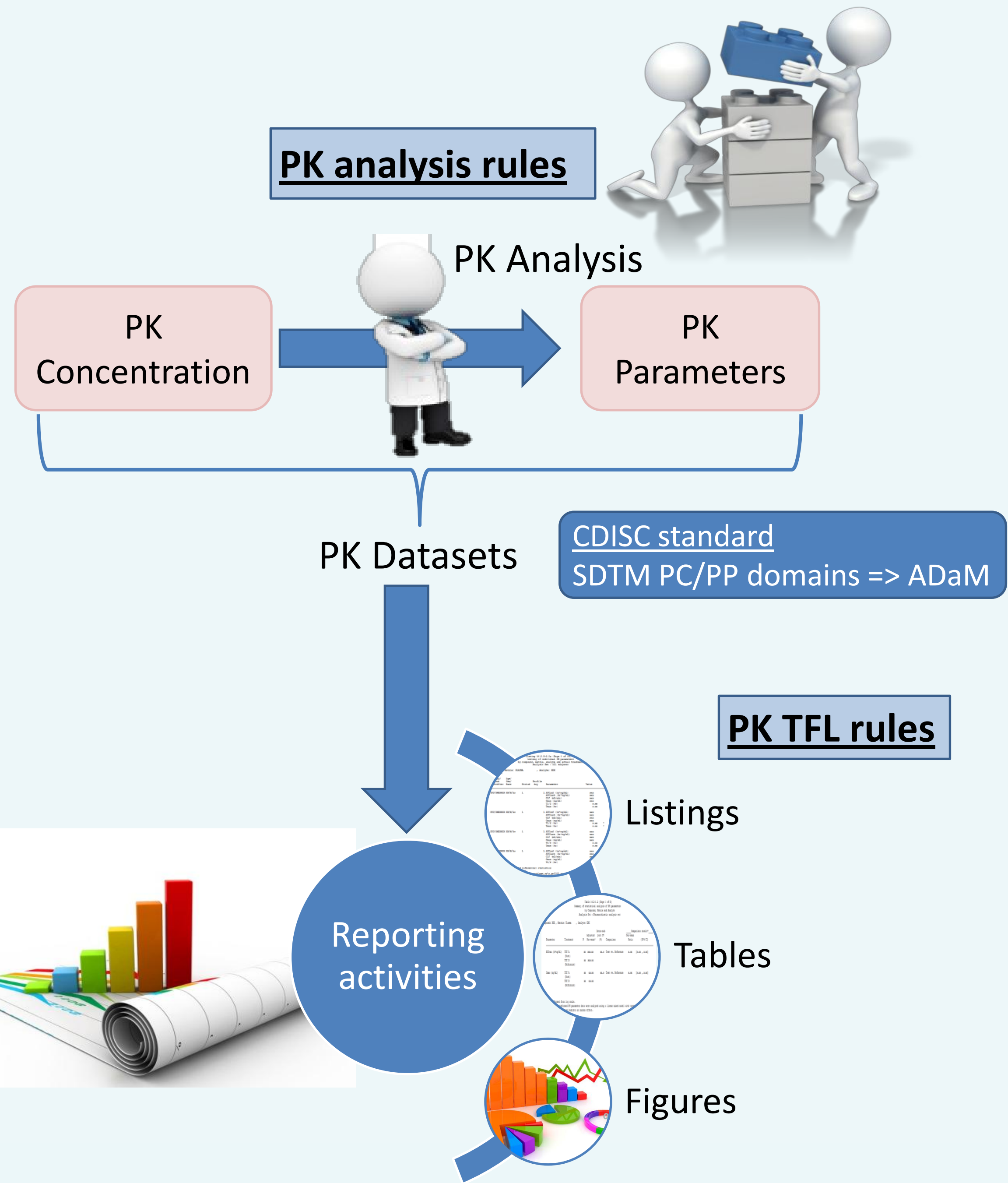
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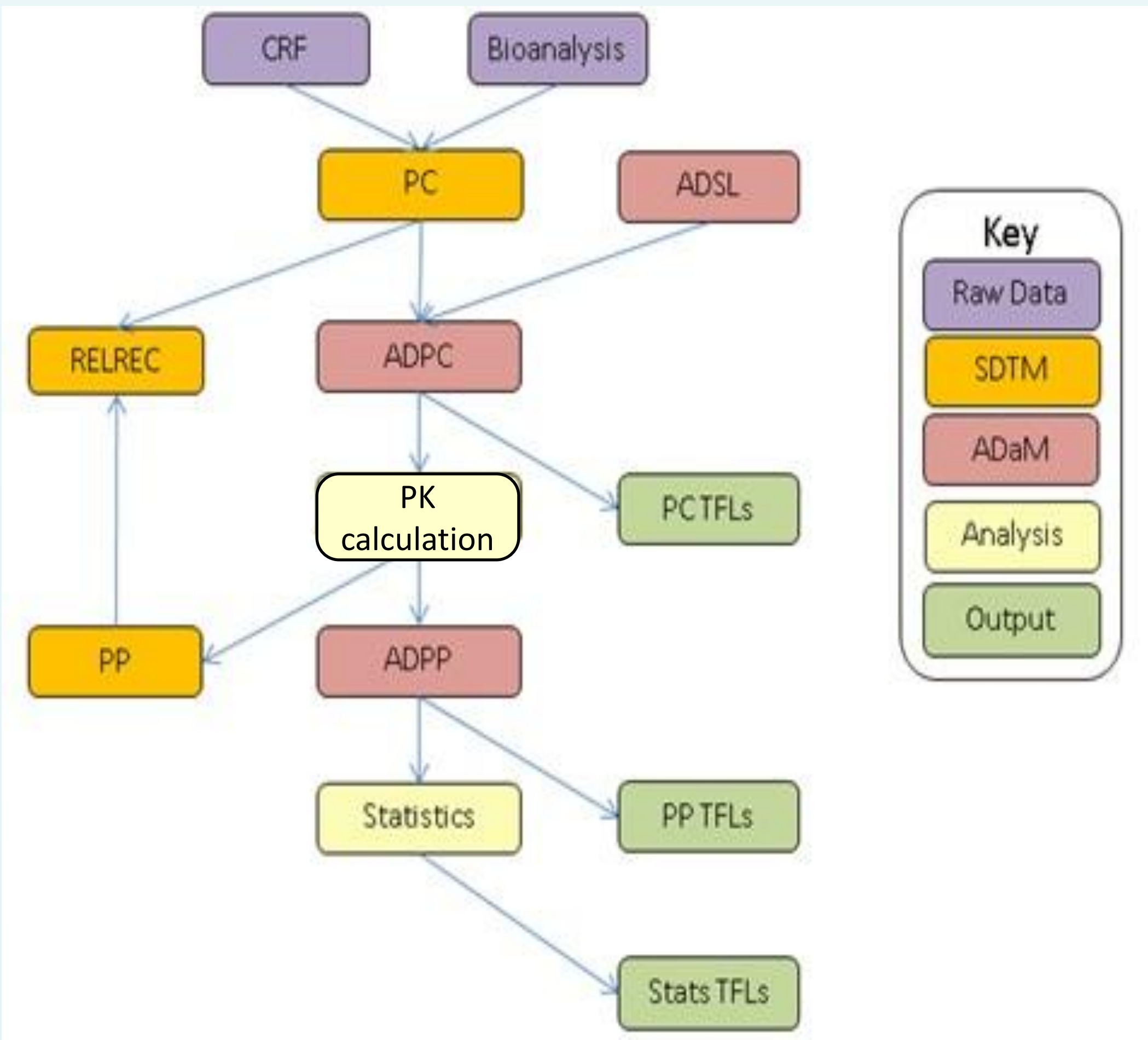
Introduction

- ✓ As part of the FDA/PhUSE CSS Working Group 5, our goal is to develop **Standard Scripts** for Analysis and Programming of **Pharmacokinetics**.
- ✓ We will issue a **white paper** to define PK standards, recommendations, imputations rules, analysis flows, standardized datasets and TFL shells.
- ✓ This poster presents the general project framework in order to create awareness and **stimulate voluntary support**.

Deliverable #1: PK reporting workflow



Deliverable #2 : CDISC Datasets workflow



Source: Quanticate CRO blog, Performing CDISC Compliant Pharmacokinetic Analyses Fri, Jul 26, 2013

Deliverable #3: Rules for PK parameters

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

Conclusion

- ✓ FDA/PhUSE CSS WG5 project 8 will be an important contribution to the standardization of PK analysis reports.
- ✓ The white paper will present standards for the reporting flow, the derived datasets, and the output shells.
- ✓ This will be the basis for the creation of automated and validated reporting programs for PK analyses.
- ✓ These programs will be published on the PhUSE Standards Script repository.
- ✓ If you want to **participate** in the creation of this white paper, please **contact us**.

Deliverable #4: Annotated PK TFLs

The WG will establish a standard list of PK TFLs. They will be annotated and assembled by modules. See 4 illustrative examples below:

STUDYNUMBER

Table 14.2-1.2a (Page 1 of xx)
Summary statistics for PK parameters
by compound, matrix, analyte and actual treatment
Analysis Set : Pharmacokinetic analysis set

Subset

Title

Compound: XXX , Matrix: PLASMA , Analyte: XXXX

Header

Group

Actual treatment

Period day

Statistic

AUCinf (hr*ng/mL)

AUClast (hr*ng/mL)

Statistics

Significant digits/format

Content

TRT A

1

n

xx

xx

xx

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

xx.x

Median

xxx

xxx

xxx

[Min; Max]

xxx;xxx

xxx;xxx

xxx;xxx

TRT B

1

n

xx

xx

xx

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

xx.x

Median

xxx

xxx

xxx

[Min; Max]

xxx;xxx

xxx;xxx

xxx;xxx

TRT C

1

n

xx

xx

xx

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

xx.x

Median

xxx

xxx

xxx

[Min; Max]

xxx;xxx

xxx;xxx

xxx;xxx

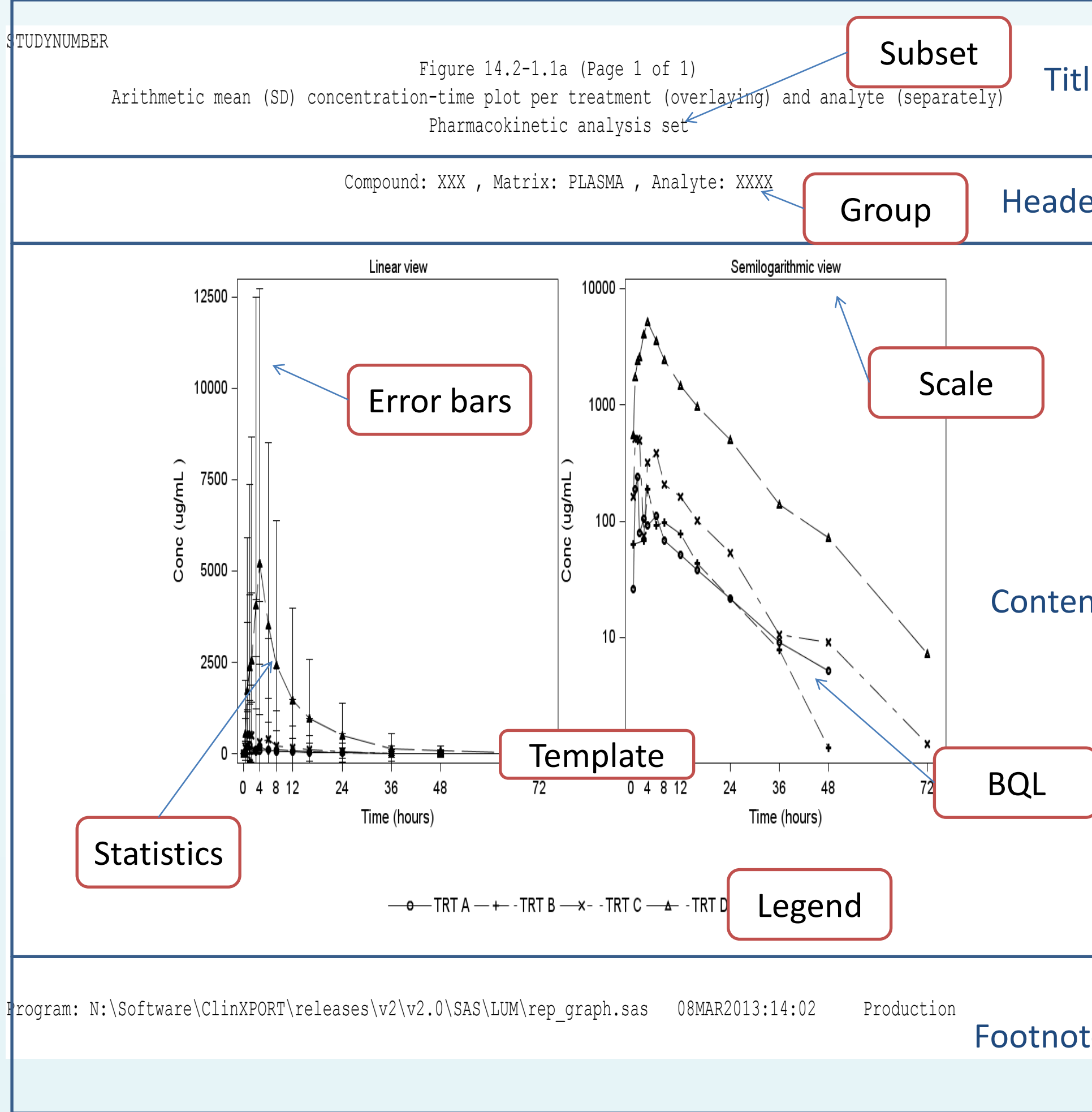
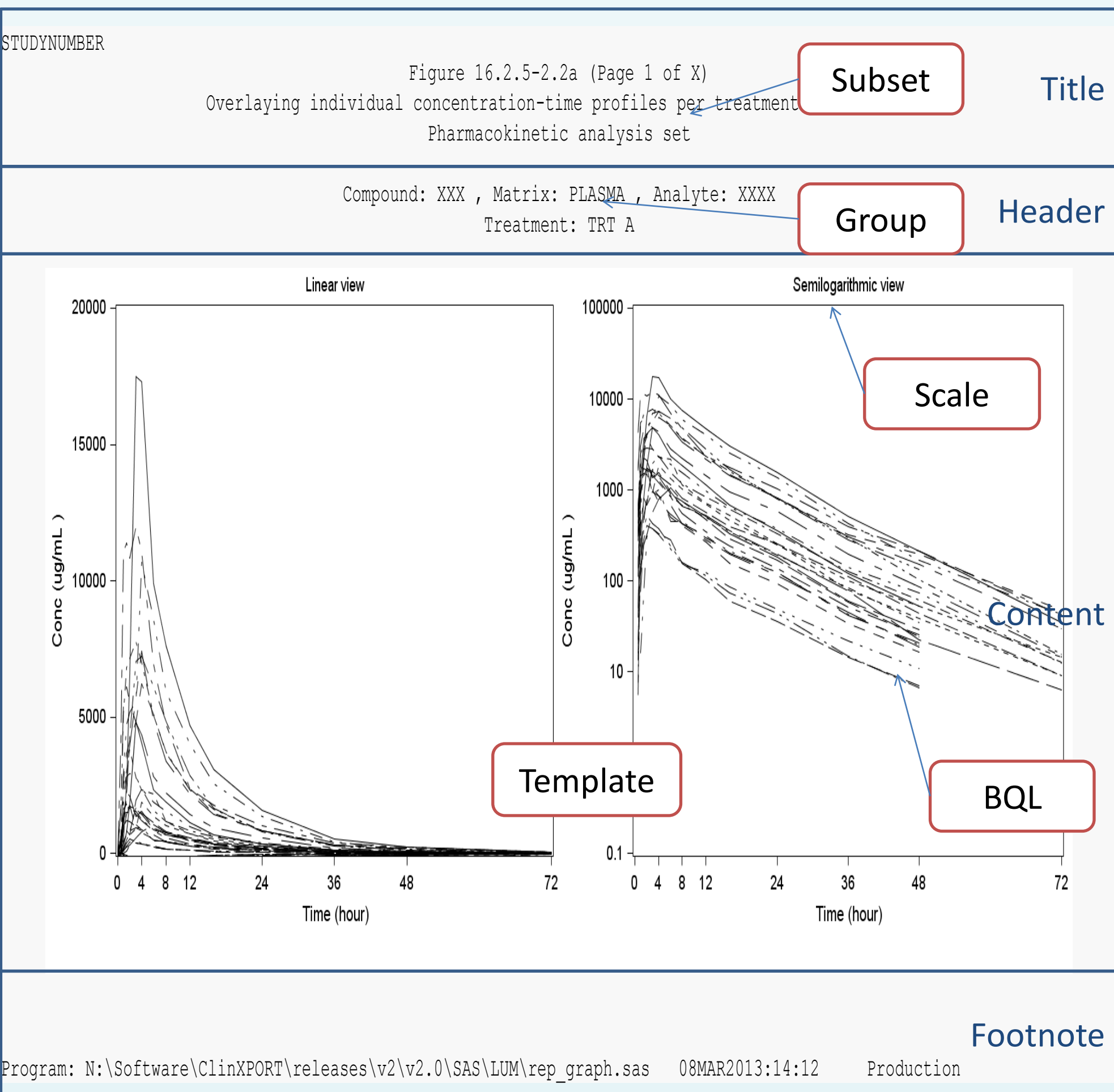
CV% = coefficient of variation (s)=sd/mean*100;
CV% geo-mean=sqrt (exp (variance for log transformed data)-1))*100
Geo-mean: Geometric mean.
Geo-mean and CV% geo-mean not presented when the minimum concentration is zero at respective timepoint.

Footnote

Program: N:\Operations\PK\Template_PK_Mat13\report\pgm_cp\p_002.sas 08MAR2013:13:05 Production

Missing values

STUDYNUMBER					Title	
Listing 16.2.5-2.1a (Page 1 of 84) Listing of PK concentration by compound, matrix, analyte and actual treatments Analysis Set : All subjects					Subset	
Compound: XXX , Matrix: PLASMA , Analyte: XXX Actual treatment: TRT A					Group	
Country/ Subject identifier	Age/ Sex/ Race	Scheduled Sampling Time (hrs)	Date/Time of collection	Elapsed Time (hrs)	Concentration (ng/mL)	Header
COU/XXXXXXXX XX/M/As		0.00 HOURS PRE DOSE	YYYY-MM-DDTHH:MM	0.00	0.00	Significant digits/format
		0.50 HOURS POST DOSE	YYYY-MM-DDTHH:MM	0.50	x.xx	
		1.00 HOURS POST DOSE	YYYY-MM-DDTHH:MM	1.00	x.xx	
		1.50 HOURS POST DOSE	YYYY-MM-DDTHH:MM	1.50	xxx	
		2.00 HOURS POST DOSE	YYYY-MM-DDTHH:MM	2.00	xxx	
		3.00 HOURS POST DOSE	YYYY-MM-DDTHH:MM	3.00	xx.x	
		4.00 HOURS POST DOSE	YYYY-MM-DDTHH:MM	4.00	xx.x	
		6.00 HOURS POST DOSE	YYYY-MM-DDTHH:MM	6.00	xx.x	
		8.00 HOURS POST DOSE	YYYY-MM-DDTHH:MM	8.00	x.xx	
		12.00 HOURS POST DOSE	YYYY-MM-DDTHH:MM	12.00	x.xx	
		16.00 HOURS POST DOSE	YYYY-MM-DDTHH:MM	16.00	x.xx	
		24.00 HOURS POST DOSE	YYYY-MM-DDTHH:MM	24.00	x.xx	
COU/XXXXXXXX XX/M/As		36.00 HOURS POST DOSE	YYYY-MM-DDTHH:MM	36.00	x.xx	Content
		48.00 HOURS POST DOSE	YYYY-MM-DDTHH:MM	47.63	x.xx	
		72.00 HOURS POST DOSE	YYYY-MM-DDTHH:MM	71.90	x.xx	
		0.00 HOURS PRE DOSE	YYYY-MM-DDTHH:MM	0.00	0.00	
		0.50 HOURS POST DOSE	YYYY-MM-DDTHH:MM	0.50	xxx	
		1.00 HOURS POST DOSE	YYYY-MM-DDTHH:MM	1.00	xxx	
		1.50 HOURS POST DOSE	YYYY-MM-DDTHH:MM	1.50	xxx	
		2.00 HOURS POST DOSE	YYYY-MM-DDTHH:MM	2.00	xxx	
		3.00 HOURS POST DOSE	YYYY-MM-DDTHH:MM	3.02	xx.x	
		4.00 HOURS POST DOSE	YYYY-MM-DDTHH:MM	4.00	xx.x	
		6.00 HOURS POST DOSE	YYYY-MM-DDTHH:MM	6.00	x.xx	
		8.00 HOURS POST DOSE	YYYY-MM-DDTHH:MM	8.00	x.xx	
- Value * was not considered for summary and inferential procedures. - Values <LOQ were considered as zero. - Age/Sex/Race: M=Male F=Female, A=Asian. Program: N:\Operations\PK\Template_PK_Mat13\report\pgm_cp\p_003.sas 08MAR2013:13:20 Production					Flags	Footnote
					BQL	



Deliverable #5: Rules for PK TFLs

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