

# IMPLEMENTATION OF CDISC ADAM IN THE PHARMACOKINETICS DEPARTMENT

Presented by Joanna Magielse, SGS Life Science Services

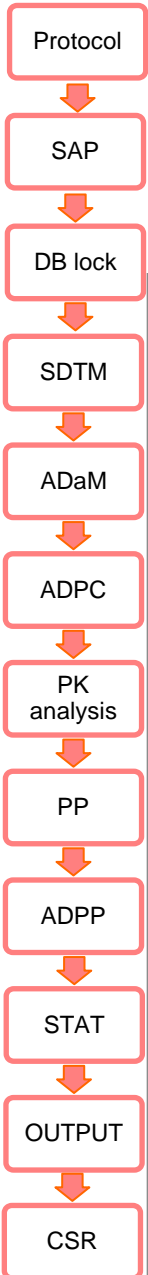
WHEN YOU NEED TO BE SURE



- Introduction
- Gain
- Pharmacokinetic analysis
- Conclusion

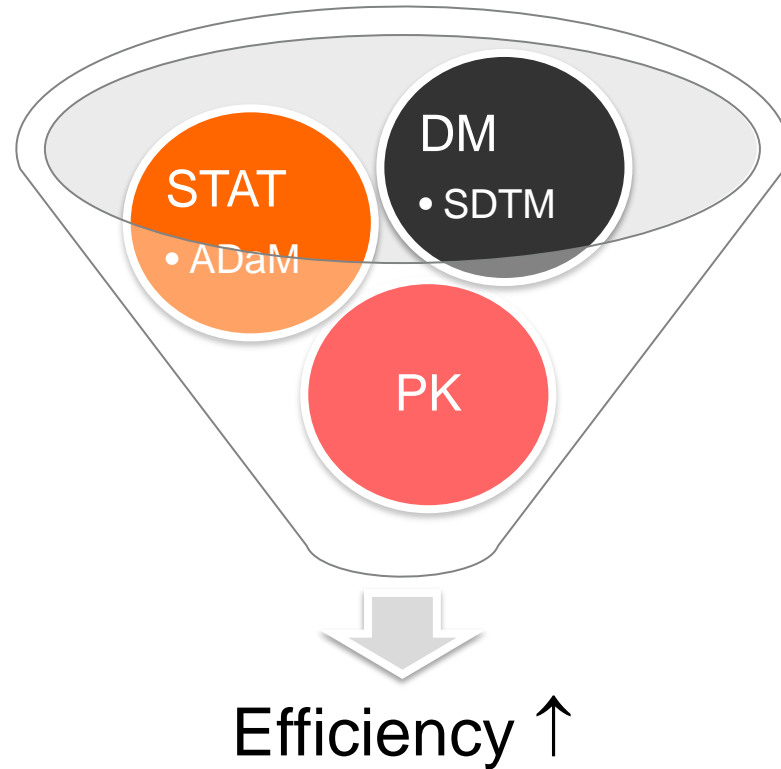
- **Introduction**
- Gain
- Pharmacokinetic analysis
- Conclusion

- Steps of PK study:
  - Protocol
  - Statistical Analysis Plan
  - Database Lock
    - SDTM datasets
    - ADaM datasets
  - Creation of ADPC dataset
  - PK analysis
  - Creation of PP dataset
  - Creation of ADPP dataset
  - Statistical analysis
  - Creation Tables, Listings, Figures
  - Clinical report

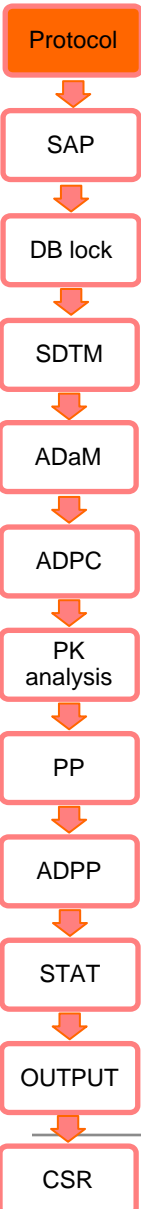


- Introduction
- **Gain**
- Pharmacokinetic analysis
- Conclusion

- Standardization
- ⇒ Efficiency ↑
- ⇒ Time ↓

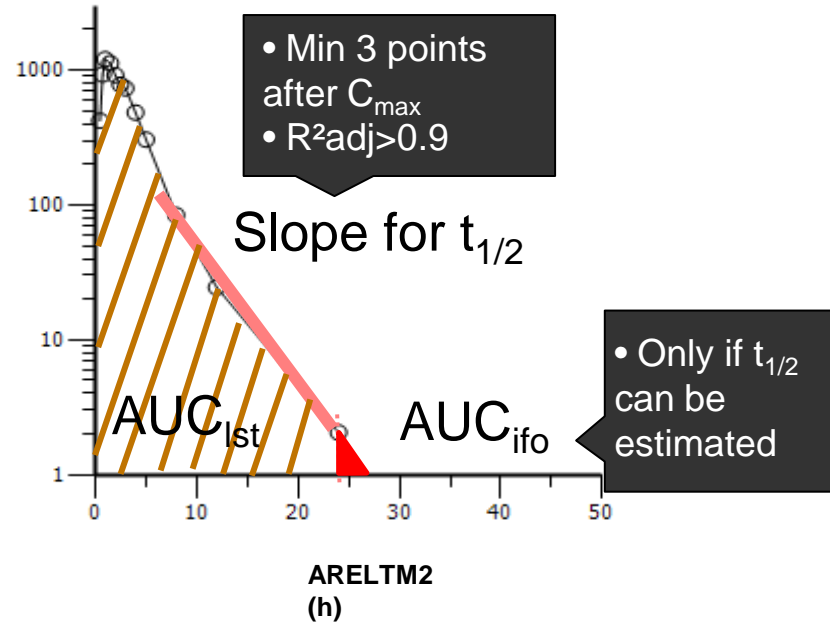
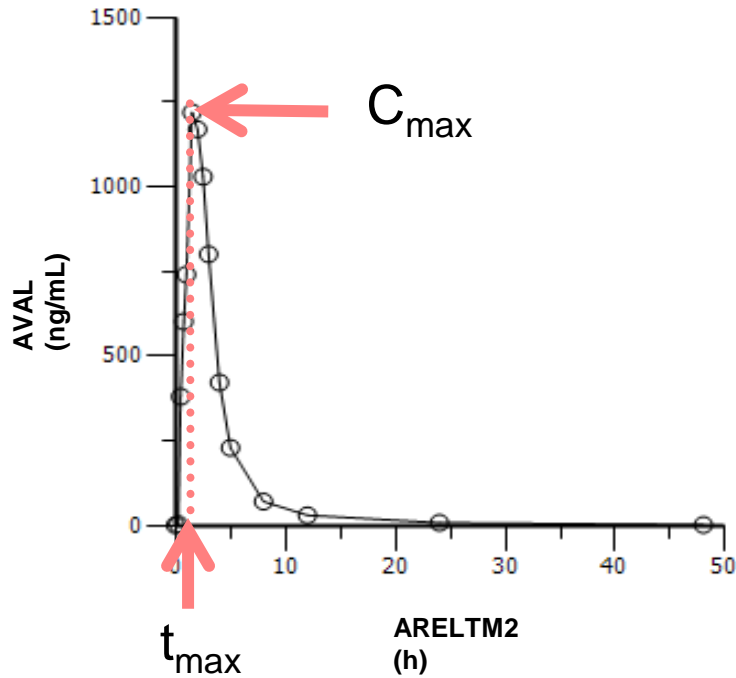


- Introduction
- Gain
- **Pharmacokinetic analysis**
- Conclusion



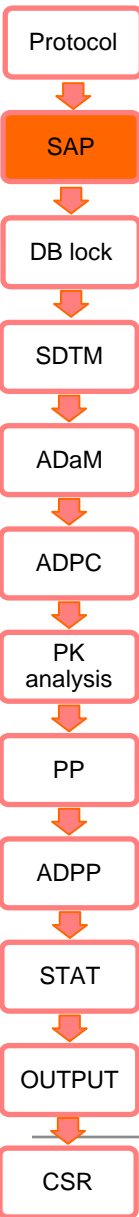
■ Protocol:

- Pharmacokinetic parameters:  $C_{max}$   $t_{max}$   $t_{1/2}$   $AUC_{lst}$   $AUC_{ifo}$

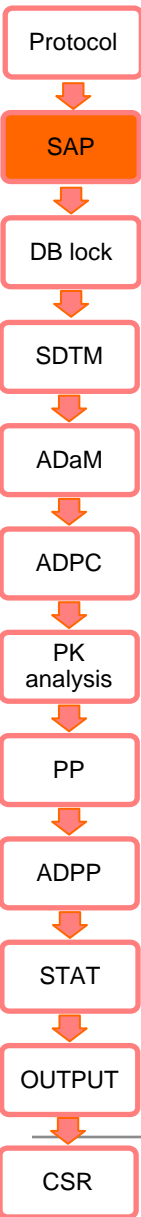


AVAL: Analysis value  
ARELTM: Analysis relative time





- Statistical Analysis Plan
  - PK population
    - Co medication:
      - Drug/drug interactions
      - Drug with motility interference
    - Adverse events:
      - Vomiting / diarrhea



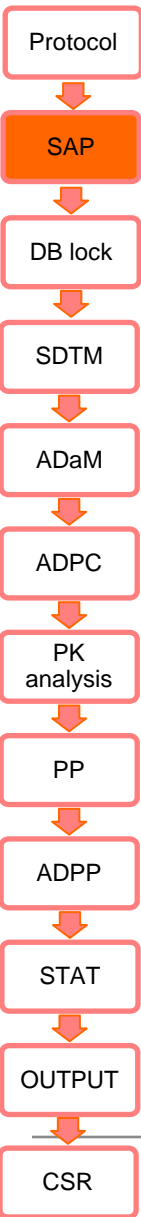
## ■ Statistical Analysis Plan

### ■ Handling of data:

- If predose missing => **AVAL = 0 for PK analysis**

SUBJID	TRTA	PCCAT	PCTPT	PCSTRESC	PCSTRESN	PCSTRESU	PCSTAT
2	TEST	COMPOUND X	PRE-DOSE	.		ng/mL	NOT DONE
2	TEST	COMPOUND X	0.25H	1590	1590	ng/mL	
2	TEST	COMPOUND X	0.5H	2070	2070	ng/mL	
2	TEST	COMPOUND X	0.75H	1490	1490	ng/mL	
2	TEST	COMPOUND X	1H	1140	1140	ng/mL	
2	TEST	COMPOUND X	1.5H	768	768	ng/mL	
2	TEST	COMPOUND X	2H	593	593	ng/mL	
2	TEST	COMPOUND X	2.5H	429	429	ng/mL	
2	TEST	COMPOUND X	3H	375	375	ng/mL	
2	TEST	COMPOUND X	4H	222	222	ng/mL	
2	TEST	COMPOUND X	5H	120	120	ng/mL	
2	TEST	COMPOUND X	8H	60.9	60.9	ng/mL	
2	TEST	COMPOUND X	12H	33.1	33.1	ng/mL	
2	TEST	COMPOUND X	24H	13.9	13.9	ng/mL	
2	TEST	COMPOUND X	48H	3.66	3.66	ng/mL	

AVAL: Analysis Value



## ■ Statistical Analysis Plan

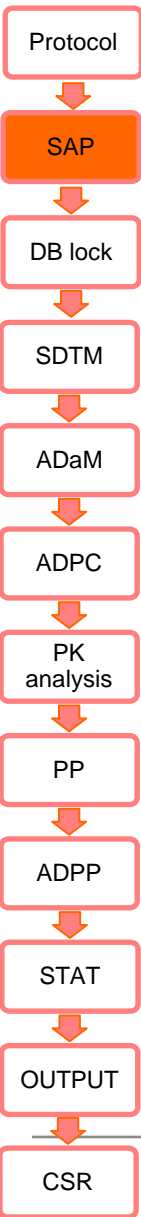
### ■ Handling of data:

- If BLoQ => AVAL = 0 for PK analysis and descriptive statistics

SUBJID	TRTA	PCCAT	PCTPT	PCSTRESC	PCSTRESN	PCSTRESU
1	TEST	COMPOUND X	PRE-DOSE	<1	.	ng/mL
1	TEST	COMPOUND X	0.25H	99	99	ng/mL
1	TEST	COMPOUND X	0.5H	1511	1511	ng/mL
1	TEST	COMPOUND X	0.75H	1718	1718	ng/mL
1	TEST	COMPOUND X	1H	1852	1852	ng/mL
1	TEST	COMPOUND X	1.5H	1360	1360	ng/mL
1	TEST	COMPOUND X	2H	1410	1410	ng/mL
1	TEST	COMPOUND X	2.5H	1030	1030	ng/mL
1	TEST	COMPOUND X	3H	799	799	ng/mL
1	TEST	COMPOUND X	4H	490	490	ng/mL
1	TEST	COMPOUND X	5H	254	254	ng/mL
1	TEST	COMPOUND X	8H	74.4	74.4	ng/mL
1	TEST	COMPOUND X	12H	16.5	16.5	ng/mL
1	TEST	COMPOUND X	24H	<1	.	ng/mL
1	TEST	COMPOUND X	48H	<1	.	ng/mL

BLoQ: Below Limit of Quantification

AVAL: Analysis Value

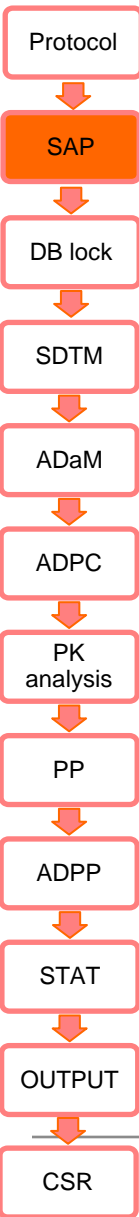


### ■ Statistical Analysis Plan

#### ■ Handling of data:

- If embedded BLoQ => **exclude from PK analysis**

SUBJID	TRTA	PCCAT	PCTPT	PCSTRESC	PCSTRESN	PCSTRESU
3	TEST	COMPOUND X	PRE-DOSE	<1	.	ng/mL
3	TEST	COMPOUND X	0.25H	251	251	ng/mL
3	TEST	COMPOUND X	0.5H	1170	1170	ng/mL
3	TEST	COMPOUND X	0.75H	1100	1100	ng/mL
3	TEST	COMPOUND X	1H	1270	1270	ng/mL
3	TEST	COMPOUND X	1.5H	793	793	ng/mL
3	TEST	COMPOUND X	2H	604	604	ng/mL
3	TEST	COMPOUND X	2.5H	566	566	ng/mL
3	TEST	COMPOUND X	3H	388	388	ng/mL
3	TEST	COMPOUND X	4H	257	257	ng/mL
3	TEST	COMPOUND X	5H	140	140	ng/mL
3	TEST	COMPOUND X	8H	41.6	41.6	ng/mL
3	TEST	COMPOUND X	12H	15.5	15.5	ng/mL
3	TEST	COMPOUND X	24H	<1	.	ng/mL
3	TEST	COMPOUND X	48H	1.15	1.15	ng/mL

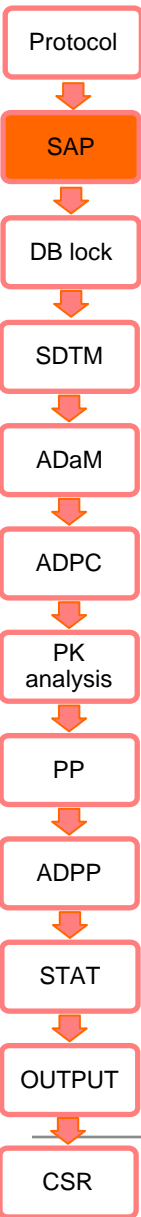


### ■ Statistical Analysis Plan

#### ■ Handling of data:

- Time deviations >10% => **exclude from descriptive statistics**

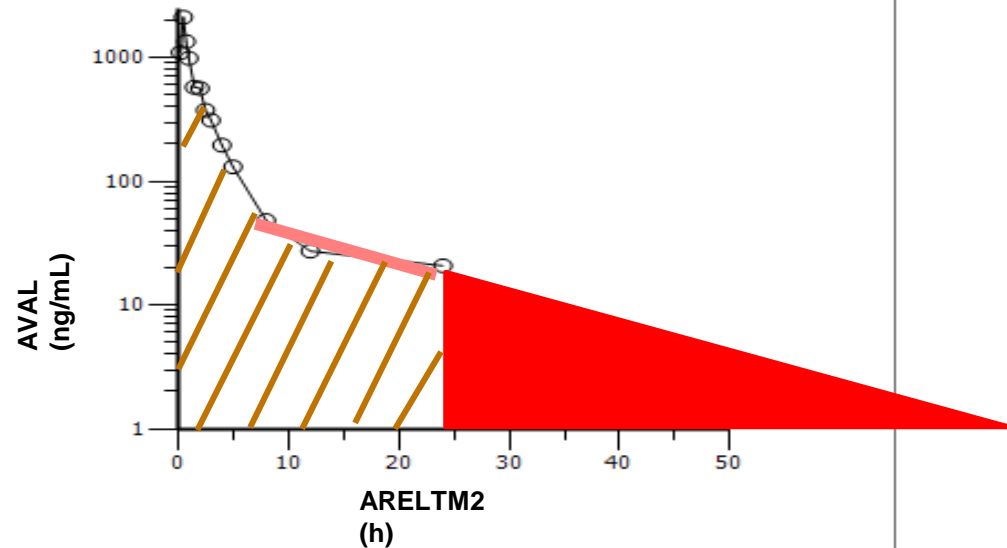
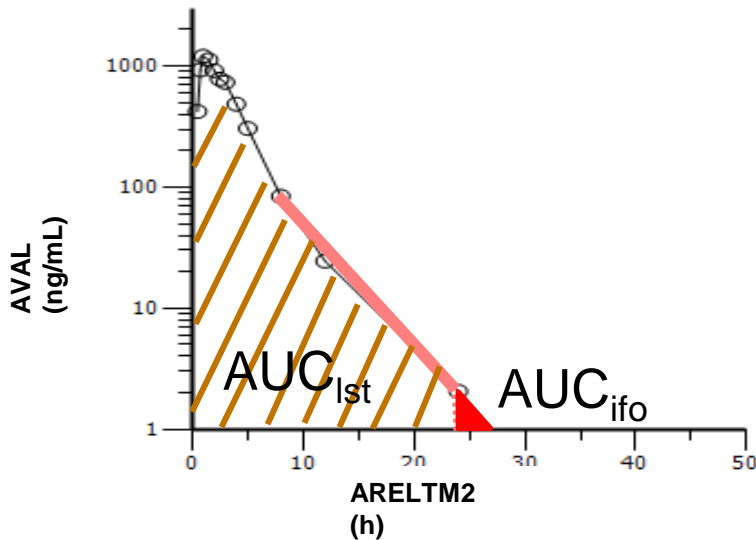
SUBJID	TRTA	PCCAT	PCTPT	EXSTDTC	PCDTC
5	TEST	COMPOUND X	PRE-DOSE	2013-07-05T09:16	2013-07-05T09:11
5	TEST	COMPOUND X	0.25H	2013-07-05T09:16	2013-07-05T09:31
5	TEST	COMPOUND X	0.5H	2013-07-05T09:16	2013-07-05T09:46
5	TEST	COMPOUND X	0.75H	2013-07-05T09:16	2013-07-05T10:01
5	TEST	COMPOUND X	1H	2013-07-05T09:16	2013-07-05T10:16
5	TEST	COMPOUND X	1.5H	2013-07-05T09:16	2013-07-05T10:46
5	TEST	COMPOUND X	2H	2013-07-05T09:16	2013-07-05T11:16
5	TEST	COMPOUND X	2.5H	2013-07-05T09:16	2013-07-05T11:46
5	TEST	COMPOUND X	3H	2013-07-05T09:16	2013-07-05T12:16
5	TEST	COMPOUND X	4H	2013-07-05T09:16	2013-07-05T13:46
5	TEST	COMPOUND X	5H	2013-07-05T09:16	2013-07-05T14:16
5	TEST	COMPOUND X	8H	2013-07-05T09:16	2013-07-05T17:16
5	TEST	COMPOUND X	12H	2013-07-05T09:16	2013-07-05T21:16
5	TEST	COMPOUND X	24H	2013-07-05T09:16	2013-07-06T09:16
5	TEST	COMPOUND X	48H	2013-07-05T09:16	2013-07-07T09:16



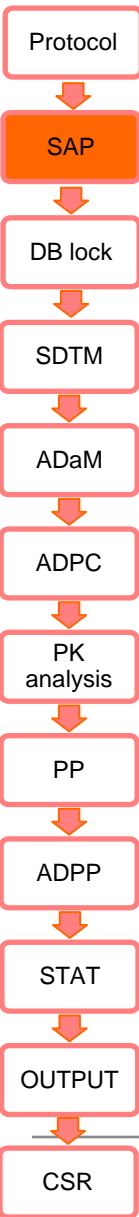
### ■ Statistical Analysis Plan

#### ■ Statistical analysis:

- $AUC_{peo} > 20\%$  => **exclude  $AUC_{ifo}$  from statistical analysis**



$AUC_{peo}$ : AUC %extrapolation  
 $AUC_{ifo}$ : AUC infinity

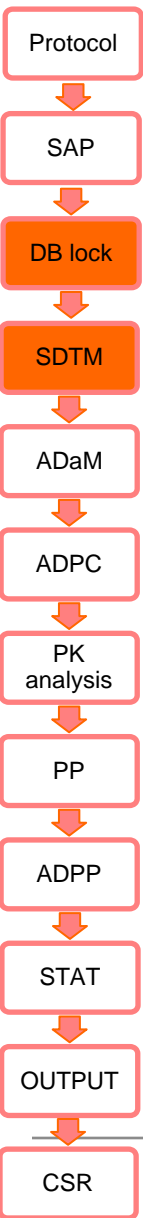


### ■ Statistical Analysis Plan

#### ■ Statistical analysis:

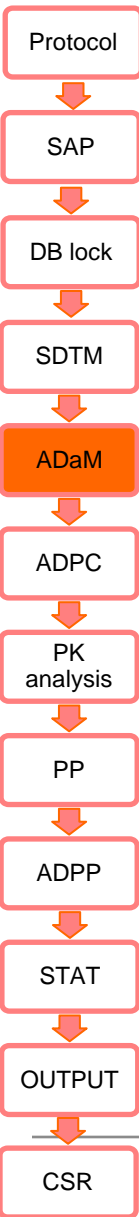
- Bioequivalence studies: If quantifiable concentration at pre-dose > 5% C<sub>max</sub> => **subject will be excluded**

SUBJID	TRTA	PCCAT	PCTPT	PCSTRESC	PCSTRESN	PCSTRESU
6	TEST	COMPOUND X	PRE-DOSE	87	87	ng/mL
6	TEST	COMPOUND X	0.25H	282	282	ng/mL
6	TEST	COMPOUND X	0.5H	965	965	ng/mL
6	TEST	COMPOUND X	0.75H	820	820	ng/mL
6	TEST	COMPOUND X	1H	547	547	ng/mL
6	TEST	COMPOUND X	1.5H	384	384	ng/mL
6	TEST	COMPOUND X	2H	336	336	ng/mL
6	TEST	COMPOUND X	2.5H	258	258	ng/mL
6	TEST	COMPOUND X	3H	202	202	ng/mL
6	TEST	COMPOUND X	4H	127	127	ng/mL
6	TEST	COMPOUND X	5H	92.4	92.4	ng/mL
6	TEST	COMPOUND X	8H	43.9	43.9	ng/mL
6	TEST	COMPOUND X	12H	57.5	57.5	ng/mL
6	TEST	COMPOUND X	24H	42.6	42.6	ng/mL
6	TEST	COMPOUND X	48H	9.93	9.93	ng/mL



- Database lock: SDTM datasets
  - DM (Demographics)
  - EX (Exposure)
  - PC (Pharmacokinetic concentrations)
  - CM (Concomitant medications)
  - AE (Adverse events)
  - DV (Protocol deviations)
  - CO (Comments)

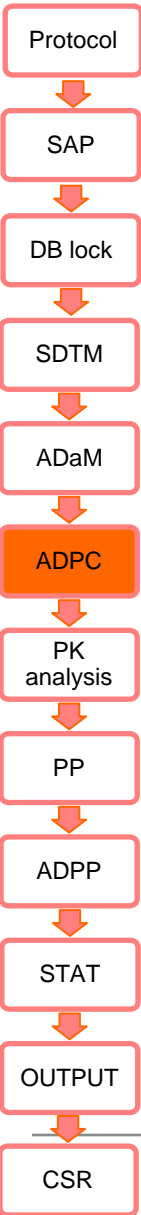




### ■ ADaM datasets

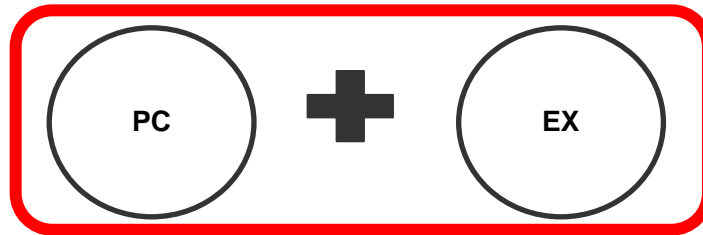
- ADSL (Subject-level Analysis Dataset)
- *ADAPER* (*Subject Analysis periods Dataset*)
- (ADEX) (Analysis Dataset containing Exposure Data)

## CREATION OF ADPC

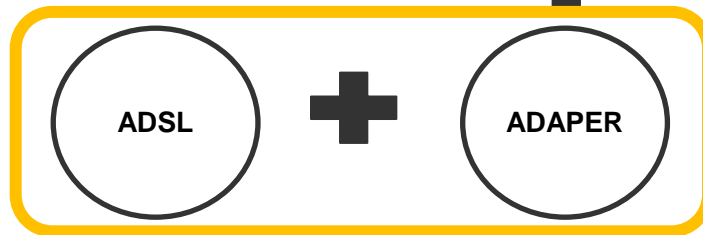


- In SAS
- Based upon define.xml

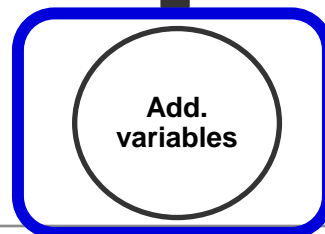
SDTM



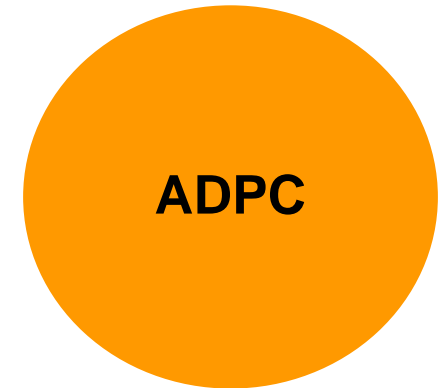
ADAM



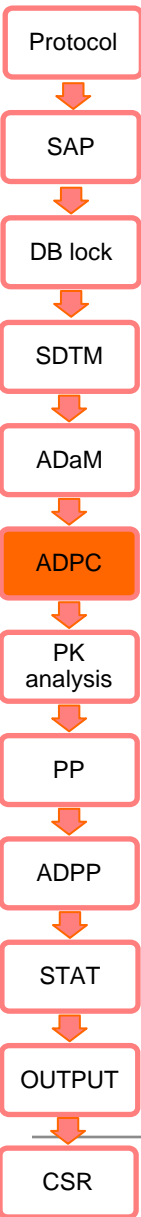
PK



=



# CREATION OF ADPC



## ■ Analysis variable metadata

Dataset name	Variable name	Source / Derivation	Core
domain	name	source	core
ADPC	STUDYID	PC.STUDYID	Req
ADPC	PART	ADSL.PART	Cond
ADPC	USUBJID	PC.USUBJID	Req
ADPC	SUBJID	ADSL.SUBJID	Perm
ADPC	ARM	ADSL.ARM	Perm
ADPC	ARMN	ADSL.ARMN	Perm
ADPC	TRTP	ADAPER.TRTP	Cond
ADPC	TRTPN	ADAPER.TRTPN	Perm
ADPC	TRTA	ADAPER.TRTA	Cond
ADPC	TRTAN	ADAPER.TRTAN	Perm
ADPC	APERIOD	ADAPER.APERIOD	Perm
ADPC	APERIODC	ADAPER.APERIODC	Perm
ADPC	PCSEQ	PC.PCSEQ	Req
ADPC	PCTESTCD	PC.PCTESTCD	Perm
ADPC	PCTEST	PC.PCTEST	Perm
ADPC	PARAM	Derived	Req
ADPC	PARAMN	Derived	Perm
ADPC	PARAMCD	Derived	Req
ADPC	PARAMTYP	Derived	Perm

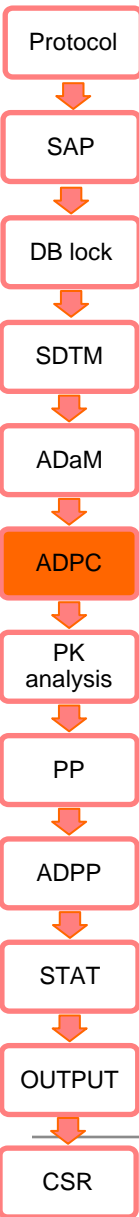
ADAM

ADAM

SDTM

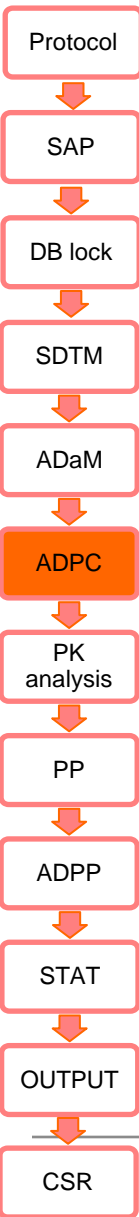
PK

## CREATION OF ADPC



- Additional/derived variables: BDS
  - PARAM, PARAMN, PARAMCD
  - ADTM, ASTDTM, AENDTM
  - AVISIT, AVISITN
  - ATPT, ATPTN
  - ARELTM, ARELTMU, *ANCHOR*
  - ANLzzFL, *ANLzzFD*
  - AVAL, AVALC
  - CRITy, CRITyFL, CRITyFN

## CREATION OF ADPC



### ■ Additional/derived variables

- PARAM, PARAMN, PARAMCD
  - PARAM: pharmacokinetic concentration used for PK analysis
  - PARAMCD: PKCONC
- ADTM, ASTDTM, AENDTM
- AVISIT, AVISITN
- ATPT, ATPTN
- ARELTM, ARELTMU, ANCHOR
- ANLzzFL, *ANLzzFD*
- AVAL, AVALC
- CRITy, CRITyFL, CRITyFN

## ■ PARAM, PARAMCD

SUBJID	PCTESTCD	PCTEST	PARAM	PARAMCD	PCCAT
1	PKCONC	Pharmacokinetic Concentration	PHARMACOKINETIC CONCENTRATION USED FOR PK CALCULATIONS	PKCONC	COMPOUND X
1	PKCONC	Pharmacokinetic Concentration	PHARMACOKINETIC CONCENTRATION USED FOR PK CALCULATIONS	PKCONC	COMPOUND X
1	PKCONC	Pharmacokinetic Concentration	PHARMACOKINETIC CONCENTRATION USED FOR PK CALCULATIONS	PKCONC	COMPOUND X
1	PKCONC	Pharmacokinetic Concentration	PHARMACOKINETIC CONCENTRATION USED FOR PK CALCULATIONS	PKCONC	COMPOUND X
1	PKCONC	Pharmacokinetic Concentration	PHARMACOKINETIC CONCENTRATION USED FOR PK CALCULATIONS	PKCONC	COMPOUND X
1	PKCONC	Pharmacokinetic Concentration	PHARMACOKINETIC CONCENTRATION USED FOR PK CALCULATIONS	PKCONC	COMPOUND X
1	PKCONC	Pharmacokinetic Concentration	PHARMACOKINETIC CONCENTRATION USED FOR PK CALCULATIONS	PKCONC	COMPOUND X
1	PKCONC	Pharmacokinetic Concentration	PHARMACOKINETIC CONCENTRATION USED FOR PK CALCULATIONS	PKCONC	COMPOUND X
1	PKCONC	Pharmacokinetic Concentration	PHARMACOKINETIC CONCENTRATION USED FOR PK CALCULATIONS	PKCONC	COMPOUND X
1	PKCONC	Pharmacokinetic Concentration	PHARMACOKINETIC CONCENTRATION USED FOR PK CALCULATIONS	PKCONC	COMPOUND X
1	PKCONC	Pharmacokinetic Concentration	PHARMACOKINETIC CONCENTRATION USED FOR PK CALCULATIONS	PKCONC	COMPOUND X
1	PKCONC	Pharmacokinetic Concentration	PHARMACOKINETIC CONCENTRATION USED FOR PK CALCULATIONS	PKCONC	COMPOUND X
1	PKCONC	Pharmacokinetic Concentration	PHARMACOKINETIC CONCENTRATION USED FOR PK CALCULATIONS	PKCONC	COMPOUND X
1	PKCONC	Pharmacokinetic Concentration	PHARMACOKINETIC CONCENTRATION USED FOR PK CALCULATIONS	PKCONC	COMPOUND X
1	PKCONC	Pharmacokinetic Concentration	PHARMACOKINETIC CONCENTRATION USED FOR PK CALCULATIONS	PKCONC	COMPOUND X
1	PKCONC	Pharmacokinetic Concentration	PHARMACOKINETIC CONCENTRATION USED FOR PK CALCULATIONS	PKCONC	COMPOUND X

## CREATION OF ADPC



### ■ Additional/derived variables

- PARAM, PARAMN, PARAMCD
- ADTM, ASTDTM, AENDTM
  - Derived from PCDTC
- AVISIT, AVISITN
- ATPT, ATPTN
- ARELTM, ARELTMU, ANCHOR
- ANLzzFL, *ANLzzFD*
- AVAL, AVALC
- CRITy, CRITyFL, CRITyFN

# CREATION OF ADPC

## ■ ADTM

SUBJID	TRTA	TRTAN	PCDTC	ADTM
1	TEST		2013-07-05T08:55	2013-07-05T08:55:00
1	TEST		2013-07-05T09:15	2013-07-05T09:15:00
1	TEST		2013-07-05T09:30	2013-07-05T09:30:00
1	TEST		2013-07-05T09:45	2013-07-05T09:45:00
1	TEST		2013-07-05T10:00	2013-07-05T10:00:00
1	TEST		2013-07-05T10:30	2013-07-05T10:30:00
1	TEST		2013-07-05T11:01	2013-07-05T11:01:00
1	TEST		2013-07-05T11:30	2013-07-05T11:30:00
1	TEST		2013-07-05T12:00	2013-07-05T12:00:00
1	TEST		2013-07-05T13:00	2013-07-05T13:00:00
1	TEST		2013-07-05T14:00	2013-07-05T14:00:00
1	TEST		2013-07-05T17:00	2013-07-05T17:00:00
1	TEST		2013-07-05T21:00	2013-07-05T21:00:00
1	TEST		2013-07-06T09:00	2013-07-06T09:00:00
1	TEST		2013-07-07T09:02	2013-07-07T09:02:00

Character

Numeric  
SAS format:  
is8601dt.



## CREATION OF ADPC



### ■ Additional/derived variables

- PARAM, PARAMN, PARAMCD
- ADTM, ASTDTM, AENDTM
- AVISIT, AVISITN
  - Derived from VISIT and VISITNUM
  - all PK conc that refer to same exposure
- ATPT, ATPTN
- ARELTM, ARELTMU, ANCHOR
- ANLzzFL, *ANLzzFD*
- AVAL, AVALC
- CRITy, CRITyFL, CRITyFN

# CREATION OF ADPC

- AVISIT, AVISITN

SUBJID	TRTA	VISITNUM	VISIT	PCTPT	AVISIT	AVISITN
1	TEST	1.001	PERIOD1_DAY1	PRE-DOSE	DAY 1	1
1	TEST	1.001	PERIOD1_DAY1	0.25H	DAY 1	1
1	TEST	1.001	PERIOD1_DAY1	0.5H	DAY 1	1
1	TEST	1.001	PERIOD1_DAY1	0.75H	DAY 1	1
1	TEST	1.001	PERIOD1_DAY1	1H	DAY 1	1
1	TEST	1.001	PERIOD1_DAY1	1.5H	DAY 1	1
1	TEST	1.001	PERIOD1_DAY1	2H	DAY 1	1
1	TEST	1.001	PERIOD1_DAY1	2.5H	DAY 1	1
1	TEST	1.001	PERIOD1_DAY1	3H	DAY 1	1
1	TEST	1.001	PERIOD1_DAY1	4H	DAY 1	1
1	TEST	1.001	PERIOD1_DAY1	5H	DAY 1	1
1	TEST	1.001	PERIOD1_DAY1	8H	DAY 1	1
1	TEST	1.001	PERIOD1_DAY1	12H	DAY 1	1
1	TEST	1.002	PERIOD1_DAY2	24H	DAY 1	1
1	TEST	1.003	PERIOD1_DAY3	48H	DAY 1	1

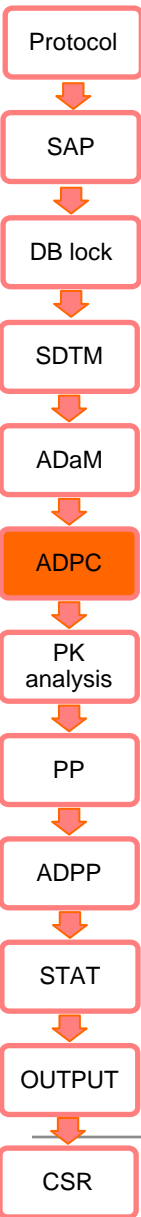
## CREATION OF ADPC



### ■ Additional/derived variables

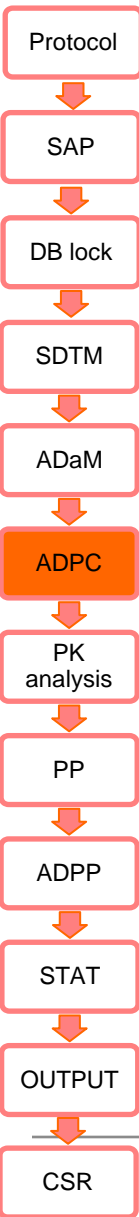
- PARAM, PARAMN, PARAMCD
- ADTM, ASTDTM, AENDTM
- AVISIT, AVISITN
- ATPT, ATPTN
  - Derived from PCTPT and PCTPTNUM
- ARELTM, ARELTMU, ANCHOR
- ANLzzFL, *ANLzzFD*
- AVAL, AVALC
- CRITy, CRITyFL, CRITyFN

## CREATION OF ADPC



### ■ ATPT, ATPTN

SUBJID	TRTA	TRTAM	PCTPT	PCTPTNUM	ATPT	ATPTN
1	TEST	2	PRE-DOSE	-1	0H	0
1	TEST	2	0.25H	15	0.25H	0.25
1	TEST	2	0.5H	30	0.5H	0.5
1	TEST	2	0.75H	45	0.75H	0.75
1	TEST	2	1H	60	1H	1
1	TEST	2	1.5H	90	1.5H	1.5
1	TEST	2	2H	120	2H	2
1	TEST	2	2.5H	150	2.5H	2.5
1	TEST	2	3H	180	3H	3
1	TEST	2	4H	240	4H	4
1	TEST	2	5H	300	5H	5
1	TEST	2	8H	480	8H	8
1	TEST	2	12H	720	12H	12
1	TEST	2	24H	1440	24H	24
1	TEST	2	48H	2880	48H	48



### ■ Additional/derived variables

- PARAM, PARAMN, PARAMCD
- ADTM, ASTDTM, AENDTM
- AVISIT, AVISITN
- ATPT, ATPTN
- ARELTM, ARELTMU, *ANCHOR*
  - *ANCHOR*: PCRFTDTC / EXSTDTC / PCDTC
  - *ARELTM1*: PCDTC – EXSTDTC
  - *ARELTM2*: if ARELTM1 < 0 (predose): ARELTM2 = 0  
others: ARELTM2 = ARELTM1
- ANLzzFL, *ANLzzFD*
- AVAL, AVALC
- CRITy, CRITyFL, CRITyFN

# CREATION OF ADPC

- ARELTM, ARELMTU, ANCHOR

SUBJID	TRTA	PCDTC	EXSTDTC	ATPT	ATPTN	ANCHOR1	ARELTM1	ANCHOR2	ARELTM2	ARELMTU
1	TEST	2013-07-05T08:55	2013-07-05T09:00	0H	0	EXSTDTC	-0.08	PCDTC	0.00	HOURS
1	TEST	2013-07-05T09:15	2013-07-05T09:00	0.25H	0.25	EXSTDTC	0.25	EXSTDTC	0.25	HOURS
1	TEST	2013-07-05T09:30	2013-07-05T09:00	0.5H	0.5	EXSTDTC	0.50	EXSTDTC	0.50	HOURS
1	TEST	2013-07-05T09:45	2013-07-05T09:00	0.75H	0.75	EXSTDTC	0.75	EXSTDTC	0.75	HOURS
1	TEST	2013-07-05T10:00	2013-07-05T09:00	1H	1	EXSTDTC	1.00	EXSTDTC	1.00	HOURS
1	TEST	2013-07-05T10:30	2013-07-05T09:00	1.5H	1.5	EXSTDTC	1.50	EXSTDTC	1.50	HOURS
1	TEST	2013-07-05T11:01	2013-07-05T09:00	2H	2	EXSTDTC	2.02	EXSTDTC	2.02	HOURS
1	TEST	2013-07-05T11:30	2013-07-05T09:00	2.5H	2.5	EXSTDTC	2.50	EXSTDTC	2.50	HOURS
1	TEST	2013-07-05T12:00	2013-07-05T09:00	3H	3	EXSTDTC	3.00	EXSTDTC	3.00	HOURS
1	TEST	2013-07-05T13:00	2013-07-05T09:00	4H	4	EXSTDTC	4.00	EXSTDTC	4.00	HOURS
1	TEST	2013-07-05T14:00	2013-07-05T09:00	5H	5	EXSTDTC	5.00	EXSTDTC	5.00	HOURS
1	TEST	2013-07-05T17:00	2013-07-05T09:00	8H	8	EXSTDTC	8.00	EXSTDTC	8.00	HOURS
1	TEST	2013-07-05T21:00	2013-07-05T09:00	12H	12	EXSTDTC	12.00	EXSTDTC	12.00	HOURS
1	TEST	2013-07-06T09:00	2013-07-05T09:00	24H	24	EXSTDTC	24.00	EXSTDTC	24.00	HOURS
1	TEST	2013-07-07T09:02	2013-07-05T09:00	48H	48	EXSTDTC	48.03	EXSTDTC	48.03	HOURS

## CREATION OF ADPC



### ■ Additional/derived variables

- PARAM, PARAMN, PARAMCD
- ADTM, ASTDTM, AENDTM
- AVISIT, AVISITN
- ATPT, ATPTN
- ARELTM, ARELTMU, ANCHOR
- ANLzzFL, *ANLzzFD*
  - Select set of records for analysis:
    - PK analysis
    - Descriptive statistics
    - Inferential statistical analysis
- AVAL, AVALC
- CRITy, CRITyFL, CRITyFN

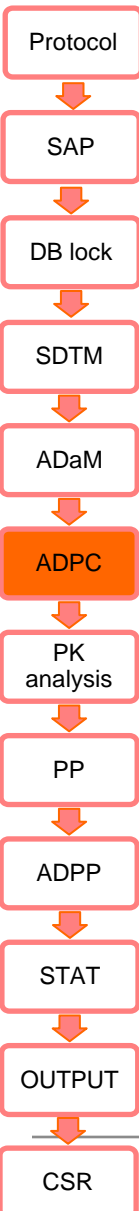
# CREATION OF ADPC

■ ANLzzFL, ANLzzFD

SUBJID	TRTA	PCCAT	PCSTRESC	PCSTRESN	PCSTRESU	AVAL	AVALC	AVISIT	ATPT	ATPTM	ANL01FL	ANL01FD	ANL02FL	ANL02FD
1	TEST	COMPOUND X	<1	.	ng/mL	0	0	DAY 1	0H	0	Y	PK ANALYSIS	Y	DESCR STAT
1	TEST	COMPOUND X	99	99	ng/mL	99	99	DAY 1	0.25H	0.25	Y	PK ANALYSIS	Y	DESCR STAT
1	TEST	COMPOUND X	1511	1511	ng/mL	1511	1511	DAY 1	0.5H	0.5	Y	PK ANALYSIS	Y	DESCR STAT
1	TEST	COMPOUND X	1718	1718	ng/mL	1718	1718	DAY 1	0.75H	0.75	Y	PK ANALYSIS	Y	DESCR STAT
1	TEST	COMPOUND X	1852	1852	ng/mL	1852	1852	DAY 1	1H	1	Y	PK ANALYSIS	Y	DESCR STAT
1	TEST	COMPOUND X	1360	1360	ng/mL	1360	1360	DAY 1	1.5H	1.5	Y	PK ANALYSIS	Y	DESCR STAT
1	TEST	COMPOUND X	1410	1410	ng/mL	1410	1410	DAY 1	2H	2	Y	PK ANALYSIS	Y	DESCR STAT
1	TEST	COMPOUND X	1030	1030	ng/mL	1030	1030	DAY 1	2.5H	2.5	Y	PK ANALYSIS	Y	DESCR STAT
1	TEST	COMPOUND X	799	799	ng/mL	799	799	DAY 1	3H	3	Y	PK ANALYSIS	Y	DESCR STAT
1	TEST	COMPOUND X	490	490	ng/mL	490	490	DAY 1	4H	4	Y	PK ANALYSIS	Y	DESCR STAT
1	TEST	COMPOUND X	254	254	ng/mL	254	254	DAY 1	5H	5	Y	PK ANALYSIS	Y	DESCR STAT
1	TEST	COMPOUND X	74.4	74.4	ng/mL	74.4	74.4	DAY 1	8H	8	Y	PK ANALYSIS	Y	DESCR STAT
1	TEST	COMPOUND X	16.5	16.5	ng/mL	16.5	16.5	DAY 1	12H	12	Y	PK ANALYSIS	Y	DESCR STAT
1	TEST	COMPOUND X	<1	.	ng/mL	0	0	DAY 1	24H	24	Y	PK ANALYSIS	Y	DESCR STAT
1	TEST	COMPOUND X	<1	.	ng/mL	0	0	DAY 1	48H	48	Y	PK ANALYSIS	Y	DESCR STAT



## CREATION OF ADPC



### ■ Additional/derived variables

- PARAM, PARAMN, PARAMCD
- ADTM, ASTDTM, AENDTM
- AVISIT, AVISITN
- ATPT, ATPTN
- ARELTM, ARELTMU, ANCHOR
- ANLzzFL, *ANLzzFD*
- AVAL, AVALC
  - AVAL= PCSTRESN
    - **Missing predose: AVAL = 0**
    - BLoQ: AVAL = 0
    - Embedded BLoQ: exclude from PK analysis
- CRITy, CRITyFL, CRITyFN

# CREATION OF ADPC

- Missing predose => 0

SUBJID	TRTA	PCCAT	PCSTRESC	PCSTRESN	PCSTRESU	AVAL	AVALC	PCSTAT	ATPT	ATPTN	ANL01FL	ANL01FD	ANL02FL	ANL02FD
2	TEST	COMPOUND X	.	.	ng/mL	0	0	NOT DONE	0H	0	Y	PK ANALYSIS		DESCR STAT
2	TEST	COMPOUND X	1590	1590	ng/mL	1590	1590		0.25H	0.25	Y	PK ANALYSIS	Y	DESCR STAT
2	TEST	COMPOUND X	2070	2070	ng/mL	2070	2070		0.5H	0.5	Y	PK ANALYSIS	Y	DESCR STAT
2	TEST	COMPOUND X	1490	1490	ng/mL	1490	1490		0.75H	0.75	Y	PK ANALYSIS	Y	DESCR STAT
2	TEST	COMPOUND X	1140	1140	ng/mL	1140	1140		1H	1	Y	PK ANALYSIS	Y	DESCR STAT
2	TEST	COMPOUND X	768	768	ng/mL	768	768		1.5H	1.5	Y	PK ANALYSIS	Y	DESCR STAT
2	TEST	COMPOUND X	593	593	ng/mL	593	593		2H	2	Y	PK ANALYSIS	Y	DESCR STAT
2	TEST	COMPOUND X	429	429	ng/mL	429	429		2.5H	2.5	Y	PK ANALYSIS	Y	DESCR STAT
2	TEST	COMPOUND X	375	375	ng/mL	375	375		3H	3	Y	PK ANALYSIS	Y	DESCR STAT
2	TEST	COMPOUND X	222	222	ng/mL	222	222		4H	4	Y	PK ANALYSIS	Y	DESCR STAT
2	TEST	COMPOUND X	120	120	ng/mL	120	120		5H	5	Y	PK ANALYSIS	Y	DESCR STAT
2	TEST	COMPOUND X	60.9	60.9	ng/mL	60.9	60.9		8H	8	Y	PK ANALYSIS	Y	DESCR STAT
2	TEST	COMPOUND X	33.1	33.1	ng/mL	33.1	33.1		12H	12	Y	PK ANALYSIS	Y	DESCR STAT
2	TEST	COMPOUND X	13.9	13.9	ng/mL	13.9	13.9		24H	24	Y	PK ANALYSIS	Y	DESCR STAT
2	TEST	COMPOUND X	3.66	3.66	ng/mL	3.66	3.66		48H	48	Y	PK ANALYSIS	Y	DESCR STAT

## CREATION OF ADPC



### ■ Additional/derived variables

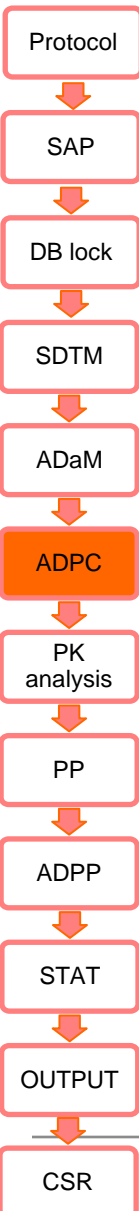
- PARAM, PARAMN, PARAMCD
- ADTM, ASTDTM, AENDTM
- AVISIT, AVISITN
- ATPT, ATPTN
- ARELTM, ARELTMU, ANCHOR
- ANLzzFL, ANLzzFD
- AVAL, AVALC
  - AVAL= PCSTRESN
    - Missing predose: AVAL = 0
    - **BLoQ: AVAL = 0**
    - Embedded BLoQ: exclude from PK analysis
- CRITy, CRITyFL, CRITyFN

# CREATION OF ADPC

■ BLoQ => 0

SUBJID	TRTA	PCCAT	PCSTRESC	PCSTRESN	PCSTRESU	AVAL	AVALC	CSTAT	PCTPT	ATPT	ATPTN	ANL01FL	ANL01FD	ANL02FL	ANL02FD
1	TEST	COMPOUND X	<1 .		ng/mL	0	0		PRE-DOSE	0H	0	Y	PK ANALYSIS	Y	DESCR STAT
1	TEST	COMPOUND X	99	99	ng/mL	99	99		0.25H	0.25H	0.25	Y	PK ANALYSIS	Y	DESCR STAT
1	TEST	COMPOUND X	1511	1511	ng/mL	1511	1511		0.5H	0.5H	0.5	Y	PK ANALYSIS	Y	DESCR STAT
1	TEST	COMPOUND X	1718	1718	ng/mL	1718	1718		0.75H	0.75H	0.75	Y	PK ANALYSIS	Y	DESCR STAT
1	TEST	COMPOUND X	1852	1852	ng/mL	1852	1852		1H	1H	1	Y	PK ANALYSIS	Y	DESCR STAT
1	TEST	COMPOUND X	1360	1360	ng/mL	1360	1360		1.5H	1.5H	1.5	Y	PK ANALYSIS	Y	DESCR STAT
1	TEST	COMPOUND X	1410	1410	ng/mL	1410	1410		2H	2H	2	Y	PK ANALYSIS	Y	DESCR STAT
1	TEST	COMPOUND X	1030	1030	ng/mL	1030	1030		2.5H	2.5H	2.5	Y	PK ANALYSIS	Y	DESCR STAT
1	TEST	COMPOUND X	799	799	ng/mL	799	799		3H	3H	3	Y	PK ANALYSIS	Y	DESCR STAT
1	TEST	COMPOUND X	490	490	ng/mL	490	490		4H	4H	4	Y	PK ANALYSIS	Y	DESCR STAT
1	TEST	COMPOUND X	254	254	ng/mL	254	254		5H	5H	5	Y	PK ANALYSIS	Y	DESCR STAT
1	TEST	COMPOUND X	74.4	74.4	ng/mL	74.4	74.4		8H	8H	8	Y	PK ANALYSIS	Y	DESCR STAT
1	TEST	COMPOUND X	16.5	16.5	ng/mL	16.5	16.5		12H	12H	12	Y	PK ANALYSIS	Y	DESCR STAT
1	TEST	COMPOUND X	<1 .		ng/mL	0	0		24H	24H	24	Y	PK ANALYSIS	Y	DESCR STAT
1	TEST	COMPOUND X	<1 .		ng/mL	0	0		48H	48H	48	Y	PK ANALYSIS	Y	DESCR STAT

## CREATION OF ADPC



### ■ Additional/derived variables

- PARAM, PARAMN, PARAMCD
- ADTM, ASTDTM, AENDTM
- AVISIT, AVISITN
- ATPT, ATPTN
- ARELTM, ARELTMU, ANCHOR
- ANLzzFL, ANLzzFD
- AVAL, AVALC
  - AVAL= PCSTRESN
    - Missing predose: AVAL = 0
    - BLoQ: AVAL = 0
    - **Embedded BLoQ: exclude from PK analysis**
- CRITy, CRITyFL, CRITyFN

■ Embedded BLoQ

SUBJID	TRTA	PCCAT	PCSTRESC	PCSTRESN	PCSTRESU	AVAL	AVALC	PCSTAT	ATPT	ATPTM	ANL01FL	ANL01FD	ANL02FL	ANL02FD
3	TEST	COMPOUND X	<1	.	ng/mL	0	0		0H	0	Y	PK ANALYSIS	Y	DESCR STAT
3	TEST	COMPOUND X	251	251	ng/mL	251	251		0.25H	0.25	Y	PK ANALYSIS	Y	DESCR STAT
3	TEST	COMPOUND X	1170	1170	ng/mL	1170	1170		0.5H	0.5	Y	PK ANALYSIS	Y	DESCR STAT
3	TEST	COMPOUND X	1100	1100	ng/mL	1100	1100		0.75H	0.75	Y	PK ANALYSIS	Y	DESCR STAT
3	TEST	COMPOUND X	1270	1270	ng/mL	1270	1270		1H	1	Y	PK ANALYSIS	Y	DESCR STAT
3	TEST	COMPOUND X	793	793	ng/mL	793	793		1.5H	1.5	Y	PK ANALYSIS	Y	DESCR STAT
3	TEST	COMPOUND X	604	604	ng/mL	604	604		2H	2	Y	PK ANALYSIS	Y	DESCR STAT
3	TEST	COMPOUND X	566	566	ng/mL	566	566		2.5H	2.5	Y	PK ANALYSIS	Y	DESCR STAT
3	TEST	COMPOUND X	388	388	ng/mL	388	388		3H	3	Y	PK ANALYSIS	Y	DESCR STAT
3	TEST	COMPOUND X	257	257	ng/mL	257	257		4H	4	Y	PK ANALYSIS	Y	DESCR STAT
3	TEST	COMPOUND X	140	140	ng/mL	140	140		5H	5	Y	PK ANALYSIS	Y	DESCR STAT
3	TEST	COMPOUND X	41.6	41.6	ng/mL	41.6	41.6		8H	8	Y	PK ANALYSIS	Y	DESCR STAT
3	TEST	COMPOUND X	15.5	15.5	ng/mL	15.5	15.5		12H	12	Y	PK ANALYSIS	Y	DESCR STAT
3	TEST	COMPOUND X	<1	.	ng/mL	0	0		24H	24	Y	PK ANALYSIS	Y	DESCR STAT
3	TEST	COMPOUND X	1.15	1.15	ng/mL	1.15	1.15		48H	48	Y	PK ANALYSIS	Y	DESCR STAT

## CREATION OF ADPC



### ■ Additional/derived variables

- PARAM, PARAMN, PARAMCD
- ADTM, ASTDTM, AENDTM
- AVISIT, AVISITN
- ATPT, ATPTN
- ARELTM, ARELTMU, ANCHOR
- ANLzzFL, ANLzzFD
- AVAL, AVALC
- CRITy, CRITyFL, CRITyFN
  - Criteria evaluation
    - Time deviation > 10%
    - Predose > 5% Cmax (cross over studies)

## ■ Time deviation

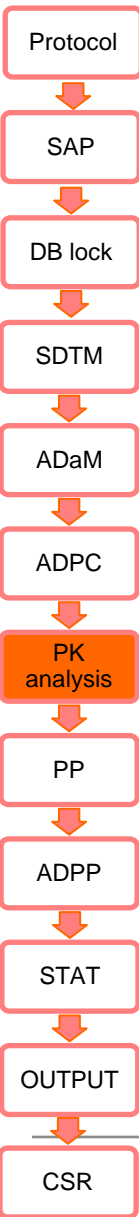
SUBJID	TRTA	TRTAN	AVAL	AVALC	ATPT	ATPTN	ANCHOR1	ARELTM1	ARELTMU	CRIT1	CRIT1FL	ANL01FL	ANL01FD	ANL02FL	ANL02FD
5	TEST	2	0	0	0H	0	EXSTDTC	-0.08	HOURS			Y	PK ANALYSIS	Y	DESCR STAT
5	TEST	2	0	0	0.25H	0.25	EXSTDTC	0.25	HOURS			Y	PK ANALYSIS	Y	DESCR STAT
5	TEST	2	8.65	8.65	0.5H	0.5	EXSTDTC	0.50	HOURS			Y	PK ANALYSIS	Y	DESCR STAT
5	TEST	2	31.5	31.5	0.75H	0.75	EXSTDTC	0.75	HOURS			Y	PK ANALYSIS	Y	DESCR STAT
5	TEST	2	50	50	1H	1	EXSTDTC	1.00	HOURS			Y	PK ANALYSIS	Y	DESCR STAT
5	TEST	2	152	152	1.5H	1.5	EXSTDTC	1.50	HOURS			Y	PK ANALYSIS	Y	DESCR STAT
5	TEST	2	372	372	2H	2	EXSTDTC	2.00	HOURS			Y	PK ANALYSIS	Y	DESCR STAT
5	TEST	2	539	539	2.5H	2.5	EXSTDTC	2.50	HOURS			Y	PK ANALYSIS	Y	DESCR STAT
5	TEST	2	566	566	3H	3	EXSTDTC	3.00	HOURS			Y	PK ANALYSIS	Y	DESCR STAT
5	TEST	2	409	409	4H	4	EXSTDTC	4.50	HOURS	TIME DEV >10%	Y	Y	PK ANALYSIS		DESCR STAT
5	TEST	2	402	402	5H	5	EXSTDTC	5.00	HOURS			Y	PK ANALYSIS	Y	DESCR STAT
5	TEST	2	171	171	8H	8	EXSTDTC	8.00	HOURS			Y	PK ANALYSIS	Y	DESCR STAT
5	TEST	2	36.4	36.4	12H	12	EXSTDTC	12.00	HOURS			Y	PK ANALYSIS	Y	DESCR STAT
5	TEST	2	5.37	5.37	24H	24	EXSTDTC	24.00	HOURS			Y	PK ANALYSIS	Y	DESCR STAT
5	TEST	2	0	0	48H	48	EXSTDTC	48.00	HOURS			Y	PK ANALYSIS	Y	DESCR STAT



# CREATION OF ADPC

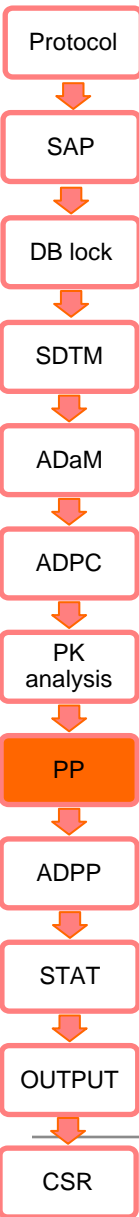
■ Predose >5% Cmax

SUBJID	TRTA	PCCAT	AVAL	IVALC	ATPT	ATPTN	CRIT2	CRIT2FL	ANL01FL	ANL01FD	ANL02FL	ANL02FD
6	TEST	COMPOUND X	87	87	0H		PREDOSE >5% CMAX	Y		PK ANALYSIS		DESCR STAT
6	TEST	COMPOUND X	282	282	0.25H	0.25				PK ANALYSIS		DESCR STAT
6	TEST	COMPOUND X	965	965	0.5H	0.5				PK ANALYSIS		DESCR STAT
6	TEST	COMPOUND X	820	820	0.75H	0.75				PK ANALYSIS		DESCR STAT
6	TEST	COMPOUND X	547	547	1H	1				PK ANALYSIS		DESCR STAT
6	TEST	COMPOUND X	384	384	1.5H	1.5				PK ANALYSIS		DESCR STAT
6	TEST	COMPOUND X	336	336	2H	2				PK ANALYSIS		DESCR STAT
6	TEST	COMPOUND X	258	258	2.5H	2.5				PK ANALYSIS		DESCR STAT
6	TEST	COMPOUND X	202	202	3H	3				PK ANALYSIS		DESCR STAT
6	TEST	COMPOUND X	127	127	4H	4				PK ANALYSIS		DESCR STAT
6	TEST	COMPOUND X	92.4	92.4	5H	5				PK ANALYSIS		DESCR STAT
6	TEST	COMPOUND X	43.9	43.9	8H	8				PK ANALYSIS		DESCR STAT
6	TEST	COMPOUND X	57.5	57.5	12H	12				PK ANALYSIS		DESCR STAT
6	TEST	COMPOUND X	42.6	42.6	24H	24				PK ANALYSIS		DESCR STAT
6	TEST	COMPOUND X	9.93	9.93	48H	48				PK ANALYSIS		DESCR STAT



- ADPC is imported in Phoenix<sup>®</sup> WinNonLin
- Include observations for analysis:
  - ANL01FL = 'Y'
- PK analysis:
  - Time: ARELTM2
  - Conc: AVAL
- Output file: PK parameters

## CREATION OF PP

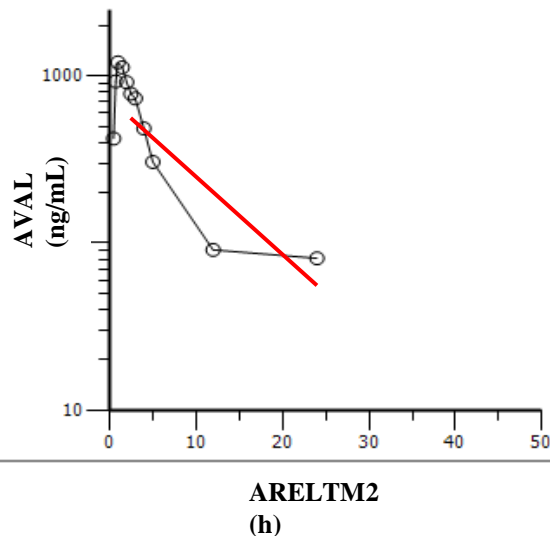


- In SAS
- Add and rename variables (SDTM IG):
  - DOMAIN PPSEQ PPCAT PPSPEC
- Calculate extra PK parameters:
  - e.g. Ratio of metabolite/parent AUC
- Pptest, Pptestcd:
  - Controlled terminology
- Relation with PC:
  - PPRFTDTC

Variable	Label	Type
STUDYID	Study Identifier	Char
DOMAIN	Domain Abbreviation	Char
USUBJID	Unique Subject Identifier	Char
SEX	Sex	Char
PPSEQ	Sequence Number	Num
PPGRPID	Group ID	Char
Pptestcd	Parameter Short Name	Char
Pptest	Parameter Name	Char
PPCAT	Parameter Category	Char
PPSCAT	Parameter Subcategory	Char
PPORRES	Result or Finding in Original Units	Char
PPORRESU	Original Units	Char
PPSTRESC	Character Result/Finding in Std Format	Char
PPSTRESN	Numeric Result/Finding in Standard Units	Num
PPSTRESU	Standard Units	Char
PPSTAT	Completion Status	Char
PPREASND	Reason Parameter Not Calculated	Char
PPSPEC	Specimen Material Type	Char

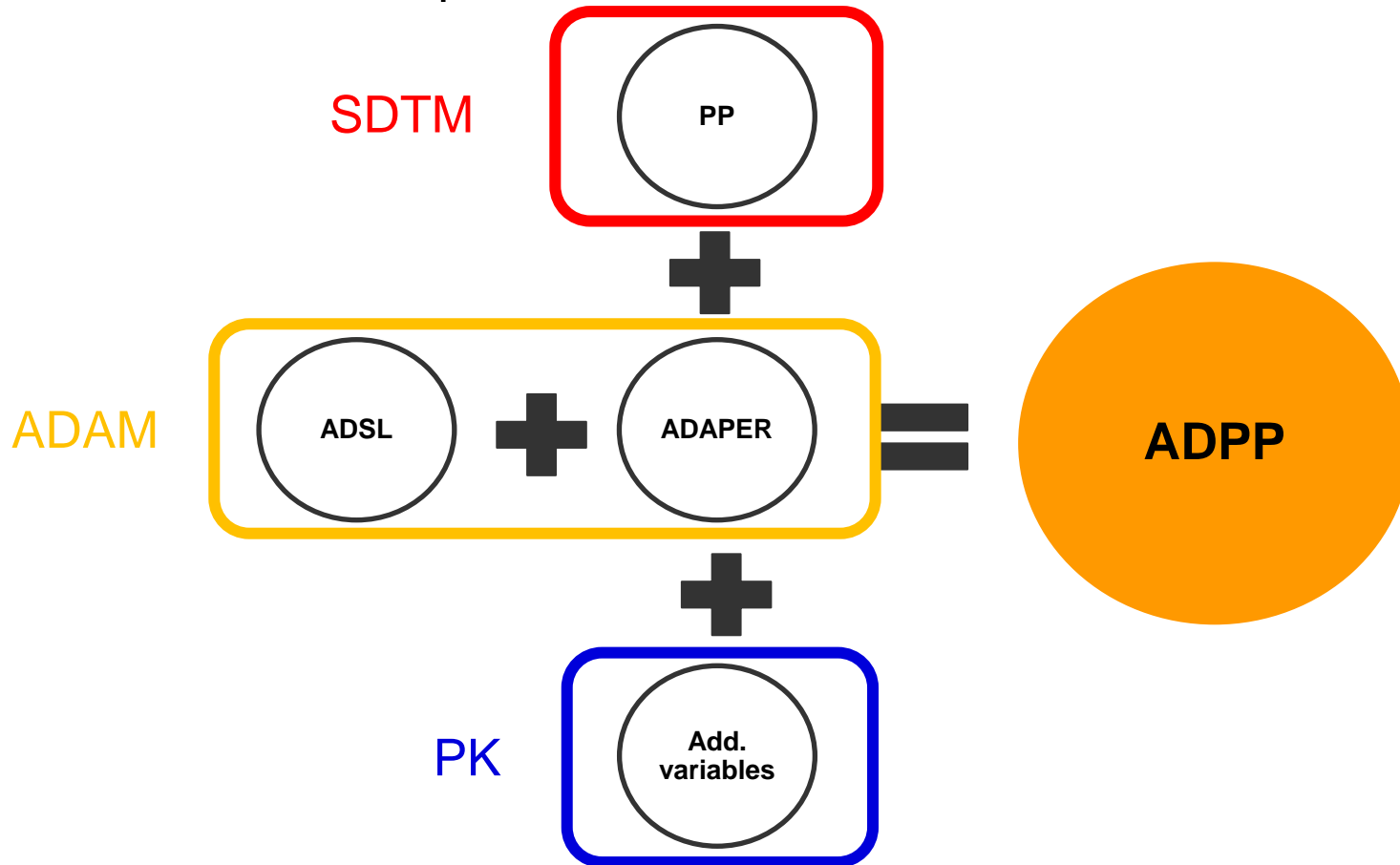
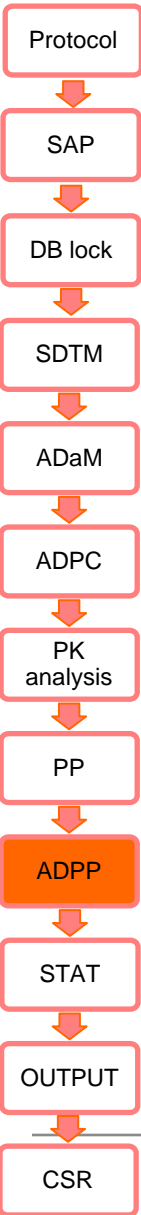
■  $R^2_{adj} < 0.9$

SUBJID	TRTA	TRTAN	PTESTCD	PTEST	PPSTRESC	PPSTRESN	PPSTRESU	PPSTAT	PPREASND
2	REF	1	C <sub>MAX</sub>	Max Conc	1850	1850	ng/mL		
2	REF	1	T <sub>MAX</sub>	Time of C <sub>MAX</sub>	1	1	h		
2	REF	1	C <sub>24H</sub>	Plasma Concentration at 24h	0	0	ng/mL		
2	REF	1	R <sub>2ADJ</sub>	R Squared Adjusted	.	.	.	NOT DONE	R <sub>2ADJ</sub> < 0.9
2	REF	1	L <sub>AMZHL</sub>	Half-Life Lambda z	.	.	.	NOT DONE	R <sub>2ADJ</sub> < 0.9
2	REF	1	L <sub>AMZ</sub>	Lambda z	.	.	.	NOT DONE	R <sub>2ADJ</sub> < 0.9
2	REF	1	A <sub>UCPEO</sub>	AUC %Extrapolation Obs	.	.	.	NOT DONE	R <sub>2ADJ</sub> < 0.9
2	REF	1	A <sub>UCIFO</sub>	AUC Infinity Obs	.	.	.	NOT DONE	R <sub>2ADJ</sub> < 0.9
2	REF	1	A <sub>UCLST</sub>	AUC to Last Nonzero Conc	5.19	5.19	µg.h/mL		
2	REF	1	R	Metabolite/Parent AUC ratio	8.76	8.76			

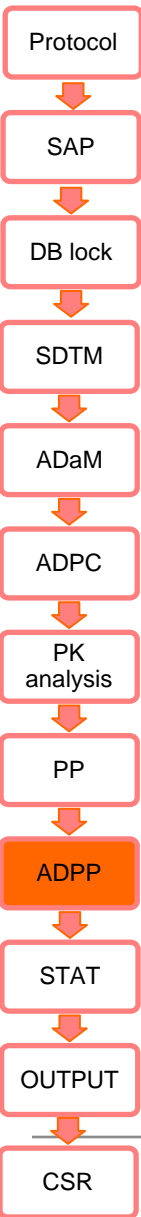


## CREATION OF ADPP

- In SAS
- Based upon define.xml



# CREATION OF ADPP



## ■ Analysis variable metadata

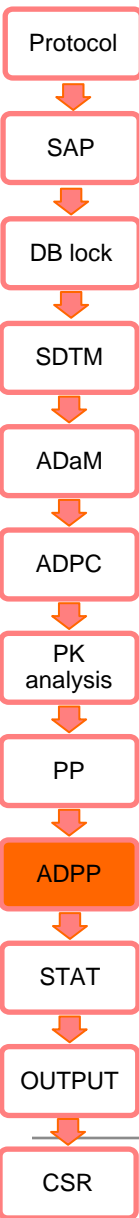
Dataset name	Variable name	Source / Derivation	Core
domain	name	source	core
ADPP	STUDYID	PP.STUDYID	Req
ADPP	PART	ADSL.PART	Cond
ADPP	COHORT	ADSL.COHORT	Cond
ADPP	COHORTN	ADSL.COHORTN	Cond
ADPP	USUBJID	PP.USUBJID	Req
ADPP	SUBJID	ADSL.SUBJID	Perm
ADPP	SEX	ADSL.SEX	Perm
ADPP	ARM	ADSL.ARM	Perm
ADPP	ARMN	ADSL.ARMN	Perm
ADPP	TRTA	ADAPER.TRTA	Cond
ADPP	TRTAN	ADAPER.TRTAN	Perm
ADPP	APERIOD	ADAPER.APERIOD	Perm
ADPP	APERIODC	ADAPER.APERIODC	Perm
ADPP	TRTSDT	ADSL.TRSDT	Perm
ADPP	TRTSDTM	ADSL.TRSDTM	Perm
ADPP	PPSEQ	PP.PPSEQ	Req
ADPP	PPGRPID	PP.PPGRPID	Perm
ADPP	PPTTESTCD	PP.PPTTESTCD	Perm
ADPP	PPTTEST	PP.PPTTEST	Perm
ADPP	PARAM	Derived	Req
ADPP	PARAMN	Derived	Perm
ADPP	PARAMCD	Derived	Req
ADPP	PARAMTYP	Derived	Perm

ADAM

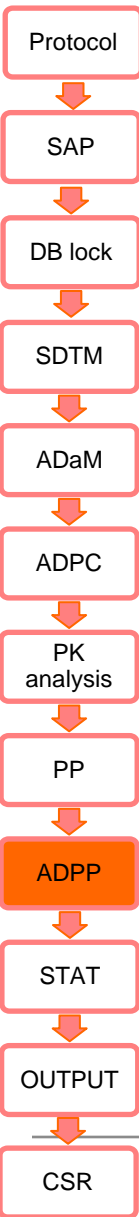
ADAM

SDTM

PK



- Additional/derived variables: BDS
  - PARAM, PARAMN, PARAMCD
  - AVISIT, AVISITN
  - ANLzzFL, *ANLzzFD*
  - AVAL, AVALC
  - CRITy, CRITyFL, CRITyFN



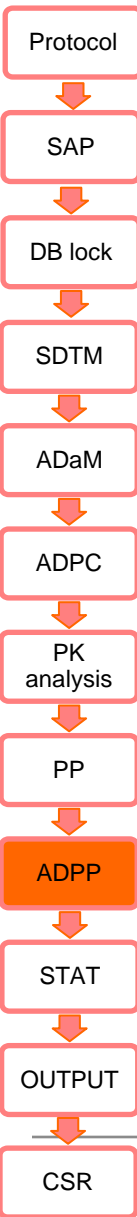
### ■ Additional/derived variables

- PARAM, PARAMN, PARAMCD
  - PARAM: Pharmacokinetic parameter used for statistical analysis
  - PARAMCD: PKPARAM
- AVISIT, AVISITN
- ANLzzFL, *ANLzzFD*
- AVAL, AVALC
- CRITy, CRITyFL, CRITyFN



## ■ PARAM, PARAMCD

SUBJID	TRTA	TRTAN	PPTSTCD	PPTST	PARAM	PARAMCD	PCAT
1	REF	2	AUCPEO	AUC %Extrapolation Obs	PHARMACOKINETIC PARAMETER USED FOR STATISTICAL ANALYSIS	PKPARAM	COMPOUND X
1	REF	2	AUCIFO	AUC Infinity Obs	PHARMACOKINETIC PARAMETER USED FOR STATISTICAL ANALYSIS	PKPARAM	COMPOUND X
1	REF	2	AUCLST	AUC to Last Nonzero Conc	PHARMACOKINETIC PARAMETER USED FOR STATISTICAL ANALYSIS	PKPARAM	COMPOUND X
1	REF	2	C24H	Plasma Concentration at 24h	PHARMACOKINETIC PARAMETER USED FOR STATISTICAL ANALYSIS	PKPARAM	COMPOUND X
1	REF	2	CMAX	Max Conc	PHARMACOKINETIC PARAMETER USED FOR STATISTICAL ANALYSIS	PKPARAM	COMPOUND X
1	REF	2	LAMZHL	Half-Life Lambda z	PHARMACOKINETIC PARAMETER USED FOR STATISTICAL ANALYSIS	PKPARAM	COMPOUND X
1	REF	2	LAMZ	Lambda z	PHARMACOKINETIC PARAMETER USED FOR STATISTICAL ANALYSIS	PKPARAM	COMPOUND X
1	REF	2	R	Metabolite/Parent Ratio AUC1st	PHARMACOKINETIC PARAMETER USED FOR STATISTICAL ANALYSIS	PKPARAM	COMPOUND X
1	REF	2	TMAX	Time of CMAX	PHARMACOKINETIC PARAMETER USED FOR STATISTICAL ANALYSIS	PKPARAM	COMPOUND X
1	REF	2	R2ADJ	R Squared Adjusted	PHARMACOKINETIC PARAMETER USED FOR STATISTICAL ANALYSIS	PKPARAM	COMPOUND X

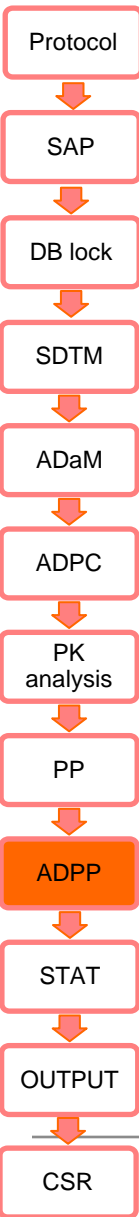


### ■ Additional/derived variables

- PARAM, PARAMN, PARAMCD
- AVISIT, AVISITN
  - Analogue to AVISIT in ADPC
- ANLzzFL, ANLzzFD
- AVAL, AVALC
- CRITy, CRITyFL, CRITyFN

■ AVISIT, AVISITN

SUBJID	TRTA	TRTAN	PPTSTCD	AVISIT	AVISITN
1	REF	2	AUCPEO	DAY 1	1
1	REF	2	AUCIFO	DAY 1	1
1	REF	2	AUCLST	DAY 1	1
1	REF	2	C24H	DAY 1	1
1	REF	2	CMAX	DAY 1	1
1	REF	2	LAMZHL	DAY 1	1
1	REF	2	LAMZ	DAY 1	1
1	REF	2	R	DAY 1	1
1	REF	2	TMAX	DAY 1	1
1	REF	2	R2ADJ	DAY 1	1

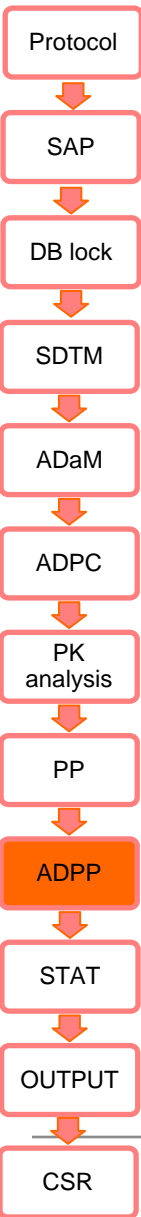


### ■ Additional/derived variables

- PARAM, PARAMN, PARAMCD
- AVISIT, AVISITN
- ANLzzFL, *ANLzzFD*
  - Select set of records for analysis:
    - Statistical analysis
    - Descriptive statistics
- AVAL, AVALC
- CRITy, CRITyFL, CRITyFN

■ ANLzzFL, ANLzzFD

SUBJID	TRTA	TRTAN	PPTSTCD	AVISIT	AVISITN	ANL01FL	ANL01FD	ANL02FL	ANL02FD
1	REF	2	AUCPEO	DAY 1	1	Y	INFER STAT	Y	DESCR STAT
1	REF	2	AUCIFO	DAY 1	1	Y	INFER STAT	Y	DESCR STAT
1	REF	2	AUCLST	DAY 1	1	Y	INFER STAT	Y	DESCR STAT
1	REF	2	C24H	DAY 1	1	Y	INFER STAT	Y	DESCR STAT
1	REF	2	CMAX	DAY 1	1	Y	INFER STAT	Y	DESCR STAT
1	REF	2	LAMZHL	DAY 1	1	Y	INFER STAT	Y	DESCR STAT
1	REF	2	LAMZ	DAY 1	1	Y	INFER STAT	Y	DESCR STAT
1	REF	2	R	DAY 1	1	Y	INFER STAT	Y	DESCR STAT
1	REF	2	TMAX	DAY 1	1	Y	INFER STAT	Y	DESCR STAT
1	REF	2	R2ADJ	DAY 1	1	Y	INFER STAT	Y	DESCR STAT

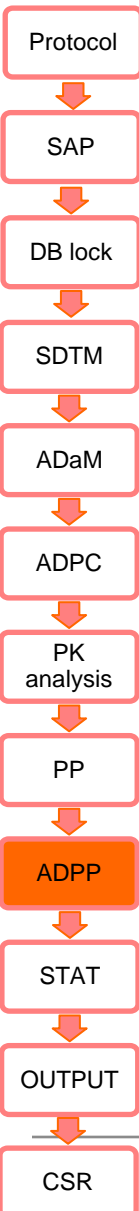


### ■ Additional/derived variables

- PARAM, PARAMN, PARAMCD
- AVISIT, AVISITN
- ANLzzFL, ANLzzFD
- AVAL, AVALC
  - AVAL = PPSTRESN
- CRITy, CRITyFL, CRITyFN

■ AVAL = PPSTRESN

SUBJID	TRTA	TRTAN	PPTSTCD	PPCAT	PPSCAT	PPSTRES	PPSTRESN	PPSTRESU	AVAL
1	REF	2	AUCPEO	COMPOUND X	NON-COMPARTIMENTAL	0.215	0.2152249	%	0.2152249
1	REF	2	AUCIFO	COMPOUND X	NON-COMPARTIMENTAL	4.2	4.2083988	ug.h/mL	4.2083988
1	REF	2	AUCLST	COMPOUND X	NON-COMPARTIMENTAL	4.2	4.1993413	ug.h/mL	4.1993413
1	REF	2	C24H	COMPOUND X	NON-COMPARTIMENTAL	2.05	2.05	ng/mL	2.05
1	REF	2	CMAX	COMPOUND X	NON-COMPARTIMENTAL	1210	1210	ng/mL	1210
1	REF	2	LAMZHL	COMPOUND X	NON-COMPARTIMENTAL	3.06	3.0625351	h	3.0625351
1	REF	2	LAMZ	COMPOUND X	NON-COMPARTIMENTAL	0.226	0.2263312	L/h	0.2263312
1	REF	2	R	COMPOUND X	NON-COMPARTIMENTAL	12.3	12.250128		12.250128
1	REF	2	TMAX	COMPOUND X	NON-COMPARTIMENTAL	1	1	h	1
1	REF	2	R2ADJ	COMPOUND X	NON-COMPARTIMENTAL	0.984	0.9839396		0.9839396



### ■ Additional/derived variables

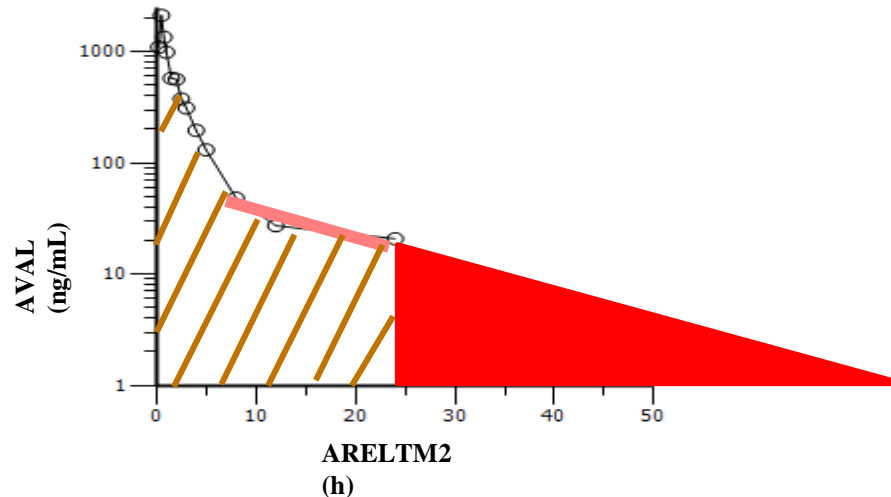
- PARAM, PARAMN, PARAMCD, PARAMTYP
- AVISIT, AVISITN
- ANLzzFL, ANLzzFD
- AVAL, AVALC
- CRITy, CRITyFL, CRITyFN
  - Criteria evaluation
    - AUCpeo > 20%

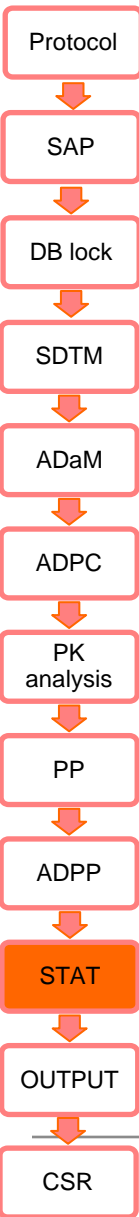


# CREATION OF ADPP

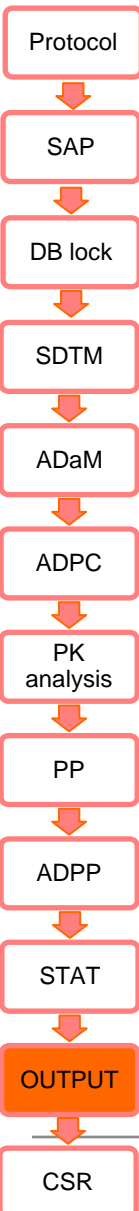
■ AUC<sub>peo</sub> > 20% AUC<sub>ifo</sub>

SUBJID	TRTA	TRTAN	PPTESTCD	PPSTRESC	PPSTRESN	PPSTRESU	AVAL	AVISIT	CRIT1	CRIT1FL	ANL01FL	ANL01FD	ANL02FL	ANL02FD
3	REF	1	AUCPEO	29	29 %	29	DAY1	AUC <sub>peo</sub> > 20% AUC <sub>ifo</sub>	Y			INFER STAT		DESCR STAT
3	REF	1	AUCIFO	5.21	5.21	µg.h/mL	5.21	DAY1	AUC <sub>peo</sub> > 20% AUC <sub>ifo</sub>	Y		INFER STAT		DESCR STAT
3	REF	1	AUCLST	4.04	4.04	µg.h/mL	4.04	DAY1			Y	INFER STAT	Y	DESCR STAT
3	REF	1	C24H	13.9	13.9	ng/mL	13.9	DAY1			Y	INFER STAT	Y	DESCR STAT
3	REF	1	CMAX	2070	2070	ng/mL	2070	DAY1			Y	INFER STAT	Y	DESCR STAT
3	REF	1	LAMZHL	11.5	11.5	h	11.5	DAY1			Y	INFER STAT	Y	DESCR STAT
3	REF	1	LAMZ	0.0604	0.0604	1/h	0.0604	DAY1			Y	INFER STAT	Y	DESCR STAT
3	REF	1	R	10.2	10.2		10.2	DAY1			Y	INFER STAT	Y	DESCR STAT
3	REF	1	TMAX	0.5	0.5	h	0.5	DAY1			Y	INFER STAT	Y	DESCR STAT
3	REF	1	R2ADJ	0.991	0.991		0.991	DAY1			Y	INFER STAT	Y	DESCR STAT

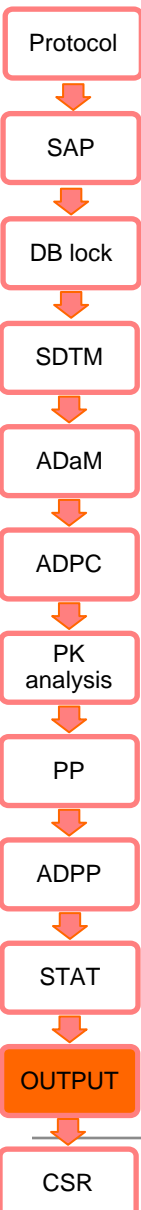




- ADPP
- Include observations from inferential statistical analysis:
  - ANL01FL = 'Y'



- ADPC
- ADPP
- Include observations from descriptive statistical analysis:
  - ANL02FL = 'Y'

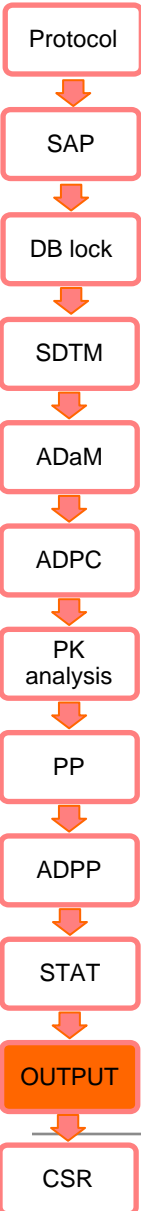


### ■ ADPC

Table 1: Plasma concentrations Compound X (ng/mL)

SUBJID	ATPTN															
	0	0.25	0.5	0.75	1	1.5	2	2.5	3	4	5	8	12	24	48	
1	0	99	1510	1720	1850	1360	1410	1030	799	490	254	74.4	16.5	0	0	
2	NR	1590	2070	1490	1140	768	593	429	375	222	120	60.9	33.1	13.9	3.66	
3	0	0	19	85.9	152	381	586	772	750	603	342	79.7	26.4	0	1.26	
4	0	0	6.72	41.1	122	399	486	605	690	518	318	68.8	0	1.25	0	
5	0	0	8.65	31.5	50	152	372	539	566	409 *	402	171	36.4	5.37	0	
N	4	5	5	5	5	5	5	5	5	4	5	5	5	5	5	
Mean	0	338	723	673	663	612	689	675	636	458	287	91	22.5	4.1	0.984	
SD	0	701	994	854	802	473	413	234	170	165	107	45.3	14.7	5.9	1.59	
Min	0	0	6.72	31.5	50	152	372	429	375	222	120	60.9	0	0	0	
Median	0	0	19	85.9	152	399	586	605	690	504	318	74.4	26.4	1.25	0	
Max	0	1590	2070	1720	1850	1360	1410	1030	799	603	402	171	36.4	13.9	3.66	

\* time deviation >10% : PK sample excluded from descriptive statistical analysis



## ■ ADPP

Table 2: PK parameters of compound X

SUBJID	AUCIFO	AUCLST	C24H	CMAX	LAMZ	LAMZHL	TMAX
1	NE	5.19	0.5	1850	NE	NE	1
2	5.21 #	4.04	13.9	2070	0.06	11.48	0.5
3	3.25	3.24	5.63	772	0.08	8.52	2.5
4	3.84	3.81	4.35	1520	0.14	4.78	0.5
5	2.97	2.94	5.37	566	0.2	3.41	3
N	3	5	5	5	4	4	5
Mean	3.36	3.84	5.95	1360	0.122	7.05	1.5
SD	0.445	0.87	4.9	661	0.065	3.66	1.17
Min	2.97	2.94	0.5	566	0.06	3.41	0.5
Median	3.25	3.81	5.37	1520	0.113	6.65	1
Max	3.84	5.19	13.9	2070	0.203	11.5	3

# AUC<sub>peo</sub> > 20% AUC<sub>ifo</sub>: AUC<sub>ifo</sub> excluded from all statistical analysis

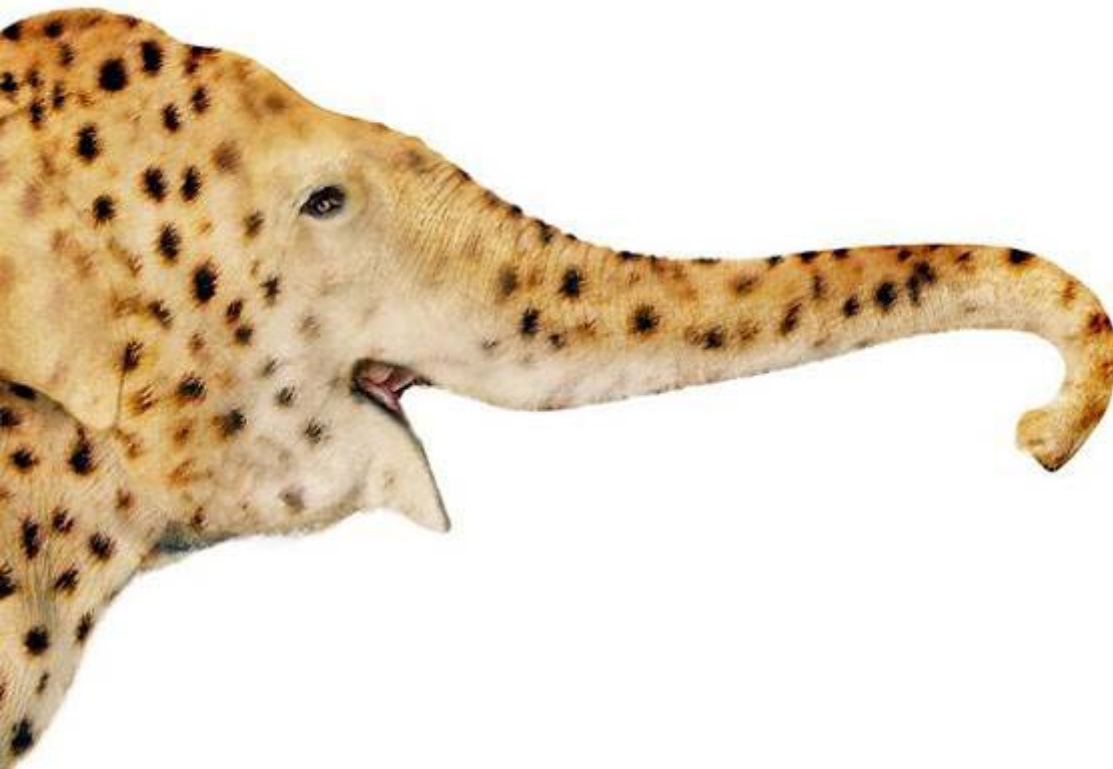
- Introduction
- Gain
- Pharmacokinetic analysis
- **Conclusion**

- ADPC/ADPP
  - SDTM + ADaM
  - Derived variables
    - Based on BDS
    - Modified variables (ANLzzFD, ARELTM1, ARELTM2)
- PK analysis
  - ARELTM2 and AVAL
- Data handling
  - CRITy and ANLzzFL
  
- Guidance from CDISC needed



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MEETS SPEED**

## CONTACT US

### CLINICAL RESEARCH

[lss.info@sgs.com](mailto:lss.info@sgs.com)

**EUROPE :** + 33 1 53 78 18 79

**AMERICAS :** + 1 877 677 2667

[www.sgs.com/lifescience](http://www.sgs.com/lifescience)

**Joanna Magielse**  
Life Science Services  
Pharmacokineticist



# SGS

**SGS Belgium NV**  
Vieux Chemin du Poète10  
1301 Wavre - Belgium  
Phone: + 32(0)15 44 01 33  
Email: [joanna.magielse@sgs.com](mailto:joanna.magielse@sgs.com)