

IMPLEMENTATION OF CDISC ADAM IN THE PHARMACOKINETICS DEPARTMENT

Presented by Joanna Magielse, SGS Life Science Services

WHEN YOU NEED TO BE SURE

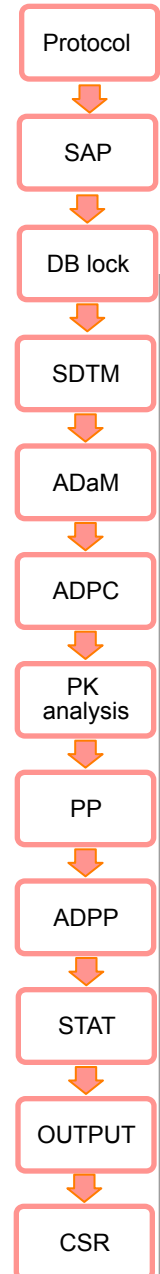


- Introduction
- Gain
- Pharmacokinetic analysis
- Conclusion

- **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

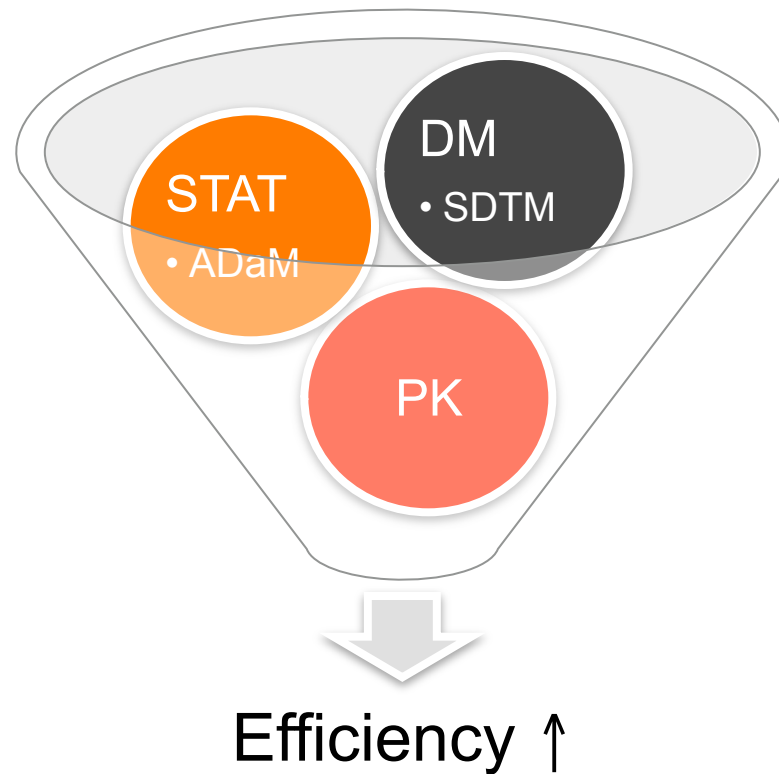


- Introduction
- **Gain**
- Pharmacokinetic analysis
- Conclusion

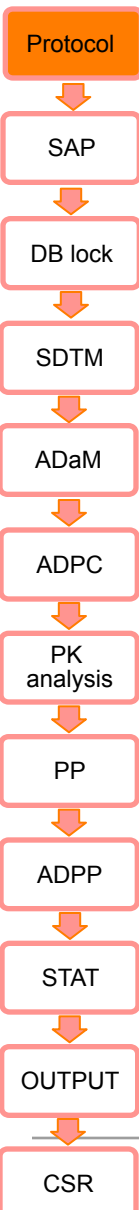
■ Standardization

⇒ Efficiency ↑

⇒ Time ↓

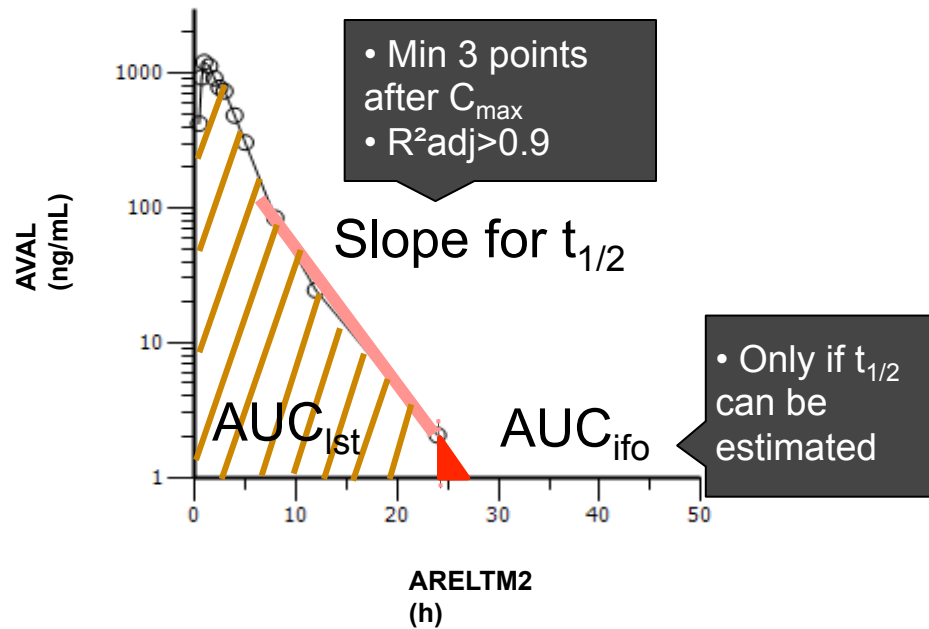
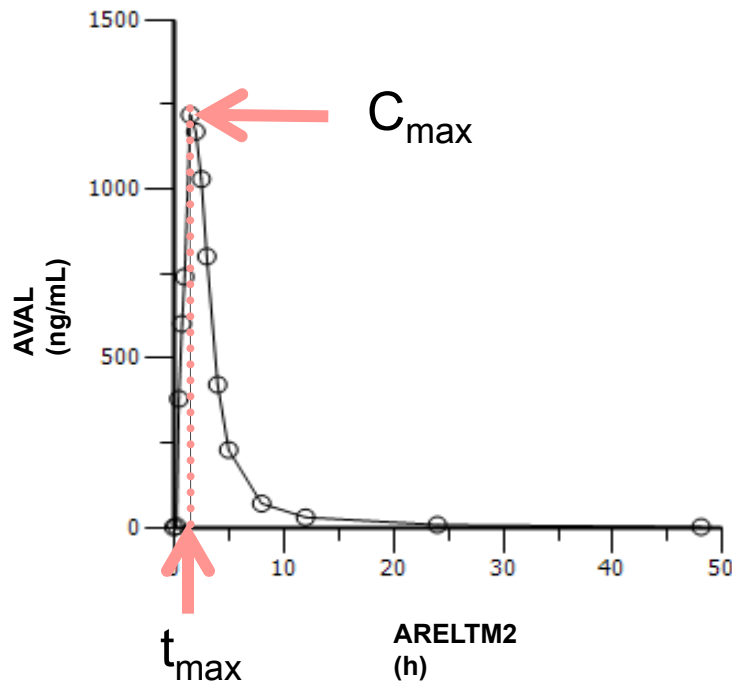


- Introduction
- Gain
- **Pharmacokinetic analysis**
- Conclusion

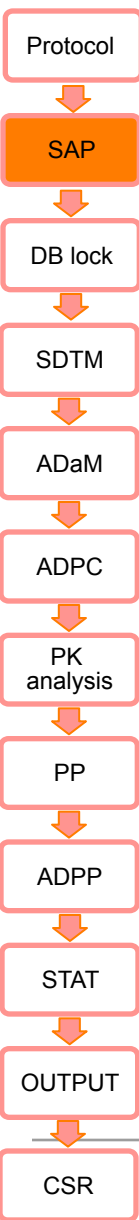


Protocol:

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

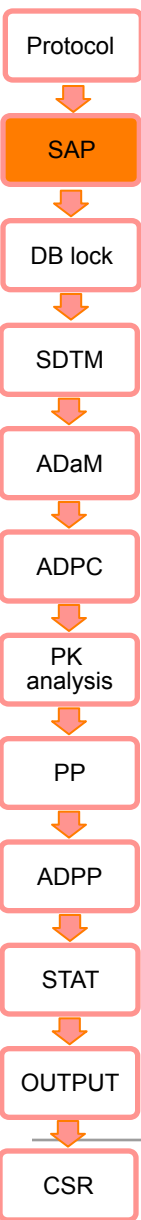


AVAL: Analysis value
ARELTM: Analysis relative time



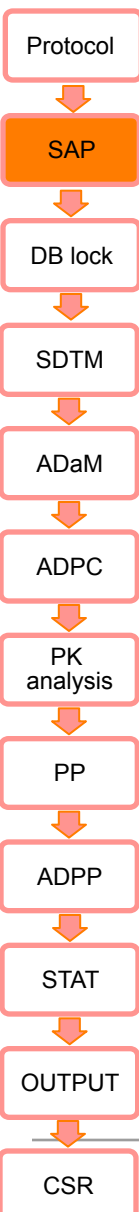
■ Statistical Analysis Plan

- PK population
- Handling of data
- Statistical analysis



■ Statistical Analysis Plan

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

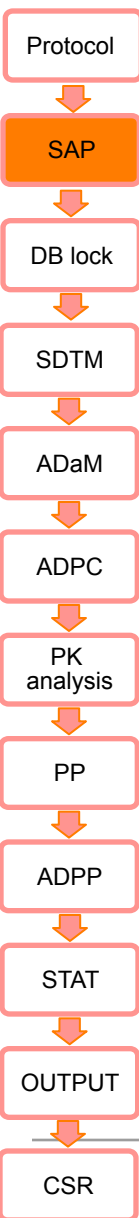


■ Statistical Analysis Plan

■ Handling of data:

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

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



■ Statistical Analysis Plan

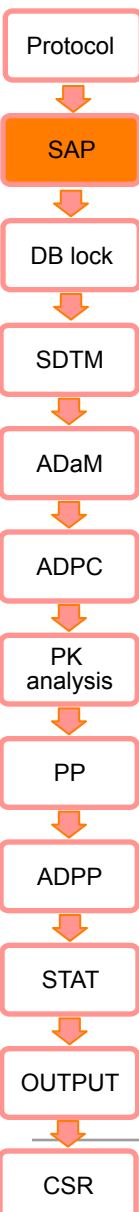
■ Handling of data:

- If BLoQ => AVAL = 0

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

BLoQ: Below Limit of Quantification

AVAL: Analysis Value

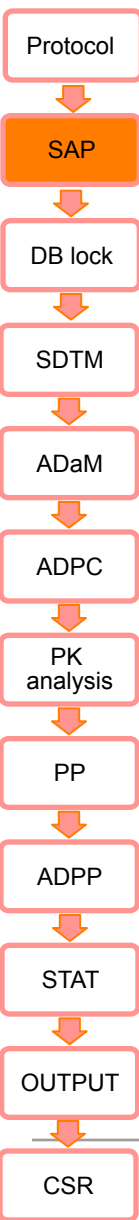


■ Statistical Analysis Plan

■ Handling of data:

- If embedded BLoQ => exclude from PK analysis

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

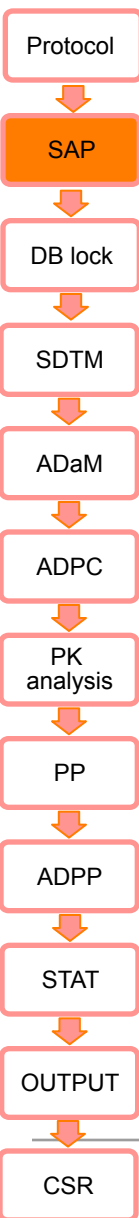


■ Statistical Analysis Plan

■ Handling of data:

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

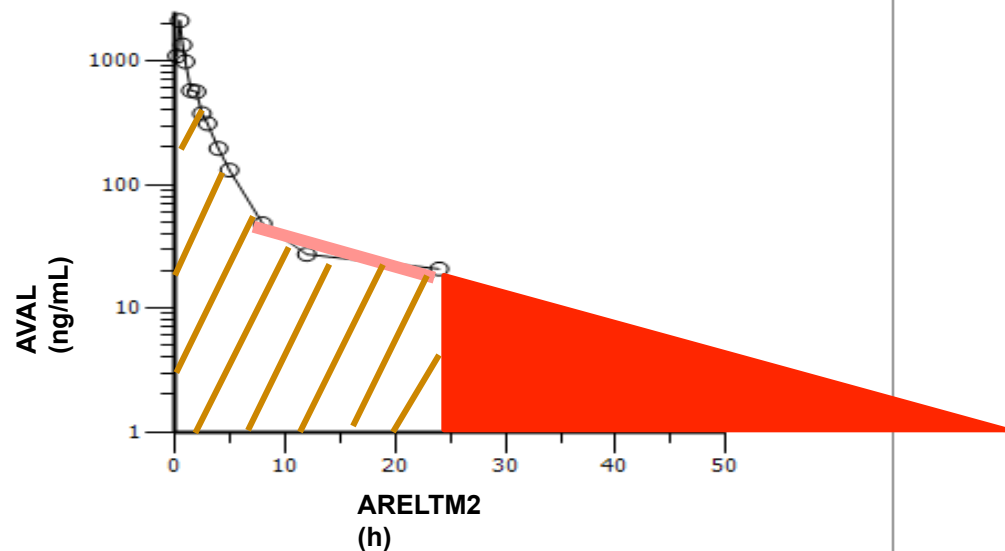
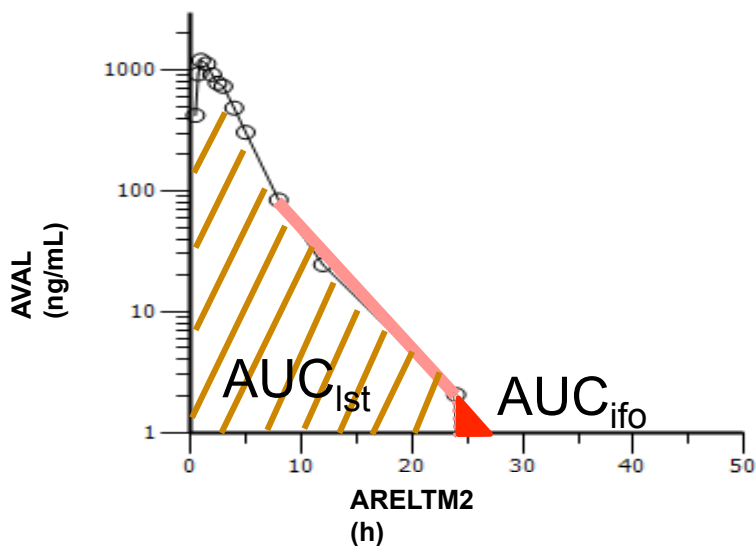
SUBJID	TRTA	PCTESTCD	PCTPT	EXSTDTC	PCDTC
5	TEST	ANAL X	PRE-DOSE	2013-07-05T09:16	2013-07-05T09:11
5	TEST	ANAL X	0.25H	2013-07-05T09:16	2013-07-05T09:31
5	TEST	ANAL X	0.5H	2013-07-05T09:16	2013-07-05T09:46
5	TEST	ANAL X	0.75H	2013-07-05T09:16	2013-07-05T10:01
5	TEST	ANAL X	1H	2013-07-05T09:16	2013-07-05T10:16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



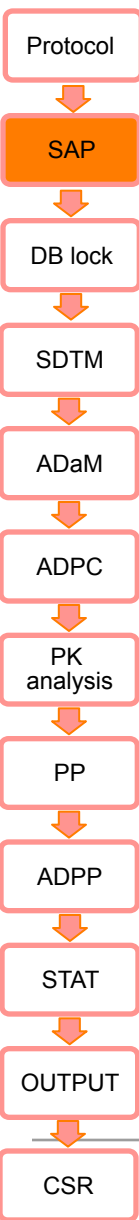
■ Statistical Analysis Plan

■ Statistical analysis:

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



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

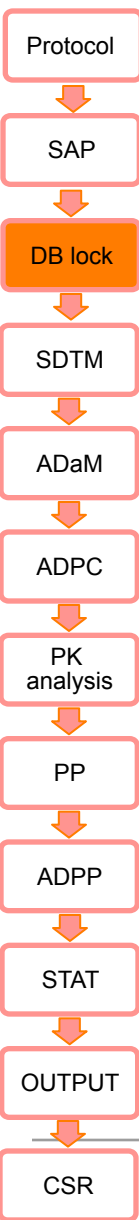


■ Statistical Analysis Plan

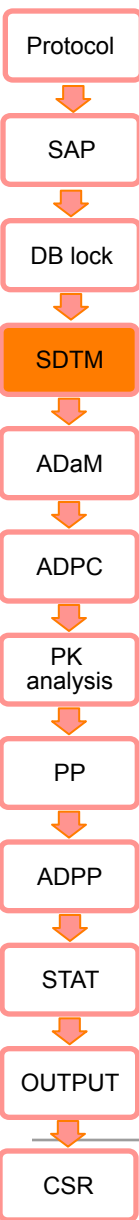
■ Statistical analysis:

- Bioequivalence studies: If quantifiable concentration at pre-dose > 5% C_{max} => **subject will be excluded**

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

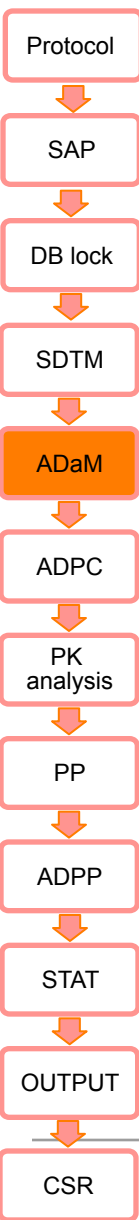


Database lock



■ SDTM datasets

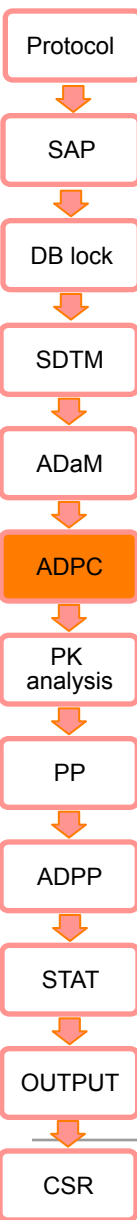
- DM (Demographics)
- EX (Exposure)
- PC (Pharmacokinetic concentrations)
- CM (Concomitant medications)
- AE (Adverse events)
- DV (Protocol deviations)
- CO (Comments)



■ ADaM datasets

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

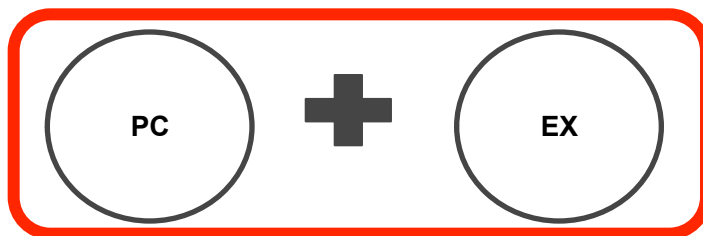
CREATION OF ADPC



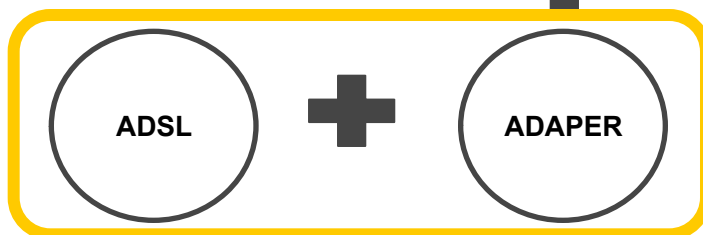
■ In SAS

■ Based upon define.xml

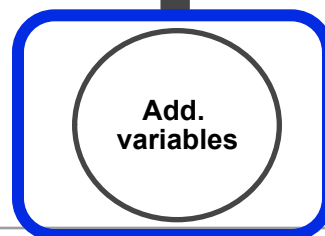
SDTM



ADaM



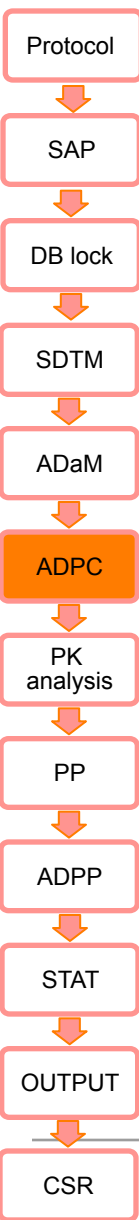
PK



=

ADPC

CREATION OF ADPC



■ Analysis variable metadata

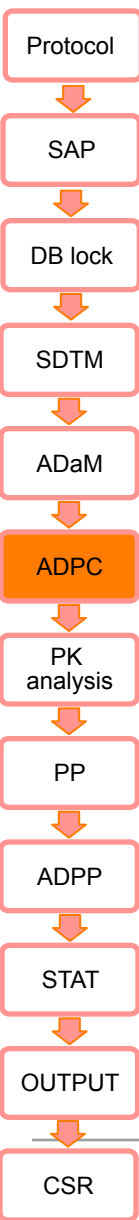
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domain	name	source	core
ADPC	STUDYID	PC.STUDYID	Req
ADPC	PART	ADSL.PART	Cond
ADPC	USUBJID	PC.USUBJID	Req
ADPC	SUBJID	ADSL.SUBJID	Perm
ADPC	ARM	ADSL.ARM	Perm
ADPC	ARMN	ADSL.ARMN	Perm
ADPC	TRTP	ADAPER.TRTP	Cond
ADPC	TRTPN	ADAPER.TRTPN	Perm
ADPC	TRTA	ADAPER.TRTA	Cond
ADPC	TRTAN	ADAPER.TR TAN	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

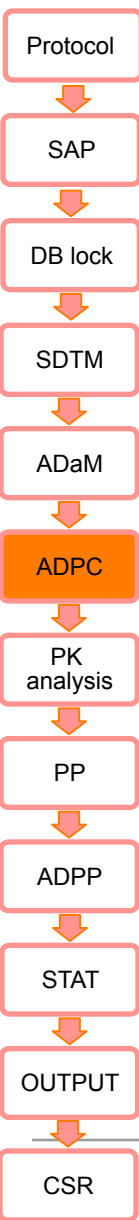
SDTM

PK



■ Additional/derived variables: BDS

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

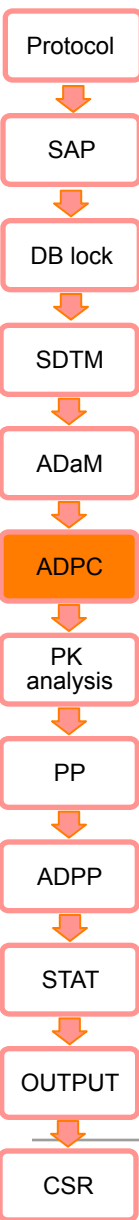


■ Additional/derived variables

- PARAM, PARAMN, PARAMCD
 - PARAM: based upon PCTEST and PCSTRESU
 - PARAMCD: abbreviation
 - PARAMN: numeric version of PARAM
- ADTM, ASTDTM, AENDTM
- AVISIT, AVISITN
- ATPT, ATPTN
- ARELTM, ARELTMU, ANCHOR
- ANLzzFL, *ANLzzFD*
- AVAL, AVALC
- CRITy, CRITyFL, CRITyFN

■ PARAM, PARAMCD

PCTESTCD	PCTEST	PARAM	PARAMCD	PCORRES	PCORRESU	PCSTRESC	PCSTRESN	PCSTRESU
ANAL X	ANALYTE X	ANALYTE X (ng/mL)	ANAL X	<1	ng/mL	<1	.	ng/mL
ANAL X	ANALYTE X	ANALYTE X (ng/mL)	ANAL X	99	ng/mL	99	99	ng/mL
ANAL X	ANALYTE X	ANALYTE X (ng/mL)	ANAL X	1511	ng/mL	1511	1511	ng/mL
ANAL X	ANALYTE X	ANALYTE X (ng/mL)	ANAL X	1718	ng/mL	1718	1718	ng/mL
ANAL X	ANALYTE X	ANALYTE X (ng/mL)	ANAL X	1852	ng/mL	1852	1852	ng/mL
ANAL X	ANALYTE X	ANALYTE X (ng/mL)	ANAL X	1360	ng/mL	1360	1360	ng/mL
ANAL X	ANALYTE X	ANALYTE X (ng/mL)	ANAL X	1410	ng/mL	1410	1410	ng/mL
ANAL X	ANALYTE X	ANALYTE X (ng/mL)	ANAL X	1030	ng/mL	1030	1030	ng/mL
ANAL X	ANALYTE X	ANALYTE X (ng/mL)	ANAL X	799	ng/mL	799	799	ng/mL
ANAL X	ANALYTE X	ANALYTE X (ng/mL)	ANAL X	490	ng/mL	490	490	ng/mL
ANAL X	ANALYTE X	ANALYTE X (ng/mL)	ANAL X	254	ng/mL	254	254	ng/mL
ANAL X	ANALYTE X	ANALYTE X (ng/mL)	ANAL X	74.4	ng/mL	74.4	74.4	ng/mL
ANAL X	ANALYTE X	ANALYTE X (ng/mL)	ANAL X	16.5	ng/mL	16.5	16.5	ng/mL
ANAL X	ANALYTE X	ANALYTE X (ng/mL)	ANAL X	<1	ng/mL	<1	.	ng/mL
ANAL X	ANALYTE X	ANALYTE X (ng/mL)	ANAL X	<1	ng/mL	<1	.	ng/mL



■ Additional/derived variables

- PARAM, PARAMN, PARAMCD
- ADTM, ASTDTM, AENDTM
 - Derived from PCDTC
 - ASTDTM and AENDTM: in case of interval (e.g. urine)
- AVISIT, AVISITN
- ATPT, ATPTN
- ARELTM, ARELTMU, ANCHOR
- ANLzzFL, *ANLzzFD*
- AVAL, AVALC
- CRITy, CRITyFL, CRITyFN

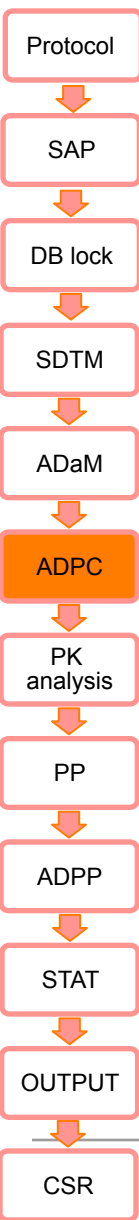
CREATION OF ADPC

■ ADTM

SUBJID	TRTA	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.

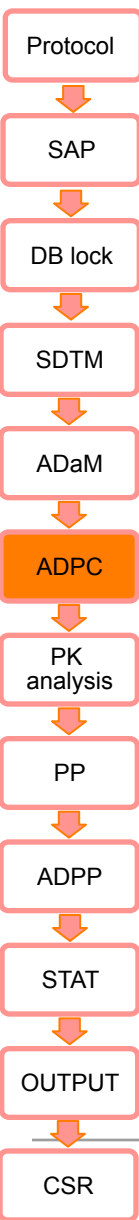


■ Additional/derived variables

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

■ AVISIT, AVISITN

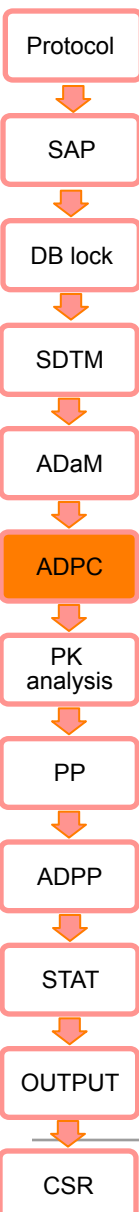
SUBJID	TRTA	VISITNUM	VISIT	PCTPT	AVISIT	AVISITN
1	TEST	1.001	PERIOD1_DAY1	PRE-DOSE	DAY 1	1
1	TEST	1.001	PERIOD1_DAY1	0.25H	DAY 1	1
1	TEST	1.001	PERIOD1_DAY1	0.5H	DAY 1	1
1	TEST	1.001	PERIOD1_DAY1	0.75H	DAY 1	1
1	TEST	1.001	PERIOD1_DAY1	1H	DAY 1	1
1	TEST	1.001	PERIOD1_DAY1	1.5H	DAY 1	1
1	TEST	1.001	PERIOD1_DAY1	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



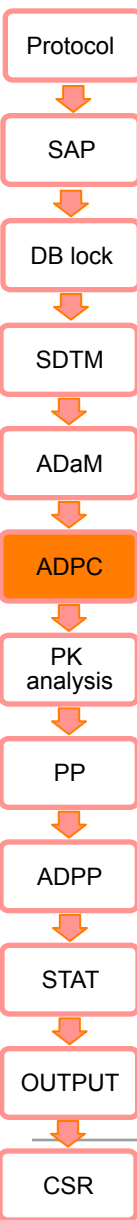
■ Additional/derived variables

- 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

■ ATPT, ATPTN



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

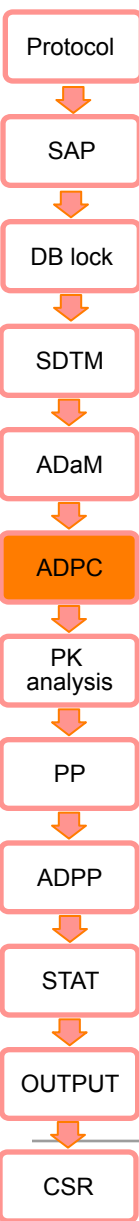


■ Additional/derived variables

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

■ ARELTM, ARELMTU, *ANCHOR*

SUBJID	TRTA	PCDTC	EXSTDTC	ATPT	ATPTN	ANCHOR1	ARELTM	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

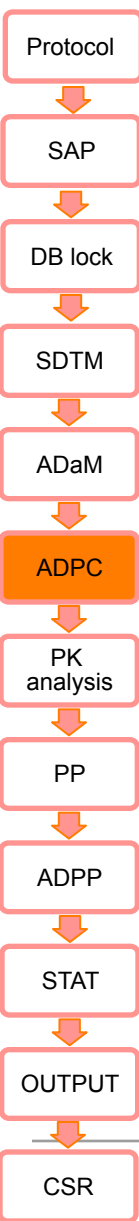


■ Additional/derived variables

- 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
 - Steady state analysis
- AVAL, AVALC
- CRITy, CRITyFL, CRITyFN

■ ANLzzFL, ANLzzFD

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

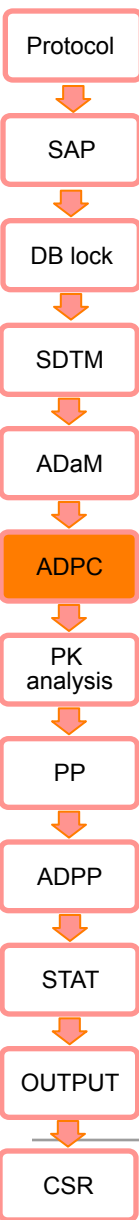


■ Additional/derived variables

- 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

- Missing predose => 0

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

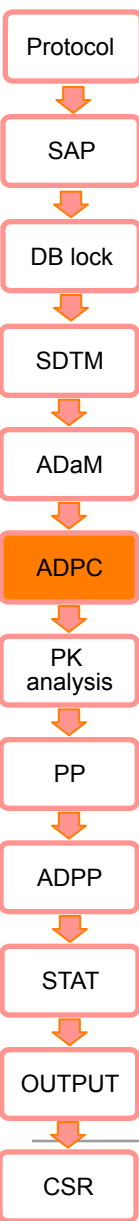


■ Additional/derived variables

- 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

■ BLoQ => 0

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

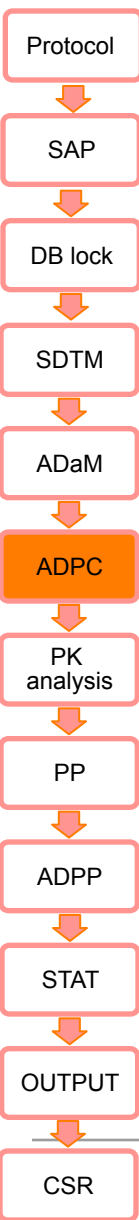


■ Additional/derived variables

- 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	PCTESTCD	PCSTRESC	PCSTRESN	PCSTRES	AVAL	AVALC	CSTAT	ATPT	ATPTN	ANL01FL	ANL01FD	ANL02FL	ANL02FD
3	TEST	ANAL X	<1	.	ng/mL	0	0		0H	0	Y	PK ANALYSIS	Y	DESCR STAT
3	TEST	ANAL X	251	251	ng/mL	251	251		0.25H	0.25	Y	PK ANALYSIS	Y	DESCR STAT
3	TEST	ANAL X	1170	1170	ng/mL	1170	1170		0.5H	0.5	Y	PK ANALYSIS	Y	DESCR STAT
3	TEST	ANAL X	1100	1100	ng/mL	1100	1100		0.75H	0.75	Y	PK ANALYSIS	Y	DESCR STAT
3	TEST	ANAL X	1270	1270	ng/mL	1270	1270		1H	1	Y	PK ANALYSIS	Y	DESCR STAT
3	TEST	ANAL X	793	793	ng/mL	793	793		1.5H	1.5	Y	PK ANALYSIS	Y	DESCR STAT
3	TEST	ANAL X	604	604	ng/mL	604	604		2H	2	Y	PK ANALYSIS	Y	DESCR STAT
3	TEST	ANAL X	566	566	ng/mL	566	566		2.5H	2.5	Y	PK ANALYSIS	Y	DESCR STAT
3	TEST	ANAL X	388	388	ng/mL	388	388		3H	3	Y	PK ANALYSIS	Y	DESCR STAT
3	TEST	ANAL X	257	257	ng/mL	257	257		4H	4	Y	PK ANALYSIS	Y	DESCR STAT
3	TEST	ANAL X	140	140	ng/mL	140	140		5H	5	Y	PK ANALYSIS	Y	DESCR STAT
3	TEST	ANAL X	41.6	41.6	ng/mL	41.6	41.6		8H	8	Y	PK ANALYSIS	Y	DESCR STAT
3	TEST	ANAL X	15.5	15.5	g/mL	15.5	15.5		12H	12	Y	PK ANALYSIS	Y	DESCR STAT
3	TEST	ANAL X	<1	.	g/mL	0	0		24H	24	Y	PK ANALYSIS	Y	DESCR STAT
3	TEST	ANAL X	1.15	1.15	g/mL	1.15	1.15		48H	48	Y	PK ANALYSIS	Y	DESCR STAT



■ 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)

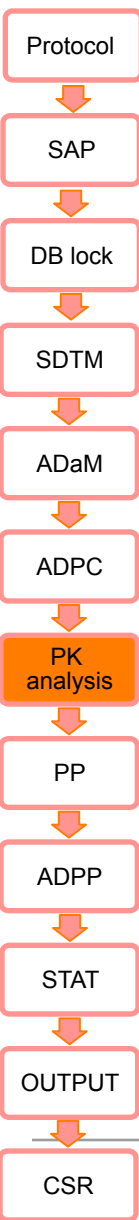
■ Time deviation

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

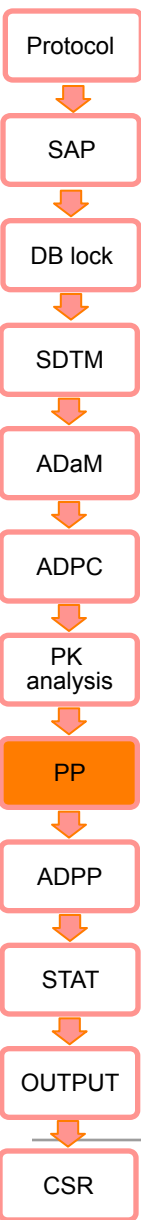
SUBJID	TRTA	PCTESTCD	AVAL	VALC	ATPT	TPTM	CRIT2	CRIT2FL	ANL01FL	ANL01FD	ANL02FL	ANL02FD
6	TEST	ANAL X	87	87	0H		PREDOSE >5% CMAX	Y		PK ANALYSIS		DESCR STAT
6	TEST	ANAL X	282	282	0.25H	0.25				PK ANALYSIS		DESCR STAT
6	TEST	ANAL X	965	965	0.5H	0.5				PK ANALYSIS		DESCR STAT
6	TEST	ANAL X	820	820	0.75H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



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



CREATION OF PP

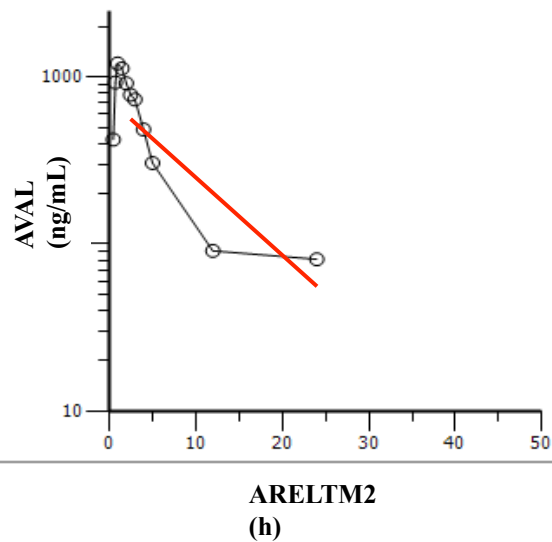


- In SAS
- Add and rename variables (SDTM IG):
 - DOMAIN PPSEQ PPCAT PPSPEC
- Calculate extra PK parameters:
 - e.g. Ratio of metabolite/parent AUC
- Pptest, Pptestcd:
 - Controlled terminology
- Relation with PC:
 - PPRFTDTC

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

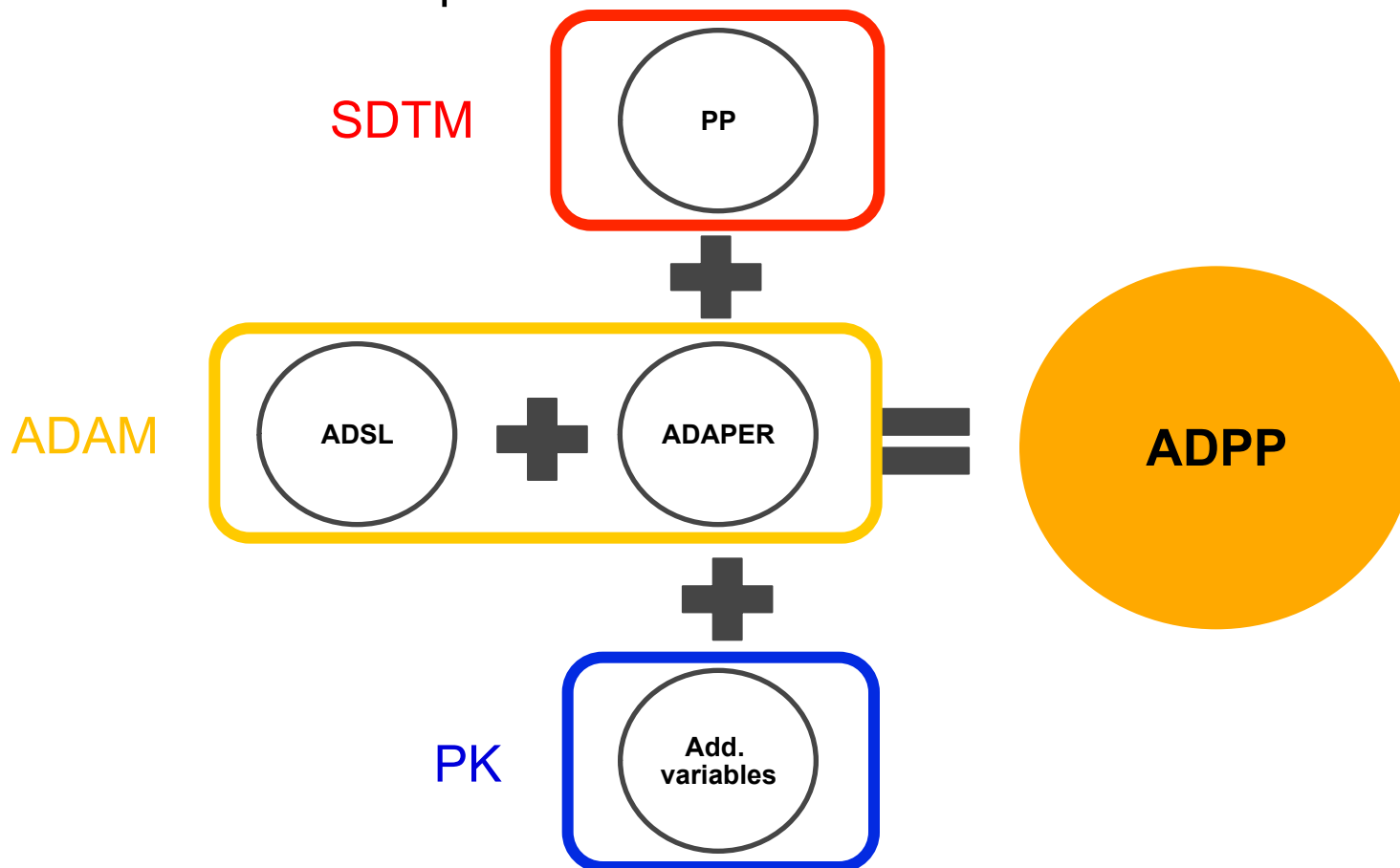
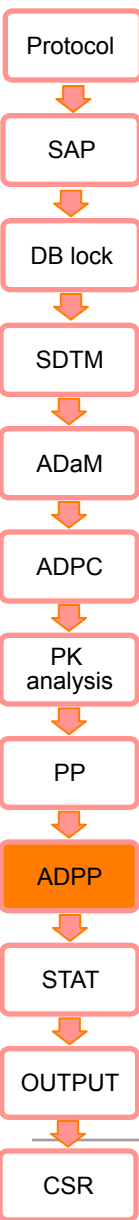
■ $R^2_{adj} < 0.9$

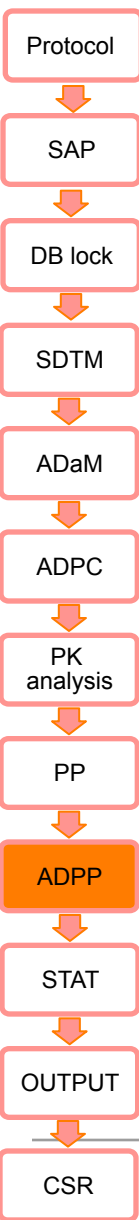
SUBJID	TRTA	PPTSTCD	PPTST	PPSTRESC	PPSTRESN	PPSTRESU	PPSTAT	PPREASND
2	REF	CMAx	Max Conc	1850	1850	ng/mL		
2	REF	TMAx	Time of CMAx	1	1	h		
2	REF	C24H	Plasma Concentration at 24h	0	0	ng/mL		
2	REF	R2ADJ	R Squared Adjusted	.	.		NOT DONE	R2ADJ < 0.9
2	REF	LAMZHL	Half-Life Lambda z	.	.		NOT DONE	R2ADJ < 0.9
2	REF	LAMZ	Lambda z	.	.		NOT DONE	R2ADJ < 0.9
2	REF	AUCPEO	AUC %Extrapolation Obs	.	.		NOT DONE	R2ADJ < 0.9
2	REF	AUCIFO	AUC Infinity Obs	.	.		NOT DONE	R2ADJ < 0.9
2	REF	AUCLST	AUC to Last Nonzero Conc	5.19	5.19	h*µg/mL		
2	REF	R	Metabolite/Parent AUC ratio	8.76	8.76			



CREATION OF ADPP

- In SAS
- Based upon define.xml





■ Analysis variable metadata

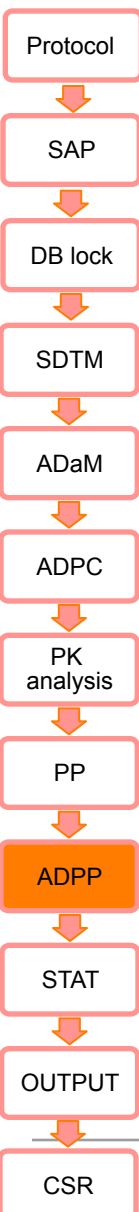
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domain	name	source	core
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ADPP	PART	ADSL.PART	Cond
ADPP	COHORT	ADSL.COHORT	Cond
ADPP	COHORTN	ADSL.COHORTN	Cond
ADPP	USUBJID	PP.USUBJID	Req
ADPP	SUBJID	ADSL.SUBJID	Perm
ADPP	SEX	ADSL.SEX	Perm
ADPP	ARM	ADSL.ARM	Perm
ADPP	ARMN	ADSL.ARMN	Perm
ADPP	TRTA	ADAPER.TRTA	Cond
ADPP	TRTAN	ADAPER.TRATAN	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	PPTESTCD	PP.PPTESTCD	Perm
ADPP	PPTEST	PP.PPTEST	Perm
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ADPP	PARAMN	Derived	Perm
ADPP	PARAMCD	Derived	Req
ADPP	PARAMTYP	Derived	Perm

ADAM

ADAM

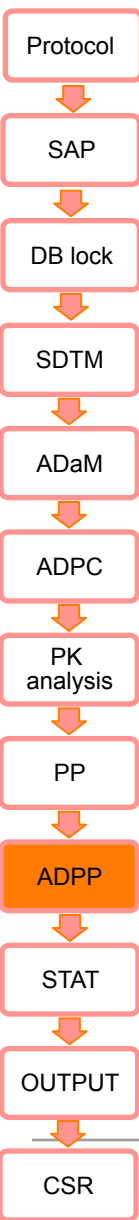
SDTM

PK



■ Additional/derived variables: BDS

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

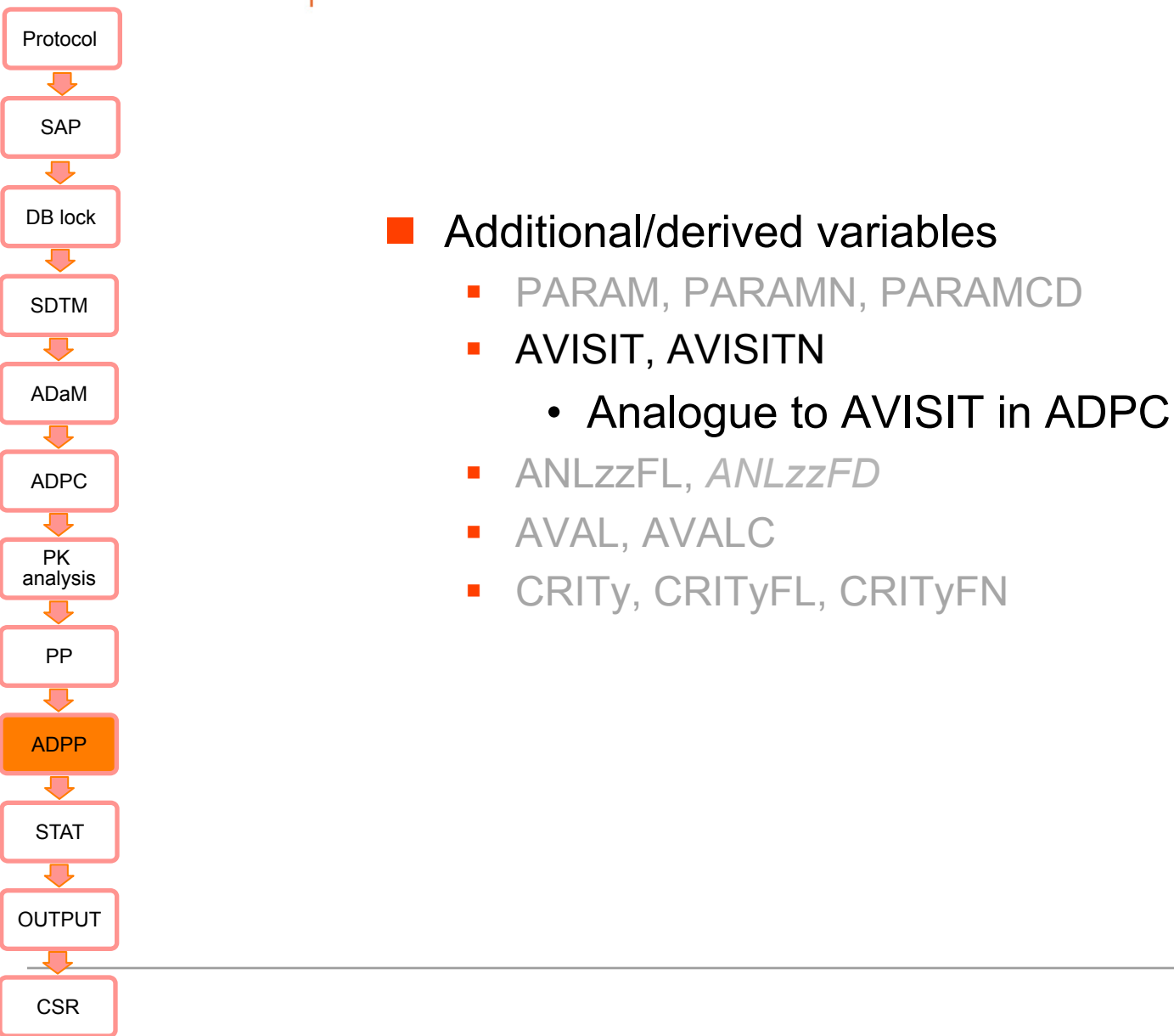


■ Additional/derived variables

- PARAM, PARAMN, PARAMCD
 - PARAM: PK parameter with unit
 - PARAMCD: abbreviation
 - PARAMN: numeric version of PARAM
- AVISIT, AVISITN
- ANLzzFL, *ANLzzFD*
- AVAL, AVALC
- CRITy, CRITyFL, CRITyFN

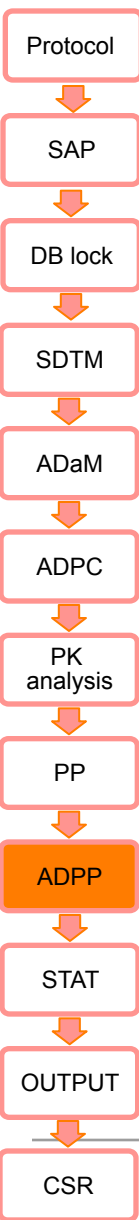
■ PARAM, PARAMCD

PPTSTCD	PPTST	PARAM	PARAMCD	PPORRES	PPORRESU	PPSTRESC	PPSTRESN	PPSTRESU
AUCPEO	AUC %Extrapolation Obs	AUCpeo (%)	AUCPEO	0.215	%	0.215	0.215224	%
AUCIFO	AUC Infinity Obs	AUCifo (h.ng/mL)	AUCIFO	4210	h*ng/mL	4.21	4.208398	h*µg/mL
AUCLST	AUC to Last Nonzero Conc	AUClst (h.ng/mL)	AUCLST	4200	h*ng/mL	4.2	4.199341	h*µg/mL
C24H	Plasma Concentration at 24h	C24h (ng/mL)	C24H	2.05	ng/mL	2.05	2.0	ng/mL
CMAX	Max Conc	Cmax (ng/mL)	CMAX	1210	ng/mL	1210	121	ng/mL
LAMZHL	Half-Life Lambda z	t1/2 (h)	LAMZHL	3.06	h	3.06	3.062535	h
LAMZ	Lambda z	Lambda z (1/h)	LAMZ	0.226	/h	0.226	0.226331	/h
R	Metabolite/Parent Ratio AUClst	R	R	12.3		12.3	12.25012	
TMAX	Time of CMAX	tmax (h)	TMAX	1	h	1		h
R2ADJ	R Squared Adjusted	Adj RSQ	R2ADJ	0.984		0.984	0.983939	



■ AVISIT, AVISITN

SUBJID	TRTA	TRTAN	PPTSTCC	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

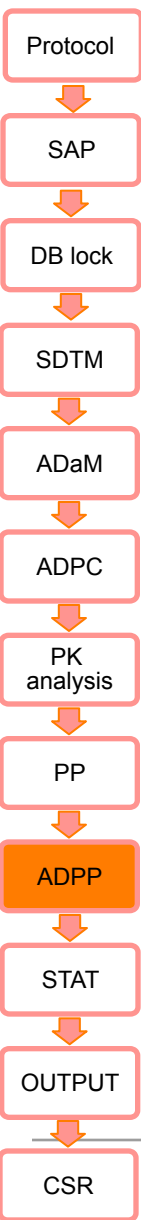


■ Additional/derived variables

- 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	PTESTCD	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

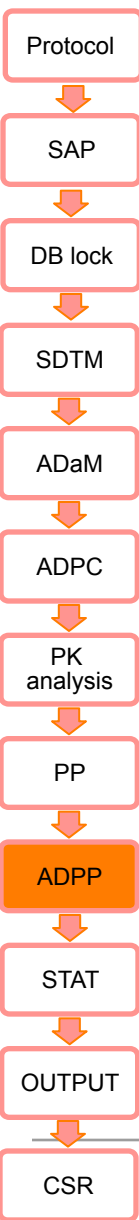


■ Additional/derived variables

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

■ AVAL = PPSTRESN

PARAM	PARAMCD	PPORRES	PPORRESU	PPSTRESC	PPSTRESN	PPSTRESU	AVAL
AUCpeo (%)	AUCPEO	0.215	%	0.215	0.2152249	%	0.2152249
AUCifo (h.ng/mL)	AUCIFO	4210	h*ng/mL	4.21	4.2083988	h*μg/mL	4.2083988
AUClst (h.ng/mL)	AUCLST	4200	h*ng/mL	4.2	4.1993413	h*μg/mL	4.1993413
C24h (ng/mL)	C24H	2.05	ng/mL	2.05	2.05	ng/mL	2.05
Cmax (ng/mL)	CMAX	1210	ng/mL	1210	1210	ng/mL	1210
t1/2 (h)	LAMZHL	3.06	h	3.06	3.0625351	h	3.0625351
Lambda z (1/h)	LAMZ	0.226	/h	0.226	0.2263312	/h	0.2263312
R	R	12.3		12.3	12.250128		12.250128
tmax (h)	TMAX	1	h	1	1	h	1
Adj RSQ	R2ADJ	0.984		0.984	0.9839396		0.9839396

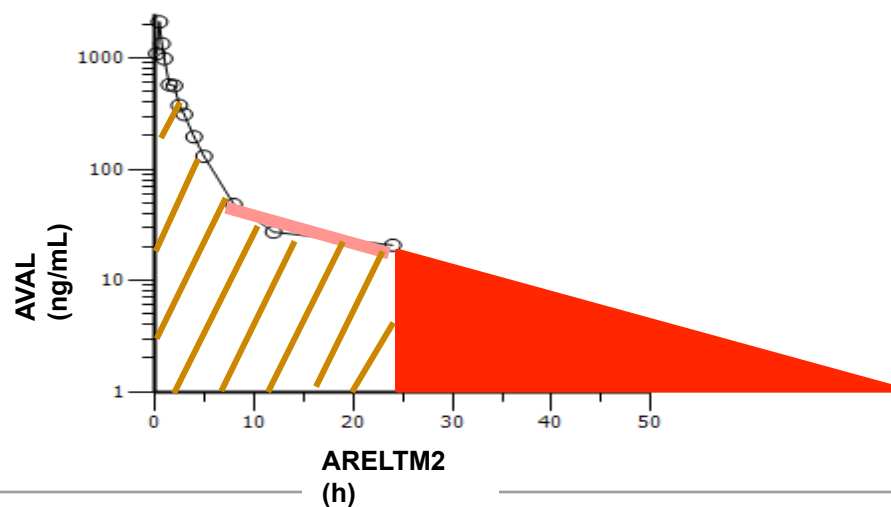


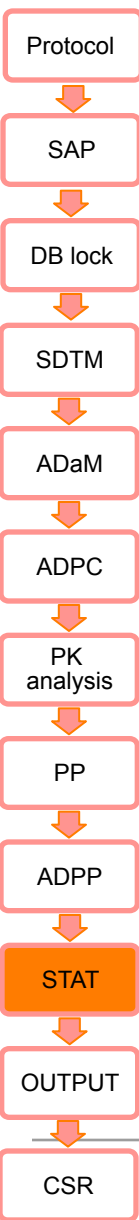
■ Additional/derived variables

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

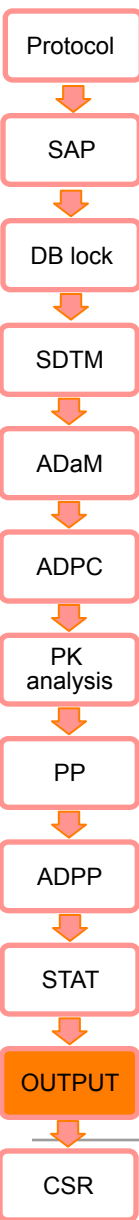
■ AUC_{peo} > 20% AUC_{cifo}

SUBJID	TRTA	TRTAM	PPTESTCD	PPSTRESC	PPSTRESN	PPSTRESU	AVAL	AVISIT	CRIT1	CRIT1FL	ANL01FL	ANL01FD	ANL02FL	ANL02FD
3	REF		AUCPEO	29	29 %		29 DAY1	AUC _{peo} > 20% AUC _{cifo}	Y			INFER STAT		DESCR STAT
3	REF		AUCIFO	5.21	5.21 h*µg/mL		5.21 DAY1	AUC _{peo} > 20% AUC _{cifo}	Y			INFER STAT		DESCR STAT
3	REF	1	AUCLST	4.04	4.04 h*µg/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 /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 Anal 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	BLOQ	99	1510	1720	1850	1360	1410	1030	799	490	254	74.4	16.5	BLOQ	BLOQ
2	NR	1590	2070	1490	1140	768	593	429	375	222	120	60.9	33.1	13.9	3.66
3	BLOQ	BLOQ	19	85.9	152	381	586	772	750	603	342	79.7	26.4	BLOQ	1.26
4	BLOQ	BLOQ	6.72	41.1	122	399	486	605	690	518	318	68.8	BLOQ	1.25	BLOQ
5	BLOQ	BLOQ	8.65	31.5	50	152	372	539	566	409 *	402	171	36.4	5.37	BLOQ
N	4	5	5	5	5	5	5	5	5	4	5	5	5	5	5
Mean	BLOQ	338	723	673	663	612	689	675	636	458	287	91	22.5	4.1	0.984
SD	NC	701	994	854	802	473	413	234	170	165	107	45.3	14.7	5.9	1.59
Min	BLOQ	BLOQ	6.72	31.5	50	152	372	429	375	222	120	60.9	BLOQ	BLOQ	BLOQ
Median	BLOQ	BLOQ	19	85.9	152	399	586	605	690	504	318	74.4	26.4	1.25	BLOQ
Max	BLOQ	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 Anal X

SUBJID	AUCIFO	AUCLST	AUCPEO	C24H	CMAX	LAMZ	LAMZHL	R	R2ADJ	TMAX
1	NE	5.19	NE	0.5	1850	NE	NE	8.76	NE	1
2	5.21 *	4.04	29	13.9	2070	0.06	11.48	10.23	0.99	0.5
3	3.25	3.24	0.48	5.63	772	0.08	8.52	18.05	0.92	2.5
4	3.84	3.81	0.78	4.35	1520	0.14	4.78	13.39	0.95	0.5
5	2.97	2.94	0.89	5.37	566	0.2	3.41	23.77	0.9	3
N	3	5	3	5	5	4	4	5	4	5
Mean	3.36	3.84	0.716	5.95	1360	0.122	7.05	14.8	0.942	1.5
SD	0.445	0.87	0.214	4.9	661	0.065	3.66	6.13	0.038	1.17
Min	2.97	2.94	0.476	0.5	566	0.06	3.41	8.76	0.905	0.5
Median	3.25	3.81	0.781	5.37	1520	0.113	6.65	13.4	0.937	1
Max	3.84	5.19	0.89	13.9	2070	0.203	11.5	23.8	0.991	3

* AUCpeo > 20% AUCifo: PK parameter excluded from statistical analysis

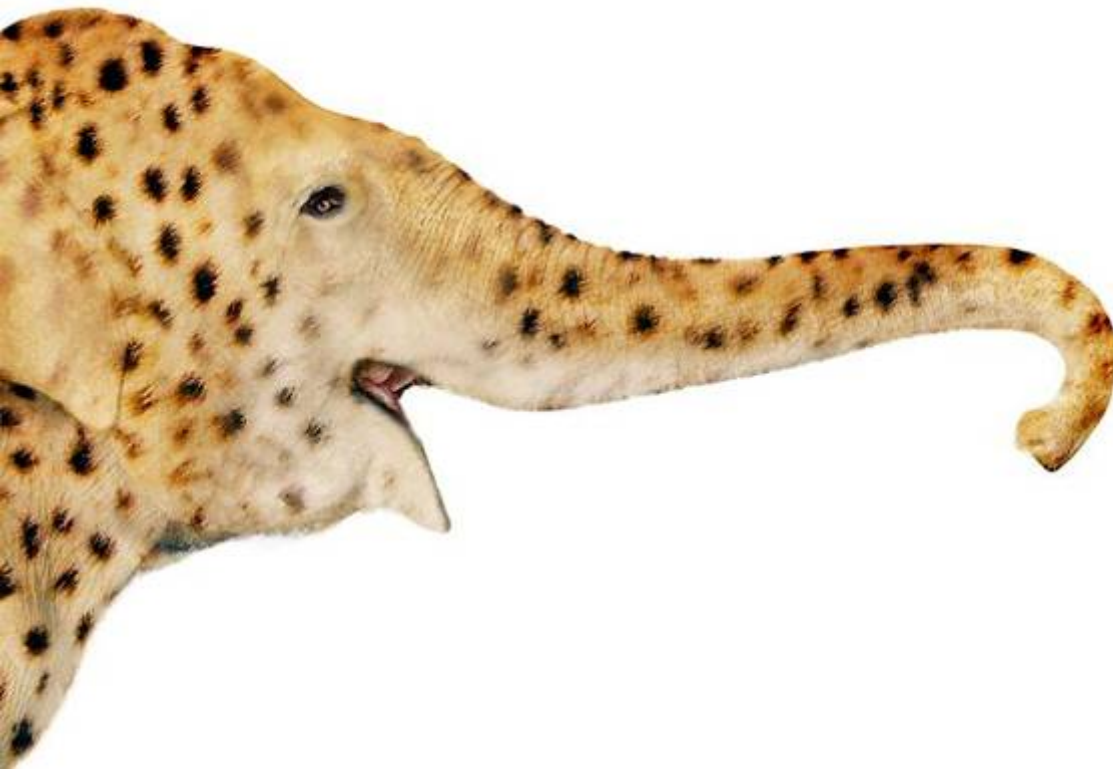
- Introduction
- Gain
- Pharmacokinetic analysis
- **Conclusion**

CONCLUSION

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



THANK YOU FOR YOUR ATTENTION



WHERE MEETS EXPERIENCE SPEED

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