

IMPLEMENTATION OF CDISC ADAM IN PHARMACODYNAMICS

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WHEN YOU NEED TO BE SURE

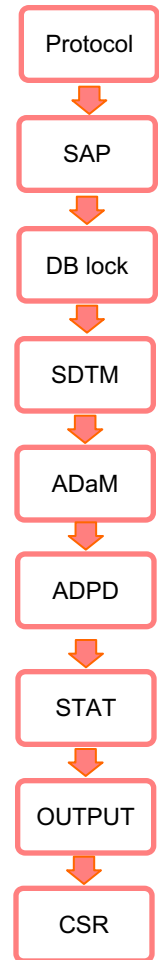


- Introduction
- CDISC ADaM in PD
- Conclusion

- **Introduction**
- CDISC ADaM in PD
- Conclusion

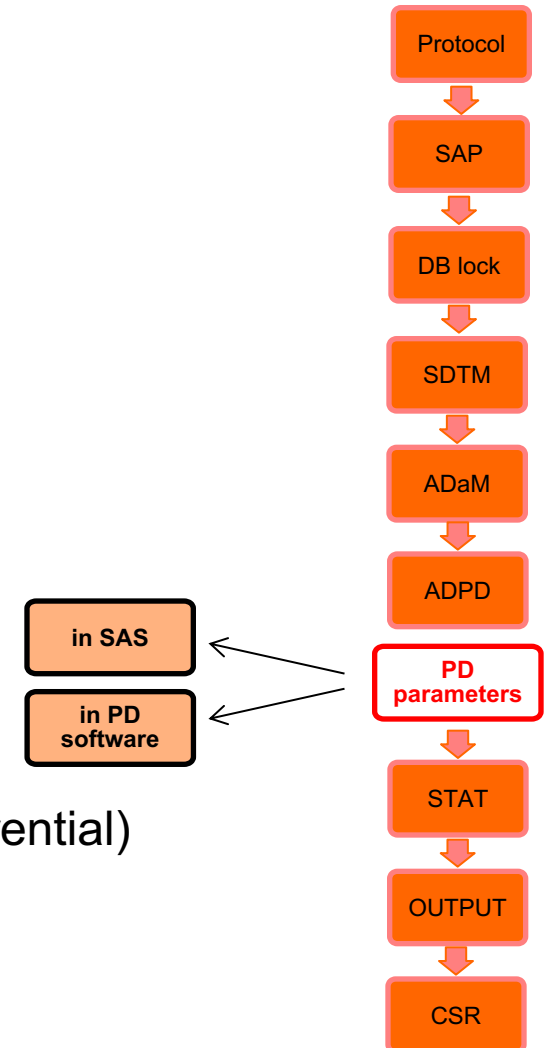
■ Steps of PD study analysis:

- Protocol
- Statistical Analysis Plan
- Database Lock
 - SDTM datasets
 - ADaM datasets
- Creation of ADPD dataset
- Statistical analysis (descriptive / inferential)
- Creation Tables, Listings, Figures
- Clinical Study Report

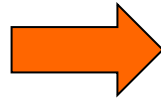


■ Steps of PD study analysis:

- Protocol
- Statistical Analysis Plan
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 - SDTM datasets
 - ADaM datasets
- Creation of ADPD dataset
- **Estimation of PD parameters**
- Statistical analysis (descriptive / inferential)
- Creation Tables, Listings, Figures
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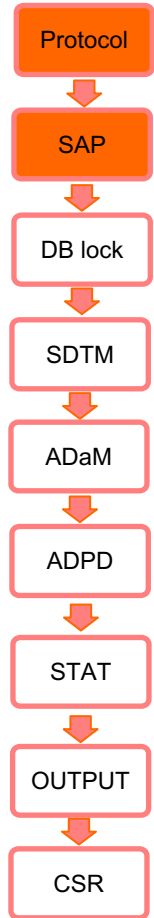


- Introduction
- **CDISC ADaM in PD**
- Conclusion



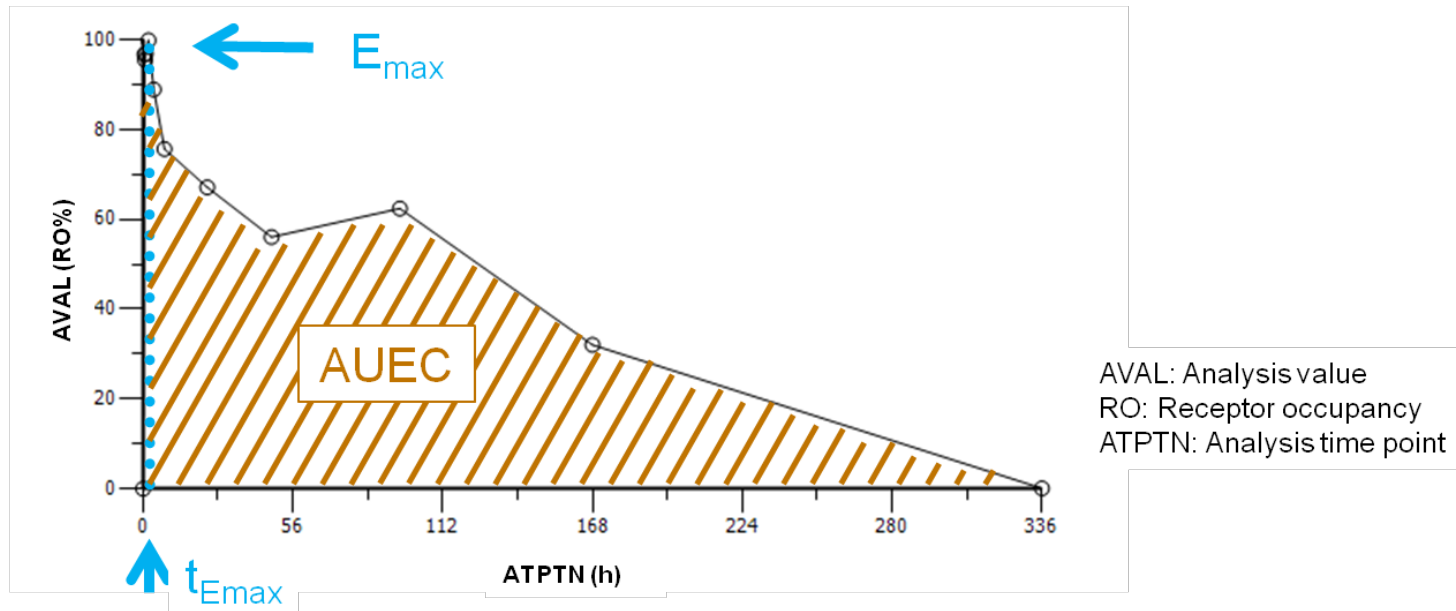
Approach to:

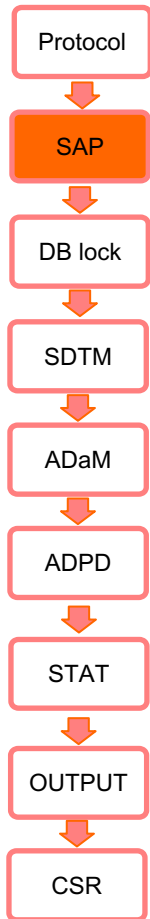
- Create the ADPD dataset
- Capture the PD parameters



Protocol / SAP:

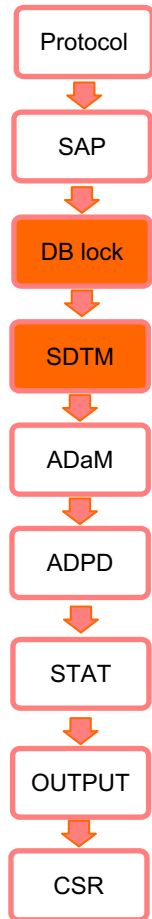
- PD **marker** to be monitored
- PD **measurement**
 - **Values already available** in SDTM PD dataset (e.g., receptor occupancy)
 - Or need to **calculate (%) change from baseline** (e.g., marker serum conc.)
- PD **parameters** : $E_{\max}$ $t_{E_{\max}}$ AUEC



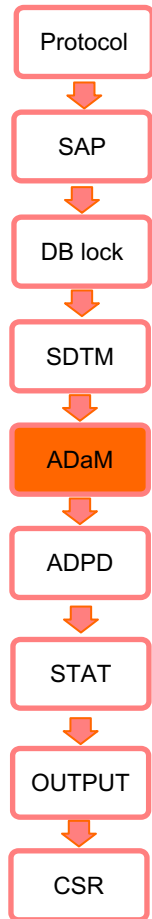


■ Statistical Analysis Plan

- PD population
- Handling of data
- Statistical analysis



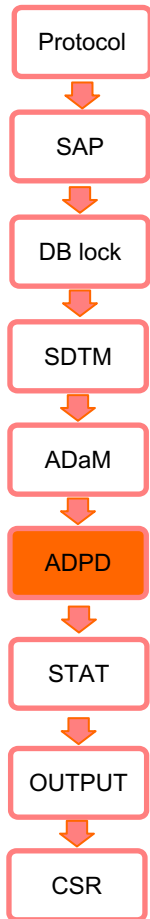
- Database lock
- SDTM datasets
 - DM (Demographics)
 - EX (Exposure)
 - PD (Pharmacodynamics)
 - CM (Concomitant medications)
 - AE (Adverse events)
 - DV (Protocol deviations)
 - CO (Comments)



■ ADaM datasets

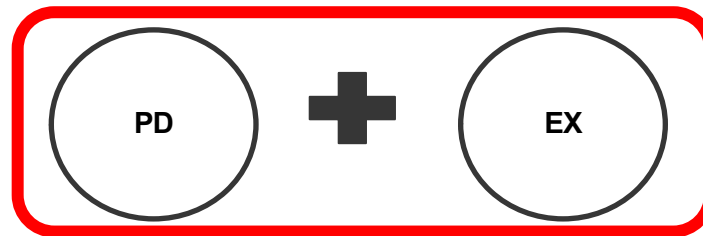
- ADSL (Subject-level Analysis Dataset)
- ADPHASE (Analysis of Subject Phases and Periods)

CREATION OF ADPD

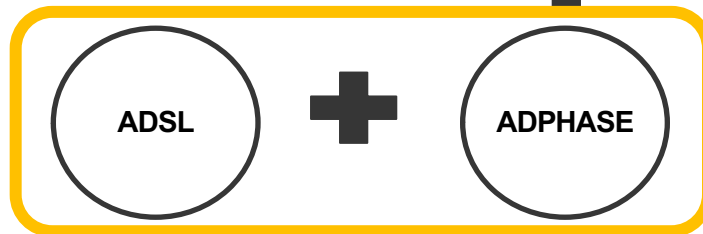


- In SAS
- Based upon define.xml

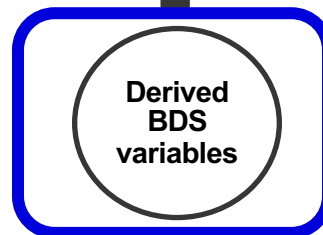
SDTM



ADaM



PD

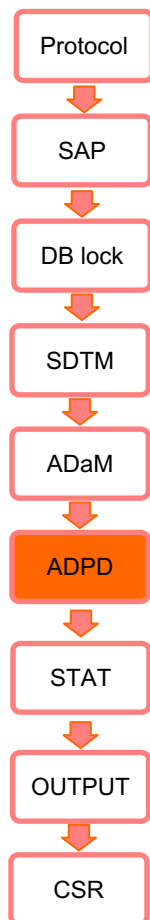


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CREATION OF ADPD

■ Analysis variable metadata



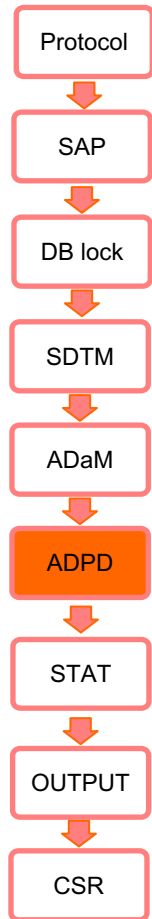
Dataset name	Variable name	Source / Derivation	Core
domain	name	source	core
ADPD	STUDYID	PD.STUDYID	Req
ADPD	USUBJID	PD.USUBJID	Req
ADPD	SUBJID	ADSL.SUBJID	Perm
ADPD	ARM	ADSL.ARM	Perm
ADPD	ARMN	ADSL.ARMN	Perm
ADPD	TRTP	ADPHASE.TRTP	Cond
ADPD	TRTPN	ADPHASE.TRTPN	Perm
ADPD	TRTA	ADPHASE.TRTA	Cond
ADPD	TRTAN	ADPHASE.TR TAN	Perm
ADPD	APHASE	ADPHASE.APHASE	Perm
ADPD	APHASEN	ADPHASE.APHASEN	Perm
ADPD	APERIOD	ADPHASE.APERIOD	Perm
ADPD	APERIODC	ADPHASE.APERIODC	Perm
ADPD	PDSEQ	PD.PDSEQ	Req
ADPD	PDTESTCD	PD.PDTESTCD	Perm
ADPD	PDTEST	PD.PDTEST	Perm
ADPD	PARAM	Derived	Req
ADPD	PARAMN	Numeric version of PARAM	Perm
ADPD	PARAMCD	Short code for PARAM	Req

ADaM (ADSL)

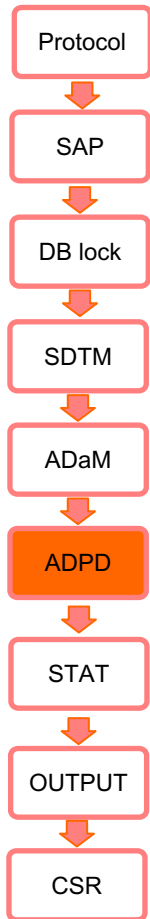
ADaM (ADPHASE)

SDTM (PD)

PD



- Additional/derived variables: BDS
 - PARAM(N), PARAMCD
 - AVISIT, AVISITN
 - ATPT, ATPTN
 - AVAL, BASE, CHG, PCHG
 - AVALCATy(N), CHGCACTy(N), PCHGCACTy(N)
 - ANLzzFL, *ANLzzFD*
 - CRITy, CRITyFL

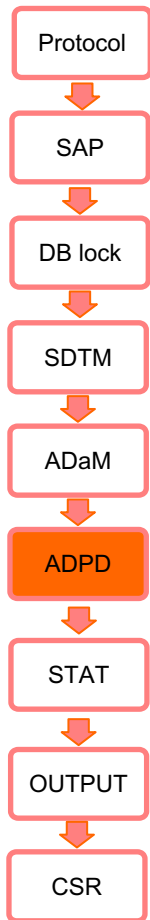


■ Additional/derived variables

■ PARAM(N), PARAMCD

- PARAM: based upon PDTEST and PDSTRESU
- PARAMCD: abbreviation

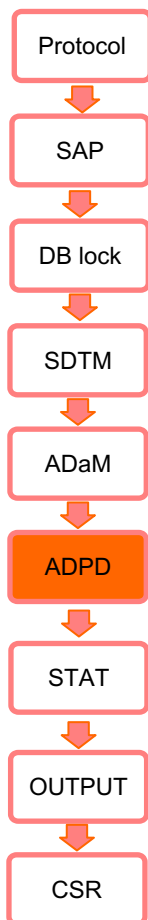
PDTESTCD	PDTEST	PARAM	PARAMCD	PDORRES	PDORRESU	PDSTRESC	PDSTRESN	PDSTRESU
TESTX	TestX	TestX (ng/mL)	TESTX	9380	ng/mL	9380	9380	ng/mL
TESTX	TestX	TestX (ng/mL)	TESTX	9870	ng/mL	9870	9870	ng/mL
TESTX	TestX	TestX (ng/mL)	TESTX	8770	ng/mL	8770	8770	ng/mL
TESTX	TestX	TestX (ng/mL)	TESTX	9590	ng/mL	9590	9590	ng/mL
TESTX	TestX	TestX (ng/mL)	TESTX	8860	ng/mL	8860	8860	ng/mL
TESTX	TestX	TestX (ng/mL)	TESTX	7270	ng/mL	7270	7270	ng/mL
TESTX	TestX	TestX (ng/mL)	TESTX	6700	ng/mL	6700	6700	ng/mL
TESTX	TestX	TestX (ng/mL)	TESTX	5920	ng/mL	5920	5920	ng/mL
TESTX	TestX	TestX (ng/mL)	TESTX	4970	ng/mL	4970	4970	ng/mL
TESTX	TestX	TestX (ng/mL)	TESTX	<3500	ng/mL	<3500	.	ng/mL
TESTX	TestX	TestX (ng/mL)	TESTX	4140	ng/mL	4140	4140	ng/mL
TESTX	TestX	TestX (ng/mL)	TESTX	4360	ng/mL	4360	4360	ng/mL



■ Additional/derived variables

- PARAM(N), PARAMCD
- AVISIT, AVISITN
 - Derived from VISIT and VISITNUM
 - PD measurements that refer to same exposure

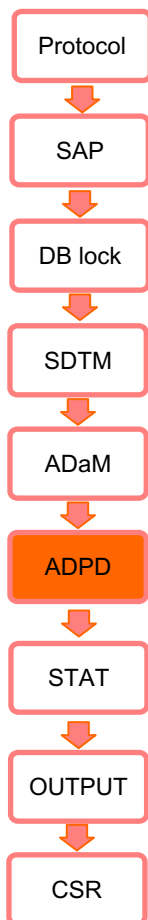
SUBJID	TRTA	VISITNUM	VISIT	PDTPT	AVISIT	AVISITN
1	TRT	1.001	PERIOD1_DAY1	PRE-DOSE	DAY1	1
1	TRT	1.001	PERIOD1_DAY1	2H	DAY1	1
1	TRT	1.001	PERIOD1_DAY1	4H	DAY1	1
1	TRT	1.001	PERIOD1_DAY1	8H	DAY1	1
1	TRT	1.002	PERIOD1_DAY2	24H	DAY1	1
1	TRT	1.003	PERIOD1_DAY3	48H	DAY1	1
1	TRT	1.004	PERIOD1_DAY4	72H	DAY1	1
1	TRT	1.005	PERIOD1_DAYS5	96H	DAY1	1
1	TRT	1.007	PERIOD1_DAY7	144H	DAY1	1
1	TRT	1.015	PERIOD1_DAY15	336H	DAY1	1
1	TRT	1.022	PERIOD1_DAY22	504H	DAY1	1
1	TRT	1.029	PERIOD1_DAY29	672H	DAY1	1



■ Additional/derived variables

- PARAM(N), PARAMCD
- AVISIT, AVISITN
- ATPT, ATPTN
 - Derived from PDTPT and PDTPTNUM
 - If estimation of PD parameters

SUBJID	TRTA	AVISIT	PDTPT	PDTPTNUM	ATPT	ATPTN
1	TRT	DAY1	PRE-DOSE	-1	PRE-DOSE	0
1	TRT	DAY1	2H	120	2H	2
1	TRT	DAY1	4H	240	4H	4
1	TRT	DAY1	8H	480	8H	8
1	TRT	DAY1	24H	1440	24H	24
1	TRT	DAY1	48H	2880	48H	48
1	TRT	DAY1	72H	4320	72H	72
1	TRT	DAY1	96H	5760	96H	96
1	TRT	DAY1	144H	8640	144H	144
1	TRT	DAY1	336H	20160	336H	336



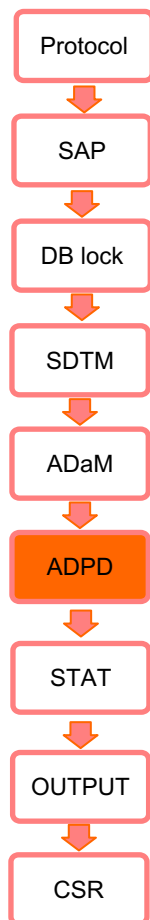
■ Additional/derived variables

- PARAM(N), PARAMCD
- AVISIT, AVISITN
- ATPT, ATPTN
- AVAL, BASE, CHG, PCHG
 - AVAL= PDSTRESN (*with possible imputations*)
 - BASE= AVAL at baseline
 - CHG= AVAL-BASE
 - PCHG= ((AVAL-BASE)/BASE)*100

PARAM	AVISIT	PDSTRESN	AVAL	DTYPE	ABLFL	BASE	CHG	PCHG
PDmeasurement(unit)	SCREENING	36	36					
PDmeasurement(unit)	BASELINE	36	36	LVPD	Y	36		
PDmeasurement(unit)	DAY1	30	30			36	-6	-16.67
PDmeasurement(unit)	DAY2	26	26			36	-10	-27.78
PDmeasurement(unit)	DAY3	22	22			36	-14	-38.89

Reduction PD (%)	DAY1	16.67
Reduction PD (%)	DAY2	27.78
Reduction PD (%)	DAY3	38.89

Percentage reduction change from baseline
 $100 - (AVAL/BASE) * 100$



■ Additional/derived variables

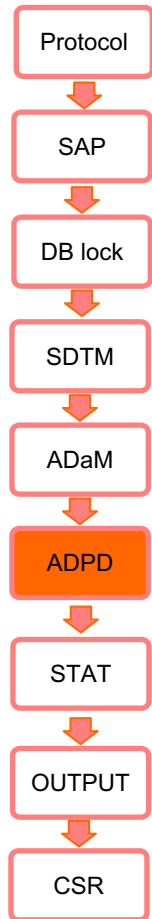
- PARAM(N), PARAMCD
- AVISIT, AVISITN
- ATPT, ATPTN
- AVAL, BASE, CHG, PCHG
- AVALCATy(N), CHGCATy(N), PCHGCATy(N)

- Percentage reduction from baseline

PARAM	AVISIT	AVAL	AVALCAT1
Reduction PD (%)	DAY1	16.67	[0, 20[%
Reduction PD (%)	DAY2	27.78	[20, 40[%
Reduction PD (%)	DAY3	38.89	[20, 40[%

- Change from baseline / percent change from baseline

PARAM	AVISIT	AVAL	BASE	CHG	CHGCAT1	PCHG	PCHGCAT1
PDmeasurement (unit)	DAY1	30	36	-6	] -10, 0] unit	-16.67	] -20, 0] %
PDmeasurement (unit)	DAY2	26	36	-10	] -20, -10] unit	-27.78	] -40, -20] %
PDmeasurement (unit)	DAY3	22	36	-14	] -20, -10] unit	-38.89	] -40, -20] %

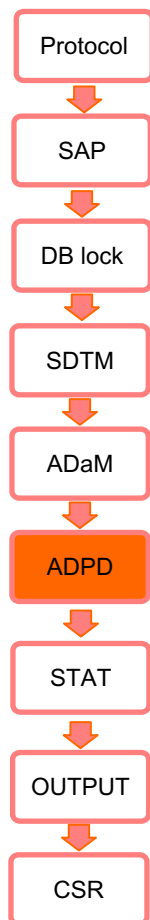


■ Additional/derived variables

- PARAM(N), PARAMCD
- AVISIT, AVISITN
- ATPT, ATPTN
- AVAL, BASE, CHG, PCHG
- AVALCATy(N), CHGCATy(N), PCHGCATy(N)
- ANLzzFL, *ANLzzFD*
 - Select set of records for analyses:
 - Descriptive statistical analysis (*ANL01FL*)
 - Inferential statistical analysis (*ANL02FL*)
 - PD analysis (estimation of PD parameters) (*ANL03FL*)
- CRITy, CRITyFL

■ ANLzzFL, ANLzzFD

SUBJID	TRTA	PARAMCD	AVISIT	ATPT	AVAL	ABLFL	PCHG	ANL01FL	ANL01FD	ANL02FL	ANL02FD	ANL03FL	ANL03FD
1	TRT	TESTX	DAY1	PRE-DOSE	9380								
1	TRT	TESTX	DAY1	BASELINE	9380	Y		Y	DESCR STAT	Y	INFER STAT	Y	PD ANALYSIS
1	TRT	TESTX	DAY1	2H	9870		5.22	Y	DESCR STAT	Y	INFER STAT	Y	PD ANALYSIS
1	TRT	TESTX	DAY1	4H	8770		-6.50	Y	DESCR STAT	Y	INFER STAT	Y	PD ANALYSIS
1	TRT	TESTX	DAY1	8H	9590		2.24	Y	DESCR STAT	Y	INFER STAT	Y	PD ANALYSIS
1	TRT	TESTX	DAY1	24H	8860		-5.54	Y	DESCR STAT	Y	INFER STAT	Y	PD ANALYSIS
1	TRT	TESTX	DAY1	48H	7270		-22.49	Y	DESCR STAT	Y	INFER STAT	Y	PD ANALYSIS
1	TRT	TESTX	DAY1	72H	6700		-28.57	Y	DESCR STAT	Y	INFER STAT	Y	PD ANALYSIS
1	TRT	TESTX	DAY1	96H	5920		-36.89	Y	DESCR STAT	Y	INFER STAT	Y	PD ANALYSIS
1	TRT	TESTX	DAY1	144H	4970		-47.01	Y	DESCR STAT	Y	INFER STAT	Y	PD ANALYSIS
1	TRT	TESTX	DAY1	336H	3500		-62.69	Y	DESCR STAT	Y	INFER STAT	Y	PD ANALYSIS
1	TRT	TESTX	DAY1	504H	4140		-55.86	Y	DESCR STAT	Y	INFER STAT	Y	PD ANALYSIS
1	TRT	TESTX	DAY1	672H	4360		-53.52	Y	DESCR STAT	Y	INFER STAT	Y	PD ANALYSIS



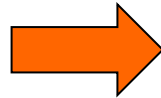
■ Additional/derived variables

- PARAM(N), PARAMCD
- AVISIT, AVISITN
- ATPT, ATPTN
- AVAL, BASE, CHG, PCHG
- AVALCATy(N), CHGCAy(N), PCHGCAy(N)
- ANLzzFL, ANLzzFD
- CRITy, CRITyFL

• Criteria evaluation

SUBJID	TRTA	PARAMCD	AVISIT	ATPT	AVAL	ABLFL	PCHG	CRIT1	CRIT1FL
1	TRT	TESTX	DAY1	PRE-DOSE	9380				
1	TRT	TESTX	DAY1	BASELINE	9380	Y			
1	TRT	TESTX	DAY1	2H	9870		5.22		
1	TRT	TESTX	DAY1	4H	5920		-36.89		
1	TRT	TESTX	DAY1	8H	9590		-62.69	PCHG <-50%	Y
1	TRT	TESTX	DAY1	24H	8860		-55.86	PCHG <-50%	Y
1	TRT	TESTX	DAY1	48H	7270		-53.52	PCHG <-50%	Y

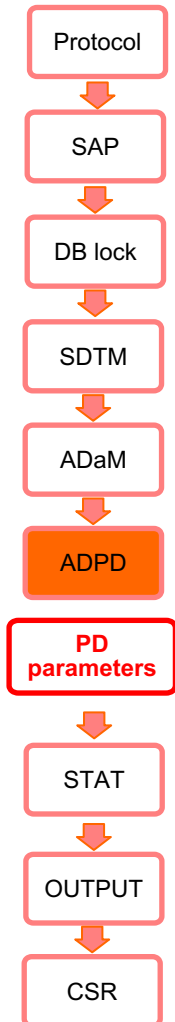
- Introduction
- **CDISC ADaM in PD**
- Conclusion



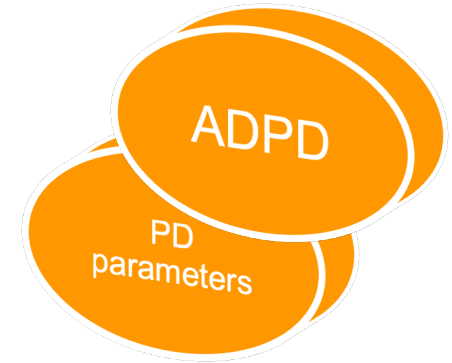
Approach to:

- ✓ Create the ADPD dataset
 - Capture the PD parameters

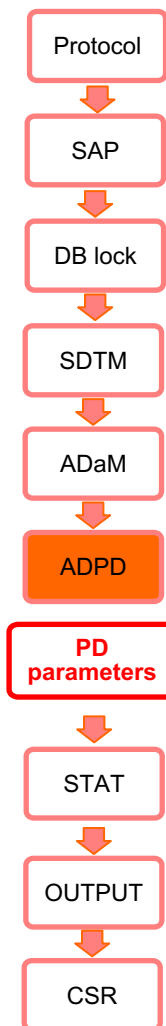
ESTIMATION OF PD PARAMETERS IN SAS WITHIN THE ADPD



- For **not complex calculations**
- Include observations for PD analysis:
 - **PD ANALYSIS** => 'Y' (*ANL03FL*)
- Estimation of PD parameters, using:
 - Time: **ATPTN**
 - Measurement: **AVAL / CHG / PCHG**



ESTIMATION OF PD PARAMETERS IN SAS WITHIN THE ADPD

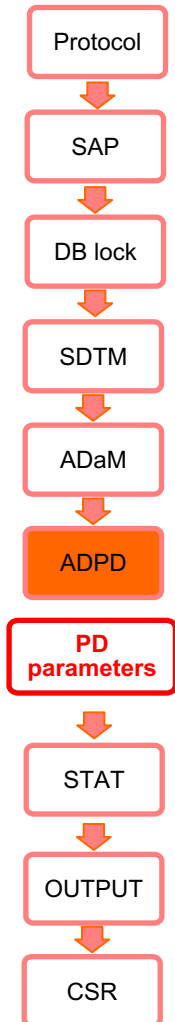


PARAM	AVISIT	ATPT	ATPTN	AVAL
PDmeasurement (unit)	DAY1	PRE-DOSE	0	0.08
PDmeasurement (unit)	DAY1	0.5H	0.5	96.58
PDmeasurement (unit)	DAY1	0.75H	0.75	95.39
PDmeasurement (unit)	DAY1	1H	1	96.77
PDmeasurement (unit)	DAY1	2H	2	99.75
PDmeasurement (unit)	DAY1	4H	4	88.82
PDmeasurement (unit)	DAY1	8H	8	75.59
PDmeasurement (unit)	DAY1	24H	24	67.06
PDmeasurement (unit)	DAY1	48H	48	56.03
PDmeasurement (unit)	DAY1	96H	96	62.37
PDmeasurement (unit)	DAY1	168H	168	32.05
PDmeasurement (unit)	DAY1	336H	336	0.17
PDmeasurement (unit)	DAY1	672H	672	0.20
PDmeasurement (unit)	DAY1	1344H	1344	0.20
PDmeasurement (unit)	DAY1	2016H	2016	0.34
AUEC (unit)	DAY1			10504.28
Emax (unit)	DAY1			99.75
tEmax (unit)	DAY1			2

Additional/derived variables

- PARAM(N), PARAMCD
- AVISIT, AVISITN
- AVAL
- ANLzzFL, ANLzzFD
- CRITy, CRITyFL

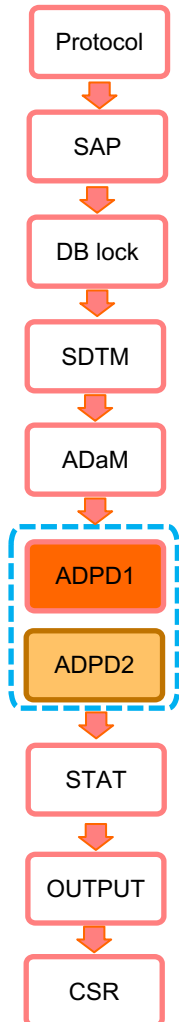
ESTIMATION OF PD PARAMETERS IN PD SOFTWARE WITH ADPD AS INPUT FILE



- For more complex calculations
- **ADPD** is imported in Phoenix® WinNonLin
- Include observations for PD analysis:
 - **PD ANALYSIS** => 'Y' (*ANL03FL*)
- Estimation of PD parameters, using:
 - Time: **ATPTN**
 - Measurement: **AVAL / CHG / PCHG**
- Output file: PD parameters
- **ADPD** is created (in SAS)



ESTIMATION OF PD PARAMETERS IN PD SOFTWARE WITH ADPD AS INPUT FILE



- For more complex calculations
- **ADPD1** is imported in Phoenix[®] WinNonLin
- Include observations for PD analysis:
 - **PD ANALYSIS** => 'Y' (*ANL03FL*)
- Estimation of PD parameters, using:
 - Time: **ATPTN**
 - Measurement: **AVAL / CHG / PCHG**
- Output file: PD parameters
- **ADPD2** is created (in SAS)

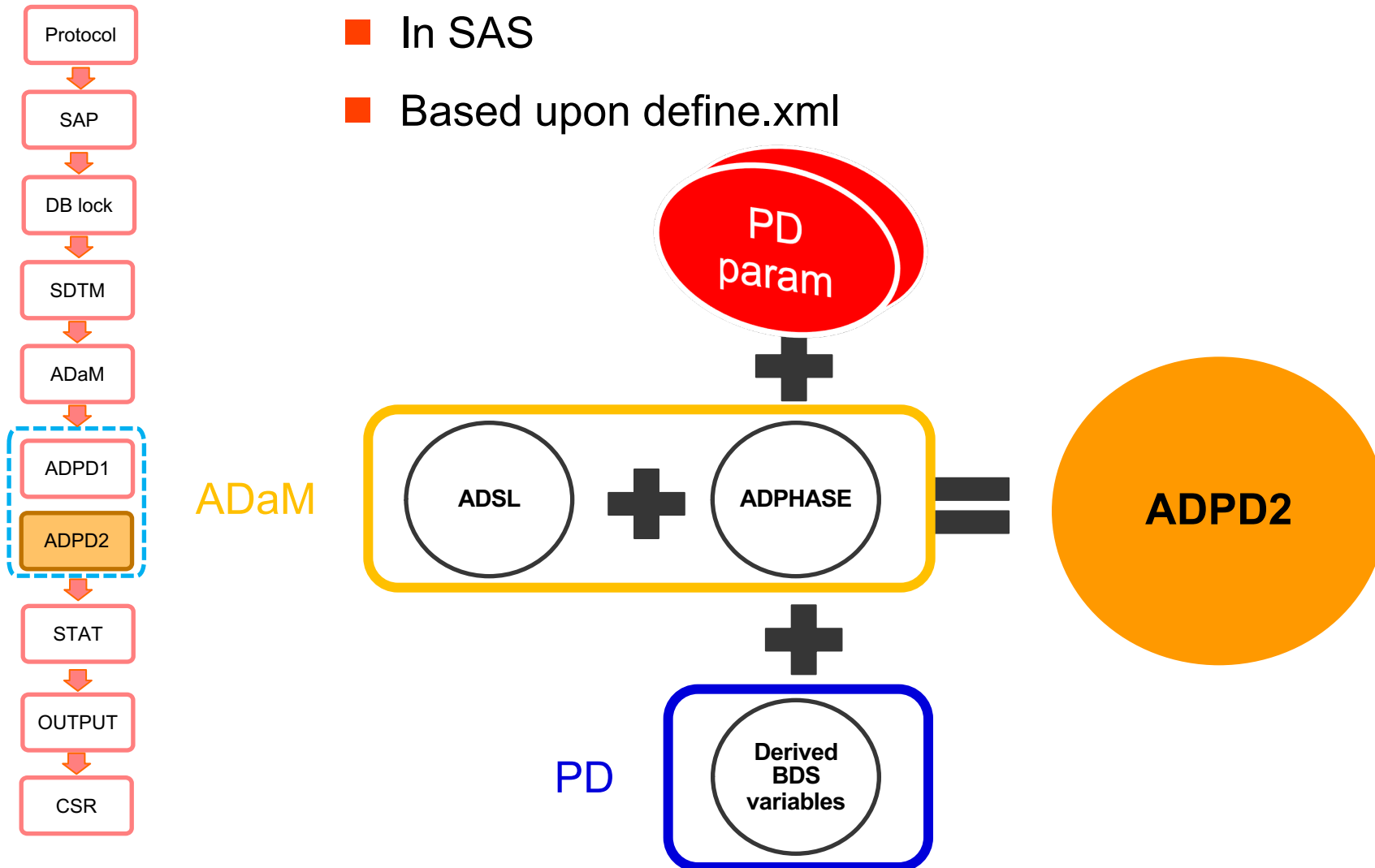


CREATION OF ADPD2

- In SAS
- Based upon define.xml

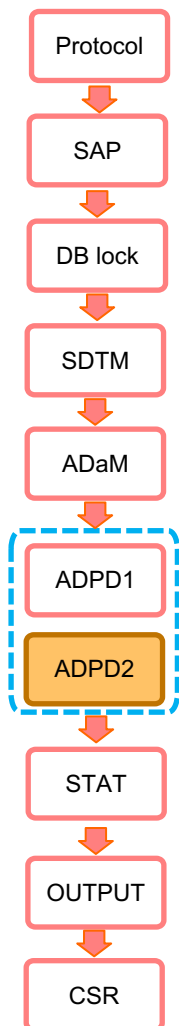
ADaM

PD



CREATION OF ADPD2

- Analysis variable metadata (same as ADPD1)



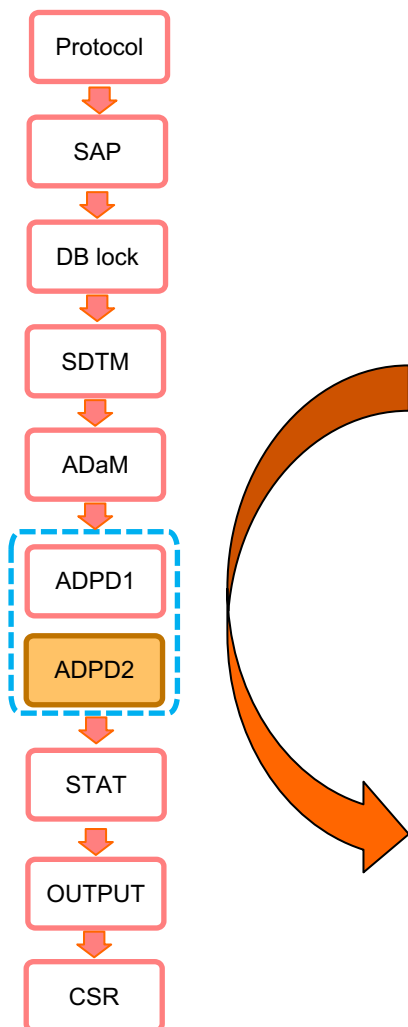
Dataset name	Variable name	Source / Derivation	Core
domain	name	source	core
ADPD	STUDYID	PD.STUDYID	Req
ADPD	USUBJID	PD.USUBJID	Req
ADPD	SUBJID	ADSL.SUBJID	Perm
ADPD	ARM	ADSL.ARM	Perm
ADPD	ARMN	ADSL.ARMN	Perm
ADPD	TRTP	ADPHASE.TRTP	Cond
ADPD	TRTPN	ADPHASE.TRTPN	Perm
ADPD	TRTA	ADPHASE.TRTA	Cond
ADPD	TRTAN	ADPHASE.TRTAN	Perm
ADPD	APHASE	ADPHASE.APHASE	Perm
ADPD	APHASEN	ADPHASE.APHASEN	Perm
ADPD	APERIOD	ADPHASE.APERIOD	Perm
ADPD	APERIODC	ADPHASE.APERIODC	Perm
ADPD	PARAM	Derived	Req
ADPD	PARAMN	Numeric version of PARAM	Perm
ADPD	PARAMCD	Short code for PARAM	Req

ADaM (ADSL)

ADaM (ADPHASE)

PD

CREATION OF ADPD2



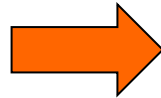
ADPD1

PARAM	AVISIT	ATPT	ATPTN	AVAL	DTYPE	ABLFL	BASE	PCHG
PD measurement (unit)	DAY1	PRE-DOSE	0	9380				
PD measurement (unit)	DAY1	BASELINE	0	9380	LVPD	Y	9380	0.00
PD measurement (unit)	DAY1	2H	2	9870			9380	5.22
PD measurement (unit)	DAY1	4H	4	8770			9380	-6.50
PD measurement (unit)	DAY1	8H	8	9590			9380	2.24
PD measurement (unit)	DAY1	24H	24	8860			9380	-5.54
PD measurement (unit)	DAY1	48H	48	7270			9380	-22.49
PD measurement (unit)	DAY1	72H	72	6700			9380	-28.57
PD measurement (unit)	DAY1	96H	96	5920			9380	-36.89
PD measurement (unit)	DAY1	144H	144	4970			9380	-47.01
PD measurement (unit)	DAY1	336H	336	3340			9380	-64.39
PD measurement (unit)	DAY1	504H	504	4140			9380	-55.86
PD measurement (unit)	DAY1	672H	672	4360			9380	-53.52

ADPD2

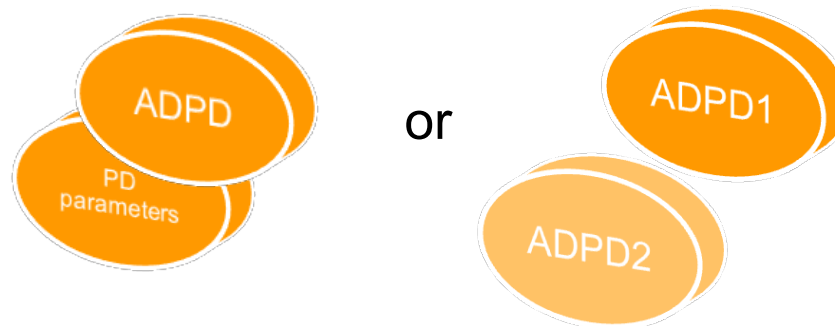
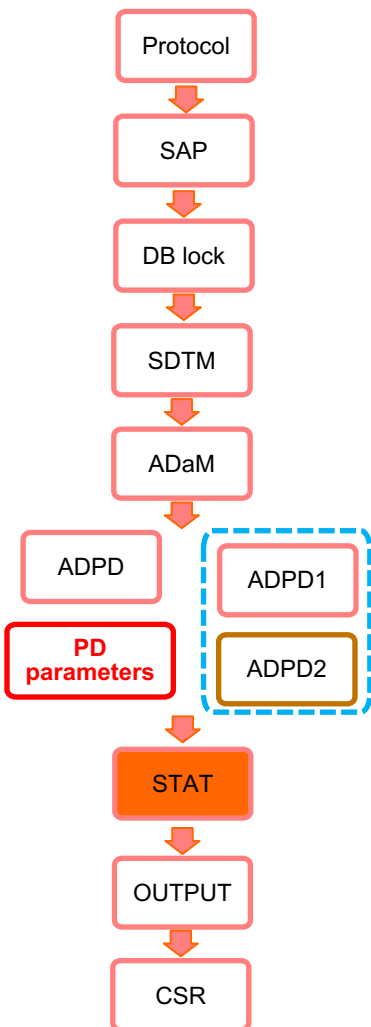
PARAM	AVISIT	AVAL	ANL01FL	ANL01FD	ANL02FL	ANL02FD	CRIT1	CRIT1FL
AUEC (unit)	DAY1	-33762	Y	DESCR STAT	Y	INFER STAT		
Emax (unit)	DAY1	-64.39	Y	DESCR STAT	Y	INFER STAT	Emax < -50%	Y
tEmax (unit)	DAY1	336	Y	DESCR STAT	Y	INFER STAT		

- Introduction
- **CDISC ADaM in PD**
- Conclusion



Approach to:

- ✓ Create the ADPD dataset
- ✓ Capture the PD parameters

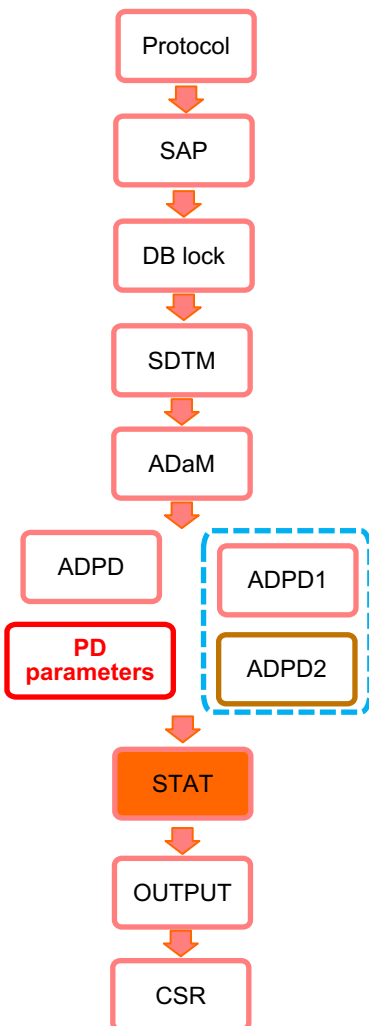


Include observations for statistical analysis:

- **DESCR STAT => 'Y'** (*ANL01FL*)
- **INFER STAT => 'Y'** (*ANL02FL*)

Example: **Percentage receptor occupancy**

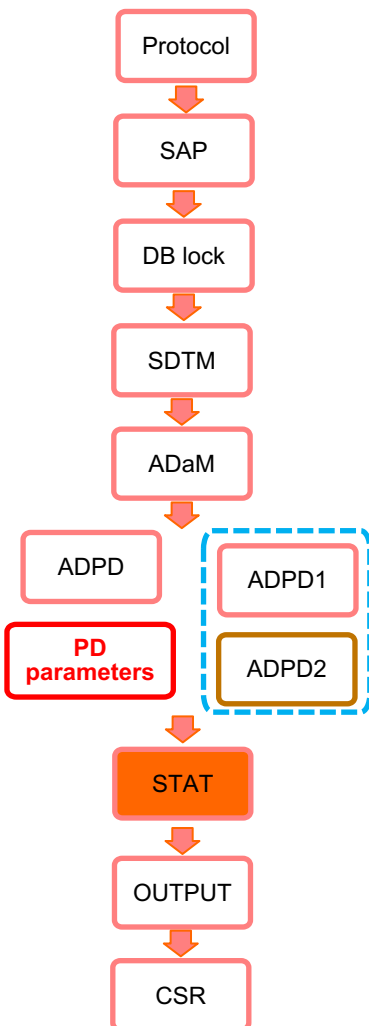
AVALCAT1 => categorization of AVAL



SUBJID	TRTA	PARAM	AVISIT	ATPT	ATPTN	AVAL	AVALCAT1
1	TRT	PD measurement (unit)	DAY1	PRE-DOSE	0	0.08	< 50%
1	TRT	PD measurement (unit)	DAY1	0.5H	0.5	96.58	[90,100] %
1	TRT	PD measurement (unit)	DAY1	0.75H	0.75	95.39	[90,100] %
1	TRT	PD measurement (unit)	DAY1	1H	1	96.77	[90,100] %
1	TRT	PD measurement (unit)	DAY1	2H	2	99.75	[90,100] %
1	TRT	PD measurement (unit)	DAY1	4H	4	88.82	[80,90[%
1	TRT	PD measurement (unit)	DAY1	8H	8	75.59	[70,80[%
1	TRT	PD measurement (unit)	DAY1	24H	24	67.06	[60,70[%
1	TRT	PD measurement (unit)	DAY1	48H	48	56.03	[50,60[%
1	TRT	PD measurement (unit)	DAY1	96H	96	62.37	[60,70[%
1	TRT	PD measurement (unit)	DAY1	168H	168	32.05	< 50%
1	TRT	PD measurement (unit)	DAY1	336H	336	0.17	< 50%
1	TRT	PD measurement (unit)	DAY1	672H	672	0.20	< 50%
1	TRT	PD measurement (unit)	DAY1	1344H	1344	0.20	< 50%
1	TRT	PD measurement (unit)	DAY1	2016H	2016	0.34	< 50%
1	TRT	AUEC (unit)	DAY1			10504.28	
1	TRT	Emax (unit)	DAY1			99.75	[90,100] %
1	TRT	tEmax (unit)	DAY1			2	



Example: Percentage receptor occupancy: Frequency Tabulation



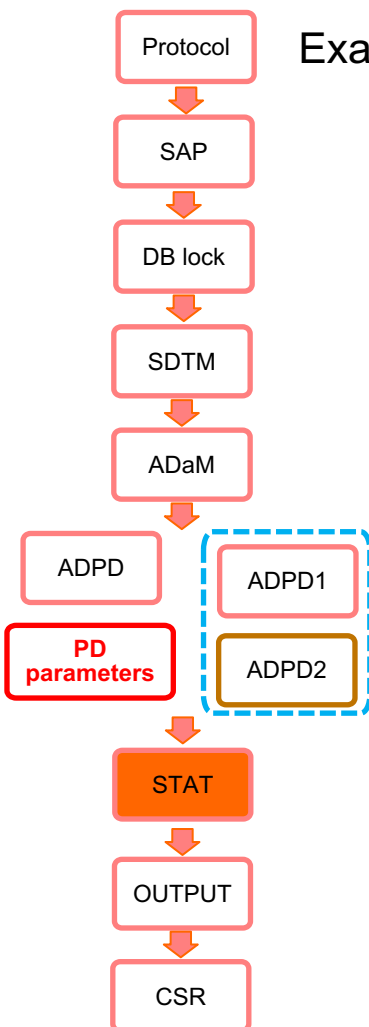
SUBJID	TRTA	PARAM
1	TRT	PD measurement
1	TRT	PD measurement
1	TRT	PD measurement
1	TRT	PD measurement
1	TRT	PD measurement
1	TRT	PD measurement
1	TRT	PD measurement
1	TRT	PD measurement
1	TRT	PD measurement
1	TRT	PD measurement
1	TRT	PD measurement
1	TRT	PD measurement
1	TRT	PD measurement
1	TRT	PD measurement
1	TRT	PD measurement
1	TRT	AUEC (unit)
1	TRT	Emax (unit)
1	TRT	tEmax (unit)

Table 1 Percentage Receptor Occupancy : Frequency Tabulation

Time point / Category	Placebo		TRT X		TRT Y		TRT	
	N=6		N=6		N=6		N=6	
	N	%	N	%	N	%	N	%
0.5h								
< 50%	6	100	6	100				
[50,60[%					3	50		
[60,70[%					3	50		
[70,80[%							2	33.3
[80,90[%							2	33.3
[90,100] %							2	33.3
...								
8h								
< 50%	6	100	3	50	4	66.6		
[50,60[%			3	50	2	33.3		
[60,70[%							3	50
[70,80[%							3	50
...								
24h								
< 50%	6	100	6	100	5	83.3		
[50,60[%					1	16.6		
[60,70[%							6	100

Example: $E_{\max}$: Maximum Percentage receptor occupancy

AVALCAT1 => categorization of AVAL



SUBJID	TRTA	PARAM	AVISIT	ATPT	ATPTN	AVAL	AVALCAT1
1	TRT	PD measurement (unit)	DAY1	PRE-DOSE	0	0.08	< 50%
1	TRT	PD measurement (unit)	DAY1	0.5H	0.5	96.58	[90,100] %
1	TRT	PD measurement (unit)	DAY1	0.75H	0.75	95.39	[90,100] %
1	TRT	PD measurement (unit)	DAY1	1H	1	96.77	[90,100] %
1	TRT	PD measurement (unit)	DAY1	2H	2	99.75	[90,100] %
1	TRT	PD measurement (unit)	DAY1	4H	4	88.82	[80,90[%
1	TRT	PD measurement (unit)	DAY1	8H	8	75.59	[70,80[%
1	TRT	PD measurement (unit)	DAY1	24H	24	67.06	[60,70[%
1	TRT	PD measurement (unit)	DAY1	48H	48	56.03	[50,60[%
1	TRT	PD measurement (unit)	DAY1	96H	96	62.37	[60,70[%
1	TRT	PD measurement (unit)	DAY1	168H	168	32.05	< 50%
1	TRT	PD measurement (unit)	DAY1	336H	336	0.17	< 50%
1	TRT	PD measurement (unit)	DAY1	672H	672	0.20	< 50%
1	TRT	PD measurement (unit)	DAY1	1344H	1344	0.20	< 50%
1	TRT	PD measurement (unit)	DAY1	2016H	2016	0.34	< 50%
1	TRT	AUEC (unit)	DAY1			10504.28	
1	TRT	$E_{\max}$ (unit)	DAY1			99.75	[90,100] %
1	TRT	tEmax (unit)	DAY1			2	



Example: $E_{\max}$: Maximum Percentage receptor occupancy: Frequency Tabulation

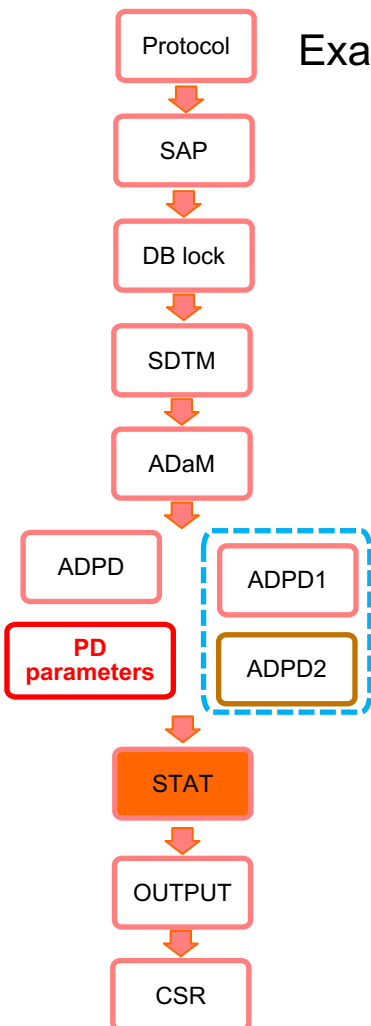
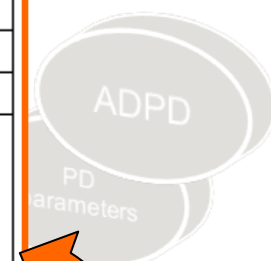


Table 2 $E_{\max}$ (%) Receptor Occupancy : Frequency Tabulation

SUBJID	TRTA	Parameter / Category	Placebo		TRT X		TRT Y		TRT	
			N=6		N=6		N=6		N=6	
			N	%	N	%	N	%	N	%
1	TRT	$E_{\max}$ (%)								
1	TRT	< 50%	6	100	3	50				
1	TRT	[50,60[%			3	50	3	50		
1	TRT	[60,70[%					3	50		
1	TRT	[70,80[%							2	33.3
1	TRT	[80,90[%							2	33.3
1	TRT	[90,100] %							2	33.3
1	TRT	PD measurement (unit)	DAY1	48H		48	56.03	[50,60[%		
1	TRT	PD measurement (unit)	DAY1	96H		96	62.37	[60,70[%		
1	TRT	PD measurement (unit)	DAY1	168H		168	32.05	< 50%		
1	TRT	PD measurement (unit)	DAY1	336H		336	0.17	< 50%		
1	TRT	PD measurement (unit)	DAY1	672H		672	0.20	< 50%		
1	TRT	PD measurement (unit)	DAY1	1344H		1344	0.20	< 50%		
1	TRT	PD measurement (unit)	DAY1	2016H		2016	0.34	< 50%		
1	TRT	AUEC (unit)	DAY1				10504.28			
1	TRT	$E_{\max}$ (unit)	DAY1				99.75	[90,100] %		
1	TRT	tEmax (unit)	DAY1				2			



- Introduction
- CDISC ADaM in PD
- **Conclusion**

CONCLUSION

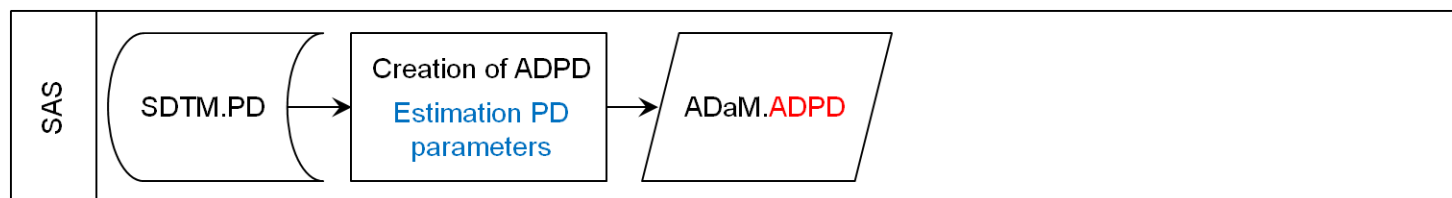
■ ADaM ADPD dataset

- SDTM + ADaM
- Derived variables
 - Based on BDS
 - Modified variables (ANLzzFD)
- **Capture of PD parameters**

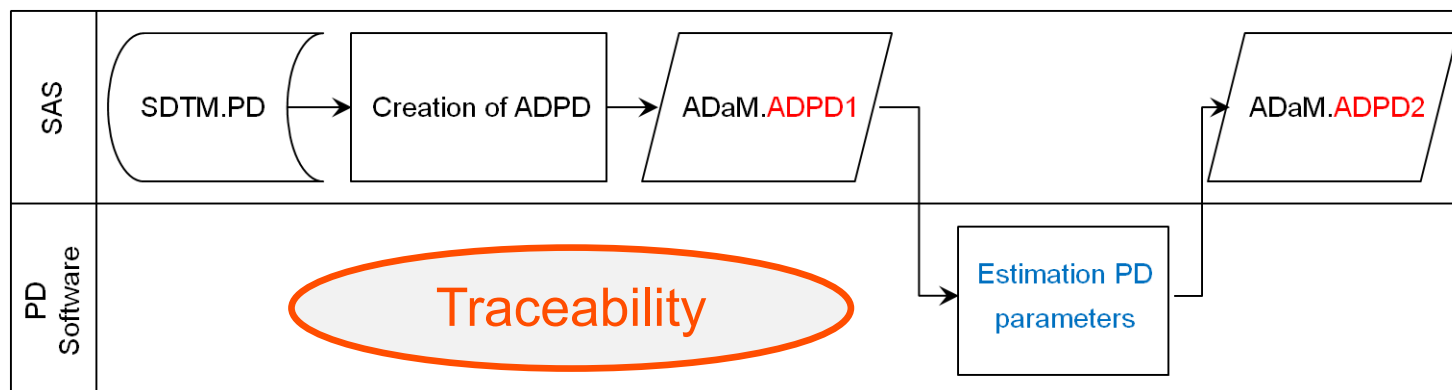
Standardized

Flexible

In SAS



Outside SAS





THANK YOU FOR YOUR ATTENTION

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BACK-UP SLIDE: PAPER EXAMPLES

- EXAMPLE 1: CHANGE FROM BASELINE

PARAM	AVISIT	AVAL	DTYPE	ABLFL	BASE	CHG	CHGCAT1	PCHG	PCHGCAT1
PD measurement (unit)	SCREENING	36							
PD measurement (unit)	BASELINE	36	LVPD	Y	36				
PD measurement (unit)	DAY 1	30			36	-6	] -10, 0] unit	-16.67	] -20, 0] %
PD measurement (unit)	DAY 2	26			36	-10	] -20, -10] unit	-27.78	] -40, -20] %
PD measurement (unit)	DAY 3	22			36	-14	] -20, -10] unit	-38.89	] -40, -20] %
PD measurement (unit)	DAY 7	14			36	-22	] -30, -20] unit	-61.11	] -80, -60] %

BACK-UP SLIDE: PAPER EXAMPLES

- EXAMPLE 2: PERCENT REDUCTION FROM BASELINE

PARAM	AVISIT	AVAL	DTYPE	ABLFL	BASE	AVALCAT1
PD measurement (unit)	SCREENING	36				
PD measurement (unit)	BASELINE	36	LVPD	Y	36	
PD measurement (unit)	DAY 1	30			36	
PD measurement (unit)	DAY 2	26			36	
PD measurement (unit)	DAY 3	22			36	
PD measurement (unit)	DAY 7	14			36	
Reduction PD (%)	DAY 1	16.67				[0, 20[%
Reduction PD (%)	DAY 2	27.78				[20, 40[%
Reduction PD (%)	DAY 3	38.89				[20, 40[%
Reduction PD (%)	DAY 7	61.11				[60, 80[%

BACK-UP SLIDE: PAPER EXAMPLES

- EXAMPLE 3: WITH PARAMETERS ASSESSED IN SAS

PARAM	AVISIT	ATPT	AVAL
PD measurement (unit)	DAY 1	PRE-DOSE	0.08
PD measurement (unit)	DAY 1	0.5H	96.58
PD measurement (unit)	DAY 1	0.75H	95.39
PD measurement (unit)	DAY 1	1H	96.77
PD measurement (unit)	DAY 1	2H	99.75
PD measurement (unit)	DAY 1	4H	88.82
PD measurement (unit)	DAY 1	8H	75.59
PD measurement (unit)	DAY 1	24H	67.06
PD measurement (unit)	DAY 1	48H	56.03
PD measurement (unit)	DAY 1	96H	62.37
PD measurement (unit)	DAY 1	168H	32.05
PD measurement (unit)	DAY 1	336H	0.17
PD measurement (unit)	DAY 1	672H	0.20
PD measurement (unit)	DAY 1	1344H	0.20
PD measurement (unit)	DAY 1	2016H	0.34
AUEC (unit)	DAY 1		10504
Emax (unit)	DAY 1		99.75
tEmax (unit)	DAY 1		2

BACK-UP SLIDE: PAPER EXAMPLES

- EXAMPLE 4: WITH PARAMETERS ASSESSED IN PHOENIX WINNONLIN

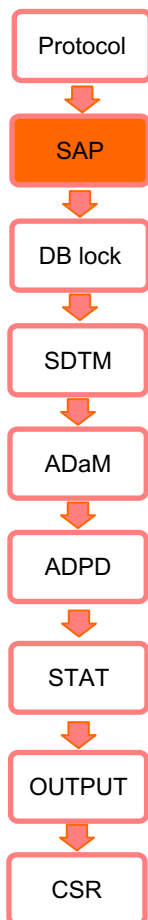
ADPD1

PARAM	AVISIT	ATPT	AVAL	DTYPE	ABLFL	BASE	PCHG
PD measurement (unit)	DAY 1	PRE-DOSE	9380				
PD measurement (unit)	DAY 1	BASELINE	9380	LVPD	Y	9380	0.00
PD measurement (unit)	DAY 1	2H	9870			9380	5.22
PD measurement (unit)	DAY 1	4H	8770			9380	-6.50
PD measurement (unit)	DAY 1	8H	9590			9380	2.24
PD measurement (unit)	DAY 1	24H	8860			9380	-5.54
PD measurement (unit)	DAY 1	48H	7270			9380	-22.49
PD measurement (unit)	DAY 1	72H	6700			9380	-28.57
PD measurement (unit)	DAY 1	96H	5920			9380	-36.89
PD measurement (unit)	DAY 1	144H	4970			9380	-47.01
PD measurement (unit)	DAY 1	336H	3340			9380	-64.39
PD measurement (unit)	DAY 1	504H	4140			9380	-55.86
PD measurement (unit)	DAY 1	672H	4360			9380	-53.52

ADPD2

PARAM	AVISIT	AVAL
AUEC (unit)	DAY 1	-33762
Emax (unit)	DAY 1	-64.39
tEmax (unit)	DAY 1	336

BACK-UP SLIDE: STATISTICAL ANALYSIS PLAN



■ Handling of data:

- If $<LLoQ \Rightarrow AVAL = LLoQ$ value

LLoQ: Lower Limit of Quantification

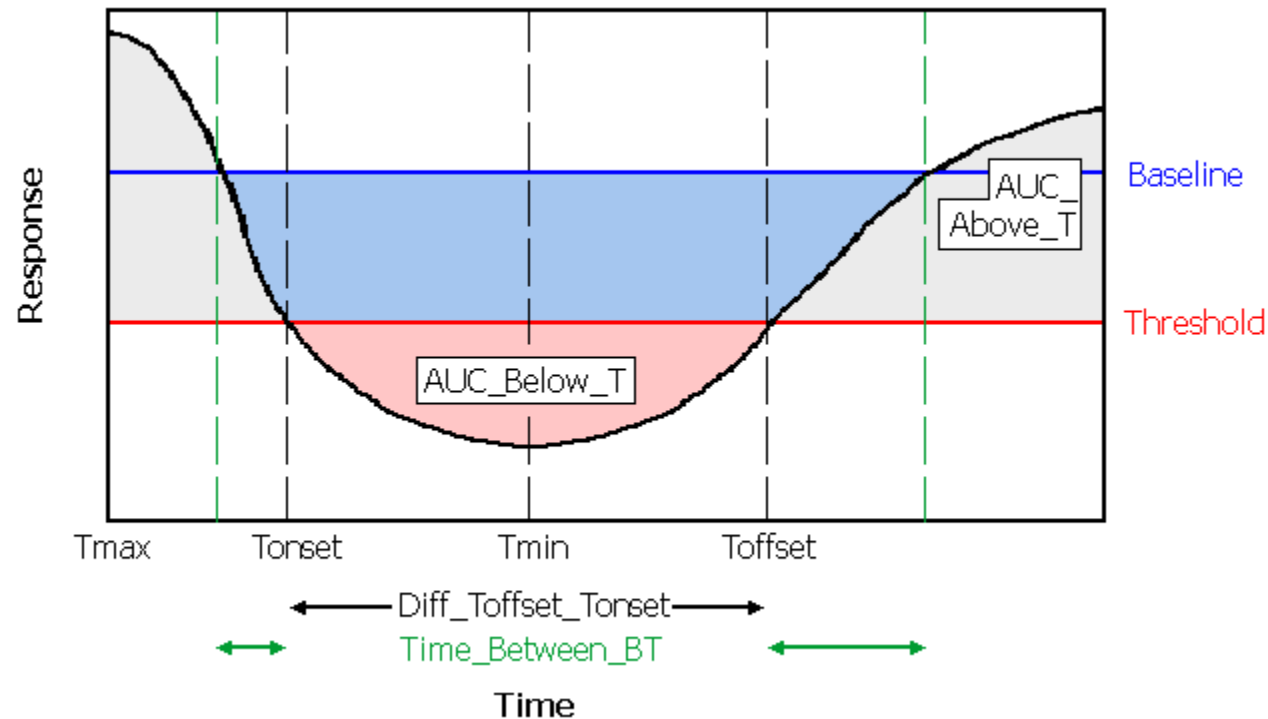
AVAL: Analysis Value

SUBJID	TRTA	PDTESTCD	PDTPT	PDSTRESC	PDSTRESN	PDSTRESU	AVAL
1	TRT	TESTX	PRE-DOSE	9380	9380	ng/mL	9380
1	TRT	TESTX	2H	9870	9870	ng/mL	9870
1	TRT	TESTX	4H	8770	8770	ng/mL	8770
1	TRT	TESTX	8H	9590	9590	ng/mL	9590
1	TRT	TESTX	24H	8860	8860	ng/mL	8860
1	TRT	TESTX	48H	7270	7270	ng/mL	7270
1	TRT	TESTX	72H	6700	6700	ng/mL	6700
1	TRT	TESTX	96H	5920	5920	ng/mL	5920
1	TRT	TESTX	144H	4970	4970	ng/mL	4970
1	TRT	TESTX	336H	<3500	.	ng/mL	3500
1	TRT	TESTX	504H	4140	4140	ng/mL	4140
1	TRT	TESTX	672H	4360	4360	ng/mL	4360

LLoQ

BACK-UP SLIDE: SAS VS. PD SOFTWARE

Drug effect data (model 220)



Extracted from Phoenix® WinNonLin user manual