

Data Abstraction Form for population PK/PD publications

MODEL BUILDING

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ARTICLE IDENTIFICATION

DATE OF PUBLICATION (YEAR)..... | | | | |

TITLE.....

.....

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FIRST AUTHOR.....

Purpose(s) of modeling

Descriptive Not reported

Estimation of PK and/or PD parameters

Estimation of parameters variability

Testing Covariate influence

Other:

Predictive Not reported

Concentrations Effects (continuous or discrete)

Time to event Probability

Other:

if predictive: Extrapolation Interpolation

Define:

Decision analysis Trial simulation Method comparison

Other:

Software Not reported

ADAPT

Bugs, PKBugs or Winbugs

Kinetica

MP2

NONMEM

NPML

P-PHARM

R (nlme) Splus (nlme)

SAS (PROC NL MIXED)

USC*PACK (NPEM)

WinNonMix

Other software:

Method (If NONMEM software used)

- | | | |
|---|------------------------------------|---------------------------------------|
| <input type="checkbox"/> FO | <input type="checkbox"/> FOCEI | <input type="checkbox"/> Not reported |
| <input type="checkbox"/> FOCE | <input type="checkbox"/> LAPLACIAN | |
| <input type="checkbox"/> FOCE CENTERED | <input type="checkbox"/> HYBRID | |
| <input type="checkbox"/> Other method : | | |

Molecule(s) included in the model ¹

Not reported

Number:

Name(s):

Data (building dataset)

For the PK study

Not reported

Number of subjects: *if not reported*, planned:

Number of observations: *if not reported*, planned:

Range of number of observations per subject per dosing interval?

min max mean/med *if not reported*, planned:

In how many occasions has PK sampling been performed?

min max mean/med *if not reported*, planned:

Occasions taken into account as different individuals

For the PD study

Not reported

Number of subjects: *if not reported*, planned:

Number of observations *if not reported*, planned:

Range of number of observations per subject per dosing interval?

min max mean/med *if not reported*, planned:

In how many occasions has PK sampling been performed?

min max mean/med *if not reported*, planned:

Occasions taken into account as different individuals

- Observation types for PD:
- | | |
|--|--|
| <input type="checkbox"/> Continuous | <input type="checkbox"/> Ordered categorical |
| <input type="checkbox"/> Binary | <input type="checkbox"/> Time to event |
| <input type="checkbox"/> Non Ordered categorical | <input type="checkbox"/> Count data |

¹ International Nonproprietary Names (=DCI) (if not published, company identification number)

Structural model (based on)**For the PK study**

(or for PKPD):

 Not reported

- | | |
|--|---|
| <input type="checkbox"/> 1 cpt. | <input type="checkbox"/> First order absorption |
| <input type="checkbox"/> 2 cpts. | <input type="checkbox"/> Zero order absorption |
| <input type="checkbox"/> 3 cpts. | <input type="checkbox"/> Other absorption |
| <input type="checkbox"/> Nonlinear elimination | |
| <input type="checkbox"/> Model for parent and metabolites | |
| <input type="checkbox"/> Joint model with sequential fit | <input type="checkbox"/> Not reported |
| <input type="checkbox"/> Joint model with simultaneous fit | |
| <input type="checkbox"/> Separate | |
| <input type="checkbox"/> Other: | |

For the PD study

(or for PKPD):

 Not reported

- | | |
|--|--|
| <input type="checkbox"/> Linear model | <input type="checkbox"/> Emax model |
| <input type="checkbox"/> Indirect model | with baseline <input type="checkbox"/> with gamma <input type="checkbox"/> |
| <input type="checkbox"/> Physiological model | <input type="checkbox"/> Effect compartment model |
| <input type="checkbox"/> Logistic model | <input type="checkbox"/> Log linear model |
| <input type="checkbox"/> Ordered categorical model | <input type="checkbox"/> Transition model (Markov) |
| <input type="checkbox"/> Time to event model | <input type="checkbox"/> Count model |
| <input type="checkbox"/> Binding model | |
| <input type="checkbox"/> Model for parent and metabolites effects | |
| <input type="checkbox"/> Effect only function of parent | <input type="checkbox"/> Not reported |
| <input type="checkbox"/> Effect only function of metabolites | |
| <input type="checkbox"/> Effect function of parent and metabolites | |
| <input type="checkbox"/> Other: | |

For the PKPD study

- Not reported
- Sequential fit (fixing PK parameters to population estimates)
- Sequential fit (fixing PK parameters to individual estimates)
- Simultaneous fit

Error model(OBS_{ij}: Observations, IPRED_{ij}: Individual Prediction, ε_{ij} : residual error)**For the PK study**

- Log transformed data Transformed both sides (log-log)
- Additive $OBS_{ij}=IPRED_{ij} + \varepsilon_{ij}$ Not reported
- Multiplicative $OBS_{ij}=IPRED_{ij} (1 + \varepsilon_{ij})$
- Combined $OBS_{ij}=IPRED_{ij} (1 + \varepsilon_{1ij}) + \varepsilon_{2ij}$
- Other:

For the PD study

- Log transformed data Transformed both sides (log-log)
- Additive $OBS_{ij}=IPRED_{ij} + \varepsilon_{ij}$ Not reported
- Multiplicative $OBS_{ij}=IPRED_{ij} (1 + \varepsilon_{ij})$
- Combined $OBS_{ij}=IPRED_{ij} (1 + \varepsilon_{1ij}) + \varepsilon_{2ij}$
- Other:

Basic model selection criteria**For the PK study**

- No building steps
- Wald test Graphs Not reported
- Akaike Criterion, Bayesian information criteria (or SC), Likelihood, Objective function
- Likelihood Ratio Test
- p value not adjusted
- p adjusted using an arbitrary criterion
- p adjusted using multiple test theory
- Randomisation test
- Residuals distribution
- Other:

For the PD study

- No building steps
- Wald test Graphs Not reported
- Akaike Criterion, Bayesian information criteria (or SC), Likelihood, Objective function
- Likelihood Ratio Test p value not adjusted
- p adjusted using an arbitrary criterion
- p adjusted using multiple test theory
- Randomisation test
- Residuals distribution
- Other:

Covariate model

For the PK study

- No covariate model
- Covariate test** Not reported

Which covariate has been.....tested?.....orkept in final model?

	↓		↓
Demographic factors	{	<input type="checkbox"/> Height	<input type="checkbox"/>
		<input type="checkbox"/> Weight	<input type="checkbox"/>
		<input type="checkbox"/> BMI	<input type="checkbox"/>
		<input type="checkbox"/> Age	<input type="checkbox"/>
		<input type="checkbox"/> Gender	<input type="checkbox"/>
		<input type="checkbox"/> BSA	<input type="checkbox"/>
		<input type="checkbox"/> Ethnic factor	<input type="checkbox"/>
Biology	{	<input type="checkbox"/> Creatinine clearance	<input type="checkbox"/>
		<input type="checkbox"/> Serum Creatinine	<input type="checkbox"/>
		<input type="checkbox"/> Hepatic markers (AST, ALT, bilirubin.....)	<input type="checkbox"/>
		<input type="checkbox"/> Genotype / Phenotype (Metabolism)	<input type="checkbox"/>

Other(s):	{	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
.....					
Number of covariates tested?	<input type="checkbox"/> Not reported			
Number of covariates in the final model?	<input type="checkbox"/> Not reported			
Covariate selection					
<u>based on post-hoc</u>	Performed <input type="checkbox"/>	Not performed <input type="checkbox"/>			
	<input type="checkbox"/> Graphs			<input type="checkbox"/> Not reported	
	<input type="checkbox"/> GAM (or bootstrap of GAM)				
	<input type="checkbox"/> Trees				
	<input type="checkbox"/> Univariate tests				
	<input type="checkbox"/> Other:				
Covariate population model building					
	<input type="checkbox"/> Forward			<input type="checkbox"/> Not reported	
	<input type="checkbox"/> Backward	<input type="checkbox"/> Stepwise (forward and backward)			
Criteria used for covariate model building					
	<input type="checkbox"/> Wald test	<input type="checkbox"/> Not reported			
	<input type="checkbox"/> Akaike Criterion, Bayesian information criteria (or SC), Likelihood or objective function				
	<input type="checkbox"/> Decrease IIV of a parameters prediction				
	<input type="checkbox"/> Decrease SE of fixed effect				
	<input type="checkbox"/> Clinical relevance				
	<input type="checkbox"/> Likelihood Ratio Test				
	<input type="checkbox"/> p value not adjusted				
	<input type="checkbox"/> p adjusted using an arbitrary criterion				
	<input type="checkbox"/> p adjusted using multiple test theory				
	<input type="checkbox"/> Randomisation test				
	<input type="checkbox"/> Other:				

For the PD study

No covariate model

Covariate test

Not reported

Which covariate has been.....tested?.....orkept in final model?

	↓		↓
Demographic factors	{	<input type="checkbox"/> Height	<input type="checkbox"/>
		<input type="checkbox"/> Weight	<input type="checkbox"/>
		<input type="checkbox"/> BMI	<input type="checkbox"/>
		<input type="checkbox"/> Age	<input type="checkbox"/>
		<input type="checkbox"/> Gender	<input type="checkbox"/>
		<input type="checkbox"/> BSA	<input type="checkbox"/>
		<input type="checkbox"/> Ethnic factor	<input type="checkbox"/>
Biology	{	<input type="checkbox"/> Creatinine clearance	<input type="checkbox"/>
		<input type="checkbox"/> Serum Creatinine	<input type="checkbox"/>
		<input type="checkbox"/> Hepatic markers (AST, ALT, bilirubin.....)	<input type="checkbox"/>
		<input type="checkbox"/> Genotype / Phenotype (Metabolism)	<input type="checkbox"/>
Other(s):	{	<input type="checkbox"/>	<input type="checkbox"/>
		<input type="checkbox"/>	<input type="checkbox"/>
		<input type="checkbox"/>	<input type="checkbox"/>
		<input type="checkbox"/>	<input type="checkbox"/>
		<input type="checkbox"/>	<input type="checkbox"/>

Number of covariates tested?

Not reported

Number of covariates in the final model?

Not reported

Covariate selection**based on post-hoc**Performed Not performed Graphs Not reported GAM (or bootstrap of GAM) Trees Univariate tests Other:**Covariate population model building** Forward Not reported Backward Stepwise (forward and backward)**Criteria used for covariate model building** Wald test Not reported Akaike Criterion, Bayesian information criteria (or SC),
Likelihood or objective function Decrease IIV of a parameters prediction Decrease SE of fixed effect Clinical relevance Likelihood Ratio Test p value not adjusted p adjusted using a arbitrary criterion p adjusted using a multiple test theory Randomisation test Other: