# Minimal model requirements

The minimal model requirements are all the requirements a model needs to meet before the author/submitter can publish the model in the DDMoRe model repository. The requirements are based on the information needed to verify the quality of the model and the minimal information needed for the next user to reproduce or re-use the model.

The minimal requirements in six essential model submission elements (ESME):

1. **Overall description of the model – Bookkeeping**
   1. Corresponding Author or Submitter (one Account)
   2. Model Name
   3. Model authors and affiliation (mandatory for unpublished models)
   4. Short model description (mandatory for published and unpublished model)
   5. Model description (mandatory for unpublished models (equivalent to abstract for published models))
   6. Long technical model description (optional external file)
2. **Context of use**
   1. Domain of application
   2. Stage of drug development
   3. Therapeutic/disease area
3. **Model**
   1. Model characteristics
   2. Structural model
   3. Statistical model
   4. Equation (not mandatory)
   5. Parameters
   6. Variables
   7. Model assumptions/limitations
4. **Design and Data**
   1. Type of trial
   2. Drug(s) modelled
   3. Data for model development
   4. Provided dataset (optional)
5. **Tasks**
   1. General tasks
   2. Software used to run the model
   3. Estimation algorithm
   4. Simulation
   5. Consistency check via DDMoRe framework
6. **Outputs**
   1. Estimation
   2. Simulation
   3. Evaluation

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| --- | --- |
| http://purl.org/dc/terms/ | dct |
| <http://xmlns.com/foaf/0.1/> | foaf |
| http://purl.org/spar/cito/ | cito |
| http://www.pharmml.org/2013/10/PharmMLMetadata | ps |
|  |  |
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|  |  |
|  |  |

## Overall description of the model

### Corresponding Author or Submitter (one Account)

Automatically retrieved from account information (name/affiliation).

:

dct:creator [

foaf:name "Maciek J Swat"

] .

dct:publisher <http://www.ebi.ac.uk> .

Note: no affiliation instead publisher linked to the model

### Model name

Free choice not more than 150 characters

Suggestions:

The nick name of the model should be used as human-friendly means of reference. It is important that model names are kept as short as practicable, to ease their adoption by the community. Additional information can be recorded in the model's description.

Two means of naming models are possible depending on whether or not they are backed by a publication either under review or that has already appeared in peer-reviewed literature. In the case of the former, the recommended approach is to combine a) the surname of the first author of the publication, b) the year in which the publication has appeared, c) the disease, d) the drug or drugs that are the object of this model, and finally e) a differentiating feature of the model. The suggested convention for models which are not yet described in a scientific paper is identical to the one above, except the first two elements are skipped. The Repository allows the name of the model to be changed, so modellers can update it once the model features in peer-reviewed article.

:

dct:title "Bergman\_1979"@en .

### Model authors and affiliations

Retrieved from publication or mandatory to provide if unpublished.

:

dct: sharesAuthorsWith [

foaf:Person [

foaf:name "John Smith";

foaf:Organisation [

foaf:name "EBI";

].

foaf:Person [

foaf:name "Ed Smith";

foaf:Organisation [

foaf:name "xxx";

].

] .

### Short model description

Free text max 200 characters. Mandatory for both published and unpublished models.

:

dct:description "Bergman\_1979 ...."@en .

### Model description

Published include Pubmed ID, DOI if available. Abstract automatically extracted from the journal article through Pubmed ID.

:

cito:citesAsAuthority <http://identifiers.org/pubmed/PMID3640682> .

Unpublished model, free text max 450 words, Could be retrieved from description tag in PharmML code.

*e.g. a template text is provided to the submitter so the information will be as consistent as possible for all models and to assure that crucial information is included, e.g. end-points, PK or PD, etc…*

:

dct:abstract “abstract text” .

### Long technical model description

Optional external file which contains elements (text paragraphs, figures, tables) to better describe and understand the model and the associated data (e.g. study design).

:

dcat:downloadURL <link to the combine archive>

Full Example:

## Context of use

Template text to be filled in and together with fixed choices of Context of use.

Fixed terms are within three dropdown lists with multiple choices.

### Domain of application

* Target selection
* Mechanistic Understanding
* Candidate Comparison, Selection, Human Dose Prediction
* Study Design Optimization
* Variability sources in PK and PD (CYP, Renal, Biomarkers)
* Similarity Assessment (MVC, Biosimilar, Formulation)
* Combination Therapy Dose Selection
* Risk & Benefit Characterization, Outcome Prediction (Clinical & design Viability)
* Comparator/Standard of Care Differentiation (Clinical & Commercial Viability)
* Dose & Schedule Selection and Label Recommendation
* Patient Population Selection and Bridging between Population (Pediatrics, Elderly, Obese)
* Disease Progression model
* Clinical end-point
* Pharmaco-economic
* Pharmaco-epidemiologic
* Social-economic
* Therapeutic Drug Monitoring
* Diagnostic model
* Veterinary
* Other: Free text

### Stages of drug development

* Fundamental/Basic research
* Clinical research
* Target selection & Validation
* Lead Generation & Optimization
* Preclinical development
  + In vitro
  + In vivo
* Early clinical development
* Late clinical development
* Approval phase
* Life cycle management & Therapeutic use

### Therapeutic/Disease area

PATO-ONTOLOGY (MESH terms from Pubmed)

* Oncology
* Diabetes
* Metabolic
* Dermatology
* Ophthalmology
* Inflammatory Diseases
* Infectious Diseases
* Central Nervous System Diseases
* Respiratory diseases
* Cardiovascular
* Other: Free text

## Model

### Model characteristics

Long list of different characteristics to be checked with PK/PD ontology

1. Type of model
   1. PK
   2. PD
   3. PK/PD
   4. PBPK
   5. Disease progression
   6. Other: Free text
2. Model characteristics
   1. PK
      1. number of compartments (1 to X)
      2. kind of elimination
         1. linear
         2. Michealis-Menten (MM)
         3. Target Mediated Drug Disposition (TMDD)
      3. kind of absorption
         1. First-order
         2. zero-order
         3. sequential absorption
         4. combined absorption
         5. transit
         6. Other: Free text
   2. PD
      1. direct
      2. indirect
      3. Compartment effect
      4. Other: Free text
   3. Type of equations:
      1. algebraic
      2. SDE
      3. ODE
      4. PDE
      5. DDE
      6. Hybrid
   4. Modelling approach:
      1. individual
      2. naïve pooled
      3. non-linear mixed effects
      4. linear mixed effects
      5. Bayesian
      6. Other
   5. Other: Free text

### Structural model

Equations automatically retrieved from pharmML code, to be displayed on the repository.

Legends to the equations (PharmML glossary), If available picture should be provided.

### Statistical model

Equations automatically retrieved from pharmML code, to be displayed on the repository.

Legends to the equations (PharmML glossary).

### Equation (not mandatory)

Extracted automatically from pharmML code using description tag **(**free text but better to use PK/PD ontology when possible).

### Parameters

Extracted automatically from pharmML code using ID tag (description, type, units, etc…).

### Variables/covariates

Extracted automatically from pharmML code using ID tag (description, type, units, etc…).

### Model assumptions/limitations

Free text.

## Design & Data

### Type of trial

Dropdown lists

exploratory

confirmatory

observational

interventional

simulated

### Drug(s) modelled

Dropdown lists

1. n/a
2. placebo
3. specified
   1. Drugbank (to be filled in)
   2. CHEBI (to be filled in)
   3. Other (to be filled in)

### Data for model development

Dropdown lists

Population:

Species (taxonomy NCBI),

Mus musculus

GMO

Rattus rattus

Homo sapiens

Healthy Volunteers

Patients

Special population

* + - * 1. Paediatrics

Premature

Neonates

Children

Young adults

* + - * 1. Adults
        2. Elderly
        3. Obese
        4. Renal impairment
        5. Hepatic impairment
        6. Genetic Polymorphism
        7. Other: free text

Single study or Multiple studies

Amount of data

Number of patients

Number of observations

Route of administration (standard term used by clinicians, CDISC, etc…)

Intravenous

oral

nasal

patch

Etc…

Others: free text

Formulation

Immediate or modified release formulation, CDISC….)

Dose regimen

No

Single

Multiple dose

Fixed dose

QD

BID

TID

QID

Continuous infusion

Etc…

Other: free text

Flexible dose

Type of measurement (PK, PD ….see ReSCU)

Type of matrix

Blood

Plasma

Serum

Urine

Faeces

Saliva

Tissue

Cellular

Etc…

Other: free text

Type of dependent variable

continuous

categorical

Binary

Ordered categorical

Not ordered categorical

Count

Frequency

time-to-event

single time to event

repeated time to event

other: free text

Data aggregation level (DAL)

individual

summarized

Sampling strategy

Rich

Sparse

Mixed

Pre-dose

One occasion

Several occassions

Other : free text

### Provided Dataset (optional)

Nature of provided data: real or simulated.

## Tasks

### General tasks

For display on the repository: automatically extracted information from pharmML code.

* Estimation
* Simulation
* Combination of simulation and estimation,
* Optimal design
* Etc…

### Software used to run the model

Dropdown list software:

* Berkeley-Madonna
* Matlab
* Monolix
* NONMEM
* Openbugs
* PFIM
* PopED
* R
* SAS
* Winbugs
* Other: free text

### Estimation algorithm

Extracted from pharmML code or list of items FO, FOCE, SAEM, etc….

### Simulation

1. Source of the parameters
   1. literature
   2. in-house values
   3. random
   4. etc…

### Consistency check via DDMoRe framework

Which software (target tools) has been successfully used after conversion from the pharmML code on the repository (Dropdown list software and need connectors to get target codes).

## Outputs

### Estimation

Estimate parameters, variance-covariance matrix (needed for level 1?).

Dropdown list software used to generate these values, Standard Output).

### Simulation

Parameters used for the simulation.

### Evaluation

Dropdown list:

* + Goodness of fit plots (Residual (CWRES) based)
  + NPC
  + VPC
  + PPC
  + NPDE
  + external validation
  + Bootstrap