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Topics: Methodology - Other topics

DDMoRe private repository linked with an in-house PK database

V. Croixmarie, S. Peigné, D. Teutonico and M. Chenel
Clinical Pharmacokinetics and Pharmacometrics division, Servier, France

Context

The **Drug Disease Model Resources (DDMoRe) Repository** is already available publically. At Servier, such repository has been implemented as an internal solution for model library. In addition to this tool, **a dedicated PK database** was designed to store individual secondary pharmacokinetics (PK) parameters derived from time-concentration profiles analysis with Population PK modeling approach. The secondary PK parameters as well as the associated final models – considered as PK parameters metadata in this context – are provided for each drug candidate in development and stored in this PK database.

Objectives

The objective of this project was to define and implement a consistent workflow for model storage with both tools and to integrate DDMoRe database capabilities to account for internal needs. In addition, the metadata available in the DDMoRe database were also integrated with additional metadata considered as relevant for model classification. Internal needs for better model sharing across modeling actors were also taken into account (tips, technical issues etc…)

Results: model metadata

Metadata capabilities of the original DDMoRe repository have been enhanced internally with technical PK and PD model characteristics in order to allow deeper search across model parameters and features.

PBPK model characteristics have been included in this enhancement work.

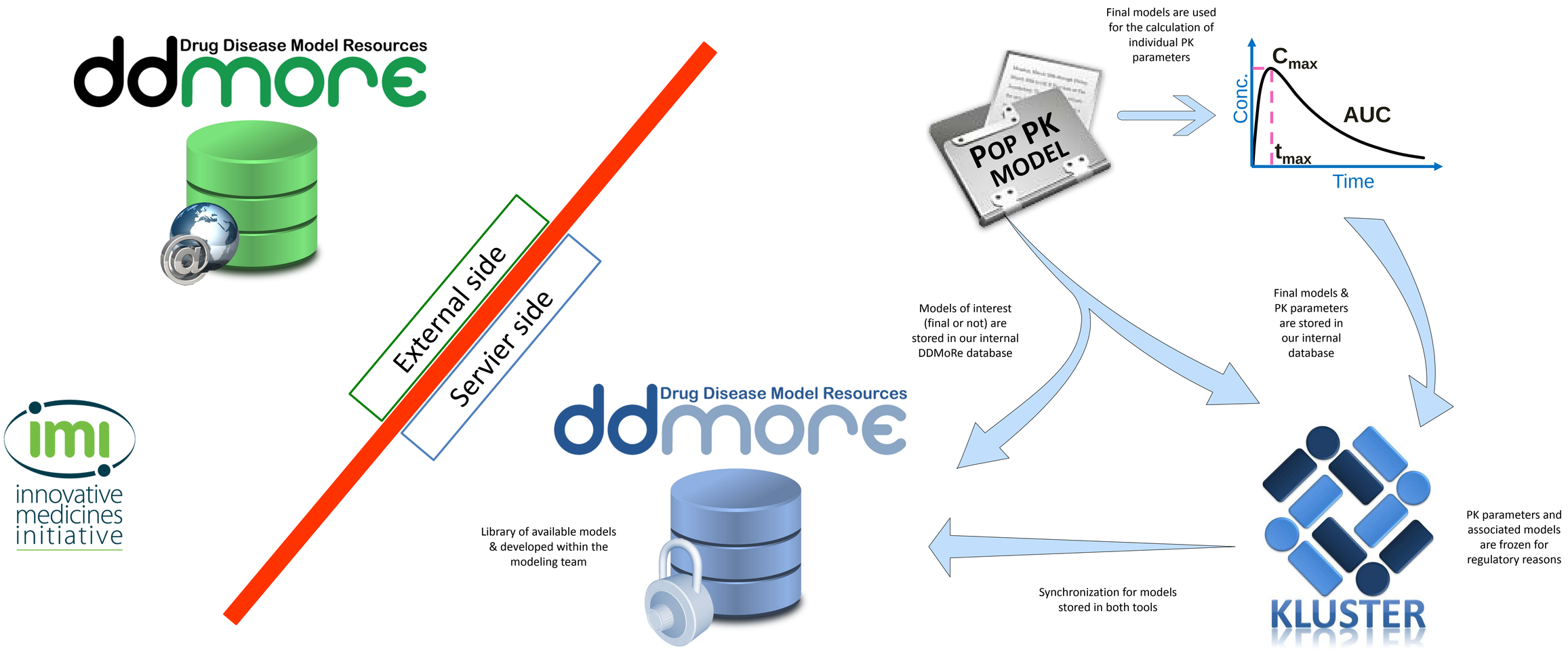
1 Design and data
1.1 Design overview
1.2 Studied Drug(s)
1.3 Observed (dependent) variable(s)
2 Model
2.1 PK model characteristics
2.2 PD model characteristics
2.3 PBPK model characteristics
2.4 Structural model elements
2.5 Statistical/variability model characteristics
3 Task execution
3.1 Software used to run the model (version)
3.2 Estimation algorithm used
3.3 Is the model identical of a model in Kluster?

2.1 PK model characteristics
2.1.1 Absorption features
2.1.2 Disposition features
2.1.3 Metabolism features
2.1.4 Elimination features
2.1.5 Other model features

Absorption features
First-order (ka)
Zero-order (Tk0/D0)
Sequential
Transit compartments
Nonlinear absorption (VM/KM)
Absolute bioavailability
Relative bioavailability
Delay with lag-time
Delay with MTIME
Delay with transit compartments
Late absorption
Parent entero-hepatic recycling (EHC)
Metabolite entero-hepatic recycling (EHC)

Example for absorption features glossary

Results: workflow



A better model sharing across modeling actors is now allowed with the use of the private Repository, with a tool inserted in our PK parameter internal workflow.
Technical model characteristics are included and can be looked for.

Impacts on the project

A workflow for model storage was shown integrating an internal storage solution for final models and model parameters with the DDMoRe model repository, which will be used as general model library as well as a technical issue resource. Such integration allows to profit from the advantage of combining a fully customized internal solution with the current and future functionalities of the DDMoRe model repository (facilitate regulatory model submission via the DDMoRe platform). Moreover, the internal DDMoRe model repository will be integrated with internal models as well as with the models which will be submitted by the DDMoRe community.

Harnisch et al. Drug and Disease Model Resources: A Consortium to Create Standards and Tools to Enhance Model-Based Drug Development. CPT: Pharmacometrics & Systems Pharmacology. 2013

http://repository.ddmore.eu/