Pharmacometric Markup Language (PharmML) & Standardised Output (SO) - Encoding Standards for Exchange of Models and Results in Pharmacometrics and Quantitative Systems Pharmacology

Maciej J Swat¹, Nadia Terranova², on behalf of all DDMoRe contributors

¹EMBL-EBI, Hinxton, UK; ²Merck Institute for Pharmacometrics, Merck Serono S.A., Switzerland.

Objectives: The definition and implementation of formats enabling a reliable exchange of pharmacometric models across software tools is one of the key goals for efficient collaborative drug and disease modelling and simulation research. PharmML, one of the key DDMoRe interoperability platform elements [1], has been designed to play the role of the exchange medium for mathematical and statistical models [2]. Similarly, SO has been developed as a complementary element, for storing typical output produced in a pharmacometric workflow.

Methods: The development of PharmML & SO is based on requirements provided by the DDMoRe community, including academic and EFPIA partners, and on use cases for estimation, simulations and optimal design tasks.

Results: PharmML supports MLE and Bayesian methods for non-linear fixed effect models, used in analysis of continuous and discrete longitudinal population data by accounting for the definition of

1. Structural model as a system of ODEs, DDEs or algebraic equations.
2. Parameter and variability models with structures allowing for the implementation of arbitrary parameter types, including discrete and continuous covariates.
3. Observation model supporting untransformed/transformed continuous, categorical, count or time-to-event data.
4. Trial design model as explicit specification of trials used for simulation and optimal design tasks.

SO, designed to be a tool-independent storage format aims at:

1. Providing a flexible structure for typical results produced in Pharmacometrics workflows, including estimation, optimal design and clinical trial simulation tasks;
2. Enabling effective data flow across tasks;
3. Facilitating information retrieval for post-processing and reporting.

Figure: Effective workflow support - the key benefit coming from PharmML and SO usage
Conclusions:
PharmML and SO offer means to encode and exchange pharmacometric models and according results across tasks and tools, thus, extending the workflow capabilities.

References:
[1] DDMoRe project, www.ddmore.eu