HMA/EMA multi-stakeholder workshop on reporting and qualification of mechanistic models for regulatory assessment

8 – 9 October 2025

In-person at the EMA building (Room 1C), Amsterdam + virtual enabled

Background and objectives

Mechanistic models are increasingly being used to support the development of medicinal products for human use. The regulatory assessment of mechanistic models is focussed on determining whether the models are qualified for their intended use. Guidance documents on the requirements for reporting on and qualification of mechanistic models, covering different types of models (physiologically based pharmacokinetic models and quantitative systems pharmacology models) are currently being developed or updated.

This multistakeholder workshop will bring together academia, regulators and industry to discuss the experience with the current regulatory landscape around the application of mechanistic models to support drug development.

The aims of the workshop are to:

- Hear the views of stakeholders and experts on the current regulatory framework around the assessment of mechanistic models.
- Share the regulatory challenges associated with the assessment of mechanistic models with stakeholders and experts.
- Identify opportunities for future regulatory qualification of mechanistic models.
- Define how the current EU regulatory framework can be refined to streamline the use and assessment of mechanistic models.

A video recording will be published after the event.

EMA Multi-stakeholder workshop on reporting and qualification of mechanistic models for regulatory assessment

Day 1 – 8 October 2025, 10:00 – 17:40 (CEST)

Chaired by Peter Arlett (EMA) & Flora Musuamba Tshinanu (FAMHP)

09:30 Joining and technical checks

10:00 Welcome and opening speech

Presentation **10'**
Peter Arlett (EMA)

Risk-based assessment of model-informed drug development approaches **20'**
Flora Musuamba Tshinanu (FAMHP)

10:30 Session 1: The qualification of mechanistic models through the EMA qualification framework and beyond.

In this session EMA wishes to interact with its stakeholders on the current landscape around the qualification of mechanistic models to support regulatory decision making. In addition, in the second part of this session, the Agency wishes to discuss with its stakeholders' applications that go beyond the current framework.

Chairs: Efthymios Manolis (EMA) & Carolien Versantvoort (MEB)

EU regulatory paths to acceptance of a mechanistic model **10'**
Efthymios Manolis (EMA) & Carolien Versantvoort (MEB)

Qualification of the Simcyp platform for CYP-mediated drug-drug interactions: a Certara perspective **20'**
Karen Rowland Yeo (CPT Division, Certara UK)

Software Verification, Validation, and Qualification of Open Source M&S Software for Regulatory Use in Translational Model-Informed Drug Development **20'**
Stephan Schaller (o.b.o. Open Systems Pharmacology Management Team)

Harmonization of PBPK platform and model qualification for regulatory assessment **20'**
Viera Lukacova (SimulationsPlus)

A Pharma industry PBPK perspective on the EMA qualification framework **20'**
Neil Parrot (Roche, o.b.o. EFPIA)

Panel discussion **30'**

Additional panellists:
Margareta Bego (HALMED)
Alexander Kulesza (UNamur, BE)

12:30 Lunch

13:30 Session 1: continued.

Chairs: Efthymios Manolis (EMA) & Carolien Versantvoort (MEB)

Holistic qualification of mechanistic models in drug development **20'**
Jan-Frederik Schlender (Novartis)

Qualification of the Simcyp platform: inter-version qualification bridging **20'**
Masoud Jamei (CPT Division, Certara UK)

Considerations for qualification of Physiologically Based Biopharmaceutics Models - Beyond the EMA framework **20'**
Xavier Pepin (SimulationsPlus)

Panel discussion **60'**

Additional Panellists:

Jörg Lippert (Bayer)
Victor Mangas (AEMPS)
Scott Marshall (representative of ICH M15 WG)

15:30 Coffee break

16:00 Session 2: Evaluation of predictive performance of mechanistic models for regulatory decision making: acceptance criteria, performance metrics, uncertainty quantification

In this session topics related to methods and tools used for platform qualification will be addressed.

Chairs: Pieter Colin (EMA) & Robin Svensson (MPA)

A regulatory perspective on performance verification of mechanistic models - application to PBPK-based DDI predictions **20'**
Pieter Colin (EMA)

Uncertainty quantification methods for complex models used in drug development and/or regulatory approval **20'**
Andrew Hooker (CONFIRMS consortium)

Industry collective experience and discussion from a PBPK working group on the predictive performance of mechanistic PBPK model platform for specific PBPK applications **20'**
Kunal Taskar (GSK, o.b.o. EFPIA)

Panel discussion **30'**

Additional panellists:
Paolo Rossato (CSL Behring, o.b.o. EFPIA)
Michael Chappell (Warwick University, UK)
Jörg Zinserling (BfArM, DE)

17:30 Closing remarks

Wrap up **10'**
Peter Arlett (EMA)

17:40 End of day 1

Day 2 – 9 October 2025, 9:00 – 16:10 (CET)

Chaired by Michael Berntgen (EMA) & Flora Musuamba Tshinanu (FAMHP)

08:45 Joining and technical checks

09:00 Welcome and opening speech

Summary of Day 1; Highlights of Day 2 **10'**
Flora Musuamba Tshinanu (EMA) and Michael Berntgen (EMA)

09:10 Session 3: Mechanistic models for the future; challenges & opportunities in the context of Model-Informed Drug Development & risk assessment

In this session applications of mechanistic models that are expected to have a high impact in future regulatory submissions will be discussed. Topics covered may include: PBPK for special populations (e.g. pregnancy, lactation, children), QSP for rare diseases, PBBM, other.

Chairs: Michael Berntgen (EMA) & Flora Musuamba Tshinanu (FAMHP)

Introduction by the session co-chairs **10'**
Michael Berntgen (EMA) & Flora Musuamba Tshinanu (FAMHP)

An industry perspective on high impact QSP and QST model applications in clinical drug development in rare diseases **20'**
Anna Sher (GSK)

Experience with software platforms qualification for mechanistic models for agent-based modelling approaches **20'**
Francesco Pappalardo (University of Catania, IT)

Panel discussion **30'**

Additional panellists:
Peter Theunissen (MEB)
Anne-Mette Hoberg (DKMA)

10:30 Coffee break

11:00 Session 3: continued

Chairs: Michael Berngten (EMA) & Gaby Wangorsch (PEI)

Opportunities for application of PBPK models in special populations and different modalities **20'**
Loeckie de Zwart (J&J, o.b.o. EFPIA/EuropaBio)

The landscape of QSP modelling and Virtual Populations: From current to best practice **20'**
Alexander Kulesza (o.b.o. ISoP QSP SIG)

Panel discussion **30'**

Additional panellists:

Sathej Gopalakrishnan (Merck, o.b.o. EuropaBio)

Saskia De Wildt (Radboud University Medical Center & Erasmus Medical Center, NL)

Elisabeth Wischnitzki (AGES)

12:10 Lunch

13:30 Session 4: Regulatory guidance on mechanistic models, gaps & challenges in guidance documents

The aim of this session is to critically review the current EMA guidance on mechanistic models and identify areas for improvement. In addition, the Agency wishes to explore opportunities for alignment of qualification requirements at the international level and with related regulatory guidance documents (ICH M15).

Chairs: Francesca Day (EMA) & Kristin Karlsson (MPA)

Introduction by the session co-chairs **5'**

Francesca Day (EMA) & Kristin Karlsson (MPA)

Guideline on assessment and reporting of mechanistic models used in the context of model informed drug development: Public comments received **20'**

Flora Musuamba Tshinanu (FAMHP)

Cross-industry feedback in implementation of regulatory guidance on mechanistic models: case studies, gaps, challenges and future perspectives **20'**

Pradeep Sharma (AstraZeneca, o.b.o. EFPIA/EuropaBio)

PBBM Qualification and Guidance: Key Challenges and Emerging Opportunities **20'**

Claire Mackie (J&J, o.b.o. EFPIA)

Shaping the Path Forward: Advancing Mechanistic Models for Regulatory Use **20'**

Hao Zhu (FDA)

Panel discussion **60'**

Additional panellists:

Christer Tannergren (AstraZeneca, o.b.o. EFPIA)

Michiel van den Heuvel (MEB)

Elin Lindhagen (MPA)

Sarem Sarem (HC)

Shinichi Kijima (PMDA)

15:55 Closing remarks

Wrap up **15'**

Flora Musuamba Tshinanu (FAMHP)

16:10 End of day 2