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

Session 1 Introduction

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Outline

- Routes for PBPK/mechanistic model Platform Qualification
- Session 1 Highlights: Qualification framework and procedure
- Session 1 Highlights: Relevance and applicability of platform qualification in the context of new drug development

Case-by-Case Model Qualification in regulatory submissions (e.g. MAA)

Purpose: Demonstrate that the model is suitable for a particular application (e.g., predicting drug-drug interactions, pediatric dosing)

✓ Tailored to compound physiochemical and clin pharm characteristics, CoU, model risk and impact

✕ Time-consuming and resource-intensive for both Developers and Regulatory Assessors

✕ Not advancing knowledge beyond development team-> Company/team silos-> No industry wide or regulatory learning

✕ Limited time for evaluation- usually timelines are driven by major efficacy and safety considerations

✕ Inconsistencies in Validation, Qualification Approaches, Reporting, and Assessment Practices (Paul CPT 2025)

EMA Qualification of novel methodologies

Purpose: Demonstrate that the platform can reliably predict the metrics of interest across a range of compounds and scenarios. Limited to 1 case: SimCYP in the specified CoU

✓ Efficient for repeated use across multiple compounds -> Reducing submission and product review efforts/timelines

✓ Improve predictability/homogeneity of regulatory assessment

✕ Qualification is tied to a design space that is defined by the qualification matrix, context of use scenario, PBPK platform and version

✕ Extrapolation or interpolation to the specific scenario/compound is needed

✕ Platform and version need to be considered in the assessment

Collaborative or Consortium-Based Qualification

Involves qualification through multi-stakeholder efforts

Purpose: Demonstrate that the platform can reliably predict the metrics of interest across a range of compounds and scenarios

✓ Leverages shared expertise and data

✓ Can address broader scientific or regulatory challenges

✓ Often leads to publication and wider acceptance

✕ **Does not automatically translate into regulatory qualification-**> prone to inconsistencies and inefficiencies discussed in earlier slides

Session 1 Highlights
Qualification Framework and Procedure

- Map the Simcyp qualification alongside other qualification approaches
- Identify opportunities for strengthening the EMA framework/procedure
- Establish a shared understanding of the EMA qualification framework's value proposition

Session 1 Highlights: Relevance and applicability of platform qualification in the context of new drug development

- Model structure has been verified
- Model evaluation by regulators is expected to focus more on it's application
  - Objectives and assumptions
  - Is the application within the qualified scope?
  - Not within the scope but having the same mechanism e.g. difference in population, food conditions, ...
  - Are the known uncertainties in the model acceptable for it's purpose? How does this relate to the therapeutic window of the new medicinal product?

Session 1 Highlights: Relevance and applicability of platform qualification in the context of new drug development

- New version of the qualified model with/without structural changes, what are the consequences of performance of the model?
- The same scope as an EMA qualified platform but different vendor/platform. Can the qualified dataset used for (partial)validation?
- Could the data submitted within a medicinal product application become public and used to update the qualified model?

Thank you

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