Title: MODEL QUALIFICATION APPROACHES FOR QUANTITATIVE SYSTEMS PHARMACOLOGY AND MECHANISTIC PHYSIOLOGICAL MODELS.

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Objectives: Quantitative Systems Pharmacology (QSP) has emerged as a powerful approach in model-informed drug development. QSP is an umbrella term for mathematical modeling that considers drug MOA in the context of biological disease mechanisms to improve understanding of human biology and pharmacology. Specific QSP modeling methods vary, and there is currently no one unifying qualification method (1). Several recent publications discuss QSP model qualification (2-4). Mechanistic physiological models are one established QSP approach in which biological mechanisms and drug MOA are represented by appropriate equations (usually ordinary differential equations) and parameters. Whole-system behavior can then be simulated to gain insights into the connections between mechanisms and outcomes. Here, we compare and contrast newly proposed QSP qualification approaches with the Model Qualification Method (MQM, Figure 1) for Rosa's PhysioPD™ Research Platforms, first presented at ACoP 2011 (5).

Methods: Recent publications discussing QSP model qualification (2-4) were analyzed and compared with the MQM.

Results: The MQM comprises eight criteria addressing relevance, uncertainty, variability, and consistency with test data. QSP qualification approaches proposed recently share several themes with each other and the MQM, and add useful details and examples for addressing several of the MQM criteria. The MQM is broader and includes additional criteria, particularly regarding biological uncertainty, that are not addressed in other published approaches.

Conclusions: The MQM developed for mechanistic physiological models can serve as a framework for qualifying QSP models. Use of the MQM would complement and enhance other proposed approaches. The industry may be converging on a set of QSP qualification criteria.
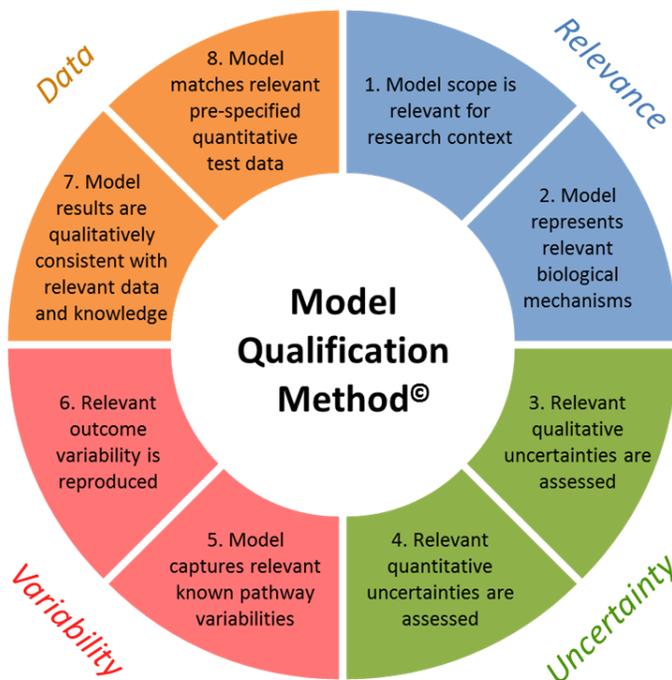

Figure 1. Rosa's Model Qualification Method for mechanistic physiological models

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