CERTARA

Status of Quantitative Systems Pharmacology Modeling in the Pharmaceutical Industry:

A Consortium Survey of the What, When and How

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A survey conducted by AbbVie on behalf of the 33 pharmaceutical member companies within the Simcyp consortia

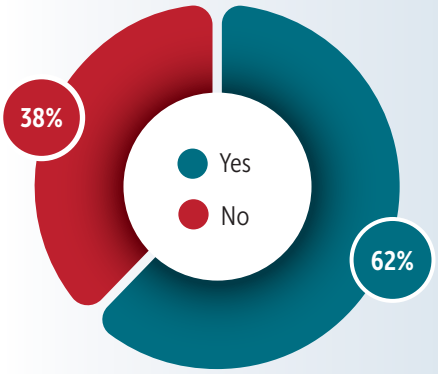
Background

A primary cause of failures in pharmaceutical research and development (R&D) was attributed to lack of efficacy (Hay et al. 2014), suggesting a lack of understanding in therapeutic targets biology and their relevance to disease progression or modulation. Quantitative systems pharmacology (QSP) has the promise of increasing probability of success in R&D by bridging scientific gaps between disciplines to enable target validation (Sorger et al., 2011). In 2014, a group of pharmaceutical industry representatives of the Simcyp consortium along with scientists from Certara initiated discussions on formation of a QSP consortium, with the objective of developing, validating and sharing pre-competitive QSP models. The idea of an industry sponsored QSP consortium managed by Certara was well received by the Simcyp member companies, and here we present results of a survey conducted recently to assess the QSP landscape in the industry. This survey was conducted among all 33 consortium members, and 21 companies returned the questionnaire, a response rate of around 60%. A poster paper of results was presented at the New York Academy of Sciences Meeting on this topic in May, 2015.

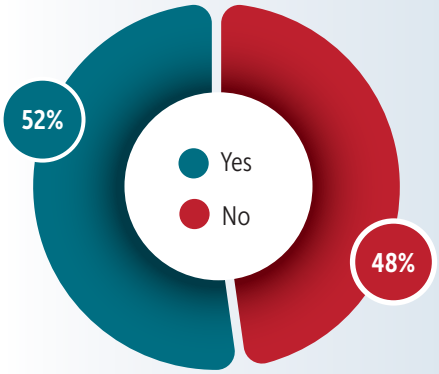
Results of the Survey

62% consider QSP modeling an in integrated part of modeling and simulations activities in their company; 52% have dedicated QSP modelers; 60% have an established or ongoing IT infrastructure to support QSP modeling. Matlab/Simbiology was the most used software or platform for QSP applications; majority of applications is for *in silico* mechanistic hypothesis testing and selecting the right pathway/target. 92% and 79% of companies have primary interest in developing QSP models for oncology and immunology, respectively; 68% interested in developing models adapted to pre-clinical pharmacology species; 90% interest in developing safety/toxicity systems models with primary focus on cardiovascular, liver and kidney. 70% have external collaborators to develop QSP models, of which 60% utilize both consulting and academic organizations. A significant number of companies (67%) plan to share pre-competitive data, experience and modeling input with the QSP consortium. Challenges were also captured and summarized under questions 3 and 9, in terms of intellectual property limitations, existing software interface and computation limitations, modeling and simulations technical challenges, logistics of sharing models with non-modelers, and the need for consortia management.

Is QSP modeling a part of your company's modeling and simulations tool box?

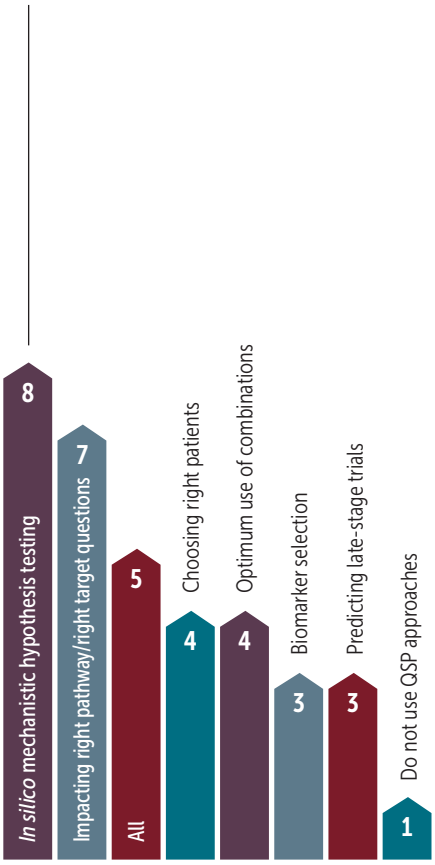


If so, do you have dedicated QSP modelers within your company?



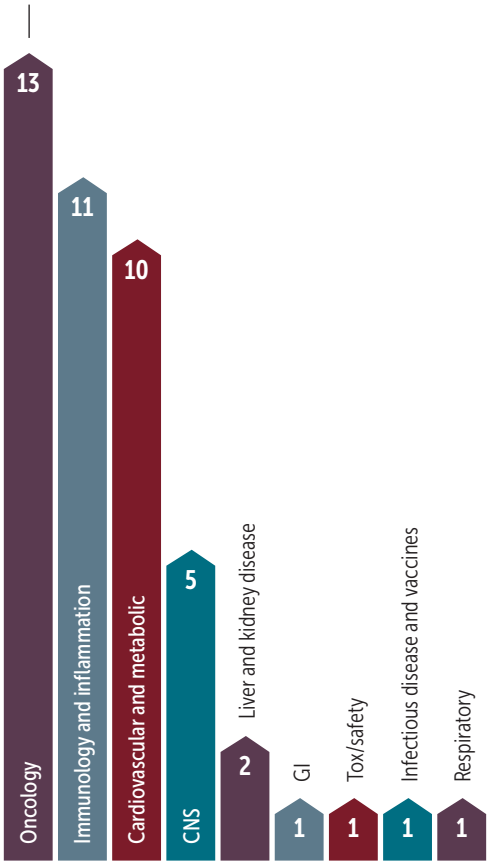
What applications does your company mostly utilize/plan to utilize QSP approaches for?

19 Responders

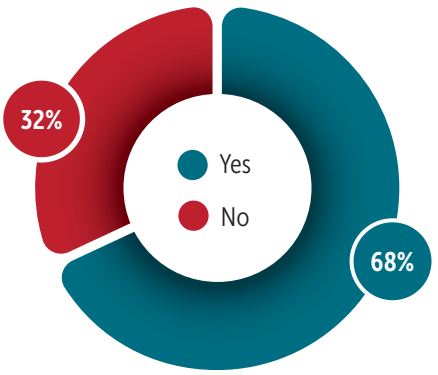


Is your company interested in developing pre-competitive QSP disease models? If so, which therapeutic areas of indications?

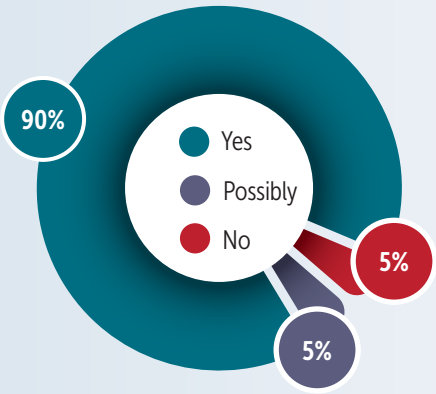
14 Responders



Is your company interested in developing disease models that are adapted to multiple species?

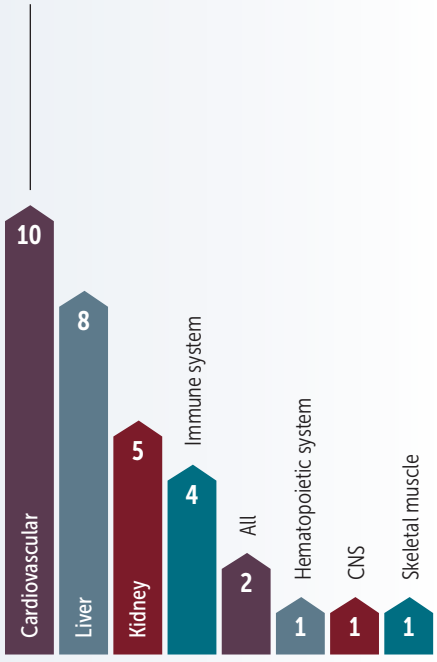


Is your company interested in developing pre-competitive QS-toxicology/safety models?



If yes, in which organs or area of focus?

20 Responders



QSP's Fit within the Drug Development Process

QSP translates PK exposure into pharmacological effect. It sits at the interface between modeling and simulation, and systems biology. A mechanistic approach, QSP facilitates the study of "what if" scenarios to determine the likely efficacy of a drug without doing any experimental analysis, facilitating lead development early in the drug development process.

Key benefits of QSP include:

- **Support discovery of new drugs:** QSP will enable Pharma to leverage the huge amount of data now being generated from the 'omics sciences' (genomics, proteomics and metabolomics) to support new therapies.
- **Provide insight into underlying mechanisms that determine pharmacological response:** For example, QSP determines the exposure at various organics to predict potential side effects, or explore which drug combinations may have the best chance of success in specific cancers.
- **Increase the likelihood of demonstrating drug efficacy:** QSP builds on insights gained from PBPK. Once we know how much drug is at the site of action, how will it modulate cellular signaling to exert a pharmacological effect? What pharmacological action will it have at that particular organ? Answering these questions will provide insight into the mechanisms of drug efficacy.
- **Support precision medicine:** In the past, we treated many diseases as monolithic. We now recognize that many diseases are actually a plethora of different diseases, affecting distinct subpopulations of patients. By leveraging QSP, sponsors can rationally select patient subgroups to target before running a Phase 2 trial, to avoid failure which still plagues Phase 2.

About Certara

Certara is a leading provider of decision support technology and consulting services for optimizing drug development and improving health outcomes. Certara's solutions, which span the drug development and patient care lifecycle, help increase the probability of regulatory and commercial success by using the most scientifically advanced modeling and simulation technologies and regulatory strategies. Its clients include hundreds of global biopharmaceutical companies, leading academic institutions and key regulatory agencies.

For more information visit www.certara.com or email sales@certara.com.

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