## Table S1. Survey Questions and Responses

| Question | Answers | Responses (%) | # of Responses | # Skipped |
|---|---|---|---|---|
| 1. How many employees does your company have? | < 500 employees | 6.25% | 2 | 1 |
| | 500-2,000 employees | 21.88% | 7 | |
| | 2,001-10,000 employees | 34.38% | 11 | |
| | > 10,000 employees | 37.50% | 12 | |
| 2. What type of therapy is the focus at your company? | Primarily small molecules | 40.63% | 13 | 1 |
| | Primarily biologics | 6.25% | 2 | |
| | Mixed | 53.13% | 17 | |
| 3. Which of the following therapeutic areas is the focus at your company (select all that apply)? | Oncology | 57.58% | 19 | 0 |
| | Neuroscience | 66.67% | 22 | |
| | Autoimmune disorders | 54.55% | 18 | |
| | Infectious diseases | 33.33% | 11 | |
| | Cardiovascular | 30.30% | 10 | |
| | Metabolic disorders | 27.27% | 9 | |
| | Rare diseases | 39.39% | 13 | |
| | Other | 39.39% | 13 | |
| 4. How well defined is the term "quantitative systems pharmacology" (QSP) at your company? | The use of the term QSP to describe models is well defined; it is clear which models are QSP models and which are not. | 18.18% | 6 | 0 |
| | The use of the term QSP to describe models is loosely defined; it is somewhat unclear which models are QSP models and which are not. | 54.55% | 18 | |
| | My company does not use the term QSP to describe its modeling activities or does not perform QSP modeling (internally or externally). | 27.27% | 9 | |
| | | | | |
| The remaining questions were not answered by the 9 responders that indicated in question 4 that they do not use QSP modeling. | | | | |
| 5. As the term is used at your company, which of the following are typical or required characteristics of QSP models (select all that apply)? | QSP models include mechanistic detail on biological and/or therapeutic processes | 83.33% | 20 | 9 |
| | QSP models represent a complex, interconnected, and multi-scale system, described by variables and/or parameters | 58.33% | 14 | |
| | QSP models utilize diverse types of data, including "-omics" data | 41.67% | 10 | |
| | QSP models incorporate effect of drugs, including PK if available | 75.00% | 18 | |
| | Other | 16.67% | 4 | |
| 6. Which of the following models would your company define as a QSP model (select all that apply)? | Mechanistic PK/PD models based on known/hypothesized biological/therapeutic mechanisms | 79.17% | 19 | 9 |
| | Comprehensive model of known/hypothesized biological/therapeutic mechanisms, including feedbacks, and redundancies | 83.33% | 20 | |
| | Mechanistic PBPK models | 50.00% | 12 | |
| | Mechanism-based pathway or signaling transduction models (e.g., deterministic ODE models) | 83.33% | 20 | |
| | Data-driven pathway or signaling transduction models (e.g., influence networks) | 41.67% | 10 | |
| | Spatial-temporal models of drug delivery and/or effects (e.g., computational fluid dynamics models) | 33.33% | 8 | |
| | Quantitative structure–activity relationship (QSAR) models | 0.00% | 0 | |
| | Machine learning approaches (e.g., Bayesian networks) applied to biological problems | 8.33% | 2 | |
| | Agent-based models applied to biological problems | 16.67% | 4 | |
| | None of these are QSP models | 0.00% | 0 | |
| | Unsure (QSP is loosely defined) | 20.83% | 5 | |
| 7. To what department do your preclinical QSP modelers belong (select all that apply)? | DMPK | 58.33% | 14 | 9 |
| | Preclinical PKPD/Modeling & Simulation group | 41.67% | 10 | |
| | Clinical Pharmacology | 29.17% | 7 | |
| | Computational Biology/Bioinformatics | 16.67% | 4 | |
| | Statistics | 0.00% | 0 | |
| | Discovery/Biology Research | 8.33% | 2 | |
| | Other | 16.67% | 4 | |
| 8. What is the academic background of your company's QSP modelers (select all that apply)? | Pharmacokinetics/Pharmaceutical Sciences | 75.00% | 18 | 9 |
| | Pharmacology | 41.67% | 10 | |
| | Computational Biology/Bioinformatics | 50.00% | 12 | |
| | Engineering | 58.33% | 14 | |
| | Computer Science | 16.67% | 4 | |
| | Mathematics | 33.33% | 8 | |
| | Statistics | 8.33% | 2 | |
| | Physical Sciences | 25.00% | 6 | |
| | Life Sciences | 29.17% | 7 | |
| | Other background | 4.17% | 1 | |

| Question | Answers | Responses (%) | # of Responses | # Skipped |
|---|---|---|---|---|
| 9. How many QSP modeling full-time equivalents (FTEs) does your company have? | < 1 | 37.50% | 9 | 9 |
| | 1-2 FTE | 16.67% | 4 | |
| | 3-5 FTE | 8.33% | 2 | |
| | 6-10 FTE | 25.00% | 6 | |
| | 10+ FTE | 12.50% | 3 | |
| 10. Do you have staff assigned as part-time QSP modelers and if so, what other functions do they serve (select all that apply) | No | 16.67% | 4 | 9 |
| | Yes, statistics | 8.33% | 2 | |
| | Yes, pharmacometrics | 29.17% | 7 | |
| | Yes, preclinical PK/PD | 58.33% | 14 | |
| | Yes, clinical pharmacology | 41.67% | 10 | |
| | Yes, DMPK | 45.83% | 11 | |
| | Yes, other | 8.33% | 2 | |
| 11. If "yes" is selected for Question 10, please provide the percentage of FTE used to develop or apply preclinical QSP models | 0-25% | 38.10% | 8 | 12 |
| | 25-50% | 38.10% | 8 | |
| | 50-75% | 9.52% | 2 | |
| | 75-100% | 9.52% | 2 | |
| | Not applicable | 4.76% | 1 | |
| 12. How are QSP modelers in your company organized? | Centralized | 41.67% | 10 | 9 |
| | Divided into therapeutic areas | 8.33% | 2 | |
| | Divided into different geographic regions | 8.33% | 2 | |
| | Other organizational structure | 41.67% | 10 | |
| 13. How do QSP modelers in your company interact with project teams? | Direct (modeler is integral part/member of project team) | 20.83% | 5 | 9 |
| | Indirect (modeler provides support only as requested by project team member) | 29.17% | 7 | |
| | Both, dependent on project or development stage | 50.00% | 12 | |
| 14. How many QSP projects are typically supported simultaneously per (part-time or full-time) QSP modeler? | 1 | 25.00% | 6 | 9 |
| | 2 | 45.83% | 11 | |
| | 3 | 20.83% | 5 | |
| | 4 | 0.00% | 0 | |
| | >4 | 8.33% | 2 | |
| 15. At what stage is QSP modeling currently initiated in your company (select all that apply)? | Target validation | 39.13% | 9 | 10 |
| | Lead identification | 21.74% | 5 | |
| | Lead optimization (LO) | 43.48% | 10 | |
| | Clinical candidate selection (pre-IND) | 73.91% | 17 | |
| | Clinical development (post-IND) | 60.87% | 14 | |
| 16. Regarding the timing in which preclinical QSP modeling is done, please select all that apply. | Modeling is initiated to facilitate/support preclinical experimental study design | 45.83% | 11 | 9 |
| | Modeling is initiated to help interpret and analyze preclinical experimental data in general | 83.33% | 20 | |
| | Modeling is initiated only when unexpected preclinical experimental results are obtained | 20.83% | 5 | |
| | Modeling is initiated to facilitate/support planning for First in Human studies | 66.67% | 16 | |
| | Not applicable (my company does not use preclinical QSP modeling, only clinical) | 4.17% | 1 | |
| 17. How does your company share QSP models internally/externally (select all that apply)? | As standalone executable tool | 20.83% | 5 | 9 |
| | As open-source code | 33.33% | 8 | |
| | As commercial code (e.g., MATLAB script) | 62.50% | 15 | |
| | As mathematical descriptions | 33.33% | 8 | |
| | As markup language model (e.g., SBML, CellML) | 25.00% | 6 | |
| | Other | 8.33% | 2 | |
| | Not applicable (company does not share QSP models) | 16.67% | 4 | |
| 18. If your company's QSP modelers are divided between preclinical and clinical, how is information shared typically? | We have a shared database of models and data with open access to both preclinical and clinical modelers | 0.00% | 0 | 10 |
| | There is an official hand-off of models, data and reports, which ends the involvement of the preclinical modelers | 0.00% | 0 | |
| | There is a gradual hand-off of models, data and reports, with the preclinical modeler working with the clinical team to keep developing the model for clinical applications | 13.04% | 3 | |
| | There is no formal process to transfer knowledge from preclinical to clinical | 39.13% | 9 | |
| | Not applicable (company does not have separate preclinical and clinical QSP modelers) | 47.83% | 11 | |

| Question | Answers | Responses (%) | # of Responses | # Skipped |
|---|---|---|---|---|
| 19. If there is an official hand-off between preclinical and clinical modelers, at what stage does this occur (select all that apply)? | Pre IND/FIH | 26.09% | 6 | 10 |
| | Pre Phase II POC | 0.00% | 0 | |
| | Post Phase II POC | 0.00% | 0 | |
| | Not applicable: preclinical and clinical QSP modelers typically work together collaboratively | 17.39% | 4 | |
| | Not applicable: company does not have separate preclinical and clinical QSP modelers or official hand-off | 56.52% | 13 | |
| 20. Does your company utilize "-omics" (genomics, transcriptomics, proteomics, metabolomics, physiomics) data in QSP models? | Often | 4.17% | 1 | 9 |
| | Sometimes | 16.67% | 4 | |
| | Rarely | 50.00% | 12 | |
| | Never | 29.17% | 7 | |
| 21. Are in-house and/or CRO experiments specifically designed to support QSP modeling activities (e.g., parameter estimation)? | Often | 8.33% | 2 | 9 |
| | Sometimes | 50.00% | 12 | |
| | Rarely | 25.00% | 6 | |
| | Never | 16.67% | 4 | |
| 22. Which of the following software tool/languages do you use for QSP modeling (select all that apply)? | Specialized systems biology/physiology/pharmacology toolbox/software or markup languages (e.g., MATLAB® SimBiology®, Entelos PhysioLab®, Immunetrics Biosimulation Platform/Aegis, DBSolveOptimum, JDesigner, Bayer's MoBi®, etc.) | 79.17% | 19 | 9 |
| | PBPK software tools (e.g., Simcyp®, GastroPlus, Bayer's PK-Sim®) | 45.83% | 11 | |
| | PK/PD modeling tools (e.g., Phoenix® WinNonlin®, Berkeley Madonna, SAAM II, ADAPT 5) | 62.50% | 15 | |
| | Population PK/PD modeling tools (e.g., Phoenix® NLME, NONMEM®, Monolix®, etc.) | 50.00% | 12 | |
| | General engineering, computational or statistical languages/tools (e.g., MATLAB®, Mathematica®/SystemModeler, C/C++, Java, Python®, FORTRAN, R, SAS®, SPlus®, etc.) | 70.83% | 17 | |
| | Others | 8.33% | 2 | |
| | Not Sure | 0.00% | 0 | |
| 23. What type of QSP models does your company develop or plan to develop? | Fit-for-purpose models (project specific, focused/pathway specific) | 33.33% | 8 | 9 |
| | Platform models (comprehensive model of a disease/therapeutic area) | 0.00% | 0 | |
| | Both types of models | 62.50% | 15 | |
| | Other | 4.17% | 1 | |
| 24. What biological scales are QSP models at your company typically focused on (select all that apply)? | Gene level | 8.33% | 2 | 9 |
| | Pathway level | 75.00% | 18 | |
| | Organelle level | 16.67% | 4 | |
| | Cell level | 58.33% | 14 | |
| | Tissue level | 66.67% | 16 | |
| | Organ level | 83.33% | 20 | |
| | Whole body level | 70.83% | 17 | |
| | Patient populations | 62.50% | 15 | |
| | Not sure | 8.33% | 2 | |
| 25. How is the quality or reliability of your preclinical QSP models assessed (select all that apply)? | Diagnostic plots/statistical tests | 50.00% | 12 | 9 |
| | Perform sensitivity analyses | 70.83% | 17 | |
| | Utilize uncertainty quantification methodologies | 29.17% | 7 | |
| | Validation simulations | 83.33% | 20 | |
| | Assessed by other modelers | 45.83% | 11 | |
| | Evaluated by biological plausibility by non-modelers | 70.83% | 17 | |
| | None | 4.17% | 1 | |
| 26. How many variables are typical of preclinical QSP models developed at your company? | < 20 | 26.09% | 6 | 10 |
| | 20-50 | 21.74% | 5 | |
| | 50-100 | 21.74% | 5 | |
| | > 100 | 30.43% | 7 | |
| 27. How long does your company typically spend on building a QSP model (select all that apply)? | 1-3 weeks | 12.50% | 3 | 9 |
| | 3-6 weeks | 20.83% | 5 | |
| | 6-12 weeks | 29.17% | 7 | |
| | 3-6 months | 37.50% | 9 | |
| | 6-12 months | 50.00% | 12 | |
| | 12+ months | 37.50% | 9 | |
| 28. What is your company's typical process for developing a QSP model (select all that apply)? | In-house development from fundamental components | 50.00% | 12 | 9 |
| | In-house development based on published models | 62.50% | 15 | |
| | External collaborations with academia or others | 37.50% | 9 | |
| | Contract with CROs | 54.17% | 13 | |
| | Both internal and external model development | 45.83% | 11 | |

| Question | Answers | Responses (%) | # of Responses | # Skipped |
|---|---|---|---|---|
| 29. In your company, preclinical QSP modeling is used for which of the following purposes (select your top 5 answers)? | Target identification, validation, or optimization | 25.00% | 6 | 9 |
| | Compound selection, optimization and prioritization | 50.00% | 12 | |
| | Biomarker identification, validation, translation and further analyses | 50.00% | 12 | |
| | Go/no-go decision making | 33.33% | 8 | |
| | Design preclinical experimental studies | 41.67% | 10 | |
| | Assess hypotheses for (patho)physiological, toxicological, and/or therapeutic mechanisms | 70.83% | 17 | |
| | Address internal or regulatory questions about unexpected PK/PD behaviors | 25.00% | 6 | |
| | Compare with competitor compounds | 45.83% | 11 | |
| | Optimize clinical PoC doses and/or dose regimens | 50.00% | 12 | |
| | Address questions regarding special population including pediatrics | 25.00% | 6 | |
| | Optimize clinical trial design (including drug/biomarker sampling times and patient selection) | 29.17% | 7 | |
| | Predict efficacy in clinical trials | 54.17% | 13 | |
| | Optimize approved drugs | 8.33% | 2 | |
| | Suggest companion diagnostics | 4.17% | 1 | |
| | Assess safety/toxicology | 25.00% | 6 | |
| | Other | 4.17% | 1 | |
| 30. How would you describe the application of QSP modeling across therapeutic areas in your company? | Applied in all therapeutic areas | 16.67% | 4 | 9 |
| | Broadly applied, but not in all therapeutic areas | 33.33% | 8 | |
| | Application limited to one or two therapeutic areas | 50.00% | 12 | |
| 31. In what therapeutic area does QSP modeling provide the most support in your organization (select all that apply)? | Oncology | 50.00% | 12 | 9 |
| | Neuroscience | 16.67% | 4 | |
| | Autoimmune disorders | 50.00% | 12 | |
| | Infectious diseases | 8.33% | 2 | |
| | Cardiovascular | 16.67% | 4 | |
| | Metabolic disorders | 25.00% | 6 | |
| | Rare diseases | 29.17% | 7 | |
| | Other | 20.83% | 5 | |
| | None | 4.17% | 1 | |
| 32. What is the general view within your company on the importance/impact of QSP modeling? | Very important/impactful | 29.17% | 7 | 9 |
| | Somewhat important/impactful | 58.33% | 14 | |
| | Not important/impactful | 8.33% | 2 | |
| | Not sure | 4.17% | 1 | |
| 33. Where QSP has been successful, what have been the main reasons for it being judged a success (select all that apply)? | Impacting projects with timely and sufficient modeling support | 66.67% | 16 | 9 |
| | Management or decision maker interest | 54.17% | 13 | |
| | Inclusion in regulatory documents and regulatory agency interest | 25.00% | 6 | |
| | Modeling findings supported by literature and experimental data | 54.17% | 13 | |
| | Model development/validation/uncertainty well performed or documented | 29.17% | 7 | |
| | Addressing the clearly defined problems within the intended scope | 66.67% | 16 | |
| | Preclinical QSP work typically get presented at governance meetings | 25.00% | 6 | |
| 34. Where QSP has failed to deliver, what have been the main reasons for it being judged a failure (select all that apply)? | Limited impacts due to delayed or insufficient modeling support (lack of resources, including funding or expertise) | 56.52% | 13 | 10 |
| | Lack of interest from management or internal decision makers (cost/benefit) | 56.52% | 13 | |
| | Lack of interest from regulatory agencies | 4.35% | 1 | |
| | Modeling findings not supported by literature and experimental data | 30.43% | 7 | |
| | Model development/validation/uncertainty poorly performed or documented | 17.39% | 4 | |
| | Not addressing clearly defined problems within the intended scope | 47.83% | 11 | |
| 35. Has the use of preclinical QSP modeling impacted communication/alignment around biological concepts within project teams? | Yes, it has had a positive impact on team communication/alignment | 66.67% | 16 | 9 |
| | Yes, it has had a negative impact on team communication/alignment | 0.00% | 0 | |
| | No, QSP modeling has not influenced team communication/alignment | 33.33% | 8 | |
| 36. When was preclinical QSP first explored in your company? | Before 2005 | 8.33% | 2 | 9 |
| | 2005-2010 | 25.00% | 6 | |
| | 2011-2015 | 50.00% | 12 | |
| | 2016 - present | 16.67% | 4 | |
| 37. How many projects does QSP significantly impact per year? | 0 | 16.67% | 4 | 9 |
| | 1 - 2 | 29.17% | 7 | |
| | 3 - 4 | 12.50% | 3 | |
| | 5 - 10 | 29.17% | 7 | |
| | >10 | 12.50% | 3 | |
| 38. Does QSP work make it into regulatory submission documents? | Frequently | 16.67% | 4 | 9 |
| | Sometimes | 8.33% | 2 | |
| | Rarely | 29.17% | 7 | |
| | Never | 45.83% | 11 | |

| Question | Answers | Responses (%) | # of Responses | # Skipped |
|---|---|---|---|---|
| 39. If QSP is included in regulatory documents, how is it used (select all that apply)? | As sole supporting evidence | 4.17% | 1 | 9 |
| | Supporting Human Efficacious Dose prediction | 66.67% | 16 | |
| | Supporting safety assessment | 29.17% | 7 | |
| | Proposing a registration (trial) dose | 20.83% | 5 | |
| | To support other arguments | 33.33% | 8 | |
| | Not applicable | 33.33% | 8 | |
| 40. At your company, how do you anticipate the number of QSP modelers changing over the next two years? | Increasing | 58.33% | 14 | 9 |
| | Stable | 37.50% | 9 | |
| | Decreasing | 4.17% | 1 | |
| 41. Within the next five years, in what therapeutic area do you anticipate the most potential for QSP modeling impact in your organization (select all that apply)? | Oncology | 62.50% | 15 | 9 |
| | Neuroscience | 33.33% | 8 | |
| | Autoimmune disorders | 62.50% | 15 | |
| | Infectious diseases | 12.50% | 3 | |
| | Cardiovascular | 25.00% | 6 | |
| | Metabolic disorders | 25.00% | 6 | |
| | Rare diseases | 29.17% | 7 | |
| | Other | 29.17% | 7 | |
| | None | 0.00% | 0 | |
| 42. What cross-functional training opportunities are planned for all modelers (including QSP modelers, PKPD modelers, statisticians, etc. ) in your organization (please select up to 5 answers)? | Mathematics, statistics, engineering, or physics concepts (e.g., nonlinear dynamics, control theory, etc.) | 45.83% | 11 | 9 |
| | Relevant biological/physiological/pathological pharmacological systems | 58.33% | 14 | |
| | Soft skills such as communication, project management, leadership, etc. | 58.33% | 14 | |
| | Systems biology/physiology, PBPK/PD, pop PK/PD | 62.50% | 15 | |
| | General ODE- or PDE-based computational modeling concepts | 29.17% | 7 | |
| | Other types of computational models (e.g., (fuzzy) logic models, agent-based models, etc.) | 4.17% | 1 | |
| | Information on “big data” or machine learning methods (e.g., Bayesian networks, artificial neural networks, deep learning, support vector machines, clustering) | 16.67% | 4 | |
| | Coding languages or software development | 33.33% | 8 | |
| | Optimization/calibration/verification techniques for complex systems | 12.50% | 3 | |
| | *In vivo* or *in vitro* experimental skills | 4.17% | 1 | |
| | Other | 4.17% | 1 | |
| | Not sure | 12.50% | 3 | |
| | None | 0.00% | 0 | |

Response (%) = 100% × [# of Responses] ÷ (33 – [# Skipped]), where 33 is the total number of survey participants. In other words, “Responses (%)” are calculated based on the number of responses divided by the number of responders to any given question.