# Quantitative Pharmacology (QP) Influence and Impact Initiative

Satyaprakash Nayak & Sandra Visser

On request of ASCPT QP Network leads

Anne Heatherington, Karthik Venkatakrishnan

Dear ASCPT Member,

On behalf of the ASCPT Quantitative Pharmacology (QP) Network (Influence and Impact) Initiative, we would like to invite you to contribute a case example which highlights the impact of Quantitative Pharmacology approaches in clinical pharmacology, translational medicine and therapeutics across the discovery, development, regulation and post-marketing applications.

The aim of this initiative is to develop a crowd-sourced compendium of high-impact QP examples to demonstrate the critical role played by QP in influencing and impacting decisions in the entire spectrum of drug development process.

Ideally, we would like the specific case example to be in the form of 1 informative slide which highlights the impact of QP approaches in answering a relevant question or guiding decisions.

We have identified a few key QP application areas for such examples:

* Translational Medicine
* Clinical Trial Design Optimization
* Drug development decision making
* Regulatory decision making
* Cost effectiveness assessment
* Therapeutic use optimization
* Novel data visualization/illustrations/simulations
* Drug-drug interactions
* Biosimilars
* Special populations
* Post-marketing applications

Please feel free to add your example even if it does not fit into the broad categories listed above.

An example case study and speaker notes are available on the following pages. Please provide your specific example in a similar format. Please note that your case example may be shared widely on the ASCPT website, with other ASCPT members via email or on groups/lists on social media websites. Case examples and speaker notes would be due December 1, 2016 (draft version) and January 31, 2017 (final version). We are planning to present selected high-impact examples during the QP Meeting at the ASCPT annual meeting in March 2017.

**If you would like to contribute, please let us know by October 17, 2016.**

In addition to the publicly available compendium, we are planning to draft a manuscript detailing the case examples with highest impact for publication consideration in an ASCPT affiliated journal. The authorship of such an article will be driven by the selected examples with a clear expectation that they meet standard ICMJE authorship criteria and take responsibility collectively for the publication.

If you have any questions regarding the scope, format or the overall goals on this initiative, please feel free to contact us (contact info below).

Thank you for your consideration and we hope to hear from you soon.

Satyaprakash Nayak & Sandra Visser

On behalf of Anne Heatherington (QP Network Chair) & Karthik Venkatakrishnan (QP Network Vice Chair)

# Aim

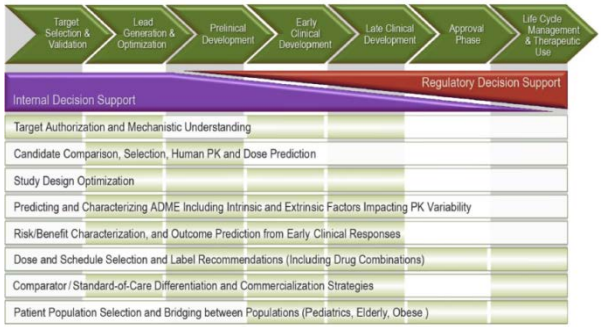
- Develop slide repository with state-of-the-art quantitative pharmacology applications
  - to increase awareness, advocacy for and education in the area of applied QP
- Develop leading publication(s) in ASCPT family of journals enhancing reputation of our community of practice in QP

# Strategic Fit

- Alignment with Goals of ASCPT 2015 Strategic Plan
  - *Influence and Impact*: ASCPT is the scientific resource that influences decision-making on therapeutic usage for patient care
  - *Education and Communication*:  ASCPT builds upon its exceptional education offerings and family of journals to create value for members and new audiences

# Building on applications listed in MID3 white paper

- How to differentiate and continue from applications surveyed in MID3 white paper?
  - Examples were compiled from the literature (up to end of 2014, see supplemental info) with the aim to illustrate the MID3 framework (key questions on compound, mechanism and disease the various modelling approaches) along the drug discovery and development path all the way into the therapeutic use. Compilation was not intended to be exhaustive for each application area
- Here: use crowd-sourcing to continue to build a repository with aim to:
  - get application owners direct input (ASCPT members, academia, industry, ….)
  - survey more applications in therapeutic use optimization
  - be more comprehensive in selected application areas for applications from the last ~ 5 years




Abstract:
http://onlinelibrary.wiley.com/doi/10.1002/psp4.12049/abstract
Paper:
http://onlinelibrary.wiley.com/doi/10.1002/psp4.12049/pdf
Supplemental info – compilation of examples:
http://onlinelibrary.wiley.com/doi/10.1002/psp4.12049/suppinfo
Podcast:
http://onlinelibrary.wiley.com/journal/10.1002/(ISSN)2163-8306/homepage/podcasts.htm

# Proposed ASCPT Quantitative Pharmacology Application Areas (1/2)

- Translational medicine
  - Human dose predictions
  - …
- Clinical trial design optimization
  - Cost reductions
  - Adaptive designs
  - …
- Drug development decision-making
  - Dose selection
  - Go/no go decisions
  - ….
- Regulatory decision-making
  - IND / NDA contributions
  - Label claims
  - …
- Cost effectiveness assessment
  - Differentiation potential
  - …..
- Therapeutic use optimization
  - Bringing drugs faster to patients
  - …..

# Proposed ASCPT Quantitative Pharmacology Application Areas (2/2)

- Biosimilars
  - Pharmacoeconomic modeling
  - Efficacy comparison
- Special Populations
  - Pediatric or Geriatric populations
  - Rare Diseases
- Novel methodology application
  - Novel data visualization to guide decisions
  - Superiority of model-based/QP method over conventional methods
- End user experience (Hospital Setting Use)
- Drug-drug interactions
- Any other QP related application

# Proposed Structure of application slide and speaker notes

# Proposed Speaker Notes Format to capture multiple aspects of application


| Case study Descriptors | | Description |
|---|---|---|
| **Application Question and Impact** | Key Question Addressed | |
| | Quantitative Pharmacology-informed conclusion | |
| | Application Area | Translational medicine; Clinical trial design optimization; Drug development decision-making; Regulatory decision-making, Cost-effectiveness / differentiation potential assessment, Therapeutic use optimization |
| **Case study Details** | Background / Introduction | |
| | Data Availability | |
| | Modeling / Analysis Method | |
| | Results | |
| | Inference /Simulation / Extrapolation | |
| | Conclusions | |
| | References / Acknowledgements | |
| **Additional Descriptions to link to MID3 Document applications** | Development Phase | Drug Development, Drug Discovery, Therapeutic Use, Regulatory Interaction |
| | MID3 Theme | Themes as listed in Table 1 of Good Practice Document (Commercial viability, Efficacy, Safety & Tolerability, PK, Risk/Benefit, Clinical viability, Study design) |
| | MID3 Level | Level as listed in Table 1 of Good Practice Document (Disease, Compound, Mechanism) |
| | MID3 Approach | Modeling Approach as listed in Table 2 of Good Practice Document (Empirical DT, Empirical PKPD, MBMA, Semi-mechanistic PKPD, Systems Pharmacology and PBPK) |
| | Low / Medium / High impact | Impact classification as described in Table 3 of Good Practice Document: Low (Describe), Medium ( Justify) or High (Replace) |

# “Quantitative Pharmacology-informed conclusion”

“Application Area “

**Key Question:** “……
……”

- **Data**
- **Modeling / Analysis Method**
- **Results**
- **Inference /Simulation / Extrapolation**

**Conclusions:** “……
……”

*“References”*

# Example of Case Study with attached speaker notes

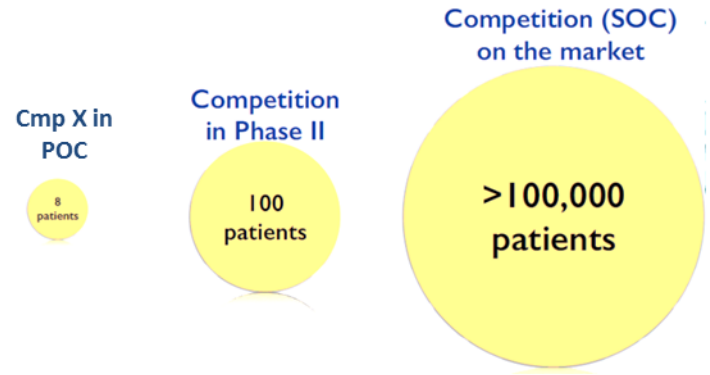
Note: Anonymized for illustration purposes, but will be completed with references and specific details in final repository

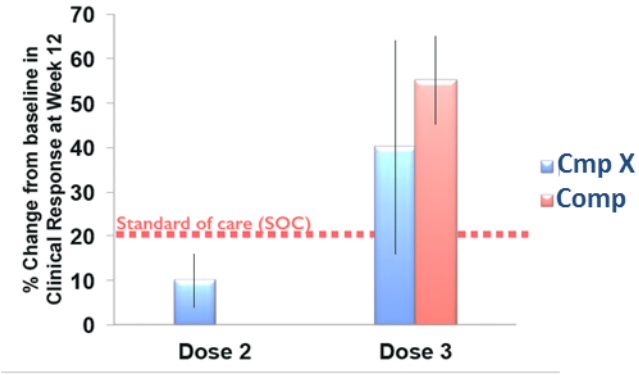
# Early Go/No Go based on differentiation potential compared to competitors and early patient data

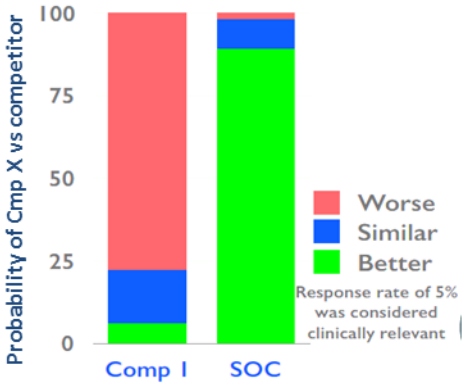
Application Area VI
Cost-Effectiveness

**Key Question:** Does the compound have sufficient differential potential to SoC to support continuation of Ph1b POC study in patients?

**Little data to assess differentiation** | **Model-Based Meta Analysis** | **Differentiation Potential**




## Inference

- Probability of Cmp X being comparable to that of the competitor was low without changes in clinical strategy, despite it would offer improvement over current standard of care.

## Conclusions

- Quantitative analysis enabled efficient decision making on a moderate effective drug despite “little” data. Based on the limited available options to revise the clinical strategy and the competitor substantially ahead in the development, the decision was made not to enroll more patients, and stop the program

Microsoft Word Document

*References: xxx, xxx*

# Further resource for communicating results with impact

# Communication of impact – guidance from a recent tutorial

Citation: CPT Pharmacometrics Syst. Pharmacol. (2016) 5, 163–172; doi:10.1002/psp4.12073


TUTORIAL

## Communicating to Influence Drug Development and Regulatory Decisions: A Tutorial

S Mehrotra and J Gobburu*

Pharmacometricians require three skills to be influential: technical, business (e.g., drug development), and soft skills (e.g., communication). Effective communication is required to translate technical and often complicated quantitative findings to interdisciplinary team members in order to influence drug development or regulatory decisions. In this tutorial, we highlight important aspects related to communicating pharmacometric analysis to influence decisions.
*CPT Pharmacometrics Syst. Pharmacol.* (2016) 5, 163–172; doi:10.1002/psp4.12073; published online 14 April 2016.

http://onlinelibrary.wiley.com/doi/10.1002/psp4.12073/abstract;jsessionid=68F862F6249B3C89AE659EFF5D359462.f04t03

Figure 5 illustrate a proposed effective way of communicating

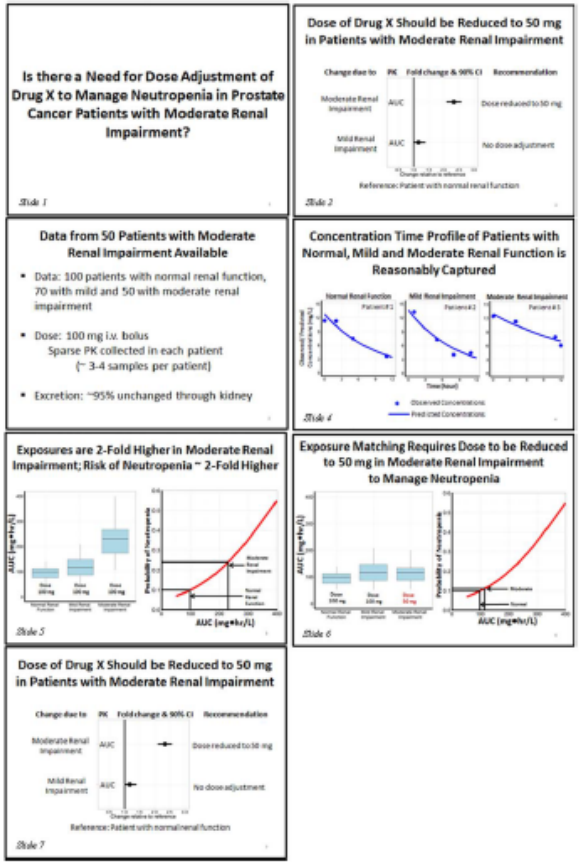



**Figure 5** Presentation B illustrates principles of effective communication. AUC, area under the curve; CI, confidence interval; PK, pharmacokinetic.