

Added value of the Data Scientist role in a Clinical Pharmacometric group



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1 – Background and Objective

The Clinical Pharmacometrics (CPM) group at Roche pRED consists of Pharmacometricians (PHME) and Clinical Pharmacology Data Scientists (CPDS). One of the main objectives of each CPM group, within the pharmaceutical industry, is to provide impactful modeling and simulation (M&S) inputs to clinical projects [1] [2]. The PHME main accountabilities are to define the M&S strategy, perform the analysis and communicate the results. The CPDS main accountabilities are to provide ready to use modeling input files from different sources, conduct data exploration, integrate important information into graphics easy to read, use previously developed models to identify and fix (if possible) data inconsistencies [3] [4], perform simulations, produce outputs for reports, etc.

The objective of this poster is to describe the current role of the CPDS group within Roche pRED and to illustrate how this role enables efficient quantitative clinical pharmacology activities.

The main added values are:

- High level of flexibility
- Data visualization expertise
- Leaner modeling and simulation flow
- Highly synergistic cross-disciplinary collaboration

2 – Flexibility



The M&S activities, contrary to biostatistics activities, are mainly data driven. Therefore, only few activities could be done proactively before database lock such as the preliminary modeling dataset building. Most of the CPDS work needs to be done in a short period of time between the database lock and the start of the modeling activity, to support the next drug development decision.



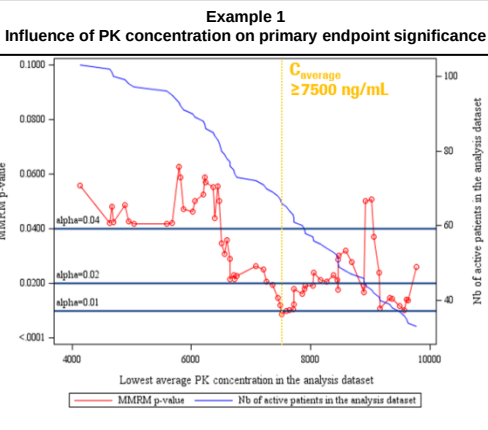
On top on the “regular” work, unexpected questions such as Health Authorities Agencies requests may arise. Recently, Clinical Pharmacology has been asked to justify the choice of the dose for a subpopulation for a drug already on the market. In less than 2 days, the CPDS has been able to generate a dataset with 7 studies, about 1000 patients and several variables in order to provide to the agency the first elements of responses.

Key elements of success:

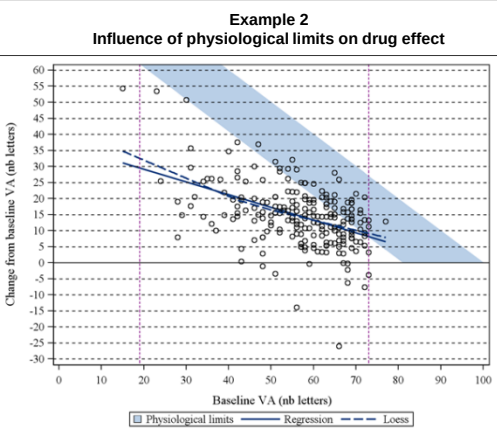
- Great values and behaviors
- Direct access to clinical database repository
- High level of understanding of clinical data standards

3 – Data Visualization

One of the most efficient ways to communicate with clinical teams, or to help PHME to decide on next steps, is to produce meaningful graphics. While some of them are easy to produce using ggplot2 in R or the SG procedures in SAS, others are much more challenging and require strong programming skills.



The example 1 illustrates the influence of removing patients with low exposure on the efficacy p-value. To produce such graphics, you need first to run all the statistical tests, to combine all results together and then to integrate all information into one graphic.



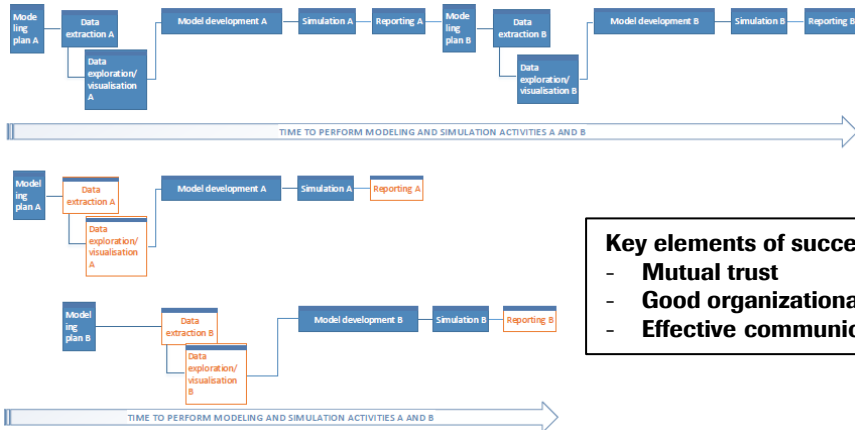
The example 2 illustrates the influence of the baseline visual acuity on the drug effect as well as the physiological limits effect on the maximum gain of letters possible. Such graphical approach was extremely useful to fine tune the inclusion criteria of a clinical study.

Key elements of success:

- High level of proficiency in SAS or R programming expertise
- High ability to display meaningful information for decision makers
- Knowledge and scripts sharing within the group

4 – Modeling and Simulation flow

A M&S activity is composed of a sequence of events (from dataset building to report writing) and M&S activities are usually conducted sequentially (e.g. PK followed by PKPD). When all those activities are conducted by one PHME, the time requires for the full analysis could become incompatible with the timing of the drug development decisions. In addition, the PHME may not have always the most appropriate skills to perform each single step in the most efficient way which contributes to further increase the time to complete the M&S activity. When the activities are split between the CPDS and the PHME based on their core skill sets then significant time reduction could be made especially as some activities could be conducted in parallel. Recently a CPDS created a phase 3 modeling dataset (+500 patients, +20 covariates) and explore most of all PK concentrations discrepancies in 2 working days only. A PHME would generally need much more time to complete such a task.

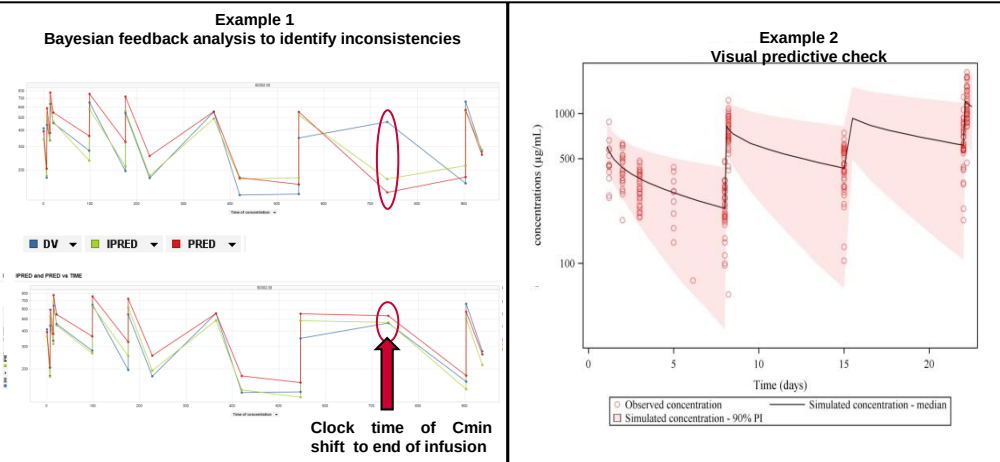


Key elements of success:

- Mutual trust
- Good organizational skills
- Effective communication

5 – Synergistic cross-disciplinary collaboration

The close connection between the CPDS and the PHME, allow the CPDS to understand how to use pharmacometrics tools and software and especially how to use previously developed models to evaluate the quality/relevance of new data by using bayesian feedback approaches (example 1) or by conducting simulation-based evaluations (example 2).



Key elements of success:

- CPDS ability and willingness to assimilate and use new methodologies
- Management support for specific education & development needs
- Increase CPDS understanding of their contribution to the big picture

6 – Discussion

Over the past few years, we have established a group of 9 CPDS, which supports M&S activities at the study, project and disease levels. Based on our experience, a CPDS free up time of a PHME around 30 to 40% allowing for more M&S activities to be conducted. Therefore, our recommendation to maximize the efficiency of a CPM group, is to have a ratio of at least one 1 CPDS for 2.5 PHME. With usually a Master degree in computational science and engineering, a CPDS brings flexibility and efficiency in the analysis process, increases the quality of the deliverables and also ensures full traceability and reproducibility. The most significant improvement is in the reduction of the time between clinical database lock and dataset ready for analysis which is usually around 70%. In order to provide impactful inputs to clinical project, Pharmacometricians have to deliver high quality works on time. Performing effectively requires many skills that not all Pharmacometricians have. It is therefore essential to work in collaboration with data scientist to maximize quality and efficiency of the M&S analysis.

7 – Acknowledgment

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8 – References

[1] FDA, March 2004: Innovation or Stagnation: Challenge and Opportunity on the Critical Path to New Medical Products. www.fda.gov/oc/initiatives/criticalpath/whitepaper.html
[2] Aarons, L. et al., Role of modelling and simulation in Phase I drug development.
[3] Buchheit, V. et al., Efficient quality review for modeling input dataset, PAGE 20 (2011) Abstr 2041 [www.page-meeting.org/?abstract=2041]
[4] Buchheit, V. and Frey, N., Data quality impacts on modeling results, PAGE 22 (2013) Abstr 2749 [http://www.page-meeting.org/default.asp?abstract=2749]