Data Scientists for improving efficiency and quality of quantitative clinical pharmacology analyses

Vincent Buchheit, MSc[1], Sebastien Jolivet, MSc[1] and Nicolas Frey, PharmD[1]

(1) Roche Pharma Research and Early Development, Pharmaceutical Sciences, Roche Innovation Center Basel, Switzerland

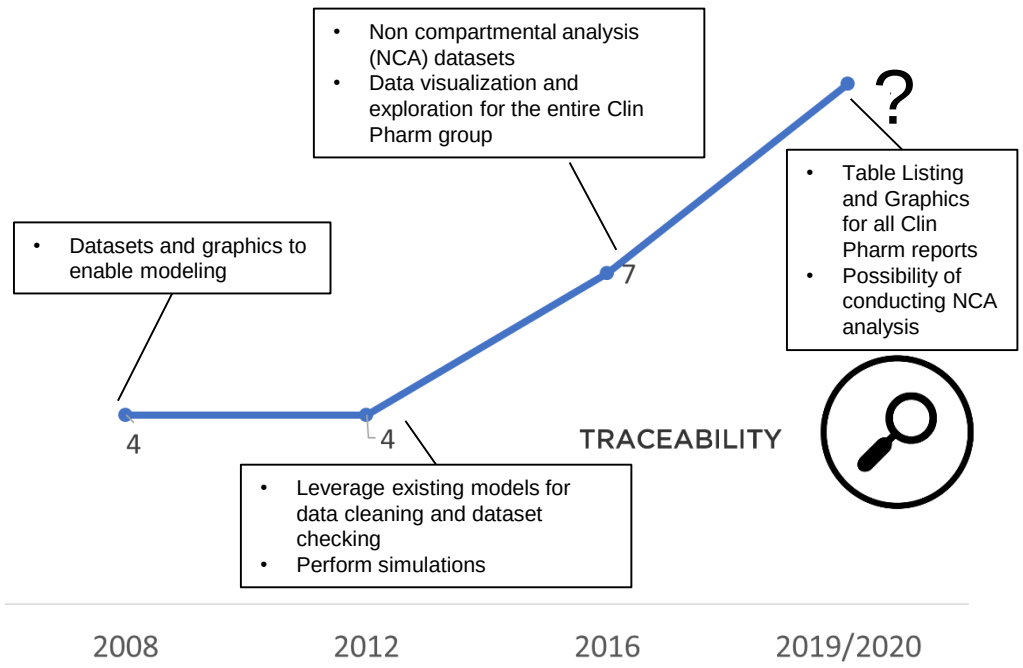
1 – Background and Objective

For the last 12 years, Roche has been having a group of Clinical Pharmacology Data Scientists (CPDS) embedded within the Clinical Pharmacometric (PMx) group. The added values of the CPDS to the conduct of PMx activities have been highlighted at previous PAGE meetings in 2013 [1] and 2016 [2]. The objective of this poster is to **describe the expansion of the CPDS role** to all the different types of Quantitative Clinical Pharmacology activities over the last few years and to highlight how it further adds efficiency and quality to the quantitative clinical pharmacology analyses.

The Clinical Pharmacology (CP) group at Roche pRED consists of clinical pharmacologists, pharmacometricians, disease modelers and CPDS. The CPDS's main accountability is to **enable those analyses and ensure full data traceability and reproducibility.** In addition to their increasing contribution to the conduct of quantitative clinical pharmacology analyses, the CPDS have also been the main drivers of two recent cross-project initiatives:

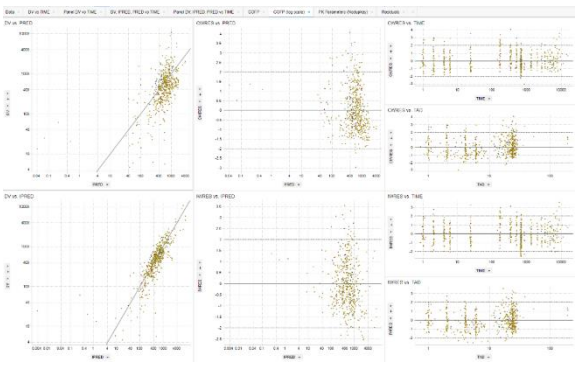
- **Implementation of a new secured and validated IT environment**
- **Early access to PK data collected in doubled blind studies to accelerate filing activities**

2 – Group Evolution



3 – Dynamic Graphical Analysis

In addition to the traditional static visualization (spaghetti plots, Goodness of fits, covariates distribution…) to explore pharmacometrics datasets and to provide tailored outputs for clinical pharmacologists, the team also provides dynamic visualization applications.

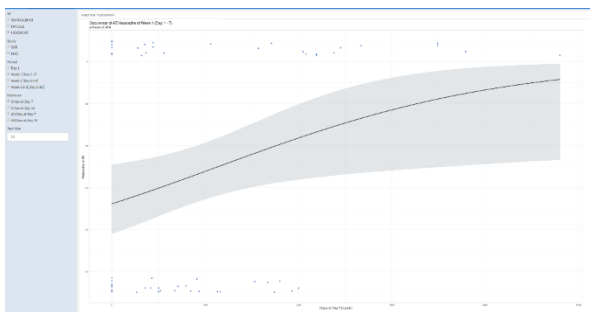


Based on spotfire® and used to dynamically explore Nonmem® output tables.The main added value of this tool is to better **identify outliers**. All graphics are automatically refreshed when one selects observations, allowing scientists to easily explore nonmem predictions and rapidly identify outliers. You can easily adapt such visualization to all your projects.

Based on R-Shiny and used:

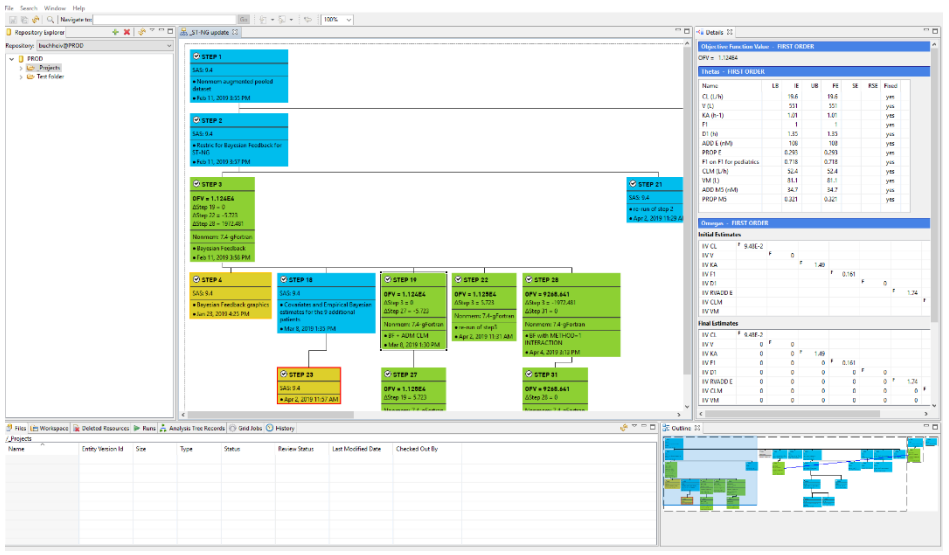
- to illustrate the model properties via interactive simulations (in combination with mrgsolve package)
- to conduct specific analyses such as exposure-response analysis for series of categorical variables.

Dynamic visualizations have been proven to be extremely effective during clinical team meetings!



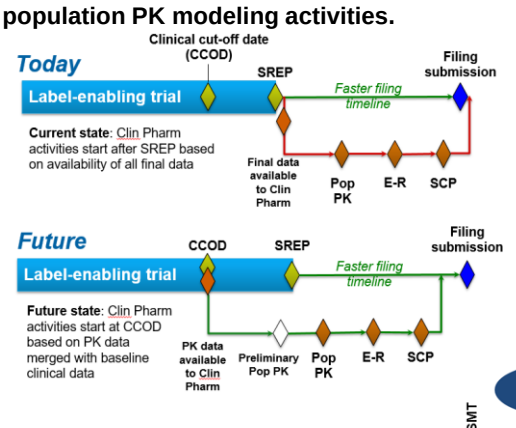
4 – Implementation of a new secured and validated IT environment

One of the added values of the CPDS team is **the full data traceability and reproducibility**. All activities are script based (mainly SAS® and R).
Since 2018, the department is using a **secured, validated** and version-controlled environment. It combines a global and secure file-repository with a robust and versatile modeling management interface for tools like NONMEM®, SAS®, R and PsN. The analysis trees allow scientists to visualize the entire analysis data flow.



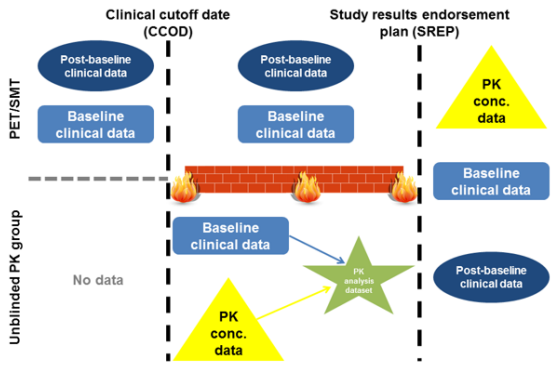
5 – Early access to PK data in doubled blind studies to accelerate filing activities

As part of a global initiative to accelerate filing timelines, we collaborated with our biometrics and regulatory colleagues to implement a new process enabling key CP team members to **have access to PK data in doubled blind studies prior to database lock to initiate population PK modeling activities.**



The main concept consists in accessing PK data (i.e.: date and time of dosing and PK samples, doses patient demographics) at the clinical cutoff date which usually takes place few weeks before the database lock date.

Between those 2 dates a firewall is put in place to avoid the PK data to be crossed with other parts of the clinical database and then ensure the study integrity.



6 – Discussion

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 data traceability and reproducibility**.
Based on our experience, a CPDS frees **up time of the quantitative clinical pharmacology scientists** allowing for more thorough scientific activities to be conducted.
As an example, one of the most significant gain we have observed, is in the time reduction between clinical database lock and PMX dataset ready for analysis. We estimate a gain in time of around 70%.
Having data scientists **fully embedded in a clinical pharmacology** department allows to **maximize efficiency and quality of quantitative clinical pharmacology analyses**.

7 – Acknowledgment

The authors would like to acknowledge the CPDS team: Claire Petry, Clarisse Chavanne, Felix Jaminion, Johann Laurent and Paul Grimsey.

8 – References

[1] 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]
[2] Buchheit, V. and Frey, N., Added value of the Data Scientist role in a Clinical Pharmacometric group, PAGE 25 (2016) Abstr 5884 [https://www.page-meeting.org/default.asp?abstract=5884]