SimDoC – Simulate Dose and Clearance

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For the development of drugs not only potency (pharmacodynamics) but also ADME (Absorption, Elimination, Meabolism, Excretion) profile (pharmacokinetics, PK) is of critical importance. To avoid drawbacks in later project stages it is essential to select the best candidate as early as possible. As a drug substance must be cleared from body but also needs be present in systemic circulation in suitable concentration, clearance (amount of elimination over time) is a key parameter. Together with other properties (from *in vitro* and *in vivo* experiment) dose can be estimated.

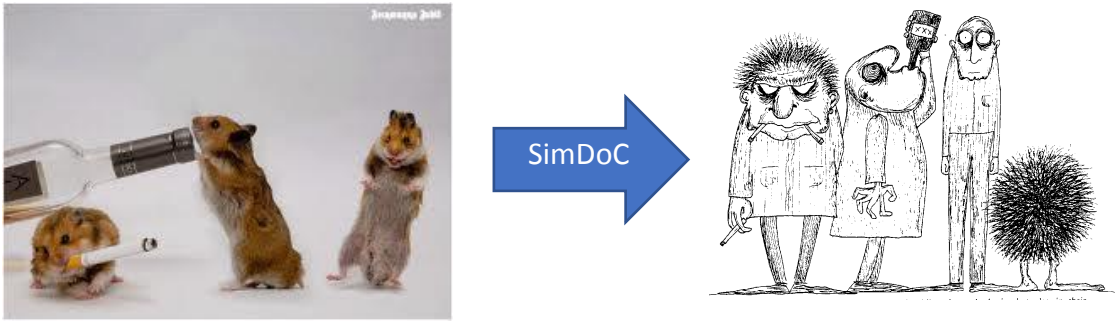
SimDoC was developed at Merck to support this process focusing on three major aspects:

1. Collect all relevant data needed for estimation of dose in human from in-house database
2. Standardize model calculation (use of same model, same physiological paramters, …)
3. Allow "what-if" simulation to gain insight in important PK processes

Elements of SimDoC are ivivc (*in vitro in vivo* correlation) and ivive (*in vitro in vivo* extrapolation) for the estimation of human clearance from experimental species data, simulation of concentration-time curves in different species and human, and sensitivity plot for dosage.

Prior to the availability of SimDoC data collection was mostly done by manual data transfer to Excel sheets followed by property calculation with Excel macros. This was cumbersome and error-prone. In addition, comparison of compounds and inter species differences was difficult or impossible.

In current version of SimDoC up to 10 compounds with 4 species plus human data are accessible and comparable. Various data visualization can guide or inspire experimental design and checks.



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