Understanding inter- and intra-individual variability in HBM spot samples

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Introduction

In many large-scale human biomonitoring (HBM) surveys, single samples of blood, urine or other biological matrices are collected from large numbers of individuals recruited from the general population. These HBM surveys aim to obtain information on the distribution of exposures in the population, the comparison of different subgroups, or the identification of high exposure groups.

The single sample analyses capture the variability of internal dose in the population, without however disentangling the variability due to variation between individuals or within an individual.

The current project, funded by CEFIC's LRI, started early in 2012 and aims at improving our understanding of the impact of inter- and intra-individual variability in large-scale HBM surveys. The project will use a combination of existing biomarker data, toxicokinetic modelling and newly generated biomarker analysis tailored to this problem. The goal of the project is to identify the most important drivers affecting the intra-individual variability of single biomarker samples for assessing an individual's internal dose.

The specific project objectives are threefold:

- To **identify the key determinants** influencing intra-individual biomarker levels (with a focus on short-lived compounds measured in urine samples);
- Development of **an easy-to-use software tool** to assist interpretation of studies utilising single human biomonitoring samples in terms of exposure;
- Where appropriate, to **propose alternative sampling schemes** that provide more representative measures of longer-term average exposures for individuals and populations.

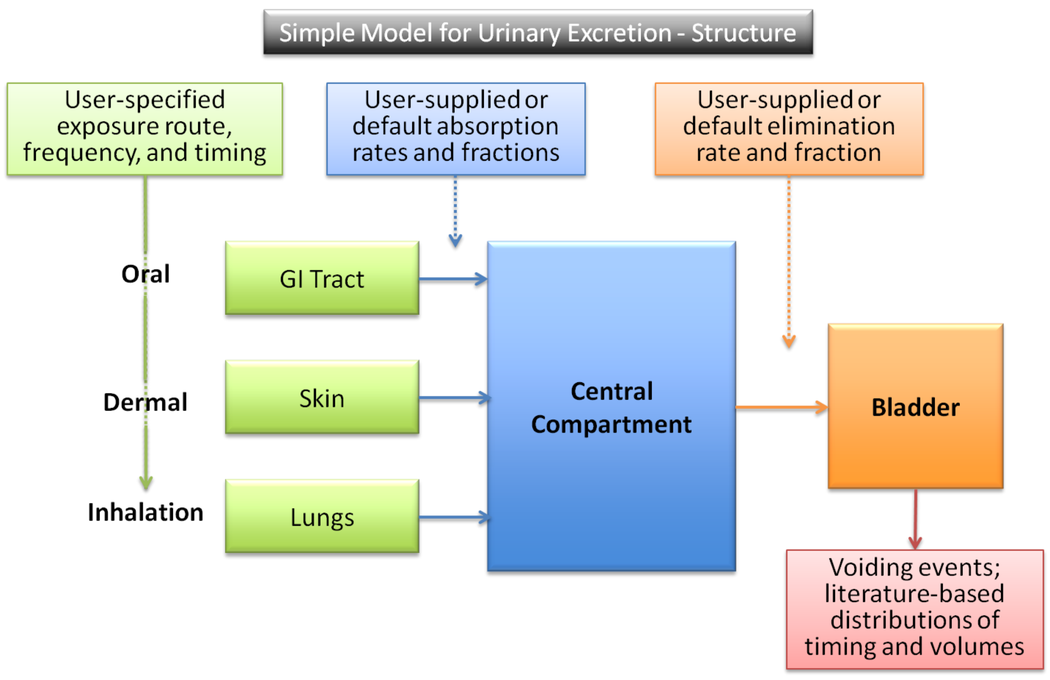

Fig 2. Outline of the structure of the model for urinary excretion

Status of the work

Currently, work within the project is focusing on WPs 1, 2 and 3 (Figure 1), i.e. identifying the key determinants that influence the representativeness of HBM sample (WP1); development of a first operational version of the software model (WP2); and setting up a dedicated HBM study in which fit-for-purpose, high quality data is collected to validate the software model (WP3). An outline of the structure of the urinary excretion model is provided in Figure 2. Figure 3 provides a first idea of what the output of the model will look like.

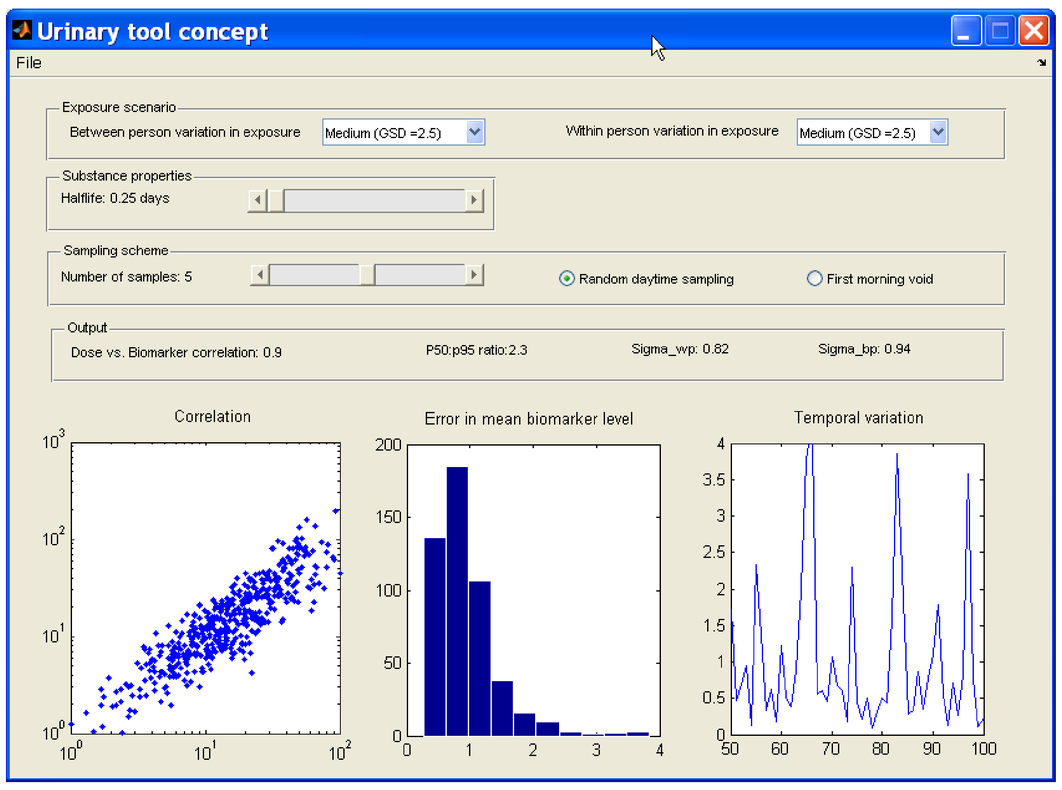

Fig 3. Outline of the structure of the model for urinary excretion

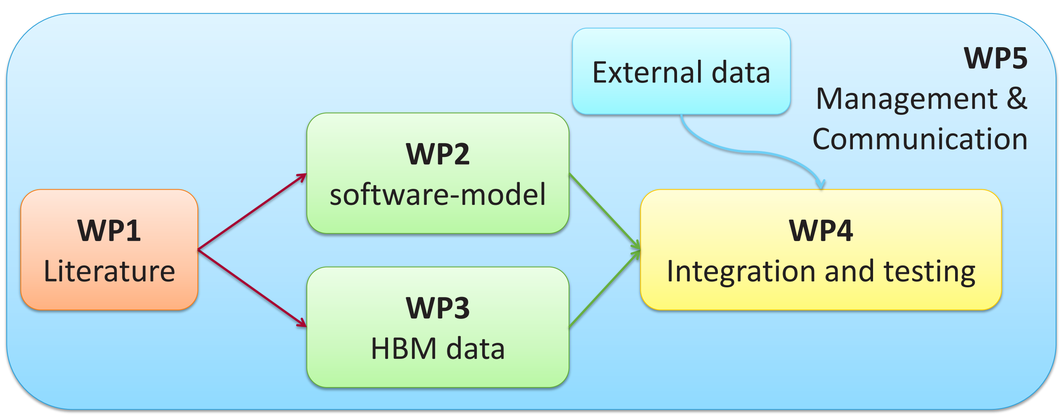

Fig 1. Schematic break-up of the work flow in different work packages (WP)

In WP3, a dedicated HBM study will be performed with the aim to collect high-quality, fit-for-purpose data to test the model developed in WP2. In this HBM study, all urinary voids will be collected from eight volunteers for a period of one week. In all samples, a set of anti-bacterial substances (parabens, triclosan, triclocaban) and a suite of metals will be measured. At the same time, volunteers will maintain a logbook with data on the timing of urinary voids, food consumption, use of cosmetics and household products, and other auxiliary information required to interpret the biomarker data and feed into the model.

Future developments

Following the completion of the alpha-version of the software model, the model will be extensively tested using both the data generated in WP3 and through additional publicly available data from both environmental and pharmaceutical trials. A user manual will be made available together with the model to warrant user-friendliness.

The project hopes to host a pre-conference workshop at the 2013 ISES/ISEE/ISIAQ meeting in Basel, Switzerland (pending), at which participants will be able to get a first taste of the functionalities of the model. Feedback from workshop participants will be used to develop the final version of the model.

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