**A hierarchical Bayesian model for an in vitro-in vivo correlation (IVIVC)**

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**INTRODUCTION**

**In vitro-in vivo correlation (IVIVC):** Defined by the FDA as "predictive mathematical model describing the relationship between an in vitro property of a dosage form and an in vivo response" → can act as a surrogate for bioequivalence or bioavailability testing in human subjects → support biowaivers → reduce costs and duration of optimization process.

**Problem:** Current IVIVC models often entail complex potentially unstable mathematical deconvolution operations, are assessed applying purely frequentist methods on averaged data.

**METHODS I**

We propose a Bayesian convolution-based IVIVC approach including:

1. a nonlinear mixed effects model for the in vitro release/permeation data;
2. a population pharmacokinetic (PK) compartment model for the in vivo immediate release (IR) data;
3. a system of ordinal differential equations (ODEs), containing the submodels (1) and (2), which approximates and predicts the in vivo controlled release (CR) data.

The innovation consists of splitting the parameter space between submodels (1) and (2) versus (3) and, subsequently, accounting for the uncertainty around the parameters via prior distributions in a Bayesian framework.

Case study example: transdermal patch, in (1) and (3), intravenous infusion, in (2).

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**METHODS II**

**I.**

**In vitro release (patch on skin portions)**

- Input function $q_{in}$

**In vivo IR (intrav. infusion in human)**

- three-compartment model

**II.**

**in vivo CR (patch on human)**

**RESULTS**

- Figure 1: Serum concentrations (dots with posterior median [black lines] and 90% credible bands of predicted individual observations in study subjects.

**DISCUSSION**

The developed IVIVC model provides a satisfactory estimation of the PK population data of a transdermal patch. The Bayesian framework allows a natural integration of knowledge from one source of information into another (in vitro to in vivo), while accounting for the parameters uncertainties. This work is an extension of the current IVIVC methodology where biased deconvolution techniques and averaged data are common.

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**REFERENCES**


