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Application of an NLME-Stochastic Deconvolution Approach to Level A IVIVC Modeling

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Abstract

Stochastic deconvolution is a parameter estimation method that calculates drug absorption using a non-linear mixed effects model in which the random effects associated with absorption represent a Wiener process. The present work compares, 1) stochastic deconvolution, and 2) numerical deconvolution, using clinical pharmacokinetic data generated for an IVIVC study of extended release (ER) formulations of a BCS class III drug substance. The preliminary analysis found that numerical and stochastic deconvolution yielded superimposable fraction absorbed (F_{abs}) versus time profiles when supplied with exactly the same externally-determined unit impulse response parameters. In a separate analysis a full population-PK/stochastic deconvolution was applied to the clinical PK data. Scenarios were considered in which immediate release (IR) data were either retained or excluded to inform parameter estimation. The resulting F_{abs} profiles were then used to model level A IVIVCs. All the considered stochastic deconvolution scenarios, and numerical deconvolution, yielded on average similar results with respect to the IVIVC validation. These results could be achieved with stochastic deconvolution without recourse to IR data. Unlike numerical deconvolution, this also implies that in crossover studies where certain individuals do not receive an IR treatment, their ER data alone can still be included as part of the IVIVC analysis.

Keywords:
Two-stage, Level A *in vitro/in vivo* correlation (IVIVC), numerical/stochastic deconvolution, population pharmacokinetics (PK), nonlinear mixed effects (NLME) modeling.

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