Exploring In Vitro Equivalence Tests Using a Bayesian Hierarchical Model

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Bayesian methods allow us to learn from data by fitting complex interconnected probability models to a range of predictor and outcome data types. Such models can handle sparse data sets, data following a zoo of probability distributions and can be updated as new information is gathered without fear of biasing results. The methods have been applied to clinical trials and explored by regulatory agencies such as EMA and FDA.

In this study the relationship between flow rate, impactor stage deposition and the certainty of passing the EMA's suggested test for comparing multistage impactor data was modelled. The model relied merely on impactor data and well-known expressions for impactor stage cut offs and confidence intervals. The connection between variable inhaler performance and uncertainty in the equivalence determination were quantified and used to track the risk of performing in vitro trials at different flow rates.

This study has shown how a Bayesian hierarchical model can be used to identify the relationship between parameters of an impactor study and the probability of determining equivalence of pharmaceutical products. The method allows the maximum insight to be gained from the data we generate, and a more complete understanding of uncertainty has the potential to de-risk expensive trials.