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June 4, Tuesday 9-10 am EST

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Title

Comparison of dissolution profiles with the Mahalanobis distance

Abstract

For some post approval changes the manufacturer has to demonstrate that the dissolution profile of the drug product before the change is statistically equivalent to the dissolution profile after the change. Guidelines suggest the so-called similarity factor f2 as standard approach for the equivalence analysis. f2 is a statistically questionable transformation of the Euclidean distance between both profile means and does not allow a control of the type I error rate. In this webinar, the T2EQ approach is introduced and suggested for dissolution profile comparisons. T2EQ is an equivalence procedure based on the Mahalanobis distance with an internal equivalence margin for comparing dissolution profiles. The equivalence margin is compliant with current dissolution guidelines. Simulation studies about the operating characteristics (size, robustness and power) show promising results: Not affected by the potential bias of the Mahalanobis distance point estimate the type I error rate can be reliably controlled for various distribution assumptions and the power of T2EQ exceeds the power of methods recently discussed in the literature.

The second part of this webinar will adress the conflicts between basic statistical principles and widely-used interpretations of current dissolution guidelines. Sample size calculations in the planning phase of the study are necessary to avoid underpowered studies especially if the number of elementary hypotheses to be tested (equivalence has to be shown for several pH values of the dissolution medium, maybe for several strengths, maybe for several active ingredients for fixed dose combinations) is high. Current developments as e.g. around the ICH M9 draft guidance will be also be discussed.

Professional Biography

Thomas Hoffelder studied Mathematics in Mainz and Biostatistics (PhD) in Heidelberg. Since 2006, he is working as a non-clinical statistician for Boehringer Ingelheim supporting the Chemistry, Manufacturing and Control (CMC) area. He is author of several publications about multivariate equivalence tests for use in pharmaceutical development. The methods can be applied for equivalence analyses of particle size distributions or dissolution profiles. Thomas is author of the R package "T2EQ" which implements a Mahalanobis distance based equivalence procedure for comparing dissolution profiles.

Sponsored by

- American Statistical Association (Boston, Connecticut, Florida, New Jersey, Princeton/Trenton, and Washington chapters)
- Boehringer Ingelheim Pharmaceuticals, Inc. (Biostatistics and Data Sciences Department)
- New England Statistical Society (NESS)

For interested participants

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