**Presentation**: Equivalence of Dissolution Profiles: Summary of statistical follow-up activities of the M-CERSI workshop 2019

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**NCS working area**: Chemistry, Manufacturing and Control (CMC) area

**Abstract**

Dissolution profile comparisons are used in the pharmaceutical industry in the context of post-approval changes where the manufacturer has to demonstrate that the quality of the product is not affected by the change. A dissolution profile comparison yields a two-sample (reference versus test product) multivariate equivalence testing problem.

The current situation: The so-called similarity factor f2, recommended in all guidelines on dissolution profile comparisons, is a series of monotone (and statistically useless) transformations of the Euclidean distance between reference and test mean profiles. It is a point estimate which does not allow Type I Error (T1E) control. A decision based on f2 is only acceptable from regulatory perspective if the variability is below some (guideline dependent) thresholds for all dissolution time points. For “highly variable” profiles, a regulatory gold standard for equivalence analyses is missing.

Some guidances and the original publication of f2 date from the mid-1990s, from a time when very few knowledge about multivariate equivalence tests was available. This has now changed. A scientific and statistical update of the dissolution profile topic is necessary leading to

* Improved T1E control in decision making by means of the use of available multivariate equivalence tests instead of f2,
* Increased power by means of an appropriate design and planning of dissolution profile studies (including sample size calculations, among others),
* International harmonization.

Follow-up working groups from the dissolution profile similarity workshop held in May 2019 in Baltimore addressed some challenges around the dissolution profile topic. One summary paper (AAPS Journal) explains the properties of various multivariate equivalence tests tailored to dissolution profiles and suggests as a result a decision tree for the selection of an appropriate statistical method depending on product characteristics.

My NCS workshop talk will present and explain the above mentioned decision tree. The second part will address the design of dissolution profile studies including a conclusion on how to evaluate profile data obtained from several batches per reference and/or test product.