Title: Equivalence of Dissolution Profiles: Time for the statistical dissolution (r)evolution?

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Presentation summary

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 gold-standard for equivalence analyses of dissolution profiles is a point estimate which does not allow Type I Error (T1E) control in the decision process. 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.

Whereas in the clinical area statistical experts from academia, regulatory agencies and industry meet at conferences and workshops to foster scientific evidence based decision making the influence of statisticians is low in the dissolution profile topic. The consequence is that basic statistical principles (balance between T1E control and power, study planning including sample size determination) are not adequately considered in the literature or the regulatory documents and thus not always implemented in practice. Ill-designed dissolution profile studies are a financial risk and do not support scientific evidence based decision making.

Another fundamental problem is that the question “what are appropriate estimands for dissolution profile studies” is not yet systematically addressed.

The presentation will be a plea for creating an international working group of statisticians from all stakeholders working on a guideline to address the statistical aspects around dissolution profiles and to harmonize the statistical requirements.

Such a statistical guideline could be used as a basis or reference for the necessary update of current dissolution guidelines.