Release testing strategies for dissolution for larger sample sizes

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A common approach for dissolution testing in conventional batch release is to measure at most 24 tablets in three subsequent stages and evaluate the results against the acceptance criteria of the dissolution chapter of the United States Pharmacopoeia (USP <711>). Recent developments in process analytical technology (PAT) have enabled testing of larger sample sizes by reducing or eliminating cost and time constraints associated with lab-based assessment. PAT has been successfully used in continuous manufacturing for blend monitoring and active pharmaceutical ingredient's (API) content uniformity in tablets. Continuous manufacture changed the batch size paradigm from fixed volumes and discrete steps into a single continuous line, so the real-time control of content is critical. PAT can provide hundreds of measurements for a single batch. Consequently, this has driven the need for methodologies on how to extend release testing to larger sample (Bergum & Vukovinsky, 2010).

PAT measurements of content together with additional process or material parameters can also be leveraged to predict dissolution. Multiple companies (see Khaki *et al*, 2023) have recently attempted to build predictive models with PAT measured API content as an input, leading to hundreds of predicted dissolution values. However, there is currently no regulatory guidance and limited literature on the topic. In line with this need, our recent publication (Otava *et al*, 2024), draws from the methods applied to API content testing as a framework for large N dissolution testing. We describe two statistical approaches towards release testing strategy for immediate release dosage forms for a large N (> 24): 1) a generalization of USP <711> three-stage acceptance criteria for any sample size N > 24, and 2) a tolerance interval approach. Both approaches are based on a sample-size independent criterion ensuring a known probability of passing USP <711> acceptance criteria. The proposed criteria can be applied to the entire batch or segmented portions of a single batch run in the context of both continuous and batch manufacturing.

References:

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Presenter's bio:

Martin Otava is an Associate director in Manufacturing and Applied Statistics in Johnson & Johnson. Martin completed his PhD at Hasselt University in 2015 and joined J&J the same year. Martin supports chemists and engineers in analytical methods and process development for manufacture of small molecules products. He focuses on continuous manufacture, design of experiments and Bayesian hierarchical modelling.