

Role of Multivariate Data Analyses In Formulation and Process Development of Oral Solid Drug Products: Encapsulation Case Studies

Shashwat Gupta

Eli Lilly and Company, Synthetic Molecule Design and Development (SMDD)

ABSTRACT

Multivariate data analysis (MVDA) methods are an important tool in a pharmaceutical drug product engineer's toolbox as part of a Quality by Design (QbD) driven framework for formulation and process development of oral solid dosage forms. This work presents such an MVDA application for two commonly used encapsulation processes in the following case studies: Case study 1: Partial least squares regression (PLSR) based enhancement of process efficiency of a vacuum-assisted drum filling encapsulation process A vacuum-assisted drum filling process was used to fill an active pharmaceutical ingredient (API). Intuitively, the drum bore volume is a function of the amount of API to be filled (combination of dose and incoming potency) and API physical properties (particle size distribution, density, etc.). Thus, selection of an appropriate drum bore volume was desired to reduce process setup time. To enable this, a PLSR model was built correlating API physical properties and drum filling process parameters to API plug density. The developed model was then used to identify drum bore volumes for manufacturing campaign support, designing a drum library that encompasses expected variability in API physical properties and potency, and a simple drum lookup table to support commercial manufacturing. Case study 2: Principal component analysis (PCA) to enable formulation development of an

excipient mixture filled with a dosing disk encapsulation process A dosing disk encapsulation process was used to fill an excipient mixture (sodium bicarbonate and dimethicone). During formulation development, the effects of varying excipient mixture properties on the encapsulation process (fill weight variability) and product performance (in-vitro dissolution) were evaluated. Varied excipient mixture properties were generated by manufacturing under a wide range of raw materials (sodium bicarbonate particle size/amount, dimethicone amount, and dimethicone viscosity) and process conditions for different mixing technologies (batch and continuous). PCA was then applied to identify excipient mixtures with the most varied physical properties that encompass all other excipient mixtures. The excipient mixtures extremes were then tested for process and product performance. The analysis demonstrated that the product and process performance was robust across the range of material properties and mixing process technologies that were evaluated for the excipient mixture.

© 2026 by the authors. Licensed to PSEcommunity.org and PSE Press. This is an open access article under the creative commons CC-BY-SA licensing terms. Credit must be given to creator and adaptations must be shared under the same terms. See <https://creativecommons.org/licenses/by-sa/4.0/>

