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A digital toolbox for pharmaceutical tablet manufacturing

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The development of pharmaceutical tablet manufacturing processes typically involves time-consuming and resource-intensive development campaigns supported by equally demanding laboratory analysis. These campaigns are designed to construct the safe operating space to deliver the desired product quality. GSK is driving the digitalization of tablet manufacturing via the use of digital twins and chemometrics through the implementation of real-time metrology. In this study, we explore the integration of digital tools on direct compression (DC) and their impact on industrial manufacturing.

DC constitutes the simplest tablet manufacturing option with the lowest number of unit operations followed by roller compaction and wet granulation. The deployment of digital tools benefits the use of this platform by **decreasing the scope and extent of development campaigns, reducing analytical burden and providing real time batch monitoring**. Detailed understanding of the relationships between raw material properties, process parameters and critical quality attributes of the intermediate and final tablet product is key to the ensuring final product quality. A DC system model provides that fundamental understanding and accelerates process and product development (Aroniada, et al., 2023). To describe the compression process, an empirical model combining established modelling approaches was developed to correlate tablet hardness to the extent of lubrication, API D90 and the API formulation strength. To generate a holistic systems model, this model was combined with blending, tablet disintegration and an in-vitro dissolution models. Upon system model scientific validation with industrial manufacturing data, very good prediction fidelity was established for predicting in vitro dissolution. The model was deployed to provide guidance during process development and support future control strategy definition to build a robust pharmaceutical manufacturing process.

To reduce the analytical requirement during development and commercialisation, process analytical tools (PAT) are deployed. PAT implemented in line provide an “eye” into the manufacturing process driving process and product understanding and robust Quality-by-Design (QbD) process characterization. NIR PAT tools provide non-destructive measurements of both physical and chemical properties of particulate material including real time quantification of the active pharmaceutical ingredient, API. NIR integration in a tablet press feedframe provides a good configuration to optimise powder material presentation prior to compression (Ward, et al., 2013). Upon successful off-line evaluation and creation of bespoke chemometrics models, this PAT approach was successfully verified during manufacturing providing satisfactory real time monitoring of API during compression. This creates the framework for reducing off line analysis of the produced tablets.

The last tool in this digital toolbox is multivariate statistical process monitoring, MSPM. MSPM is a multivariate analysis technique that can be used for analysing highlycorrelated, highly-dimensional and noisy process data, hence streamlining process understanding, monitoring and control. In this data-driven approach, compression process variables are correlated through a principal component analysis (PCA) algorithm enabling the monitoring of batch performance through key model metrics. Monitoring the model metrics not only establishes a robust real-time batch monitoring

tool but also allows comparing batch data over time to derive insights into process robustness and creates the basis for predictive maintenance.

Type of presentation

Contributed Talk

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