Advanced process control practices for continuous pharmaceutical twin-screw wet granulation.

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State of the art

Continuous manufacturing offers great potential to improve the economic and environmental impact hailing from the production of solid pharmaceutical drug products. Recently, considerable work has been performed to understand the effect of process dynamics on product quality, as well as the design of appropriate measurement systems for the real-time monitoring of these production lines. Few studies have, however, made an attempt to include automated supervision using the knowledge and on-line measurements available for twin-screw wet granulation processes. Nowadays, controlling intermediate and final quality attributes in this industry is still mainly based on fixed recipe parameters optimised for a steady-state combined with offline acceptance sampling strategies. Hence, not taking into account the impact of stochastic disturbances which vary in time. Therefore, an approach with automated corrective actions is proposed to meet the real-time release requirments of continuous pharmaceutical manufacturing.

Objectives and Results

This work exemplifies the use of time-domain system identification and linear model based control theory for automated process supervision, i.e. advanced process control, on a commercial continuous twin-screw wet granulation line, type ConsiGma-25^{TM}. With the help of complementary GMP approved PAT instruments as well as legally compliant data management software, it is shown that both chemical (granule moisture content) and physical (granule size distribution) product characteristics can be subjected to user defined reference values. Above all, it is shown that process disturbances coming from feeder fluctuations and physical wear are effectively tackled. This work also presents some challenges related to instrument interfacing and control integration which are especially relevant for equipment, instrument and software suppliers.