Mechanistic modelling for process understanding of fluidized bed drying process part of a full continuous pharmaceutical manufacturing line

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Nowadays, the pharmaceutical industry is increasingly moving towards continuous production processes, requiring understanding and monitoring to deal with the PAT regulations. In this work, the continuous formulation of APIs into final drug products is of interest, and more specifically a six-segmented fluidized bed drying process part of the Consigma^{TM}. In traditional batch processes, product quality evaluation mostly relies on off-line, time-consuming and, hence, less efficient laboratory testing. The continuous approach possesses clear advantages. The efficiency can be improved by relying on in-line measurements and real-time adjustment of sensitive variables. Monitoring and controlling the process during operation can be much more economical through significant decreases in product loss.

A mechanistic model describing the drying process of one single granule has been developed and validated with experimental data. This model has then been extended towards a model for a population of granules using PBM. A scenario analysis has been performed to investigate the influence of changing operating.

Another part focuses on the continuously logged process, which are processed using a mass and energy balance. These can be be used to calculate the moisture content of the granules leaving the drying unit. The energy balance, which predicts the gas outlet temperature, is useful to have an immediate check of the mass balance. The balances are a powerful tool to gain information about the process during operation without the need for time-consuming off-line measurements. Based on several datasets, it can be concluded that it is possible to monitor the process and draw drying endpoint and residual moisture conclusions.

The combination of the detailed understanding of the drying process, gained by mechanistic models, and the process monitoring by using balances enables the operator to monitor and control the process during operation in order to stay within the design space.