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MC. Martinetz, A-P. Karttunen, S. Sacher, P. Wahl, J. Ketolainen, J.G. Khinast, O. Korhonen

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RTD-based Material Tracking in a Fully-Continuous Dry Granulation Tableting Line

M. C. Martinetz[1,3,§], A-P. Karttunen[2,3,§], S. Sacher[1,3], P. Wahl[1], J. Ketolainen[2,3], J. G. Khinast[1,3,*], O. Korhonen[2,3]

[1] Research Center Pharmaceutical Engineering (RCPE), 8010 Graz, Austria
[2] School of Pharmacy, Promis Centre, University of Eastern Finland, 70210 Kuopio, Finland
[3] European Consortium on Continuous Pharmaceutical Manufacturing, 8010 Graz, Austria

[§,#] Both authors contributed equally to this work.
* Corresponding authors: khinast@tugraz.at

Abstract

Continuous manufacturing (CM) offers quality and cost-effectiveness benefits over currently dominating batch processing. One challenge that needs to be addressed when implementing CM is traceability of materials through the process, which is needed for the batch/lot definition and control strategy. In this work the residence time distributions (RTD) of single unit operations (blender, roller compactor and tablet press) of a continuous dry granulation tableting line were captured with NIR based methods at selected mass flow rates to create training data. RTD models for continuous operated unit operations and the entire line were developed based on transfer functions. For semi-continuously operated bucket conveyor and pneumatic transport an assumption based the operation frequency was used. For validation of the parametrized process model, a pre-defined API step change and its propagation through the manufacturing line was computed and compared to multi-scale experimental runs conducted with the fully assembled continuous operated manufacturing line. This novel approach showed a very good prediction power at the selected mass flow rates for a complete continuous dry granulation line. Furthermore, it shows and proves the capabilities of process simulation as a tool to support development and control of pharmaceutical manufacturing processes.

Keywords: Continuous manufacturing, process modeling, PAT, residence time distribution, material tracking, dry granulation, roller compaction, validation