Accepted Manuscript

A review of PAT strategies in secondary solid oral dosage manufacturing of small molecules

S. Laske, A. Paudel, O. Scheibelhofer, Stephan Sacher, Theresa Hoermann, Adrian Kelly, Jukka Rantannen, Ossi Korhonen, Fanny Stauffer, Fien De Leersnyder, Thomas De Beer, Jerome Mantanus, Pierre-Francois Chavez, Benjamin Thoorens, Patrizia Ghiotti, Martin Schubert, Pirjo Tajarobi, Gunnar Haeffler, Satu Lakio, Magnus Fransson, Anders Sparén, Susanna Abrahmsén-Alami, Staffan Folestad, Adrian Funke, Ivo Backx, Barbara Kavsek, Francois Kjell, Marc Michaelis, Trevor Page, John Palmer, Alexander Schaepman, Sonja Sekulic, Steve Hammond, Birgit Braun, Brenda Colegrove, Johannes Khinast

PII: S0022-3549(16)41849-6

DOI: 10.1016/j.xphs.2016.11.011

Reference: XPHS 565

To appear in: *Journal of Pharmaceutical Sciences*

Received Date: 22 August 2016

Revised Date: 14 October 2016

Accepted Date: 8 November 2016

Please cite this article as: Laske S, Paudel A, Scheibelhofer O, and the author team, Sacher S, Hoermann T, Kelly A, Rantannen J, Korhonen O, Stauffer F, De Leersnyder F, De Beer T, Mantanus J, Chavez PF, Thoorens B, Ghiotti P, Schubert M, Tajarobi P, Haeffler G, Lakio S, Fransson M, Sparén A, Abrahmsén-Alami S, Folestad S, Funke A, Backx I, Kavsek B, Kjell F, Michaelis M, Page T, Palmer J, Schaepman A, Sekulic S, Hammond S, Braun B, Colegrove B, Khinast J, A review of PAT strategies in secondary solid oral dosage manufacturing of small molecules, *Journal of Pharmaceutical Sciences* (2016), doi: 10.1016/j.xphs.2016.11.011.

A review of PAT strategies in secondary solid oral dosage manufacturing of small molecules

S. Laske, A. Paudel, O. Scheibelhofer and the author team*

*Author team:
Stephan Sacher (RCPE GmbH)
Theresa Hoermann, Johannes Khinast (Graz University of Technology)
Adrian Kelly (University of Bradford)
Jukka Rantannen (University of Copenhagen)
Ossi Korhonen (University Eastern Finland)
Fanny Stauffer, Fien De Leersnyder, Thomas De Beer (University Gent)
Jerome Mantanus, Pierre-Francois Chavez, Benjamin Thoorens, Patrizia Ghiotti, Martin Schubert (UCB)
Pirjo Tajarobi, Gunnar Haeffler, Satu Lakio, Magnus Fransson, Anders Sparén, Susanna Abrahmsén-Alami, Staffan Folestad (AstraZeneca)
Adrian Funke (Bayer AG)
Ivo Backx, Barbara Kavsek, Francois Kjell (Siemens)
Marc Michaelis (Hüttlin GmbH)
Trevor Page, John Palmer, Alexander Schaepman (GEA Process Engineering Ltd.)
Sonja Sekulic, Steve Hammond (Pfizer Inc.)
Birgit Braun, Brenda Colegrove (The Dow Chemical Company),

Abstract:
Pharmaceutical solid oral dosage product manufacturing is a well-established, yet revolutionizing area. To this end, process analytical technology (PAT) involves interdisciplinary and multivariate (chemical, physical, microbiological and mathematical) methods for material (e.g. materials, intermediates, products) and process (e.g. temperature, pressure, throughput, etc.) analysis. This supports rational process modelling and enhanced control strategies for improved product quality and process efficiency. Therefore, it is often difficult to orient and find the relevant, integrated aspects of the current state-of-the-art. Especially, the link between fundamental research, in terms of sensor and control system development, to the application both in laboratory and manufacturing scale, is difficult to comprehend. This review compiles a non-exhaustive overview on current approaches from the recognized academia and industrial practices of PAT, including screening, selection and final implementations in solid oral dosage manufacturing, through a wide diversity of use cases. Finally, the authors attempt to extract a common consensus towards developing PAT application guidance for different unit operations of drug product manufacturing.