brought to you by I CORE





A retrofit strategy to achieve "Fast, Flexible, Future (F3)" pharmaceutical production processes

Singh, Ravendra; Rozada-Sanchez, Raquel; Wrate, Tim; Muller, Frans; Gernaey, Krist V.; Gani, Rafiqul; Woodley, John

Publication date: 2011

Document Version Publisher's PDF, also known as Version of record

Link back to DTU Orbit

Citation (APA):

Singh, R., Rozada-Sanchez, R., Wrate, T., Muller, F., Gernaey, K., Gani, R., & Woodley, J. (2011). A retrofit strategy to achieve "Fast, Flexible, Future (F3)" pharmaceutical production processes. Poster session presented at 21st European Symposium on Computer Aided Process Engineering, Chalkidiki, Greece.

DTU Library

Technical Information Center of Denmark

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.



A retrofit strategy to achieve "Fast, Flexible, Future (F³)" pharmaceutical production processes



Ravendra Singh,^a Raquel Rozada-Sanchez,^b Tim Wrate,^b Frans Muller,^b Krist V. Gernaey,^a Rafigul Gani,^a John M. Woodley^a

 a Department of Chemical and Biochemical Engineering, Technical University of Denmark, DK-2800 Lyngby, Denmark ^bAstraZeneca Limited, Charter Way, Silk Road Business Park, Macclesfield, Cheshire SK10 2NA, UK



Introduction: A "Substrates Adoption Methodology (SAM)" and a generic nitro reduction process-plant template for a series of substrates with similar molecular functionality has been developed. The main idea is to combine the flexibility of batch processes with the efficiency of continuous processes.

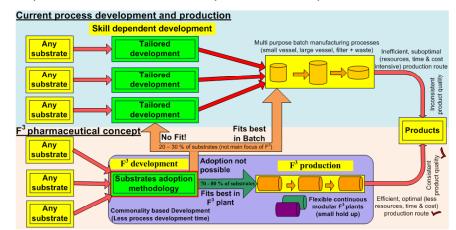
SAM identifies changes to a process-plant template:

- Reagents (e.g. reducing agent, solvent, catalyst)
- Process equipment configuration
- Process operational conditions (e.g. T, P, F)

Char.: Characteristics

feasible output Experiments are needed

Does considered step of the SAM gives



Substrates Adoption Methodology (SAM)

Input for SAM 1. Hazard assessment Reagent identification 2. Inital solubility screen 3. Reactivity & selectivity assessment F³ process v condition: Generate desired Yes process operational scenario 4.2. Generate process (nowledge base (unit operations charact.) flowsheet Yes F experiments, mathematical models R: Reactant, P: Product Feasibility analys Modify Re: Reducing agent Around 20% substrates S: Solvent C: Catalyst SAM: Substrates Adoption Methodology Proposed adapt from SAM may not be feasible to

Validation (exp.)

Accepted ▼
Final adaptation

Nitro reduction case study

Amines are used in many pharmaceutical products and therefore make a good target for a generic process.

Problem definition: Adapt a generic nitro reduction process-plant template for the adoption of 2-Nitro-4'-chlorodiphenylamine

Generic case: Catalyst Reducing R-NO, R-NH₂ + By-product Solvent agent Specific case: Catalyst Reducing Solvent ΝO, Ĥ ŃΗ.Ĥ

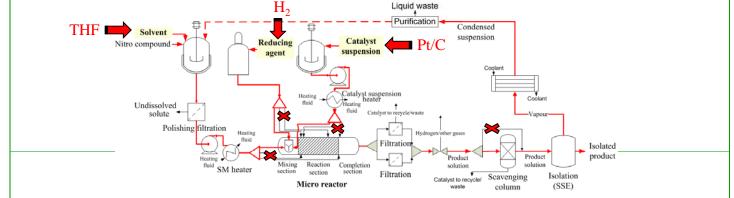
Generic nitro reduction process-plant template: Proposed adaptation (one alternative)

Experimental

verifications

Not accepted

produce in F3 way



Conclusions: A generic nitro reduction Process-Plant template and Substrates Adoption Methodology (SAM) including the supporting tools (knowledge base, model library, graphical tool (operational window), solubility prediction and solvent selection tool) has been developed to achieve a flexible and fast production process.

Acknowledgement: This work is funded by European Community's 7th Framework Program under grant agreement n° 228867, F³ Factory.

ESCAPE21