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

A retrofit strategy to achieve "Fast, Flexible, Future (F^3)" pharmaceutical production processes

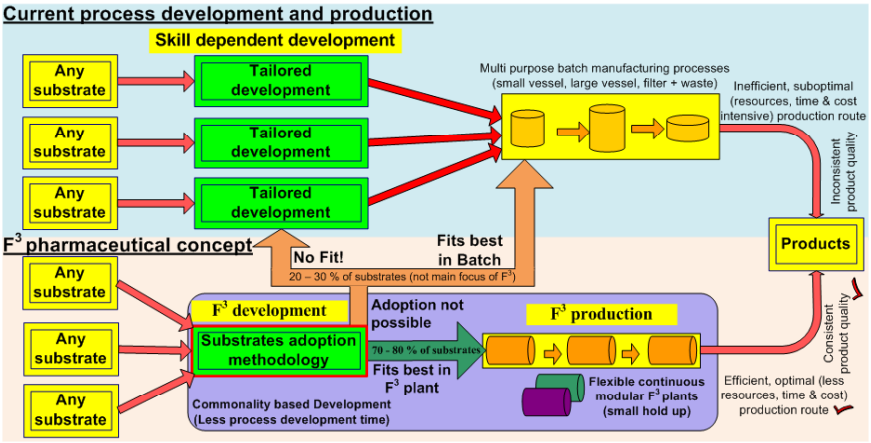
Ravendra Singh,[a] Raquel Rozada-Sanchez,[b] Tim Wrate,[b] Frans Muller,[b] Krist V. Gernaey,[a] Rafiqul Gani,[a] John M. Woodley[a]

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

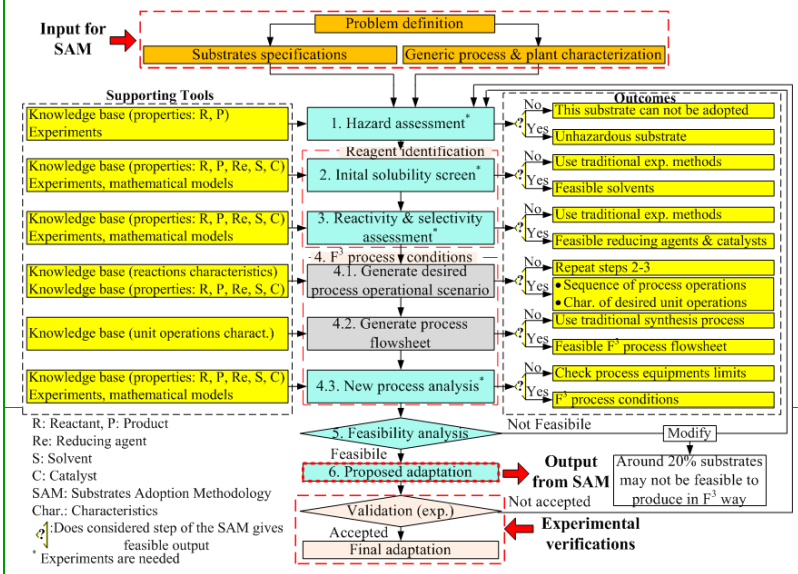
Introduction: A "Substrates Adoption Methodology (SAM)" and a generic nitro reduction process-plant template for a series of substrates with similar molecular functionality has been developed. The main idea is to combine the flexibility of batch processes with the efficiency of continuous processes.

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)



Substrates Adoption Methodology (SAM)



Nitro reduction case study

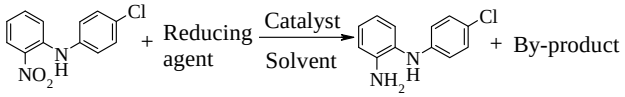
Amines are used in many pharmaceutical products and therefore make a good target for a generic process.

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

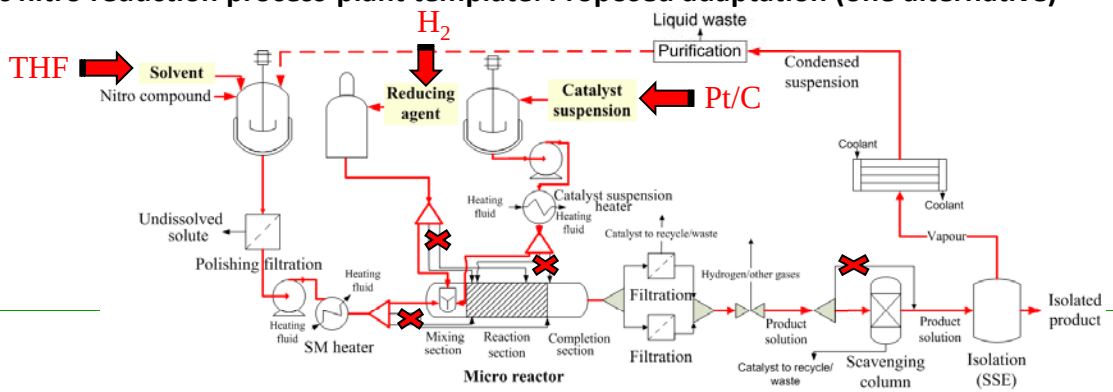
Generic case:

$$R\text{-}NO_2 + \text{Reducing agent} \xrightarrow[\text{Solvent}]{\text{Catalyst}} R\text{-}NH_2 + \text{By-product}$$

Specific case:



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



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, F^3 Factory.