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):
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 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)**

**Input for SAM**

- Knowledge base properties: R, P, C, X, E, experiments, mathematical models
- Knowledge base properties: R, P, C, X, E, experiments, mathematical models
- Knowledge base properties: R, P, C, X, E, experiments, mathematical models
- Knowledge base properties: R, P, C, X, E, experiments, mathematical models
- R, Standard, P, Product
- R, Reducing agent
- C, Catalyst
- S, Solvent
- C, Catalyst

**Output**

- Not accepted
- Accepted Final adaptation
- Evolutes
- Substrate conditions
- Process conditions and characteristics

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

**Generic case:**

R-NO₂ + Reducing agent → Catalyst → Solvent → R-NH₂ + By-product

**Specific case:**

R-NO₂ + Reducing agent → Catalyst → Solvent → R-NH₂ + By-product

**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.