

Sustainable Pharmaceutical Process R&D Enabled by Continuous Manufacturing

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Continuous Manufacturing is the result of industrializing flow chemistry, and the focus of this presentation will be the application to synthesizing medicines.¹ The fundamental principles of how continuous processes can impact a chemical reaction are outlined, and the connection to green chemistry is given, relying on metrics such as Process Mass Intensity (PMI) and Total Carbon-dioxide Release (TCR).²

The key learnings from three case-studies in the areas of hydrosilylative reduction and organometallic chemistries will be highlighted,³⁻⁵ taking the listener from the lab discoveries to the final processes and equipment rigs used for manufacturing on kilogram scale. Decision making as to when to use flow equipment, and when to use batch, as well as strengths and weaknesses of the new processes will be shared.

The aim is to showcase continuous manufacturing as a mature enabling technology which has green credentials, and can be relied upon to support the synthesis of complex pharmaceutical building blocks.



References

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- [3] A Multistep Flow Process for the Synthesis of Highly Functionalized Benzoxazoles, *Org. Lett.*, 21 (15), **2013**, 5546
- [4] Match-making reactors to chemistry: a continuous manufacturing-enabled sequence to a key benzoxazole pharmaceutical intermediate, *Org. Process Res. Dev.*, **2017**, 21, 1779
- [5] Application of transition-metal catalysis, biocatalysis, and flow chemistry as state-of-the-art technologies in the synthesis of LCZ696, *J. Org. Chem.* **2020**, 85, 6844