## From flow chemistry to continuous processing: shifting the mindset in drug synthesis

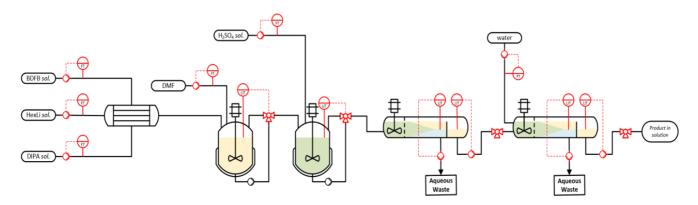
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The adoption of continuous processing in the pharmaceutical industry represents a paradigm shift from traditional batch processing methods to a more efficient and controlled approach, particularly for the manufacturing of synthetic molecules. Continuous processing leverages a seamless and uninterrupted production flow, which significantly enhances the speed, consistency, quality, and environmental sustainability of drug synthesis. Using advanced automation with real time process parameter controls and process analytical technology also enables stringent control of reaction conditions, ensuring consistent product quality and minimizing variability.

In this context, flow chemistry addresses several challenges associated with organometallic compounds, particularly their handling and stability. The continuous flow environment minimizes the exposure of sensitive intermediates to undesired conditions, thereby reducing the risk of degradation or unwanted side reactions. Continuous flow techniques thus offer a versatile platform for conducting organometallic reactions on large scale.



As the pharmaceutical industry incrementally transitions towards more complex synthetic challenges, continuous processing is poised to become a fundamental component of the drug development and production landscapes. This paradigm shift will be fueled by concurrent advancements in technology, refinements of regulatory support, and the growing need for more efficient and adaptable production methods.

Seeberger, Gillmore et al. Chem. Soc. Rev., **2020**, 49, 8910–8932

Noël et al. Chem. Sci. 2023, 14, 4230-4247

Kappe et al. Chemistry–Methods **2021**, 1, 454–467

Kelly et al. Org. Process Res. Dev. 2024, 28, 1546-1555

Kaldre, Sedelmeier et al. Org. Process Res. Dev. 2024, 28, 1576-1586

ICH guideline Q13 on continuous manufacturing of drug substances and drug products