Special Feature Section: Engineering Contributions to Chemical Process Development

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Editorial

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Upon initial consideration, the idea of a special *Organic Process Research & Development* (OPRD) feature devoted to "Engineering Contributions to Chemical Process Development" may seem unnecessary. After all, chemical engineering principles are deeply embedded in the strategy of process development, especially as it relates to the consistent, safe, and robust scale-up of processes for the manufacturing scale. However, there are specific examples where the application of chemical engineering principles leads to new or improved capabilities for the development of organic processes. This special feature section highlights such aspects of chemical process development.

Reaction kinetics analysis can provide insight into the controlling mechanisms of reactions and thus enable successful reaction scale-up even for complex heterogeneous systems. Crump et al. illustrate this through their first-principles analysis of the kinetics of a metal-catalyzed nitro reduction where they determined the relative importance of hydrogen gas−liquid mass transfer, liquid-phase diffusion, and surface reaction as a function of hydrogen pressure.

The recent development of metal-free hydrogenation catalysts, particularly for imine reduction, is a significant advance, but the commercial implementation of these catalysts has been hampered by their sensitivity to catalyst poisoning. Thompson and his associates demonstrate how the use of inexpensive scavengers can lead to robust reactions and significantly improve the industrial feasibility of these catalysts.

Scale-up and design-space mapping of batch reactive distillation are approached by Figueroa et al. through first-principles modeling and experimentation by considering both scale-dependent and scale-independent factors for reaction kinetics and chemical equilibrium, VLE, LLE, and heat transfer. This technique enabled on-scale prediction and design-space mapping, providing acceptable ranges of the parameters for on-scale operation.

Active pharmaceutical ingredients (APIs) are often isolated as crystalline or amorphous solids. Processing steps include solids formation steps (crystallization and precipitations), slurry filtrations, agitated drying, wet and dry milling operations, delumping, and blending. Engineering approaches are frequently needed to ensure not only that the desired physical and chemical properties are obtained but also that the purification and isolation steps are completed safely. Several articles in this special feature section describe advances in these processing areas.

Computational fluid dynamics (CFD) is shown to be useful in the development and scale-up of a crystallization of a thermally unstable API in a helical coil heat exchanger (Vashistha et al.). CFD analysis afforded greater process understanding and a rapidly optimizable process evaluation resulting in a more robust, finalized process successfully meeting the targeted yield and quality on scale.

The article by Ivan Lee describes the use of antistatic additives during the crystallization of pharmaceutical compounds. Minimal impact on physical and chemical properties of the isolated particles was demonstrated, and the use of only low (ppm) levels of a pharmaceutically acceptable additive should minimize regulatory hurdles.

Zhou et al. present the application of a highly integrated and automated experimental platform for developing crystallization processes with targeted powder properties. This platform enabled the authors to calibrate FTIR and FBRM in an automated fashion. The authors successfully demonstrated the use of this platform in various modes of crystallization including cooling, antisolvent addition, and fed-batch crystallizations.

The article by Allison Harter et al. describes a new high-shear rotor−stator mill for achievement of sizes smaller than previously possible with this type of technology. They also propose a new Slot Event model for scaling performance from the laboratory to the pilot plant and beyond.

Finally there are two excellent articles by David am Ende et al. and Ivan Marziano et al. which describe small-scale laboratory methods for assessing particle breakage and granulation behavior during drying of APIs in agitated filter dryers. A ranking system relative to the risk for particle breakage and granulation is proposed, and recommendations to minimize scale-up risks and improve dryer productivity are provided.

In summary, these papers describe a wide variety of engineering techniques to enable efficient process development. We hope that OPRD readers find these papers interesting and are inspired to apply some of these engineering approaches to their process development work.

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