Poster Presentations

[MS24-P32] Layered solid forms and crystalline defects in multi-component continuous crystallisation.

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Crystallisation is a vital step in the manufacture of many pharmaceuticals and fine chemicals, producing solids in a form ideal for manufacturing processes. Unlike others, these industries have not kept pace with advances in continuous production and for centuries industrial crystallisation has operated as a batch process relying heavily on stirred tank reactors which bring batch to batch variations and limited control over particle attributes. Continuous crystallisation can offer improved product quality, less waste and access to new products more efficiently.

The continuous oscillatory baffled crystalliser (COBC) [1] is a jacketed tubular crystalliser containing equally spaced baffled cells. The material is added as a hot solution and crystallisation is facilitated by cooling through a temperature gradient as the suspension is pushed through the system by motor driven bellows. The crystalliser offers the benefit of uniform mixing through the generation of eddies in each cell from the oscillatory flow and therefore improved product quality. There is also potential for real-time monitoring of the crystallisation, via ports that allow for in-line measurements using process analytical technology.

Disordered molecular materials (at the extreme, amorphous) can bring enhanced properties, such as solubility and compressibility [2], but have not been widely exploited to date as they can be difficult to control and characterise as solid forms. Multi-component crystallisation can encourage orientational disorder and layering within the crystal lattice by choice of the appropriate co-former and by utilising the principles of crystal engineering. In this work small scale evaporative multi-component crystallisations have been carried out in order to screen the conditions under which disorder appears, towards the future goal of developing controllable multi-component molecular systems that are accessible in a continuous crystallisation environment. Examples will be presented in which layered and disordered molecular materials have been produced from multi-component crystallisations, initially targeting APIs (Active Pharmaceutical Ingredients) including the anti-inflammatory piroxicam.

Accelerating the adoption of continuous manufacturing processes is the vision of the EPSRC Centre for Innovative Manufacturing in Continuous Manufacturing and Crystallisation [3]. The work presented is carried out in the context of the newly established Doctoral Training Centre, which aims to deliver a multi-institutional, multi-disciplinary training and research programme spanning the breadth of the Centre's research scope from a range of academic and industrial perspectives.

[1] Caldeira, R. L. F.; Ni, X. Org. Process Res. Dev. (2009), 13, 1080–1087; Lawton, S., Steele, G., Schering, P., Zhao, L., Laird, I., Ni, X. (2009). *Org. Process Res. Dev.* 13, 6, 1357-1363.
[2] Saleki-Gerhardt, A., Ahlneck, C., Zografi, G. Int. J. Pharm. (1994), 101, 237-247
[3] www.cmac.ac.uk

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