

Poster Presentations

[MS39-P05] **Towards Multi-component Crystallisation in a Continuous Flow Environment.** Kate Wittering^{1, 2}, Chick C. Wilson² Ali N. Saleemi^{1, 3}.

¹CMAC, EPSRC Centre for Continuous Manufacturing and Crystallisation;

²Department of Chemistry, University of Bath, Bath BA2 7AY, UK;

³Department of Chemical Engineering, Loughborough University, Loughborough LE11 3TU, UK.

E-mail: k.wittering@bath.ac.uk

As a valuable tool in materials development, crystal engineering and more specifically co-crystallisation have facilitated the production of new materials which retain their original function but with enhanced physical properties. As an example, the important function may be the bioavailability of an active pharmaceutical ingredient (API), while the target physical property might be improved solubility or optimised morphology [1]. It is possible to tune these desired physical or physicochemical properties through systematic alteration of crystallisation conditions and the co-formers used. It has also been shown that such techniques present a route to crystal form (polymorphism) control in single component systems through crystallisation in a multi- component environment.

In addition to new materials discovery for property optimisation, multi-component crystallisation also offers a means of modifying and improving processes for the bulk production of desired materials. To date, much of the work in this area has focused around the use of batch or static crystallisation methods. As part of a collaborative effort in Continuous Manufacturing and Crystallisation, (CMAC, an EPSRC Centre for Innovative Manufacturing), our research is focused on translating both new and previously identified multi-component systems into a continuous flow crystallisation environment. The continuous flow environment in this investigation is predominantly

achieved using a continuous oscillatory baffled crystalliser (COBC) [2]. This brings about the challenge of producing multi-component systems via cooling crystallisation instead of using tried and tested small scale evaporative crystallisation techniques. The move to continuous crystallisation aims to address scale up issues previously encountered when using the more common stirred tank batch reactor; increase productivity via higher throughput and promote increased manufacturing flexibility and product quality [3].

The work to be presented explores crystallisation of new multi-component molecular complexes with enhanced properties, as well as optimising the non- evaporative crystallisation conditions for production of established multi-component molecular materials, including complexes of barbituric acid and urea [4], which were previously obtained via evaporative crystallisation. We will describe how these complexes can successfully be obtained by cooling crystallisation, detail attempts to ascertain the crystallisation conditions required to isolate a specific complex via cooling crystallisation and give an account of progress towards the overarching aim of transferring these systems into the continuous crystallisation environment.

[1] Vishweshwar, P., McMahon, J. A., Bis, J. A., Zaworotko, M. J. (2006). *J. Pharm. Sci.* 95, 3, 499-516. [2] Lawton, S., Steele, G., Schering, P., Zhao, L., Laird, I., Ni, X. (2009).

Org. Process Res. Dev. 13, 6, 1357-1363. [3] Quon, J. L., Zhang, H., Alvarez, A., Evans, J., Myerson, A. S., Trout, B. L. (2012). *Cryst. Growth Des.* 12, 6, 3036-3044.

[4] Gryl, M., Krawczuk, A., Stadnicka, K. (2008). *Acta Cryst.* B64, 623-632.

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