**Poster Presentation**

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*Redefining Solution-Mediated Transformations: Pharmaceutical Systems*

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Engineering the isolation of a metastable or stable crystalline phase of an active pharmaceutical ingredient (API) is of critical importance when crystallizing from solution as an uncontrolled outcome can directly affect API manufacture and performance. The theoretical framework for understanding solution-mediated crystal phase or polymorphic transformation (SMPT) was first established by Cardew & Davey.[1] The process is defined to consist of a metastable phase that dissolves and a stable phase that nucleates and grows independently from the solution. That paper also identified that in terms of a reaction pathway, SMPT could be controlled in either of two ways: by growth of the stable phase or dissolution the metastable phase. Studies concerning SMPT since then have brought the definition and those conclusions into question. Firstly, the recent case of the SMPT from FI to FIII carbamazepine and FII to FIII piractem were studied separately where data on both the solid state composition and solution concentration were collected during the transformation using powder X-ray diffraction and in situ infra-red spectroscopy, respectively. These studies, in combination with a brief review of the literature, reveal that SMPT can be controlled not only in the two ways described by Cardew & Davey but rather in 4 principal ways (Figure 1).[2] Secondly, many studies now identify that nucleation of the stable phase often occurs on the surface of the metastable phase during SMPT [3] and not independently from solution. Again when the literature is examined, this surface supported nucleation event is identified as being either epitaxial in nature or having no or inconclusive evidence of epitaxy. It is concluded that the term "independently" in the definition by Cardew & Davey be redefined to recognize that the crystallization of the stable phase during SMPT is often dependent on the surface of the metastable phase in solution.

***[1]*** *[1] P. T. Cardew, R. J. Davey, Proc. Royal. Soc. A 1985, 398, 415.,* ***[2]*** *[2] M. O'Mahony, A. Maher, D. M. Croker et al. Cryst. Growth & Des. 2012, 12, 1925.,* ***[3]*** *[3] D. Croker, B. K. Hodnett, Cryst. Growth & Des. 2010, 10, 2806.*

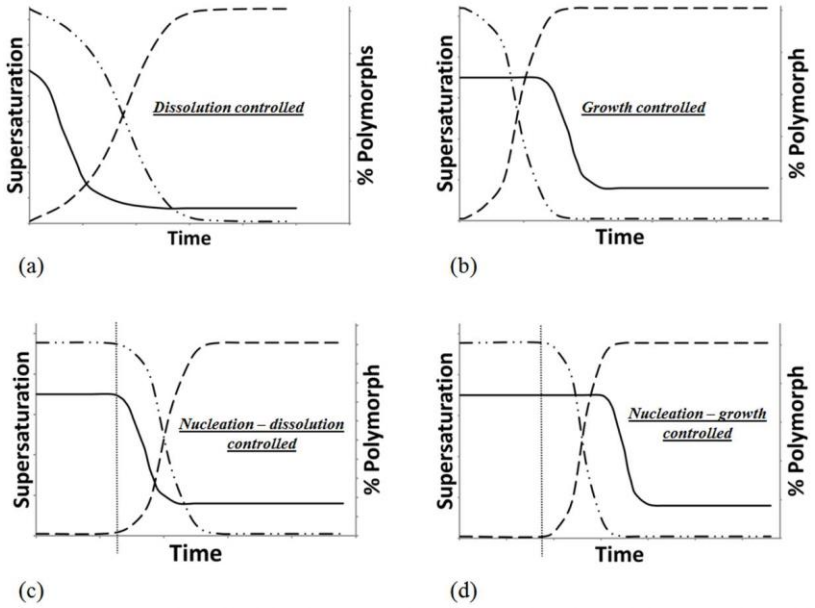


**Figure 1. Representations of principal scenarios for solution mediated crystal phase or polymorphic transformations assessed from a review of the literature with supersaturation (solution concentration) profiles and solid state compositional data. – Supersaturation profile, - - - stable phase composition and –•• metastable phase composition. Vertical line indicates limit of the induction time for nucleation of the stable phase.**

**Keywords:** phase transformation, polymorphs