INSTITUTE OF PARTICLE SCIENCE & ENGINEERING

hool of Process Environmental & Materials Engineering

Engineering Building

University of Leeds

IPSE Staff Seminar

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4:00pm, 9th February 2012

NUCLEATION, GROWTH & HABIT MODIFICATION OF *N*-PHOSPHONOMETHYL GLYCINE (PMG) IN THE ABSENCE AND PRESENCE OF CRYSTAL GROWTH MODIFIER (CGM)

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Crystallisation is a separation technique for products that exist as solids at room temperature, and is the most important means of purifying high value chemical products and then delivering them into forms that can be efficiently formulated. Crystallisation from solution phase provides a direct route to designing and controlling the solid form properties of product crystals (Figure 1). It is known that many organic molecules can adopt more than one solid crystalline form, as polymorphs (only differ in the arrangement of the molecules) and/or solvates. In particular, pharmaceutical and agrochemical companies spend much effort in investigating how many different forms a crystalline product can adopt, and to develop detailed understanding of process variability that can leads to undesired formation of other crystal forms. If a new polymorphic crystalline form appears unexpectedly during production or storage, this can have a profound impact on the product performance.

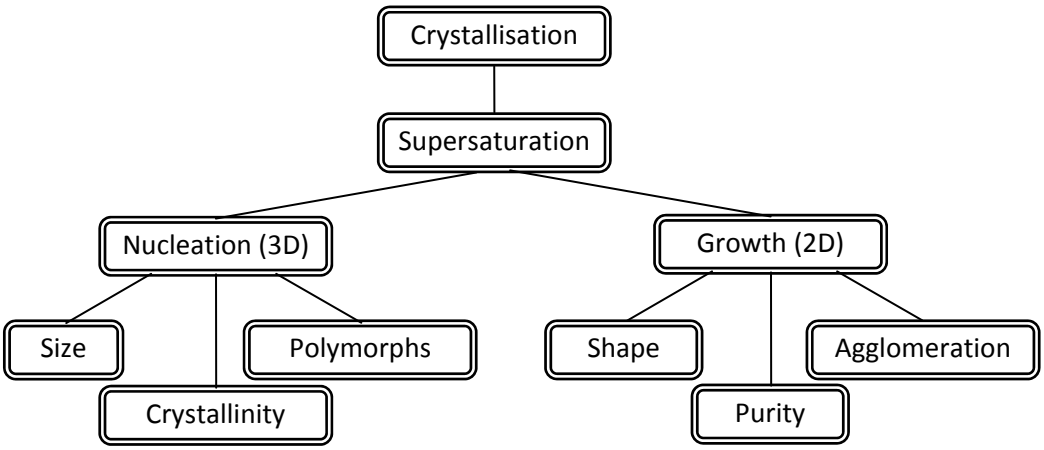

Figure 1: ***A route map showing designing and controlling of the solid product crystals.***

Crystallisation processes need to deliver the product into a solid form (morphology, size, surface) that is suitable for separation, drying, powder handling, milling and formulation. Crystal Growth Modifiers (CGMs) are molecular analogues of the active ingredient generated in synthesis or additives incorporated into the formulation that strongly influence the crystal formation process. Synthetic impurities (in-process CGMs) can often influence process throughput, yield and robustness of formulations, and requires methods for their removal or moderating their effect. On the other hand, controlling molecular assembly with CGMs as formulation additives (i.e. pre-designed CGMs) can enhance product performance and reduce development time since CGMs can affect particle size and shape by effecting nucleation and crystal growth rate respectively, thus help to produce the desired physical properties of the particles in question.

N-Phosphonomethyl glycine (PMG) is an agrochemical compound whose crystallisation is affected by the presence of iminodimethyl phosphonic acid (IMPA) which acts as a CGM mediating the nucleation and growth rate. This work will demonstrate the effects of IMPA on PMG nucleation and growth rates using high-throughput methodology with morphological characterisation carried out using both conventional optical and digital video microscopy. Furthermore, crystal imaging methodology developed at Leeds University will be coupled with the commercial high throughput screening equipment. This will allow rapid discovery of potent CGMs including early quantification of their impact on process and product performance by chemical companies.