Is Crystallization a Black Box?

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Crystallization is an essential operation in pharmaceutical industry, because the majority of active pharmaceutical ingredients are produced in solid form. The operating conditions of the crystallization process determine the physical properties of the solid product, such as crystal purity, shape, size distribution, surface and bulk. Active substances may crystallize well or badly, quickly or slowly. Many monographs and journal articles tackle the question of whether crystallization can be controlled and the properties of the final material predicted. The disadvantage of these studies is that they tend to focus on one aspect of the properties, whether it is the purity of the final material, the final particle size distribution, polymorphic purity, or surface properties. This paper has two goals. The first is to facilitate the understanding of the fundamental properties of crystallization and the impact of these properties on crystallization process development (especially with emphasis on nucleation step, which is the process of phase transformation and the resulting creation of crystalline materials from liquid-phase precursors).
The second is to show the progress that has been made in controlling the crystallization process and the facilities and methods by which it is possible to prepare "a good crystalline material". Great advances have been made in the systems which are able to detect the nucleation event and dynamically monitor the crystal size, shape and crystal size distribution in the course of the crystallization processes without sampling for external analysis, e.g. the FBRM probe, the EasyViewer probe or the Blaze system.
And last but not least, we intended to demonstrate how the view of API crystallization has changed over the last twenty years in the non-academic sphere.