SPECIAL FEATURE SECTION: POLYMORPHISM & CRYSTALLIZATION

Editorial

This is the third special issue on the subject of Polymorphism and Crystallisation, the last one appearing in Nov/Dec 2003. Since that time there have been new developments, particularly in the area of process analytical technology. Also there has been an increasing interest in what happens after crystallisation during the filtration and drying processes, and how this affects the particle size distribution and the physical properties of the active pharmaceutical ingredient (API). In many cases this affects the drug product too. A few of the papers in this issue reflect these developments.

I have an advantage over many scientists in that I visit, either through in-house training courses or consultancy, a large number of companies, from small, virtual or emerging biotech/pharmaceutical companies, who subcontract most of their API manufacture, to large pharmaceutical companies, most of whom carry out the last steps of API manufacture in-house. My perception is that almost 100% of APIs coming through development in the last couple of years are polymorphic or form solvates (some with as many as 20 forms) and that this can be a nightmare if a full understanding of the interrelationships is not acquired. Understanding then leads to control in production. The earlier the knowledge is acquired, the better; I find that companies are carrying out polymorph and salt-form screening at earlier and earlier stages in the development of the API.

A potential problem with this is that impurities are present in early batches at levels unlikely in later batches after full process optimisation has been carried out. Since even 0.1% of an impurity can be sufficient to inhibit the crystallisation of the most stable polymorph, then it follows that using an impure batch of API for polymorph/solvate/salt-form screening may not give all the desired forms. A purer grade of API might be needed to guarantee that the most stable form is obtained.

Perhaps guarantee is the wrong word—there are no guarantees when it comes to polymorphism. Therein lies the frustration of the topic and, to some extent, the fascination. I hope you are fascinated by this special issue and that we will be able to have more special issues on this topic.

My thanks go to all authors who submitted papers for this issue, and to the reviewers for their comments which always improve the quality of papers.

Trevor Laird

Editor

OP050196T

10.1021/op050196t CCC: $30.25
Published on Web 10/26/2005