SL01 Crystal & Particle Engineering Strategies to Enable Efficient Direct Compression Tablet Development of Pharmaceuticals

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Direct compression (DC) is preferred over granulation processes for tablet manufacturing because of its significant advantages in economy. The DC process is particularly preferred for continuous tablet manufacturing. However, the development of DC tablet products is often challenged with several problems, including unsatisfactory content uniformity for low dose active pharmaceutical ingredients (API); poor tabletability and flowability for medium to high dose APIs. For this reason, DC has been only passively applied to only a small percentage of APIs within a narrow range of API loading where the aforementioned problems are not severe.

A proactive and efficient development approach is that guided by the material science tetrahedron, where API deficient properties can be engineered out through appropriate particle and crystal engineering on the basis of structural understanding of the properties. Several crystal and particle engineering strategies have been recently developed to overcome deficient properties of APIs. Appropriate implementation of these strategies would facilitate the design of high-quality robust drug products, as stipulated by the Quality-by-Design framework.

In this lecture, we will first discuss some effective crystal and particle engineering strategies to overcome problems in tastes, content uniformity, compression, and flow. These include nano-particle coating, surface polymer coating, forming a composite with porous carrier, cocrystallization, and spherical crystallization. The focus is on the underlying materials science, which is the foundation for effective API engineering to improve pharmaceutical properties. Then, we will demonstrate the applications of these strategies to enabling successful DC tablet development for problematic drugs at both very low and very high doses. For examples, a DC formulation platform based on the API-carrier composite strategy can overcome the problem of poor content uniformity; the integrated crystal and particle engineering enabled the expedited development of DC tablets; the spherical crystallization enables the development of very high API loading by effectively improving API flow and compression properties. In a recent example, we have demonstrated a record high 99% API loading in a DC tablet formulation.