Multi-scale Modeling of Spray Drying

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Developing pharmaceutical product formulations in a timely manner and ensuring quality is a complex process which requires a systematic, science based approach and combination of information at multiple spatial and temporal scales. Advances in quantitative analysis techniques (e.g. mechanistic models) in combination with modern measurement tools enable engineers to design and scale-up pharmaceutical unit operations and processes with more confidence and reliability.

Spray drying is becoming an important unit operation in pharmaceutical industry to produce solid amorphous dispersions which are frequently used to improve the solubility and thus the bioavailability of poorly soluble active pharmaceutical ingredients.

Goal of the presentation is to share our experience how to develop, calibrate and combine mathematical models of spray drying at different levels/scales. This is accomplished through combination and solution of governing balance equations and using empirical data defining boundary conditions and input/output properties at following levels/scales of drying:

Scale 1: Single droplet. A detailed distributed parameter model was developed for simulation of a single droplet drying. The model describes heat and mass transfer inside the droplet/particle, shrinking of the particle, the skin formation followed by skin thickening, crust formation and the final drying of non-shrinking particle. The model also calculates exchange of heat and mass between the particle and external drying gas and the decreasing particle density needed for the momentum balance at scale 2. This model was calibrated against single droplet drying experimental results.

Scale 2: Spray dryer. A detailed Computational Fluid Dynamics (CFD-DPM) model was developed for simulation of drying of multiple droplets (sprays) using a mixed Eulerian/Lagrangian approach. Iterative coupling is employed to account for exchange of momentum, heat and mass between the particles and continuous phase. The single droplet model (Scale 1) is combined with the CFD code (Scale 2) in the form of a Fluent User Defined Function. The model (after calibration) also predicts the outlet gas composition needed for the dryer mass balance specification at scale 3.

Scale 3: Spray drying process. The Aspen Plus software was employed for development of a process model containing the different unit operations of the spray drying process. The key unit operations of the process (in addition to the stream dividers, mixers, etc.) are the simplified spray dryer, heater and condenser used for the recycle stream purification. Detailed simulations of the CFD model (Scale 2) are used for improvement of the Aspen Dryer model (Scale 3) predictability and the Aspen model is used for calculation of the solvent content in the recycle stream and mixing with the fresh drying gas before entering the spray dryer.