1. Purpose

Spray drying is nowadays a well established technology in the pharmaceutical industry. In such a competitive and fast-paced area, the need for robust and lean process development methodologies is critical in order to minimize the consumption of resources, namely time and materials. Moreover, the product quantities required in the early stages of the development are usually small but may quickly increase by several orders of magnitude as the drug candidate advances through the clinical phases and reaches the market. CMC development is therefore increasingly critical on the path of drug development, especially for drug candidates with compressed clinical development timelines.

The current work describes a systematic methodology for the development of spray drying processes with minimal expenditure of drug substance. Laboratory tests are used to build scale-independent correlations that are used to support the scale-up to larger units, while the costly experiments such as process intensification and process design space definition are deferred to latter stages of the process development. Concurrently, modelling tools are used to estimate the spray drying conditions required to target specific powder properties.

2. Methodology

- Systematic methodology for scale-up based on scale independent correlations
- Main goal is to reduce the experimental burden of multiple scale-up stages by focusing the resources when really needed – later in the development process

3. Process Development Toolbox

1 - Thermodynamic Modelling
- Mass and energy balance and L-V equilibrium equations
- Accurate knowledge of the thermodynamic space and spray drying conditions estimation
- Anticipation of spray drying conditions impact on ASD stability: e.g. RS, out = SDD T

2 - Atomization Modelling
- Droplet size is the main factor affecting particle size and it can be tuned for attaining a specific particle size
- Droplet size = f (nozzle, feed pressure / atomization ratio, solution properties)

3 - Drying Kinetics
- Droplet and particle size are intrinsically connected, however particles can follow different formation pathways depending on the drying kinetics and product properties
- Drying kinetics can be controlled by the temperature, relative saturation and flow rates

4 - CFD Modelling
- Models developed for all spray dryers scales provide detailed flow and temperature profiles
- Used to support scale-up and for troubleshooting

5. Conclusions

An effective knowledge management and a strong scientific understanding of the spray drying process (thermodynamics, atomization, CFD and drying kinetics) make process scale-up across different production scales a straightforward task. A methodology based on such modelling tools and on laboratory data is nowadays used at Hovione to manage process development in a timely and cost effective manner. The advantages are a leaner process development with minimal resources use.