Case Study: Formulation, Optimization & SD Scale Up

Background

A leading global non-profit research institute engaged CritiTech to solve formulation issues related to their novel inhaled treatment for tuberculosis. Their initial formulation utilized spray drying (SD) but had significant issues with bulk density and the inability to scale up. The issues led to inadequate capsule fill weight and suboptimal aerodynamic performance.

The client transferred their existing SD process to CritiTech on a Buchi B290. Initial runs successfully achieved targeted density . Following completion of confirmation batches, we immediately began scale-up on our SD30 spray dryer. Scale-up was quickly achieved with the necessary increase in bulk density while maintaining other specifications in the target product profile (TPP). GMP material was produced for preclinical trials including two GLP animal tox trials. While awaiting clinical results, the client engaged CritiTech on additional spray drying and other formulation projects and opportunities.

GOALS

- **Optimize dry powder formulation to achieve capsule fill weight and aerosolization performance specifications**
- **Scale up manufacturing to support clinical trials**

Challenges

- Initial formulation density required potentially detrimental compacting and prevented appropriate capsule loading for the necessary dosage
- Original formulation had not been scaled beyond laboratory
- Inadequate aerodynamic particle attributes to achieve desired aerosolization performance

Approach

- Developed and executed experiment design once initial POC conditions were replicated on the B290
- Using experimental data from improvements made during scale up, performed modeling on JMP software to forecast production results and hone in on achieving the TPP

Results

Optimized formulation to achieve TPP

- Over 50% increase in bulk density (see Figure 1)
- Decreased moisture by 45% (See Figure 2)
- Increased capsule fill weight by over 20%

Delivered clinical supplies with TPP at scale

- Reduced SD processing time by over 50% with changes to feed flow rate and feed solution concentration
- Achieved aerodynamic particle target product profile at scale
- Produced multiple GMP batches for client GLP studies

Figure 1: Bulk Density & Capsule Fill Weight

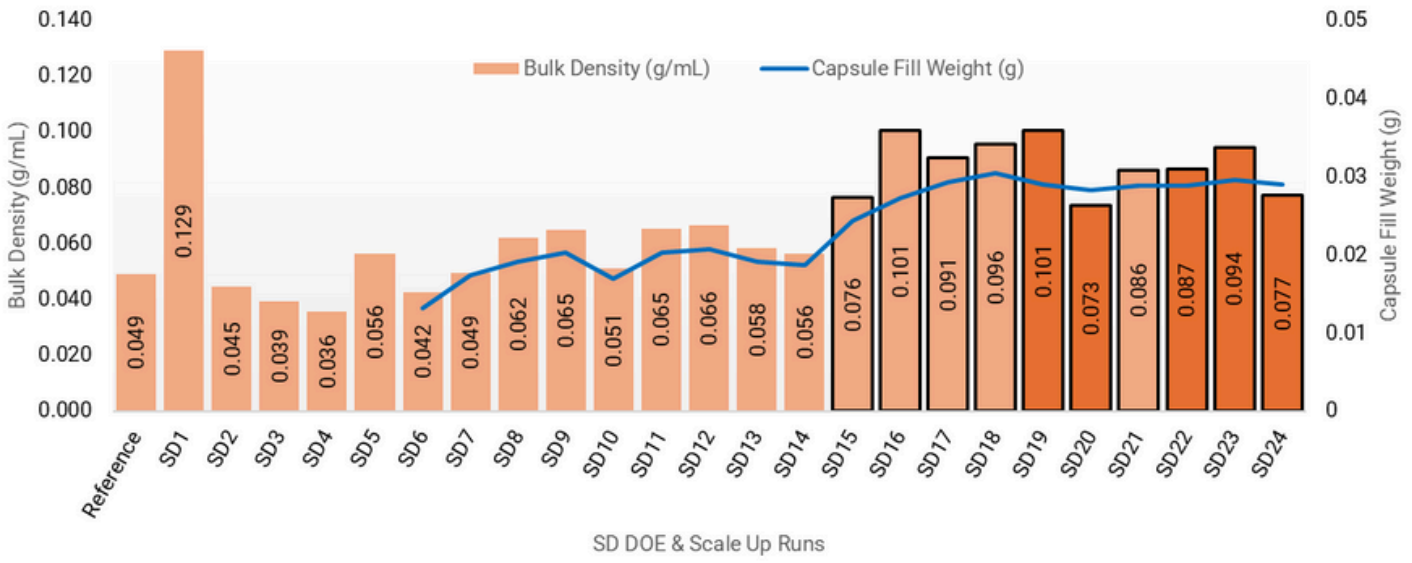

Figure 1 represents the bulk density and capsule fill-weights of each manufacturing run. SD19, 22, 23, 24 used the optimized conditions, which enabled desirable results regarding capsule loading and density. The runs highlighted in dark orange represent the runs that used the increased production rate and the runs outlined in black represent the runs with an increased feed concentration.

Figure 2: Moisture Content & Particle Size

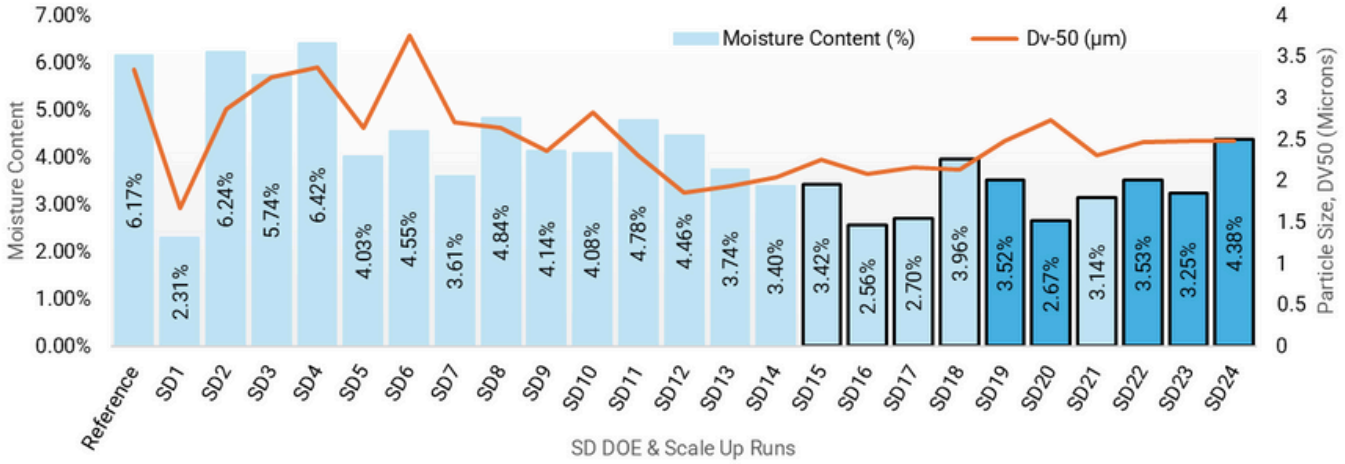

Figure 2 represents the moisture content (%) and particle size, Dv50 (µm) of each manufacturing run. SD19, 22, 23, 24 used the optimized conditions, which enabled desirable results regarding capsule loading and density. The runs highlighted in dark blue represent the runs that used the increased production rate and the runs outlined in black represent the runs with an increased feed concentration.

Client Impact

- Achieved necessary density specifications and capsule fill weight to allow program to proceed to clinical trials

- Published research paper on the scale-up and optimization in conjunction with CritiTech as co-authors
  - Stewart, I.E., Durham, P.G., Sittenauer, J.M. et al. Optimization and Scale Up of Spray Dried CPZEN-45 Aerosol Powders for Inhaled Tuberculosis Treatment. Pharm Res 39, 3359-3370 (2022).

I know I can speak for my entire team when I say we love working with the CritiTech team and we look forward to what we will achieve!

-Drug Product Development Leader