Capsule Filling of Spray Dried Powders for Inhalation using a Drum Filling Technology: From Lab to Pilot Scale

DDL2022 DRUG DELIVERY TO THE LUNGS

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BACKGROUND

Pulmonary drug delivery is an interesting route of administration and **dry powder inhalers (DPIs)** are very attractive as **they provide improved stability.**

Highly engineered particles by **spray drying** present several flowability challenges with **cohesiveness** and **poor flowability**

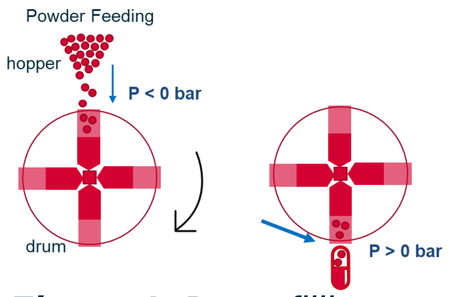
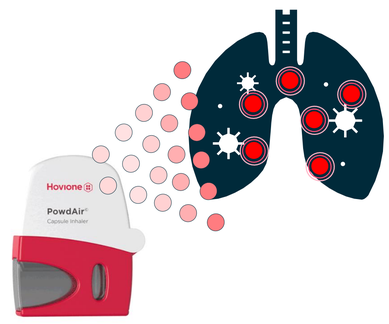


Figure 1. *Drum filling*

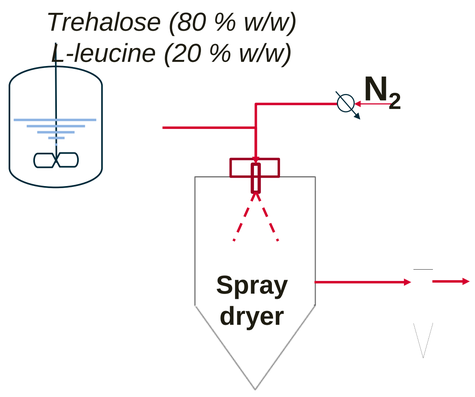
OBJECTIVES

- Low dosage capsule filling process development for **pulmonary delivery**.
- Identification of **critical process parameters** (CPPs) for drum filling technology



MATERIALS & METHODS

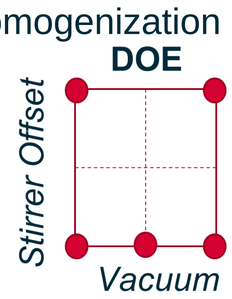
SPRAY DRIED COMPOSITES



- Highly engineered particles for inhalation
- Dv50 ~ 2.2 µm

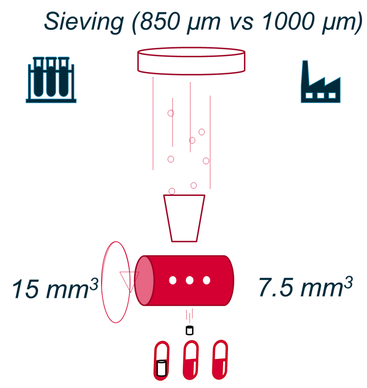
POTENTIAL CPPS

- Vacuum pressure for plug formation
- Stirrer offset
- Powder sieving for bed homogenization



SCALE-UP METHODOLOGY

DrumLab **Modu-C LS**



Capsules were filled at a target weight of 5 ± 0.4 mg using a 7.5 mm3 dosing bore volume at the Modu-C LS and at a target weight of 8 ± 0.6 mg using a 15 mm3 dosing bore volume at the Drum Lab.

PROCESS / PRODUCT PERFORMANCE

Process Performance

- Scale transfer process performance assessment: capsules RSD
- Feeding system: Accepted capsules

Product Performance

- Aerodynamic performance by ACI
- Fine particle fraction (FPF) determined as the percentage of the powder mass emitted from the capsule with an aerodynamic diameter below 5 µm.

RESULTS AND DISCUSSION

Feeding vacuum was found to affect filling performance significantly (P < 0.05).

Increasing vacuum may eventually have negative consequences on the product therapeutic efficiency, hindering deagglomeration of the powder during its aerosolization and release from the capsule.

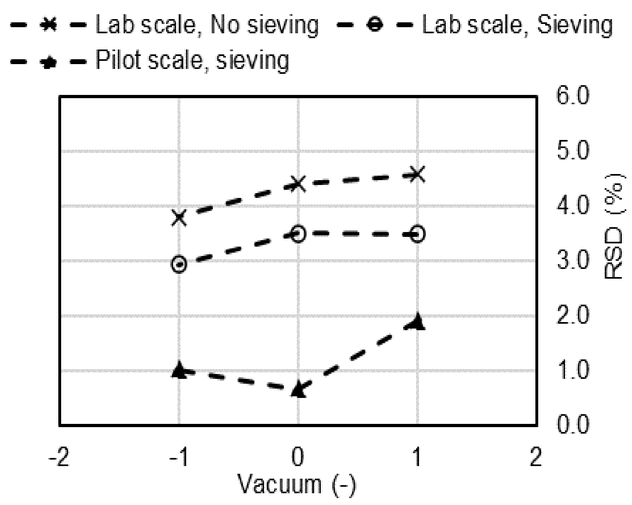


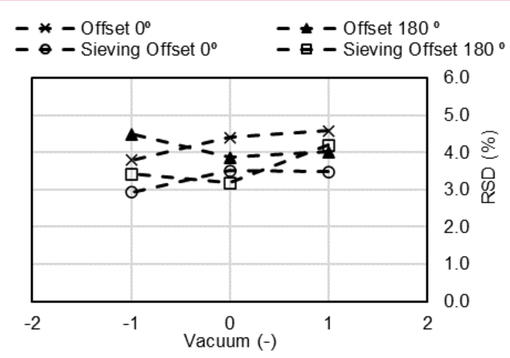
Figure 2. *Capsule filling process performance for the sieving and scale tests.*

Lab-scale drum filling represents a worst case

Can be a consequence of environmental RH.

Results show that the process responds equally to the different vacuum pressures.

Such alignment suggest that **lab-scale results can be used for process development at scale**, de-risking the scale-up of capsule filling process.



The stirrer offset resulted into non-significant differences (P > 0.05)

The tested stirrer configuration (i.e. design, rotation) at lab-scale, the impact of the stirrer offset in capsule filling performance was negligible.

Figure 3. *Capsule filling process performance offset tests at the lab-scale.*

Sieving improves operational and process performance

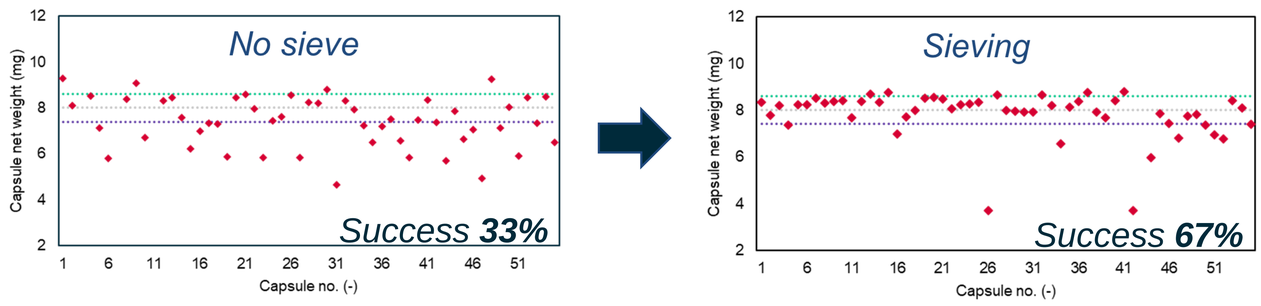


Table 1. Aerodynamic performance (N=3).

Lab scale	Vacuum (-)	ED (%)	FPF (%ED)
No sieving	1	86.1 ± 1.0	64.2 ± 9.7
	0	90.3 ± 1.5	68.1 ± 4.6
	-1	86.7 ± 0.9	69.9 ± 3.1
Sieving	1	72.8 ± 1.7	73.5 ± 6.6
	0	76.4 ± 0.6	65.1 ± 5.4
	-1	71.3 ± 5.3	74.1 ± 7.6

Sieving improves the aerodynamic performance

Nevertheless, a **higher emitted dose is obtained for the non-sieved powders**, which may be explained by the **increased powder cohesivity observed in loose fine particles,** leading to a higher capsule retainment.

CONCLUSION

- Capsule filling process was successful at all the tested conditions, with **RSD below 5% across scales**.
- Vacuum was found to significantly affect performance, while stirrer offset did not.
- Variables such as **powder fluidization** can be a **key driver** for improving process performance and reduce the difference between RSD across scales.

REFERENCES: Besenhard, M.O., et al., Eur. J. Pharm. Biopharm.,2015,94, 264-272; Sibum, I. et al., Pharmaceutics 2020,12, 1-14; Hebbink, G.A., et al., Adv. Drug Deliv. Rev 2022,189, 114527