Assessment of the Delivery Performance of a Novel Soft Mist Inhaler Using a Pre-Filled Syringe Based Container Closure System

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Key Message

Biological drugs are primarily delivered as water-based liquid formulations and require efficient delivery platforms when being delivered via the inhalation route. The soft mist inhaler tested within this study uses a container closure system that is compatible with biological drug products and achieves a high lung deposition of about 63%.

Background

- There is a necessity for inhalers capable of delivering larger amounts of liquid drugs and providing container closure systems that allow aseptic filling compatible with available technologies like pre-filled syringes or cartridges.
- Soft Mist Inhalers (SMIs) deliver liquid formulations through a slow-moving cloud of aerosol generated solely by mechanical energy.
- Novel SMIs are now being developed for larger molecules and biological drug products that require the delivery of higher amounts of the drug.
- The objective of this study is to characterize the delivery performance and lung deposition efficiency of Resyca's soft mist inhaler.

Methods

- The pre-filled syringe inhaler (PFSI) is a mechanical, pocket-sized, portable device that utilises a disposable cartridge to provide 10 to 30 metered dosages.
- The multi-dose cartridge is based on a pre-filled glass syringe containing the drug solution, to which a spray nozzle and a mouthpiece are attached.
- The formulation is aerosolised by the micro spray nozzle with a low shear force by means of Rayleigh breakup. This technique allows the generation of nearly mono-disperse droplets under very low shear condition, ideally suited for sensitive biological formulations.

Figure 1: *Pre-filled syringe inhaler (PFSI™) with multi-use cartridge*

- Device under test: PFSI™ (Resyca BV, Enschede, Netherlands), using a cartridge filled with 2,5% saline with a target dosing volume of 30 µL.
- Measurement of particle size: Malvern Spraytec laser diffraction, emitted mass and delivered dose uniformity: DUSA and weight loss; Both at 30 L/min inspiratory flow rate.
- Lung deposition modelled using Mimetikos Preludium V 1.1.7 (Emmace) using the parameters as described in Table 1.

Table 1: *Parameters for lung deposition modeling*

Parameter	PFSI™
Model	Weibel A
Tidal breath volume	1000 mL
Inspiratory flow rate	30 L/min
Flow pattern	rectangular
Breath hold	1 sec
I/E ratio	1:1
Bolus volume	950 mL
Delay volume	50 mL

Results

Table 2: *Particle size data at 30 L/min*

Parameter	VMD (µm)	GSD (-)	FPF <5µm (%)
PFSI	4.3 (0.3)	1.4 (0.04)	65.2 (6.2)

- Mean VMD, GSD and FPF (Percentage emitted aerosol < 5 µm), is presented in Table 2.
- Average emitted metered is 30.4 mg (95% CI, 30.18 – 30.65 mg).
- The device exhibits good device-to-device and shot-to-shot variability with all doses falling within the 75 – 125% interval (Figure 2).
- The total modelled lung deposition is 63% (Figure 3).

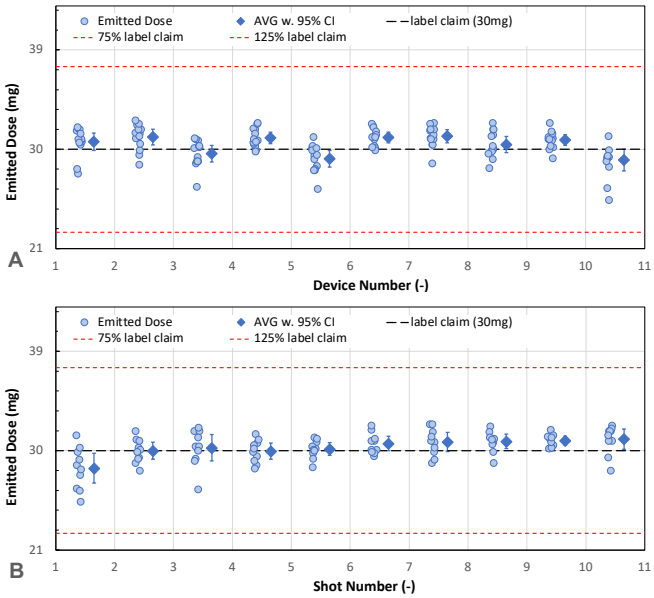

Figure 2: *Distribution of individual and mean (95% CI) emitted dose; (A) inter device comparison; (B) Shot-to-shot comparison for all devices.*

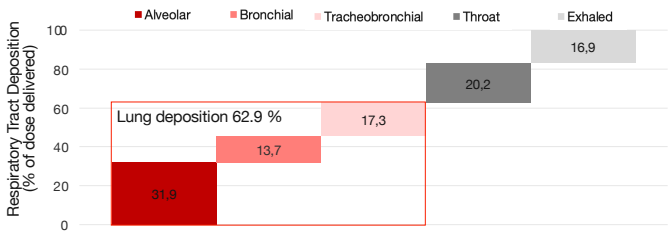

Figure 3: *Modelled regional lung deposition in the % of delivered dose.*

Conclusion

Particle size, emitted dose and inhalation flow rate play a crucial role in determining the delivery efficiency and the lung deposition. Test results from aerosol characterisation of the PFSI device show a volumetric median diameter of 4.3 µm with a narrow size distribution (GSD of 1.4) and FPF of 65.2%. Results from emitted dose measurements confirm that the targeted dose of 30 mg was reached with 30.4 ± 0.24 mg over 10 dose actuations and across different devices. The uniformity of single doses fulfils dose uniformity requirements are in the range of 75%–125% of the label claim. Regional respiratory lung deposition modelling shows a high deposition in the lung and the lung periphery of 62.9% and 31.9%, respectively.

1. Komalla V, Wong CY, Sibum I, Muellinger B, Nijdam W, Chaugule V, Soria J, Ong HX, Buchmann NA, Traini D: Advances in soft mist inhalers, Expert Opinion on Drug Delivery 2023; 10: pp 1 – 6.
2. B. Olsson and S. C. Kassinos. On the Validation of Generational Lung Deposition Computer Models Using Planar Scintigraphic Images: The Case of Mimetikos Preludium, J. of Aerosol Medicine and Pulmonary Drug Delivery 202134:2