

Development of a Blow-Fill-Seal (BFS) Nasal Vaccine Device

INTRODUCTION

Intranasal vaccination requires delivery systems that are simple to use, suitable for sterile manufacturing, scalable and compatible with unit-dose administration. **Blow-Fill-Seal (BFS) technology** offers an attractive platform for the aseptic filling of single-use containers, providing high production capacity at competitive cost.

The partnership between Unither Pharmaceuticals and Nemera aims to develop a nasal vaccine delivery system, based on Unither's proprietary BFS technology and Nemera's nasal spray technology. The resulting product concept consists of a customised spray nozzle connected to a pre-filled Euroject® BFS container after removal of the BFS cap (Figure 1 & 2).

MATERIALS & METHODS

Euroject® BFS containers filled with 250 µL of water were opened and then coupled with prototype swirl-based spray nozzles (Figure 1). Devices were manually actuated by a single operator by pinching the container held at a 45° downward angle.

Droplet Size Distribution was characterised by laser diffraction (Spraytec, Malvern Panalytical). Shot weight was measured as the mass differential of the sample before and after actuation.

A qualitative deposition assessment was performed in a CUBO nasal cast (Nemera) using an aqueous fluorescein solution (5 g/L). The cast orientation simulated administration to a patient lying on his back, with a dry nasal wall and breath hold condition. (Figures 2 & 3).



Figure 1: Illustration of Euroject® BFS container and prototype swirl-chamber based spray nozzles.

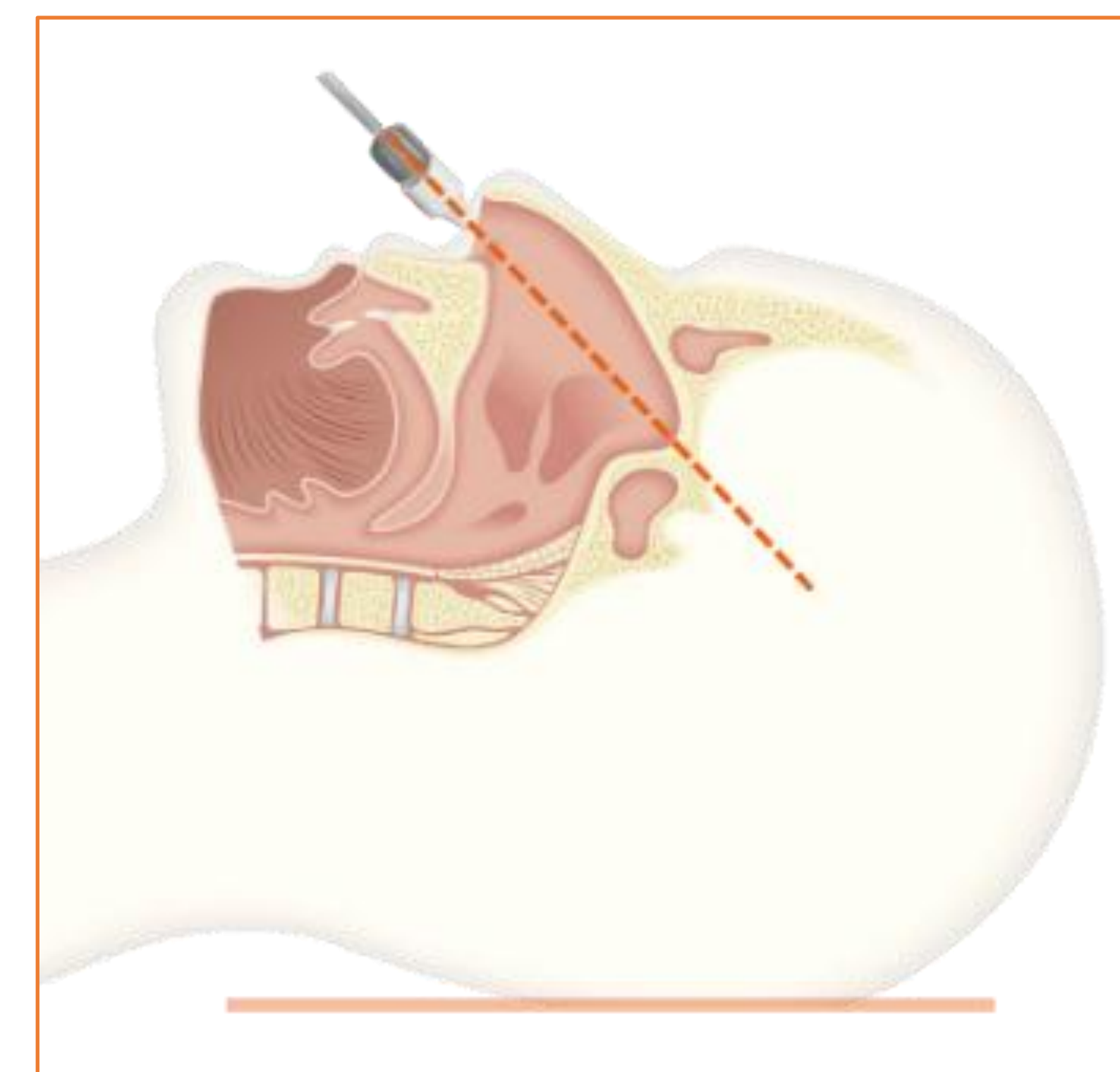


Figure 2: Graphic representation of administration with Euroject® BFS nasal device on a patient in a horizontal lying-down position.

RESULTS

The emitted dose ranged from 136 to 162 µL (mean 150,9 µL, SD 9,2 µL) and D50 values from 230 to 565 µm (mean 425 µm, SD 128 µm) (Figures 4 & 5).

Qualitative assessment showed deposition mainly in the front of the respiratory zone and in the middle meatus. The observed nasopharyngeal deposition may indicate potential delivery to the Nasal-Associated Lymphoid Tissue (NALT) (Figure 6).

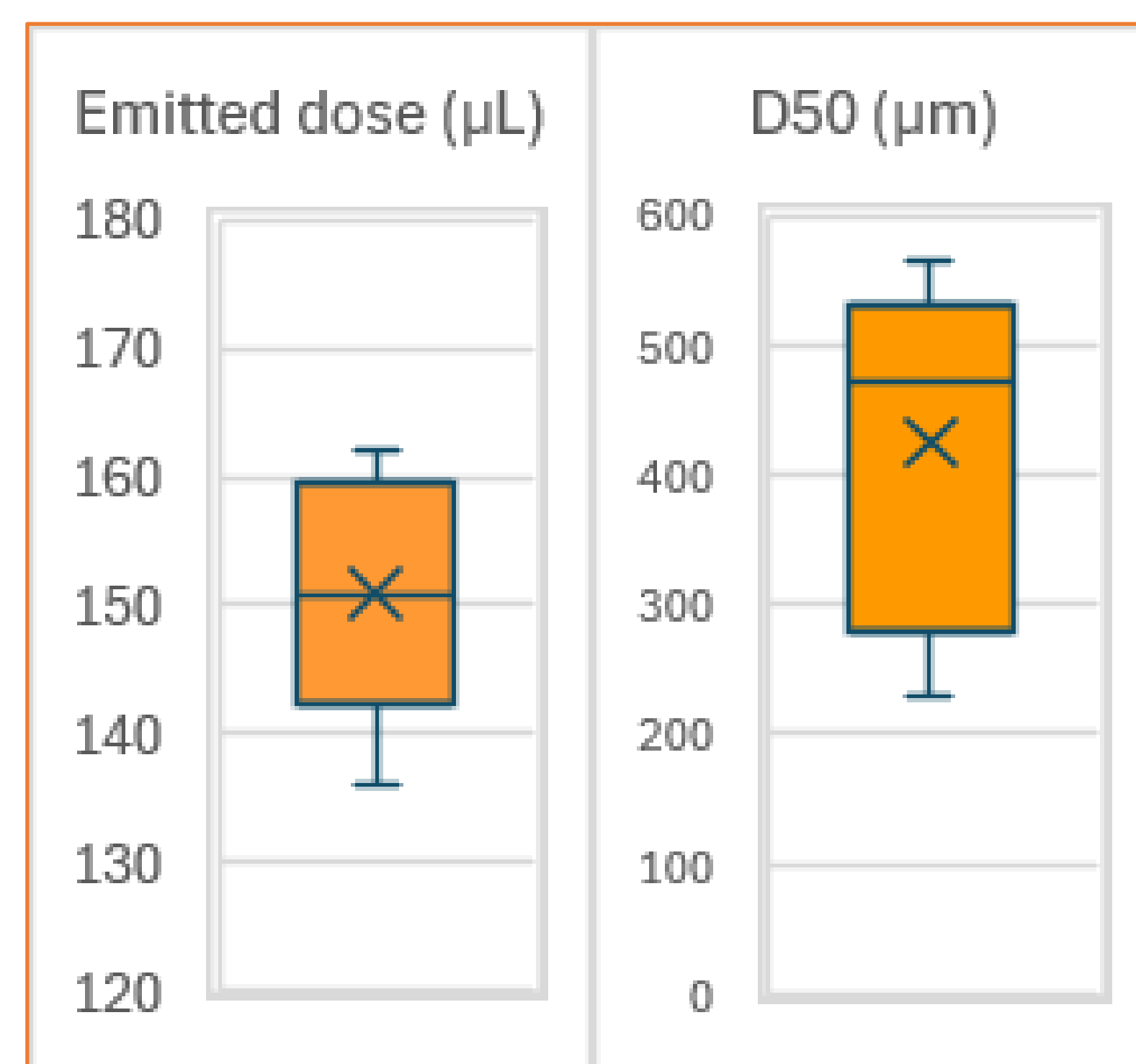


Figure 4: Emitted dose and droplet size.



Figure 5 : High speed imaging of the Euroject® BFS nasal spray.



Figure 6: Administration in CUBO nasal cast simulating intended horizontal patient position.

DISCUSSION

Manual pinching of the BFS container generates a transient pressurization of the air-liquid system, expelling liquid through the spray nozzle. The limited pressure and sensitivity to user-dependent pinching force results in large, variable droplets.

However, the emitted dose (136-162 µL) is in the same order of magnitude as the 100 µL per nostril, which is the common dose volume of marketed intranasal influenza vaccines. Large-particle atomization has been shown to achieve efficient vaccine delivery in humans [1]. Deposition in the middle nasal meatus and run-off toward the nasopharyngeal region may be relevant for intranasal vaccine delivery.

CONCLUSION

This proof-of-concept study demonstrates the feasibility of combining Unither's Euroject® BFS container with a specially designed nasal spray nozzle for intranasal vaccine delivery.

The concept offers potential advantages in simplicity, unit-dose presentation and quick-to-scale manufacturability.

Ongoing development will focus on improving reproducibility, optimizing spray performance and assessing regional nasal deposition.

REFERENCES

- [1] Gruber WC et al. Comparative Trial of Large-Particle Aerosol and Nose Drop Administration of Live Attenuated Influenza Vaccines. J Infect Dis. 1993;168(5):1282-1285.