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Designing a Sustainable Ipratropium HFA-152a pMDI: Actuator Geometry Considerations

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KEY WORDS: Global Warming Potential (GWP), HFA-152a Propellant, Ipratropium Bromide Pressurised Metered Dose Inhaler (pMDI), Actuator Geometries.

INTRODUCTION

The pharmaceutical industry is actively exploring sustainable alternatives to the currently used propellants for pressurised metered dose inhalers (pMDIs) [1]. The new propellant HFA-152a has a tenfold reduction in GWP compared with the current HFA-134a propellant. Differences in the physicochemical properties of the new propellants have led to the redevelopment of existing pMDIs. Actuator geometries (Figure 1) are critical parameters which influence the delivered dose uniformity (DDU), aerodynamic particle size distribution (APSD) and the shape and size of the aerosol plume, thereby affecting the overall efficacy of the product for the patient [2].

This study focuses on

- Comparison of Ipratropium HFA 152a pMDI with the currently marketed Atrovent HFA-134a pMDI.
- Effect of actuator geometries on APSD and Spray pattern (SP).

MATERIALS AND METHODS

Materials:

- Ipratropium Bromide solution formulation (20 µg/actuation with approximately 15%w/w ethanol as cosolvent, citric acid as excipient and HFA-152a as propellant) was filled in H&T Presspart's plasma canisters and crimped with Bespak 50 µL valves at H&T Presspart's Inhalation Product Technology Centre (IPTC) facility.
- Atrovent HFA134a marketed product.
- Actuators with different geometries manufactured by H&T Presspart were chosen for the study (Table 1).

Methods:

All test parameters were tested with sample size n=3

- **DDU:** was performed on ten doses per inhaler using a through-life testing regime.
- **Tail off:** by testing additional doses after 200 doses.
- **Actuator Retention:** By performing two prime shots and one delivered dose.
- **APSD:** was performed on ten doses using NGI at 30 L/min.
- **Spray pattern:** testing was performed using Proveris Spray VIEW® at 3.0 cm and 6.0 cm distance from the actuator mouthpiece [3].

Table 1: H&T Presspart Actuator Geometries and tests performed.

Tests Performed	Orifice Diameter (OD) mm	Jet Length (JL) mm
DDU, Tail Off, Actuator retention, APSD, Spray Pattern	0.25	0.35
APSD and Spray Pattern	0.20	0.70
	0.22	0.70
	0.25	0.40
	0.35	0.70

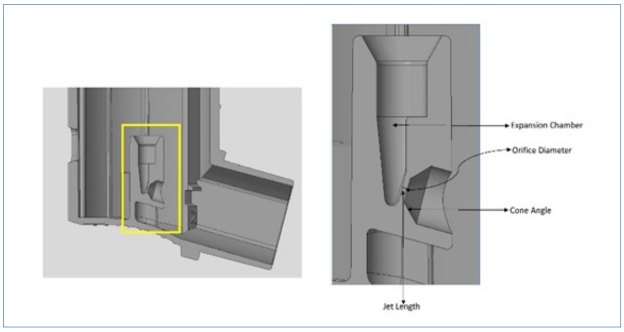

Figure 1: Schematic of Actuator geometry

RESULTS

Delivered dose uniformity and tail off

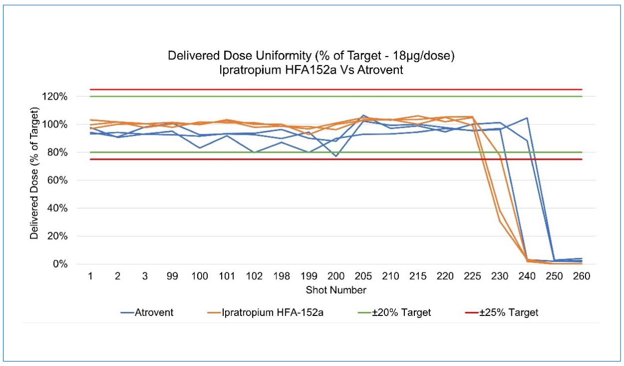

Figure 2 - DDU and Tail-Off - Atrovent Vs Ipratropium HFA-152a

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Drug retention within the Actuator

Table 2 - Actuator Retention

Sample	Average Delivered Dose (µg/dose)	Average Actuator Retention (µg/dose)
Ipratropium HFA-152a	18.0	3.1
Atrovent HFA-134a	15.9	4.9

Aerodynamic Particle Size Distribution

Consistent APSD performance was observed through the life for the Ipratropium HFA-152a formulation whereas the Atrovent product exhibited lower Fine Particle Mass (FPM) at the EOL stage.

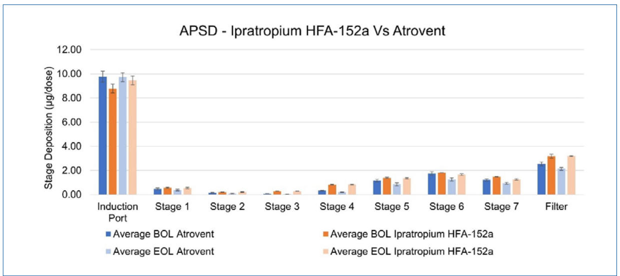

Figure 3 - Comparison of APSD Ipratropium HFA152a vs Atrovent

Comparison of FPM: Diff. Actuator geometries

All but one of the different actuator geometries (Table 1) demonstrated a higher FPM highlighting further actuator optimisation or changes in the formulation composition might be required [4] to match the Atrovent product. The HFA-152a product had a significantly higher FPM than the Atrovent product ($p<0.05$, Student T-Test).

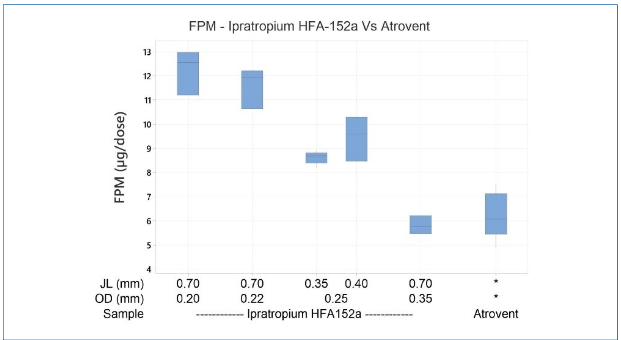

Figure 4 – FPM: Diff. Actuator geometries, Ipratropium HFA-152a vs Atrovent

Spray Pattern (SP)

The actuator geometry OD and JL significantly impact the spray area. The study showed a statistically significant difference for the actuator geometries studied with as seen with Ipratropium HFA-152a formulation vs Atrovent ($p<0.05$, Student T-Test).

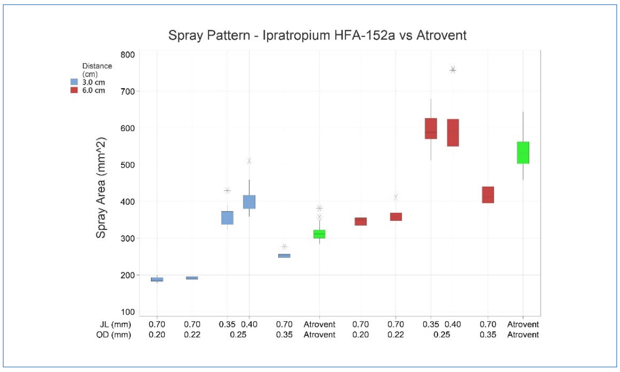

Figure 5– SP: Diff. Actuator Geometries: Ipratropium HFA-152a vs

CONCLUSION

The actuator geometries have a significant impact on invitro performance parameters i.e. FPM and Spray Pattern. Understanding the formulation properties and container closure systems (Canister, Valve and Actuator) is crucial for product development. The Ipratropium HFA-152a formulation and actuator geometry studied here is promising as a low GWP propellant alternative to the current HFA-134a product.

ACKNOWLEDGEMENTS

The authors would like to thank H&T Presspart's commercial team for their support to the study.

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