Assessment of Potential Mouth/Throat Deposition and Lung Delivery of Suspension- and Solution-Formulated Inhaled Corticosteroid Formulations Delivered by Pressurized Metered Dose Inhaler without and with Valved Holding Chamber Using an Anatomic Adult Upper Airway

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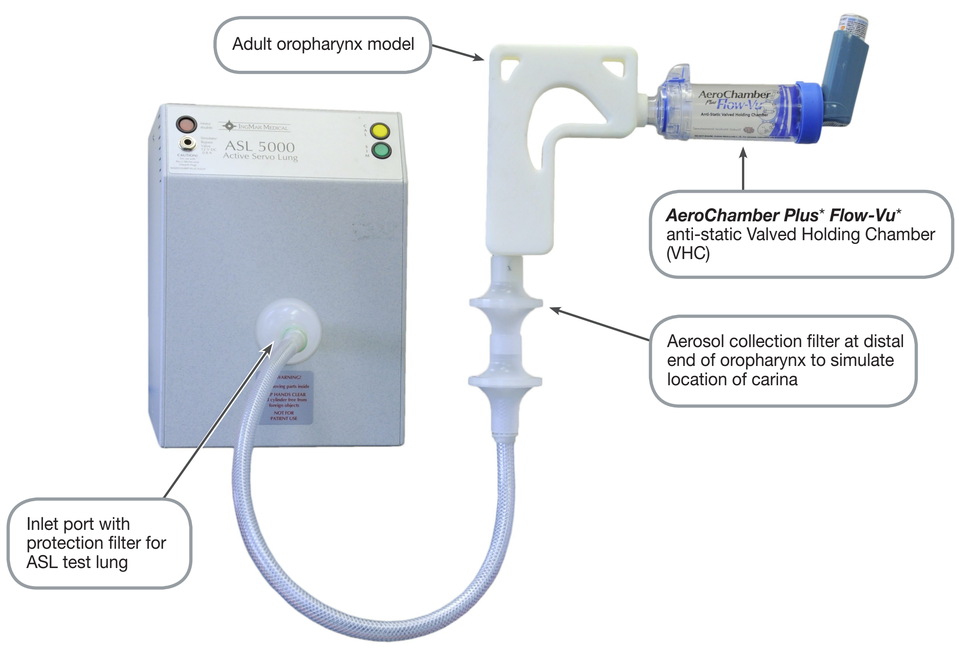
INTRODUCTION / STUDY PURPOSE

- The present laboratory study explored how insertion of a Valved Holding Chamber (VHC) in the pathway between pMDI and the mouth might affect the transfer of particles from inhaler mouthpiece to the airways of the lungs
- An anatomically correct adult oropharyngeal airway was used in conjunction with simulated patient inhalation, and both suspension and solution corticosteroid pMDIs were assessed

MATERIALS AND METHODS

Figure 1: Experimental Arrangement Showing Adult Oropharyngeal Inlet; The Same Configuration was Utilized for Evaluation of pMDI Alone or with VHC Present



- The location of filter represents the approximate location of the carina[1], so that the mass of active pharmaceutical ingredient (API) collected thereon was deemed to be indicative of potential lung deposition
- The following standardized[2] adult profile based on tidal breathing was used throughout the investigation
  - Tidal volume = 770 mL
  - Inspiratory/expiratory ratio = 1:2
  - Rate per minute = 12
- Antistatic ***AeroChamber Plus**** ***Flow-Vu**** VHCs (Trudell Medical International, London, ON, Canada) were used as a representative VHC
- Three replicate measurements were made at each condition with each of the pMDI products
- Two actuations of the pre-primed pMDI canister were actuated into the entry of the airway, the second timed to take place following 6 breathing cycles after the initial actuation.

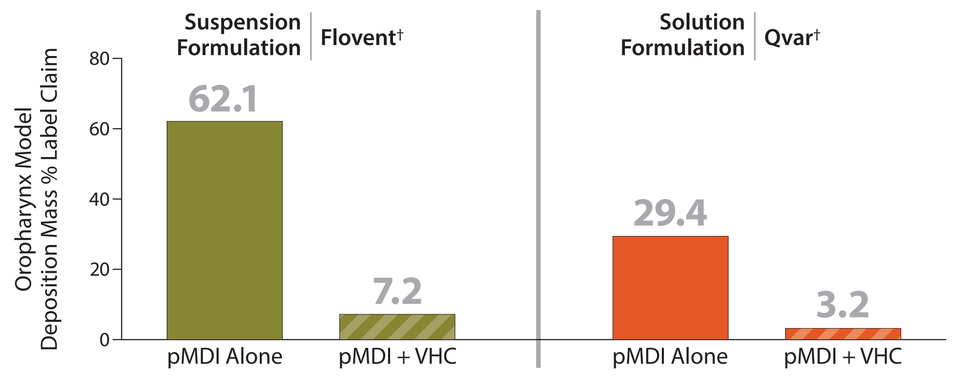
Table 1: Study Design and Outputs

pMDI product	API/mass per actuation	Formulation type	VHC present	Outputs Measured
Flovent† 125	FP/125 µg	HFA Suspension	No	Model airway and filter deposition related to potential oropharyngeal and lung deposition respectively
			Yes	
Qvar† 100	BDP/100 µg	HFA Solution	No	
			Yes	

- Following each test, an internally validated HPLC-UV spectrophotometric assay was used to determine the mass of the relevant API recovered at each location

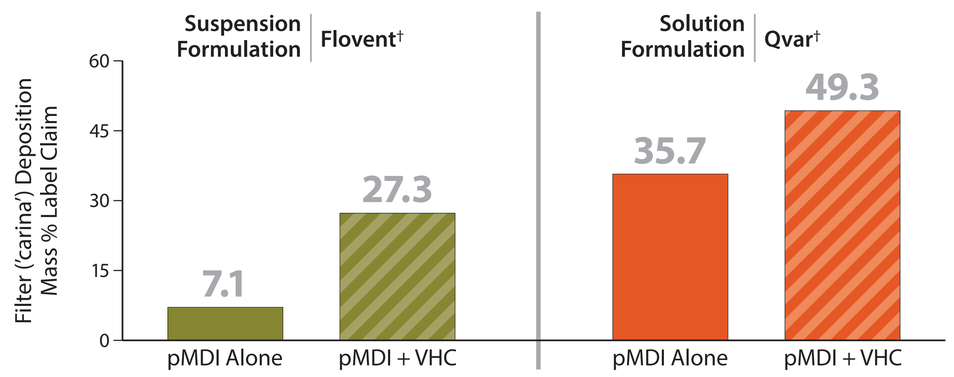
RESULTS

Figure 2: Particle Deposition in the Oropharynx of the Adult ADAM Airway
» Representative of Oropharyngeal Deposition



- When the VHC was absent, the FP (suspension) formulation was deposited in the oropharyngeal passageway at approximately double the extent to that observed with the BDP (solution) formulation (62% v 29%)
- Significant oropharyngeal airway deposition still occurred, even with the ultrafine HFA solution product, which was greatly reduced when the VHC was present (29% v 3%, $p < 0.001$).

Figure 3: Particle Deposition on Filter Located at the Distal End of the ADAM Adult Airway
» Representative of Delivery to the Lungs



- As expected, the finer aerodynamic particle size distribution of the ultrafine Qvar† solution aerosol resulted in greater delivery to the filter ('carina') compared with the coarser Flovent† suspension aerosol ($p < 0.001$) when the VHC was absent, although the large degree of difference (7% v 36%) is potentially surprising (see Figure 3)
- Filter deposition was increased for both pMDI products when the VHC was present ($p < 0.001$). The increase was more pronounced with the suspension product; however, an increase was still evident even when used with the solution HFA pMDI
- Given the findings for both oropharyngeal and filter deposition in the present study, the view that a VHC might not add value with the solution type of product for oropharyngeal deposition [5], therefore appears to be an overstatement of reality

CONCLUSIONS

- This laboratory-based pilot study, using a new replicated adult airway, provides new data supporting the fact that finer solution HFA pMDI products are likely to deposit in the oropharynx to a lesser extent and be delivered to the lungs to a greater extent, than suspension HFA pMDIs
- The combination with a VHC, for either type of product, resulted in significantly less drug deposited in the modelled oropharynx and increased potential for lung delivery
- Hence the potential value of a VHC, even within an adult population, is demonstrated.

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