

***In vitro* Performance of Space Chamber Plus™ and Compact Space Chamber Plus™ compared with Aerochamber Plus Flow Vu™ Anti-static**

Study Objective:

To compare particle size distribution, and therefore *in vitro* performance, of three different classes of drug (albuterol sulfate, beclomethasone dipropionate and ipratropium bromide) when delivered from three different valved holding chambers (VHCs).

Study Design:

Particle size distribution was performed in an independent cGMP laboratory using a Next Generation Impactor (NGI) at a flow rate of 15 L/min according to compendial technology. Aerosol emitted from the pressurised metered dose inhaler (pMDIs) (6 actuations each for albuterol and beclomethasone and 12 actuations for ipratropium) is directed into the NGI cascade either directly or through a VHC. Aerosol passing through the NGI impactor impacts on the impactor throat and various cascade stages on the basis of its aerodynamic size. Aerosol residue deposited at each stage is collected and quantified by HPLC against USP drug standards.

VHCs compared:

- Space Chamber Plus and Compact Space Chamber Plus (Medical Developments International).
- Aerochamber Plus Flow Vu Anti-static (Trudell Medical International)

pMDIs used:

- Albuterol sulfate (Ventolin HFA, GSK USA)
- Ipratropium bromide (Atrovent HFA, Boehringer Ingelheim USA)
- Beclomethasone dipropionate (QVR, Teva USA)

Three units of each VHC were tested. The VHCs were treated according to each respective manufacturer's Instruction for Use leaflets prior to the start of testing.

Results:

The results are summarised graphically for particle size (mass median aerodynamic diameter or MMAD), total delivered and respiratory doses as well as respirable fractions obtained with each VHC and pMDI combination, and each pMDI alone in Figures 1 – 4 respectively.

Figure 1: Mean Mass Median Aerodynamic Diameter

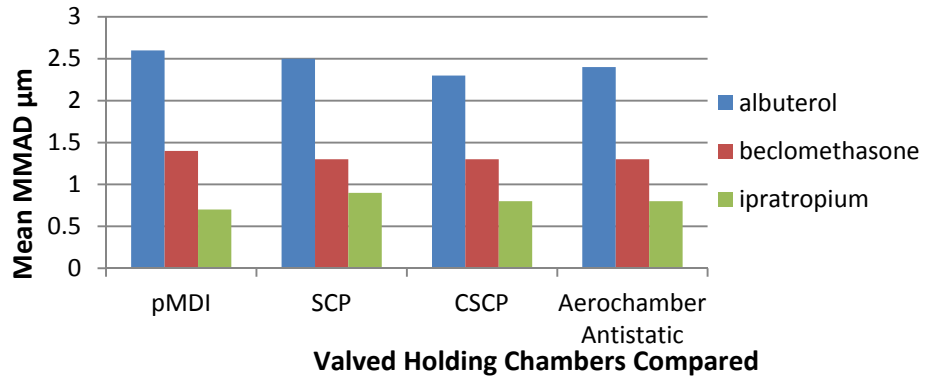


Figure 2: Mean Total Delivered Dose

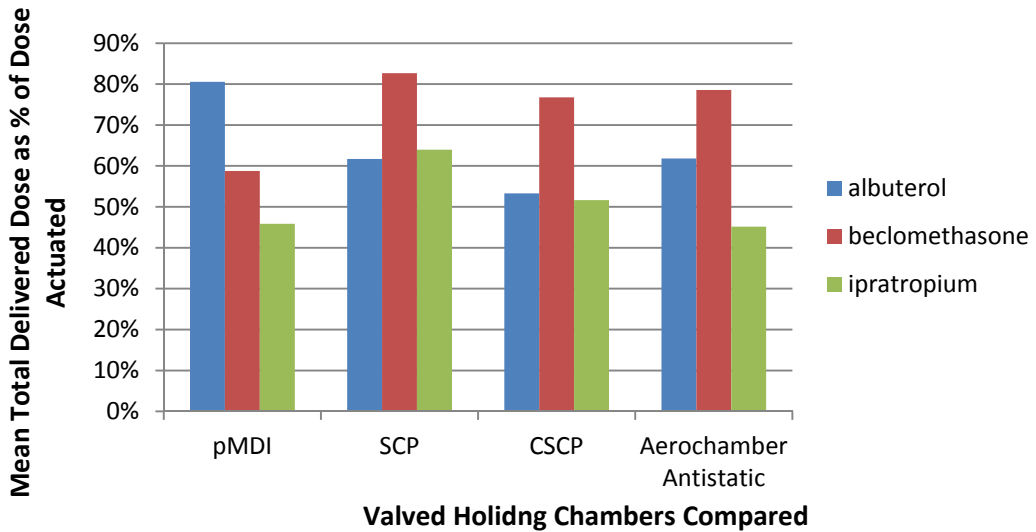


Figure 3: Mean Total Respirable Dose

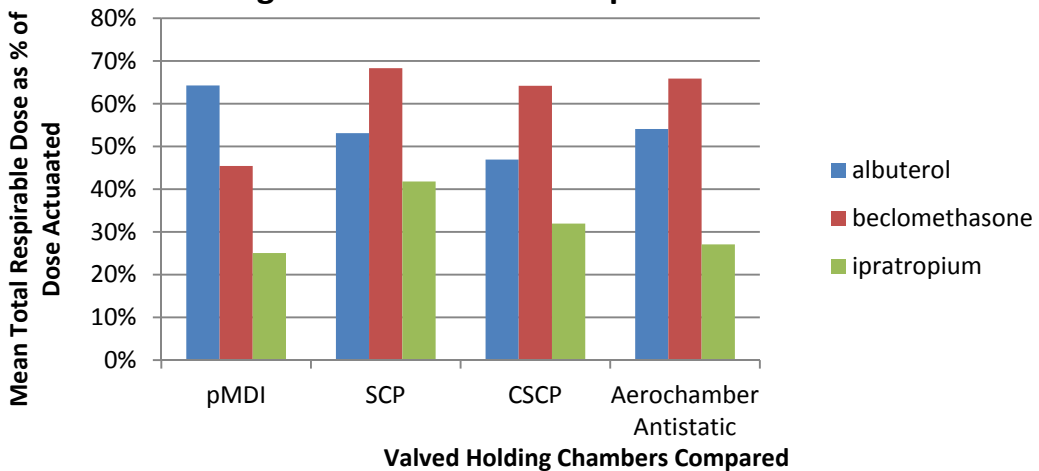
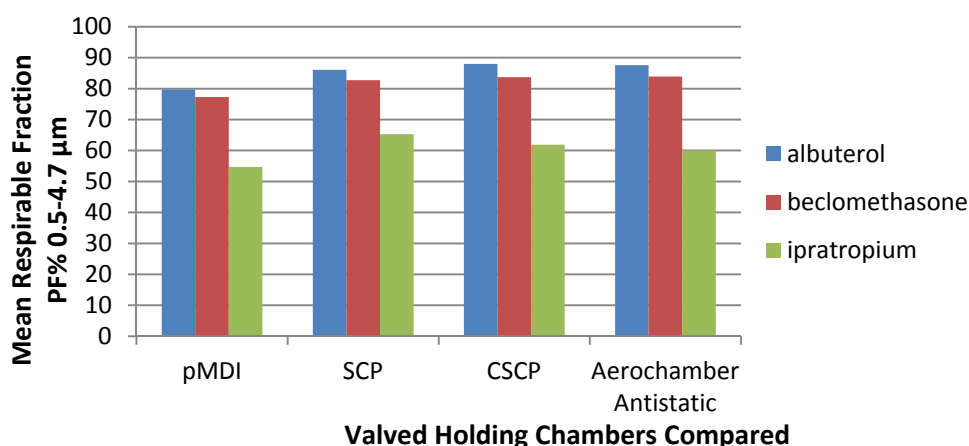


Figure 4: Mean Respirable Fraction



Discussion:

The VHC acts as a reservoir for the medication from the puffer or pMDI; it does not require patient-coordinated actuation and inhalation for maximum efficiency. It reduces the amount of medication deposited in the upper respiratory tract (large aerosol particles of $>5 \mu\text{m}$) and increases the amount of medication reaching the lungs (particles of $0.5 - 4.7 \mu\text{m}$), the respirable dose.

In this study, the performance of Space Chamber Plus and Compact Space Chamber Plus was compared against that of Aerochamber Plus Flow Vu Anti-static. Both Space Chamber Plus and Compact Space Chamber Plus are made of the same materials. The shorter length of the Compact Space Chamber Plus easily fits into school bags, handbags or briefcases to allow easier storage and handling. Both these VHCs have a transparent body so that the respiratory valves and their movement can be easily seen and therefore enables the confirmation of correct product operation and usage.

The performance of the three VHCs was evaluated by:

- MMAD or mass median aerodynamic diameter, i.e. the diameter above and below which lies 50% of the mass of the particles recovered in the impactor;
- Respirable fraction (Particle Fraction % $0.5-4.7 \mu\text{m}$);
- Mean total respirable doses (as percentage of total delivered dose); and
- Mean total delivered doses (as percentage of total delivered dose).

Comparable results were obtained for all VHCs tested. However, for each pMDI tested, the respirable fractions delivered by the VHCs are greater than those delivered by the pMDIs alone.

The results therefore showed that use of VHCs with the pMDIs increased the proportion of particles in the respirable range (respirable fraction) that would reach the lungs.

Importantly, the results of the study demonstrate that Space Chamber Plus and Compact Space Chamber Plus are equivalent to Aerochamber Plus Flow Vu Antistatic in performance.

Conclusion:

Results of the aerodynamic particle size distribution study indicate that Medical Development International's non-antistatic VHCs, Space Chamber Plus and Compact Space Chamber Plus, have equivalent *in vitro* performance to Trudell's Aerochamber Plus Flow Vu Anti-static.