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

Study Objective:

To compare drug output and aerodynamic particle size distribution of combination inhalers, for the treatment of both the bronchoconstriction and inflammatory aspects of asthma and chronic obstructive pulmonary disease (COPD), when delivered from different valved holding chambers (VHCs): Space Chamber Plus (SCP), Compact Space Chamber Plus (CSCP), Aerochamber Plus Flow Vu and Aerochamber Plus Flow Vu Anti-static.

Study Design:

Particle size distribution was performed by an independent laboratory using a Next Generation Impactor (NGI) at a flow rate of 30 L/min according to compendial methodology. Aerosol emitted from a pMDI (20 actuations) is directed into the NGI cascade either directly or through a VHC. Aerosol passing through the NGI 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 a linear standard curve plotted from standard solutions.

VHCs compared:

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

pMDIs compared:

- Seretide: Fluticasone proprionate 250 µg and salmeterol xinaofate 25 µg (GlaxoSmithKline Australia Pty Ltd)
- Fostair: Beclomethasone dipropionate 100 µg and formoterol fumerate 6 µg (Chiesi Ltd UK)

In the first part of the study, Seretide was used for the comparison. Six units of each VHC were tested. In the second part of the study, Fostair was used, and similarly 6 units of MDI's VHCs were tested, but only 3 each of Aerochamber Plus Flow Vu and Aerochamber Plus Flow Vu Anti-static. The VHCs were treated according to each respective manufacturer's Instruction for Use leaflets prior to testing.

Results:

The results for the respirable fraction are graphed and presented in Figure 1 for Seretide and Figure 3 for Fostair. As shown by the Figures, the respirable fractions delivered by the VHCs are greater than those delivered by the pMDIs alone. The respirable fractions delivered by the Space Chamber Plus and Compact Space Chamber Plus are equivalent to those delivered by Aerochamber Plus Flow Vu and/or Aerochamber Plus Flow Vu Anti-static.

Likewise, the results for average total dose delivered per actuation, as a percentage of total amount of drug recovered, are graphed and presented in Figures 2 and 4 for Seretide and Fostair,

respectively. The percentage of average dose delivered by all the VHCs tested are equivalent and within 15% of each other. However, it is of note that, numerically, of the four VHCs tested with Fostair, Space Chamber Plus performs best, and Aerochamber Plus Flow Vu Anti-static, the worst.

Figure 1: Respirable Fractions compared using Seretide

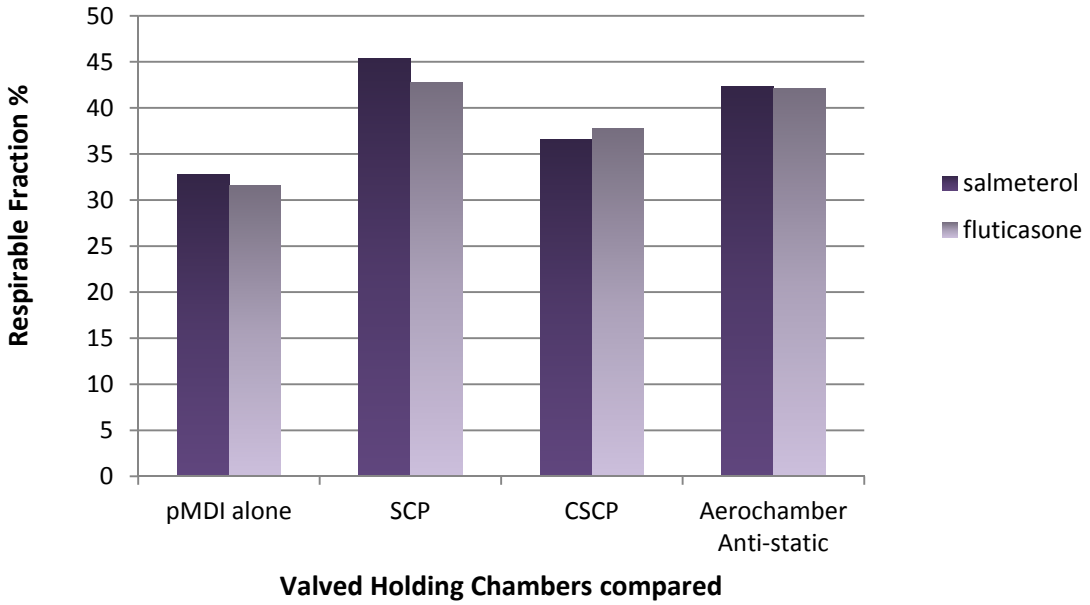


Figure 2: Total Delivered Dose compared using Seretide

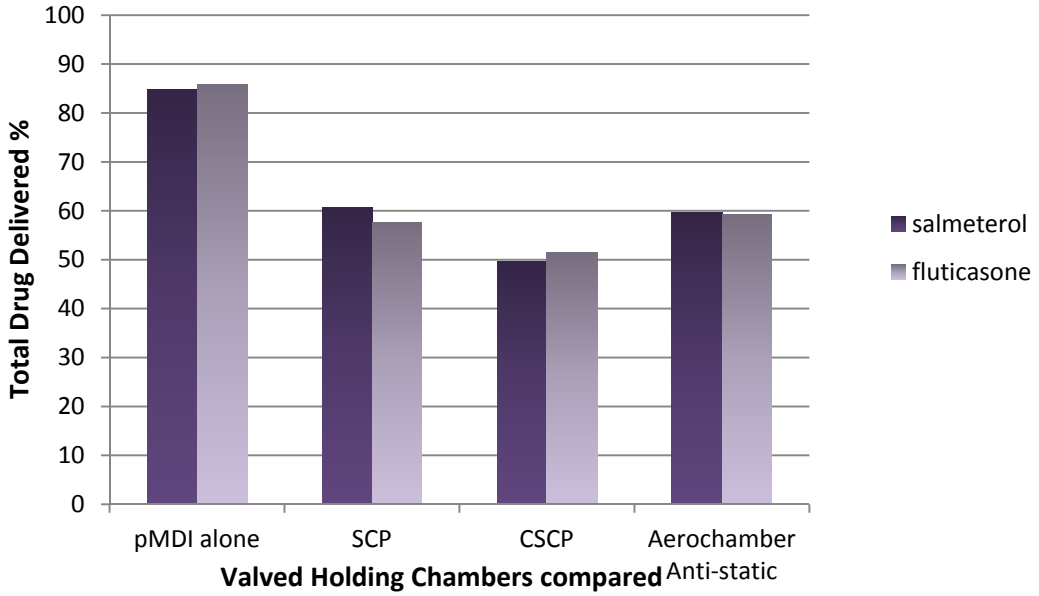


Figure 3: Respirable Fractions compared using Fostair

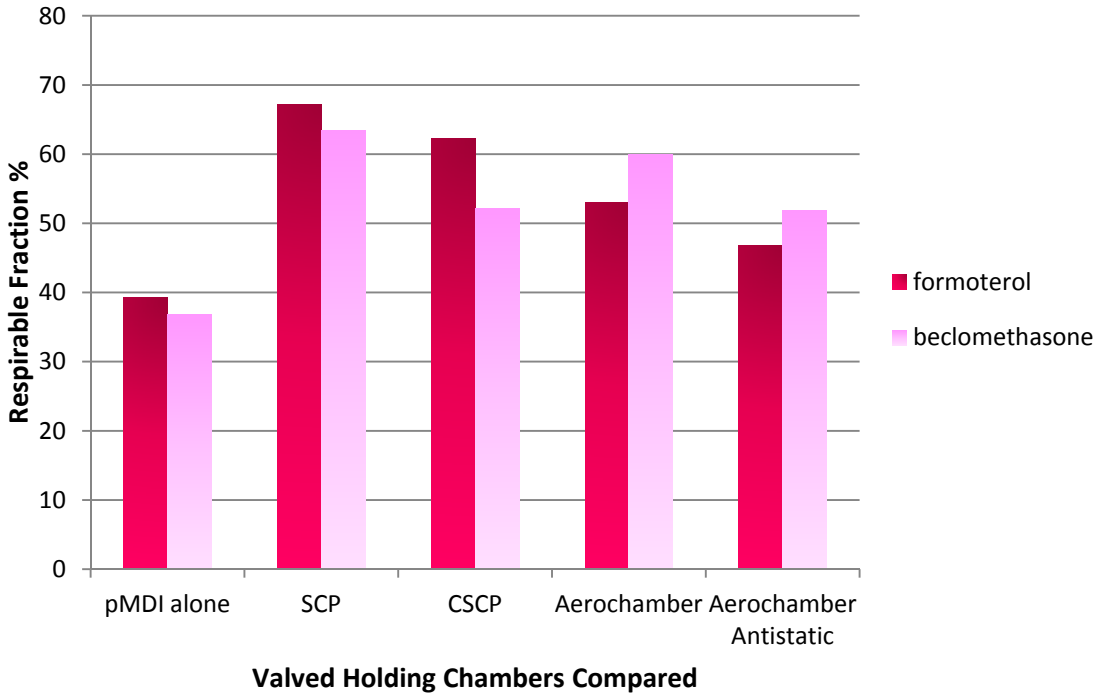
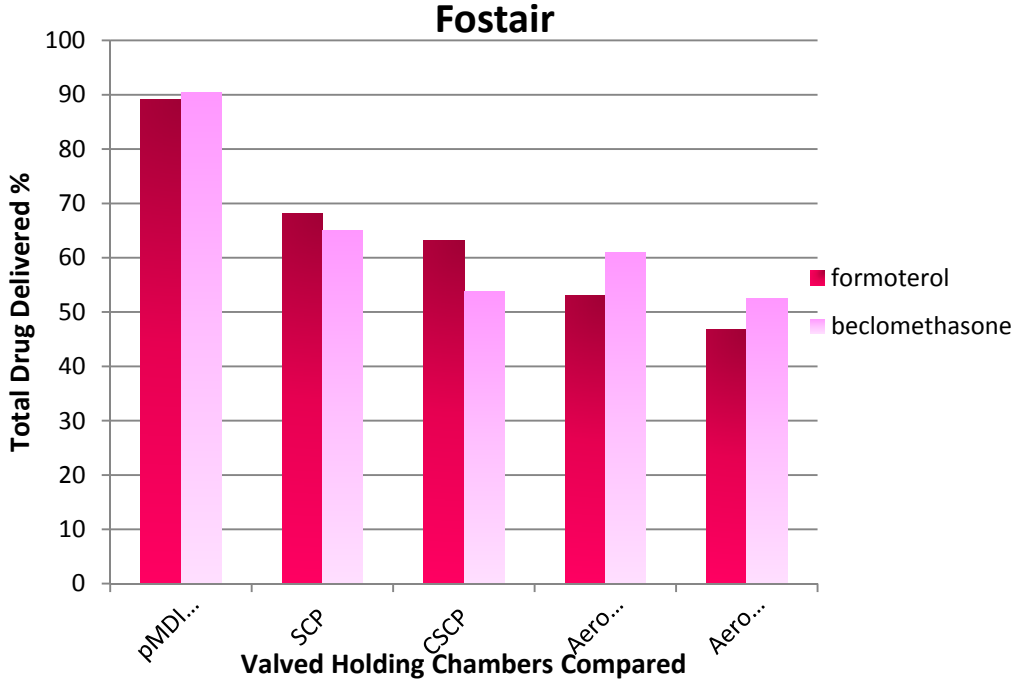


Figure 4: Total Delivered Dose compared using Fostair



Discussion:

The VHC acts as a reservoir for the medication from the puffer or pMDI (pressurised metered dose inhaler); it does not require patient-coordinated actuation and inhalation for maximum efficiency. It reduces the coarse component of medication deposited in the upper respiratory and increases the amount of medication reaching the lungs.

In this study, the performance of the four VHCs was evaluated using an NGI. The NGI measures Aerodynamic Particle Size Distribution (APSD) which is widely recognised as a critical quality attribute in the *in vitro* characterisation of inhaled medications. It is the APSD of an aerosol cloud that defines where the particles in that cloud are deposited in the respiratory system following inhalation. It is generally accepted that to be therapeutically effective, the particles should be < 5 µm in aerodynamic diameter since particles > 5 µm will generally impact in the oropharynx and be swallowed. Particles < 5 µm are usually labelled fine particles fraction, or respirable fraction, and are those that generally deposit in the lungs for therapeutic action.

The performance of the VHCs, in this study, has been compared for total drug delivered (as a percentage of total drug recovered) and for respirable fraction (total drug delivered < 5 µm as a percentage of total drug recovered) using two commonly used combination pMDI medications for asthma and COPD, Seretide and Fostair. The results demonstrate the four VHCs are comparable in performance.

In terms of total drug delivered, the pMDIs alone deliver more drug than any of the VHCs. However, as expected, the VHCs perform better in terms of respirable fractions than the pMDIs alone, and therefore deliver more medication to the lungs. The Space Chamber Plus, having a larger volume than the other VHCs, tends to deliver slightly more drug in the case of Fostair. Similarly and for the same reason, Space Chamber Plus appears to perform numerically better in terms of respirable fraction.

Conclusion:

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

References:

1. Devadason S. Report on particle size and output measurements of formoterol fumarate and beclomethasone dipropionate, delivered via prototype spacers, the Space Chamber *plus* and Compact Space Chamber *plus* (Medical Developments International) compared with the AeroChamber *plus* with *Flow-Vu* and the AeroChamber *plus* with *Flow-Vu* Antistatic (Trudell Medical International, University of Western Australia, Subiaco, 11 July 2013.
2. Devadason S. Report on particle size and output measurements of salmeterol xinafoate and fluticasone propionate, delivered via prototype spacers, the Space Chamber plus and Compact Space Chamber plus (Medical Developments International) compared with the AeroChamber plus with Flow-Vu Antistatic (Trudell Medical International), University of Western Australia, Subiaco, 20 August 2013.