Improving spacer delivery for low flow (paediatric) use.

Mark Sanders[1], Ronald Bruin[1], Cuong Tran[2]

[1] Clement Clarke International Ltd., Edinburgh Way, Harlow, CM20 2TT, UK.
[2] i2c Pharma Services, Cardiff Medicentre, Heath Park, Cardiff, CF14 4UJ, UK.

Background

- Children struggle to coordinate pMDI actuation with correct inhalation.
- Receipt of drug via tidal breathing is an attractive solution.
- All paediatric pMDI users should have a spacer or valved holding chamber (VHC).
- What factors are important when choosing a VHC — recommendation, prescription status, practicality, lung function ?

Introduction

- Selection is rightly influenced by scientific evaluation. However :
  - usual 30L/min flow rate assessments do not represent paediatric tidal breathing. [1]
  - at low flow rates, VHCs with open exhaust valves 'steal' inspired air and reduce drug lung deposition (**Figure 1**). [2]

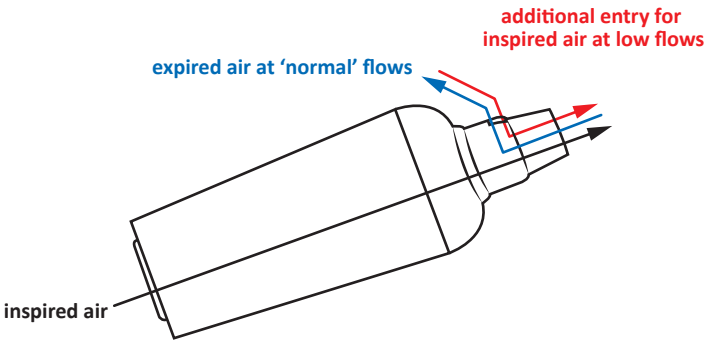

Figure 1 - **VHC routes of air flow**

Objectives

- Valve technology research to improve Able Spacer®-2 function at low flow rates.
- Deliver improved utility for young children.

Assessments

- Exemplar pMDI - 100µg salbutamol (Ventolin Evohaler®).
- Standard flow 30L/min Next Generation Impactor aerosol performance.
- Low flow 10L/min Dosage Unit Sampling Apparatus (DUSA) quantifying drug retention within the VHC.
- Three Able Spacer-2 valve assembly comparisons plus Ventolin pMDI alone.

References

1. Mitchell JP, Nagel MW. In vitro performance testing of three small volume-holding chambers under conditions that correspond with use by infants and small children. J Aerosol Med 1997; 10 (4): 341-349 (https://doi.org/10.1089/jam.1997.10.341, accessed 14/09/2017).
2. Furon E, Vanel F, Porée T, Dubus J-C. Computational fluid dynamics simulations and in vitro testing on the importance of expiratory valves for spacers. J Aerosol Med Pulmon Drug Del 2017; 30(3): A-12. Full poster available on researchgate.net
3. Oliveira RF, Silva MV, Teixeira SFCF, Cabral-Marques HM, Teixeira JCF. Efficiency of valved holding chambers: experimental full dose assessment. J Aerosol Med Pulmon Drug Del 2015; 28: A-2. Full poster available on researchgate.net

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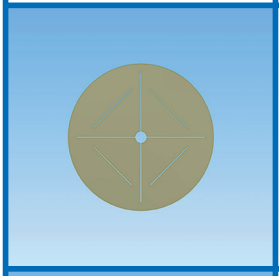
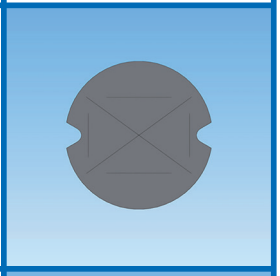
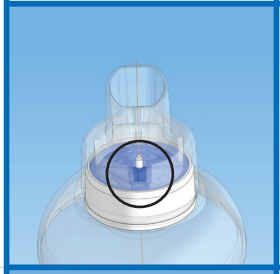
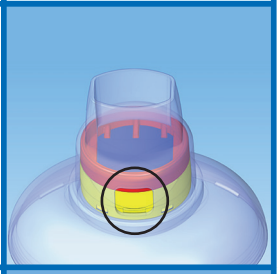
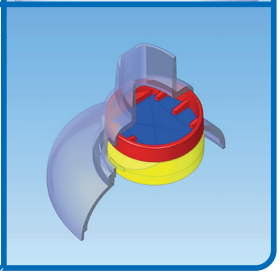
Development work

Able Spacer-2 VHC mouthpiece and valve

Current		Development examples
	Valve — additional cuts and shape change	
	Valve and chamber top support — exit port enlarged (circled)	
	New two-piece valve support — closes during inhalation	

Results

	Fine Particle Fraction (%<5µm)	Fine Particle Dose (µg<5µm)
pMDI only	47.9 ± 2.4	41.7 ± 4.4
+ Current valve	55.0 ± 2.0	55.8 ± 9.2
+ Development-1	51.8 ± 2.4	52.2 ± 9.9
+ Development-2	55.4 ± 2.5	53.1 ± 10.3

Table 1 - **Similar key aerosol characteristics at 30 L/min (mean ± SD)**

	µg recovered per actuation	% recovered of emitted dose
pMDI only	82.1 ± 5.8	≡ 100.0
+ Current valve	43.6 ± 6.5	49.4 ± 6.3
+ Development-1	45.1 ± 2.8	56.6 ± 4.4
+ Development-2	52.7 ± 4.5	58.0 ± 2.1

Table 2 - **Improved DUSA recovery at 10 L/min (mean ± SD)**

Conclusions

- *"In vitro measurements made at constant high flow rates in excess of 20 L/min do not reveal [these] differences in performance that are clinically significant, and may lead the physician to prescribe a device that under certain conditions may not deliver any drug to infants or small children."* [1]
- At low flow rates, the current research demonstrates improved performance using new valve assemblies.
- The data also demonstrate improvements on previous low flow, dose uniformity comparator research. [3]