

# Differences among three pMDI products labeled to deliver the same dose of albuterol sulfate

## An example of the Importance of Holding Chambers

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### Introduction

Three albuterol sulfate (AbS) pressurized metered-dose inhaled (pMDI) products (Ventolin® HFA, Proventil® HFA and ProAir® HFA) are labeled to deliver the same Total Dose (TD) of drug per actuation (108 µg AbS or 90 µg Albuterol).<sup>1,2,3</sup> It is widely known within the field of inhalation drug delivery that the portion of the dose which is “respirable” (i.e. reaches the lungs) and therefore results in the desired efficacy, has a particle size <5 µm.<sup>4</sup> This is often called the Fine Particle Dose (FPD). The difference between the TD and the FPD is “non-respirable” and referred to as the Course Particle Dose (CPD). Therefore, equivalence in dose for inhaled medications should be based upon the “respirable” FPD, and not the CPD or TD.

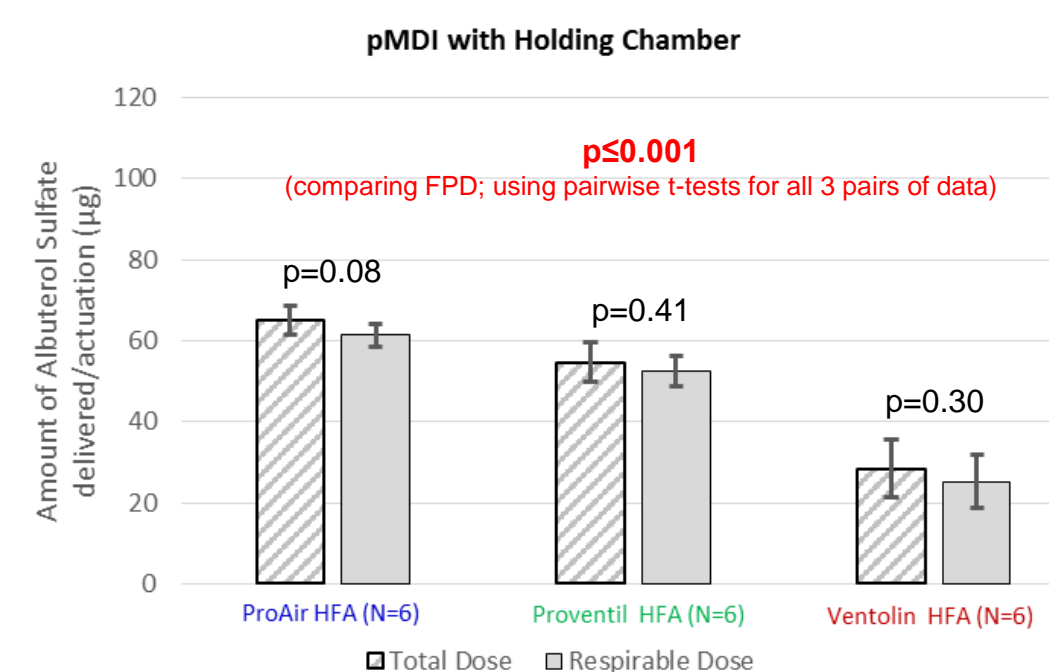
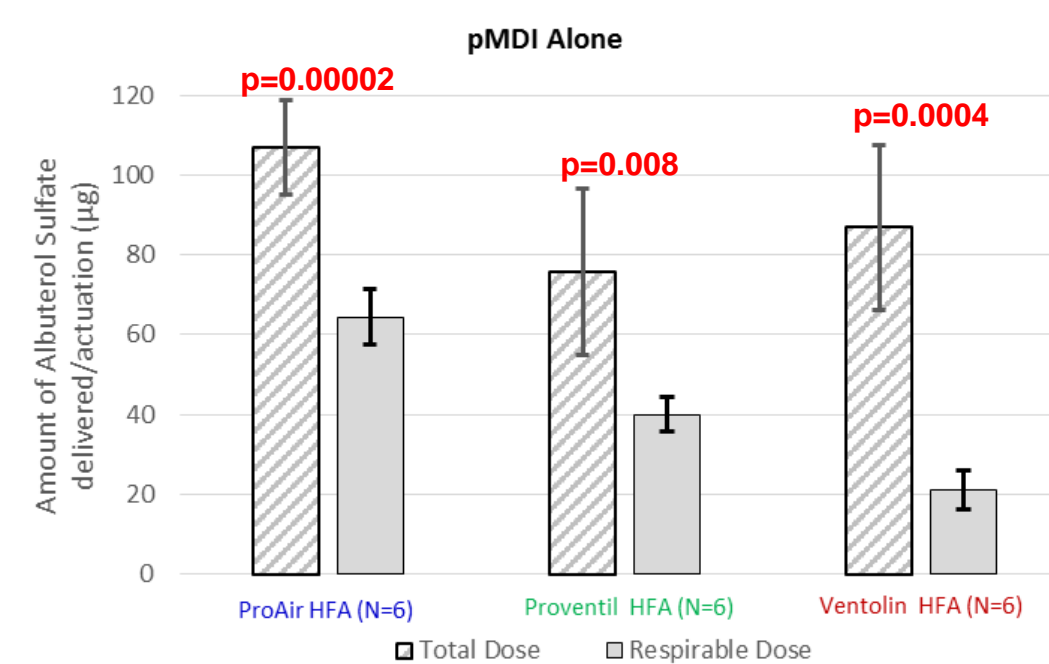
### Methods

Ventolin® HFA, Proventil® HFA and ProAir® HFA, were each purchased in triplicate. Particle size distributions of AbS in each product were obtained 6 times by 8-stage Anderson Cascade Impactor and analyzed by validated HPLC using UV detection at 276 nm. Repeat analyses were again carried out 6 times for each drug product, but also added the use of a collapsible Valved Holding Chamber (VHC) called the LiteAire®.<sup>5</sup> Various data comparisons were made.

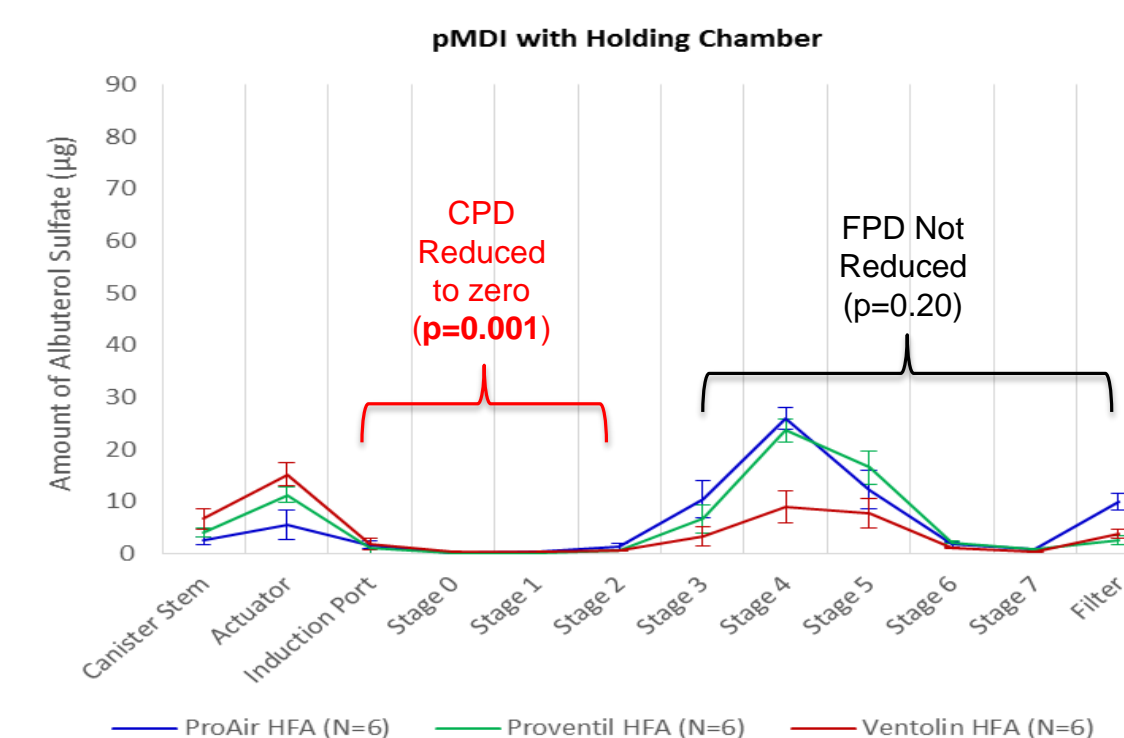
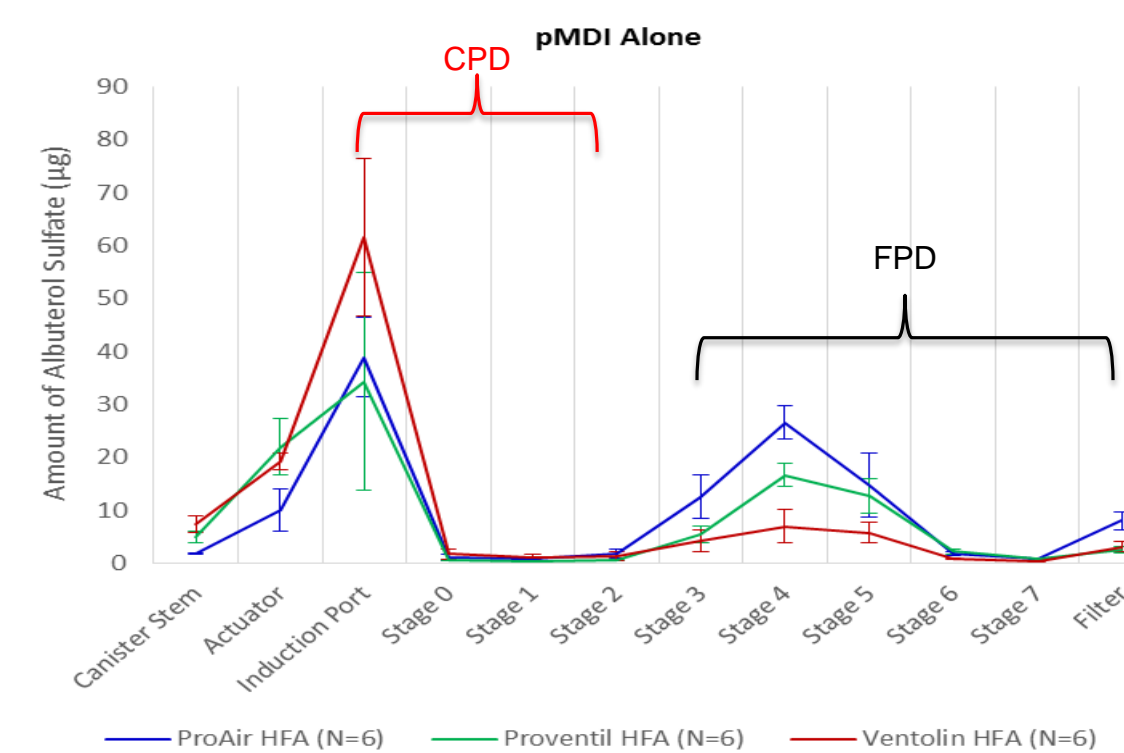


**Figure 1.** Products tested. Ventolin® HFA<sup>1</sup>, Proventil® HFA<sup>2</sup> and ProAir® HFA<sup>3</sup> (shown on the left) and LiteAire® VHCs<sup>5</sup> (shown on the right) are displayed in both collapsed and popped up form.

### Results



**Figure 2.** Resulting Total Dose (TD) and Fine Particle Dose (FPD) testing of ProAir HFA, Proventil HFA and Ventolin HFA without a VHC (top graph) and with a VHC (bottom graph).



**Figure 3.** Resulting particle size distributions obtained from Anderson Cascade Impactor testing of ProAir HFA, Proventil HFA and Ventolin HFA without a VHC (top graph) and with a VHC (bottom graph).

**Table 1.** Cost Comparison of pMDIs based on FPD normalization

	ProAir® HFA	Proventil® HFA	Ventolin® HFA
Mean Price/MDI <sup>1</sup>	\$61.88	\$73.23	\$54.22
Mean Price/actuation <sup>2</sup>	\$0.31	\$0.37	\$0.27
FPD/TD	58%	49% (w/ VHC) or 37% (pMDI alone)	22%
Actuations necessary for FPD=Mfr Label Claim	2	2 or 3	5
Price to achieve 108 µg AbS dose in FP size <sup>3</sup>	\$0.62	\$0.74 or \$1.11	\$1.35
Number of 108 µg AbS doses in FP size present in pMDI	100	100 or 66	40

<sup>1</sup>Mean values are the result of CVS, Target, Walgreens, Walmart and Fry's Pharmacy non-discounted prices.

<sup>2</sup>Assuming 200 actuations/canister.

<sup>3</sup>All 3 products are labeled to deliver 108 µg of albuterol sulfate (90 µg of albuterol) in each actuation.

### Conclusions

**Dose collection and Sizing studies [Figures 2 & 3] suggest the following may be true:**

- Without the VHC, the FPD in each product is significantly less than the TD ( $p \leq 0.008$ ). [Figure 2, top graph]
- AbS FPDs in all 3 products ProAir® HFA (~64 µg), Proventil® HFA (~40 µg) and Ventolin® HFA (~21 µg) are significantly different from each other ( $p \leq 0.0001$ ). [Figure 2, bottom graph, red font]
- With the VHC, the CPD is reduced to ~0 µg ( $p = 0.001$ ) while the FPD is not reduced ( $p = 0.20$ ). [Figure 3]

**Cost/Dose Analysis [Table 1] suggests the following may be true:**

- ProAir® HFA is 2.5 times more economical than Ventolin® HFA.
- ProAir® HFA is 1.5 times more economical than Proventil® HFA without a VHC; but equivalent when a VHC is used.
- Proventil® HFA is 2.5 times more economical than Ventolin® HFA with a VHC and 1.6 times without a VHC.
- Reported TD may not be the most appropriate way to label MDI products
- The value of using a VHC can be dramatic

### References

- ProAir HFA Package Insert. TEVA Respiratory. LLC/IVAX Pharm, © 2012
- Proventil HFA Package Insert. 3M Pharm/Key Pharm/Merck & Co, © 2012
- Ventolin HFA Package Insert. Glaxo Smith Kline, © 2012
- Brocklebank, D. *et al*, *Health Technol Assess*, 2001; 5, p 1-149.
- LiteAire VHC Package Insert, Thayer Medical, © 2015