

# PARTICLE SIZE CHARACTERIZATION ANALYSIS – A COMPARISON STUDY BETWEEN ANDERSEN CASCADE IMPACTOR, NEXT GENERATION IMPACTOR, AND MALVERN SPRAYTEC®

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## INTRODUCTION

The particle size analysis of aerosols generated from pressurized metered dose inhalers (pMDIs) is typically characterized using a multistage impactor to obtain aerodynamic particle size, which is an indication of anticipated deposition site within the respiratory tract<sup>1</sup>.

Recently introduced in the United States Pharmacopeia (USP), the Next Generation Impactor (NGI) was developed to improve the aerodynamic characteristics<sup>2</sup>. However, multistage impactor testing is labor intensive and time consuming. Therefore, in this study, the Malvern Spraytec® 97 system which provides in-situ, real-time measurements of the particle size distribution of aerosol droplets was evaluated and compared to particle size analysis obtained from Andersen Cascade Impactor (ACI) and NGI.

Tempo™ breath synchronized, plume controlled inhaler (BSPCI, Figure 1) is a breath synchronous trigger device with a flow control chamber that releases drug upon patient inhalation and controls the aerosol plume to drive enhanced aerosol performance.



Figure 1: Tempo BSPCI

## MATERIALS AND METHODS

- Compound A micronized crystals (volume median diameter < 3.0 µm) were formulated into aluminum canisters with HFA propellant. Proventil® Hydrofluoroalkane (HFA) pMDI (3M) was investigated as a comparison commercially available product.
- Aerosol performance was performed using a 0.3 mm commercially available reference actuator and Tempo using the following techniques:
  - 8-stage Andersen Cascade Impactor, operating at 28.3 L/min.
  - Next Generation Impactor, operating at 30 L/min.
  - Malvern Spraytec coupled with the inhalation cell (400 ms data collection in flash mode with USP induction port attached) operating at 28.3 L/min.
- The analysis was performed where appropriate using HPLC with a UV detection at 276 nm.

## RESULTS

• Overall drug deposition profiles from ACI and NGI (Figures 2 and 3) appeared to be similar.

• Aerosol performance generated from Tempo was improved with the following key results:

> Throat deposition from ACI and NGI was reduced 27.8% by Tempo.

> Fine particle dose (FPD) < 4.7µm was increased 30.8% relative to the reference actuator.

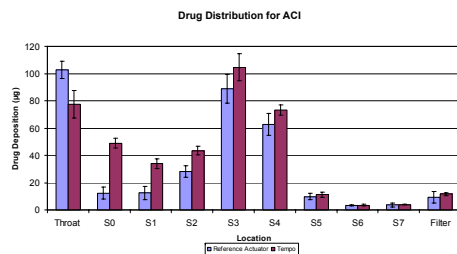


Figure 2: ACI drug deposition profile of Compound A pMDI from reference actuator vs. Tempo (n = 3).

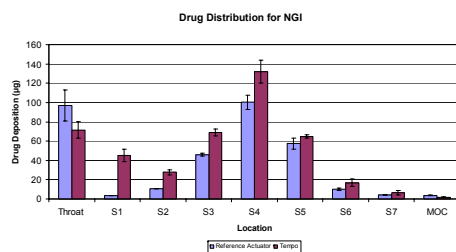


Figure 3: NGI drug deposition profile of Compound A pMDI from reference actuator vs. Tempo (n = 3).

\*MOC = Micro orifice collector

## RESULTS CONTINUED

• Comparison of particle size generated from Proventil, Compound A pMDI using reference actuator, and Compound A using Tempo was evaluated with ACI, NGI, and the Spraytec (Figure 4). As expected, NGI suggested smaller MMADs (Mass Median Aerodynamic Diameters) than the ACI<sup>2,3</sup>.

• Correlation between the Spraytec Dv50 laser diffraction values and the MMAD values from the ACI and NGI data was found to be 0.9949 and 0.9594, respectively.

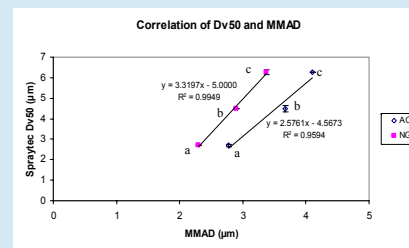


Figure 4: The correlation of Dv50 (µm) and MMAD (µm) values from Spraytec, ACI, and NGI (a) Proventil HFA (b) Cmpd A pMDI using reference actuator (c) Cmpd A using Tempo (n = 5).

## DISCUSSION

• For Compound A pMDI using reference actuator and Tempo, the Dv50 values were found to be larger than MMADs which may be due to Spraytec measurements that occur within milliseconds from the point of the release of aerosol droplets<sup>3</sup>.

• When sampling at 30 L/min from the ACI or NGI, there was a two-second residence time which would allow more time for the evaporation to occur<sup>4</sup>.

• The presence of non-spherical particles may result in an upward shift in volume distribution.

• Dv50 values were in close agreement to MMADs for Proventil HFA. This correlation may be due to the finer particle size of Proventil which allows a more complete evaporation.

## CONCLUSION

Although the laser diffraction technique provides measurement data of particle size rapidly, the presence of non-spherical particles in the formulation may reduce the potential to establish meaningful correlations due to aerodynamic differences.

This study demonstrated discrepancies when light scattering was used to quantify particle size distribution in comparison to cascade impactors.

A careful selection of aerodynamic particle size characterization techniques for new aerosol drug formulations should be considered and evaluated. No single technique is appropriate for all formulations.

## REFERENCES

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