

The Effects of Inhalation Flow Rate on Aerodynamic Particle Size Distribution of Commercial Solution and Suspension Metered Dose Inhalers (MDIs)

Abhinav R. Mohan¹; Sneha Dhapare¹; Bryan Newman¹; Mårten Svensson²; Peter Elfman²; Lawrence Winner³; Jürgen Bulitta⁴; and Günther Hochhaus⁴

¹ Office of Research and Standards, Office of Generic Drugs, Center for Drug Evaluation and Research, Food and Drug Administration, Silver Spring, MD, US

² Emmace Consulting AB, Medicon Village, SE-223 81 Lund, Sweden

³ Department of Statistics, College of Liberal Arts and Sciences, University of Florida, Gainesville, FL, US

⁴ Department of Pharmaceutics, College of Pharmacy, University of Florida, Gainesville, FL, US

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Disclaimer

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Introduction

- The goal of this research is to investigate the **effects of inhalation flow rates on the in vitro APSD** of various commercial suspension and solution MDIs available in the United States
- A systematic evaluation of the effect of four flow rates - **30, 45, 60, and 90 LPM** on the APSD in 11 commercial MDIs was conducted

Product	Strength(s)	Formulation Type
ADVAIR® HFA	0.045 mg/inh; EQ 0.021 mg base/inh	Suspension
ALBUTEROL SULFATE INHALATION AEROSOL METERED*	EQ 0.09 mg base/inh	Suspension
ALVESCO®	0.08 mg/inh	Solution
ASMANEX® HFA	0.05 mg/inh	Suspension
ATROVENT® HFA	0.021 mg/inh	Solution
BEVESPI AEROSPHERE™	0.0048 mg/inh; 0.0090 mg/inh	Suspension
FLOVENT® HFA	0.044 mg/inh	Suspension
PROAIR® HFA	EQ 0.09 mg base/inh	Suspension
PROVENTIL® HFA	EQ 0.09 mg base/inh	Suspension
QVAR® REDIHALER™	0.04 mg/inh	Solution
SYMBICORT®	0.08 mg/inh; 0.0045 mg/inh	Suspension

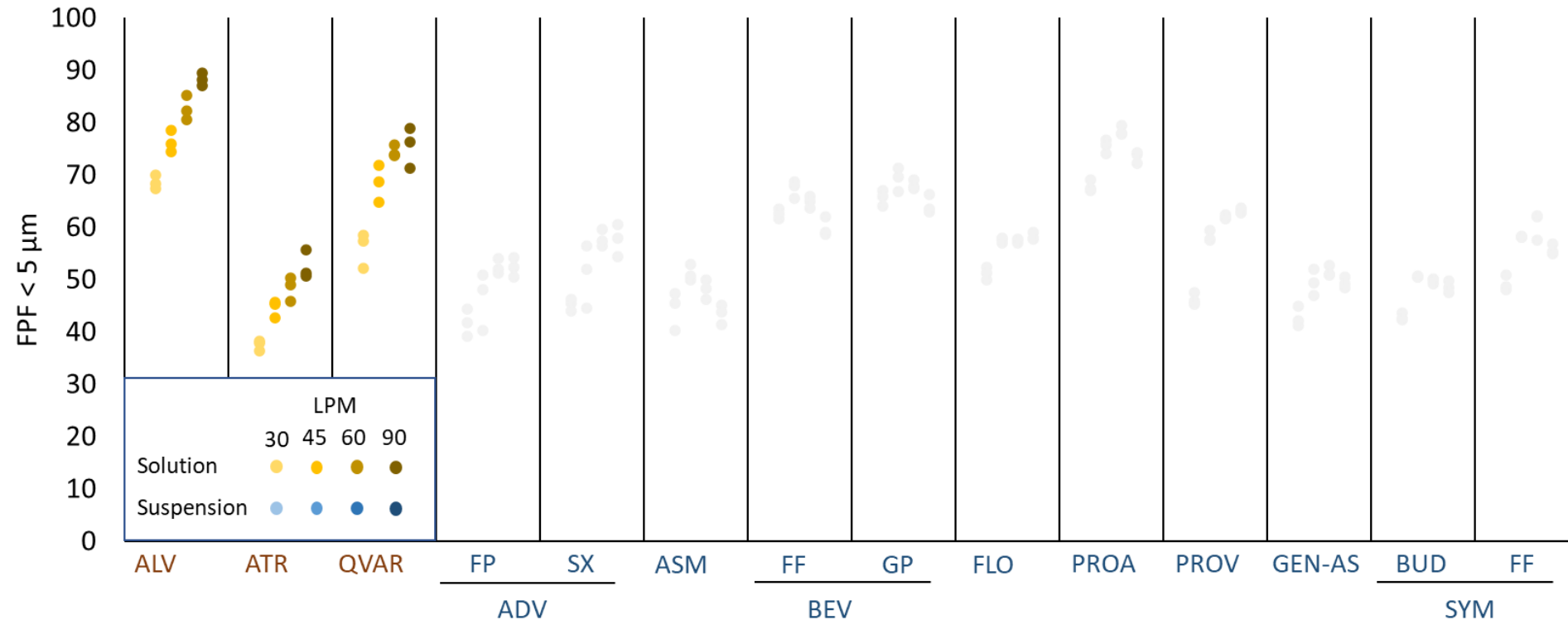
* Manufactured by Cipla Ltd.

Methods

- **Fine particle fractions** of particles smaller than $5\ \mu\text{m}$ ($\text{FPF} < 5\ \mu\text{m}$; fine particle dose divided by total emitted dose), **mass median aerodynamic diameter** (MMAD) and **impactor stage mass** (ISM) were determined from the next generation impactor (NGI) stage deposition as described in USP <601> at different flow rates.
- A statistical model built in RStudio using **flow rate**, **formulation type**, and their interaction as effect factors in a linear regression were evaluated to distinguish effects of flow rate by formulation type (solution vs. suspension).

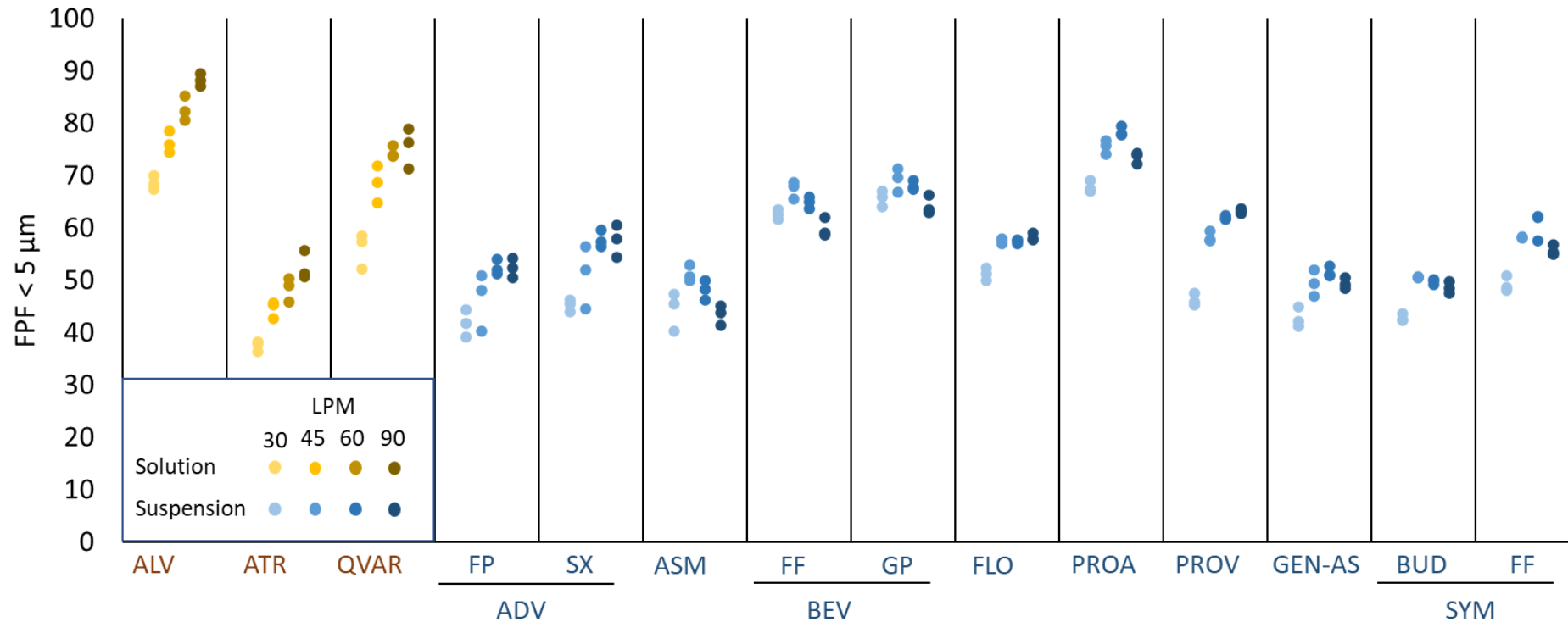


Results: FPF < 5 μm



- **Solution** MDIs exhibited a linear change in FPF < 5 μm with respect to flow rate

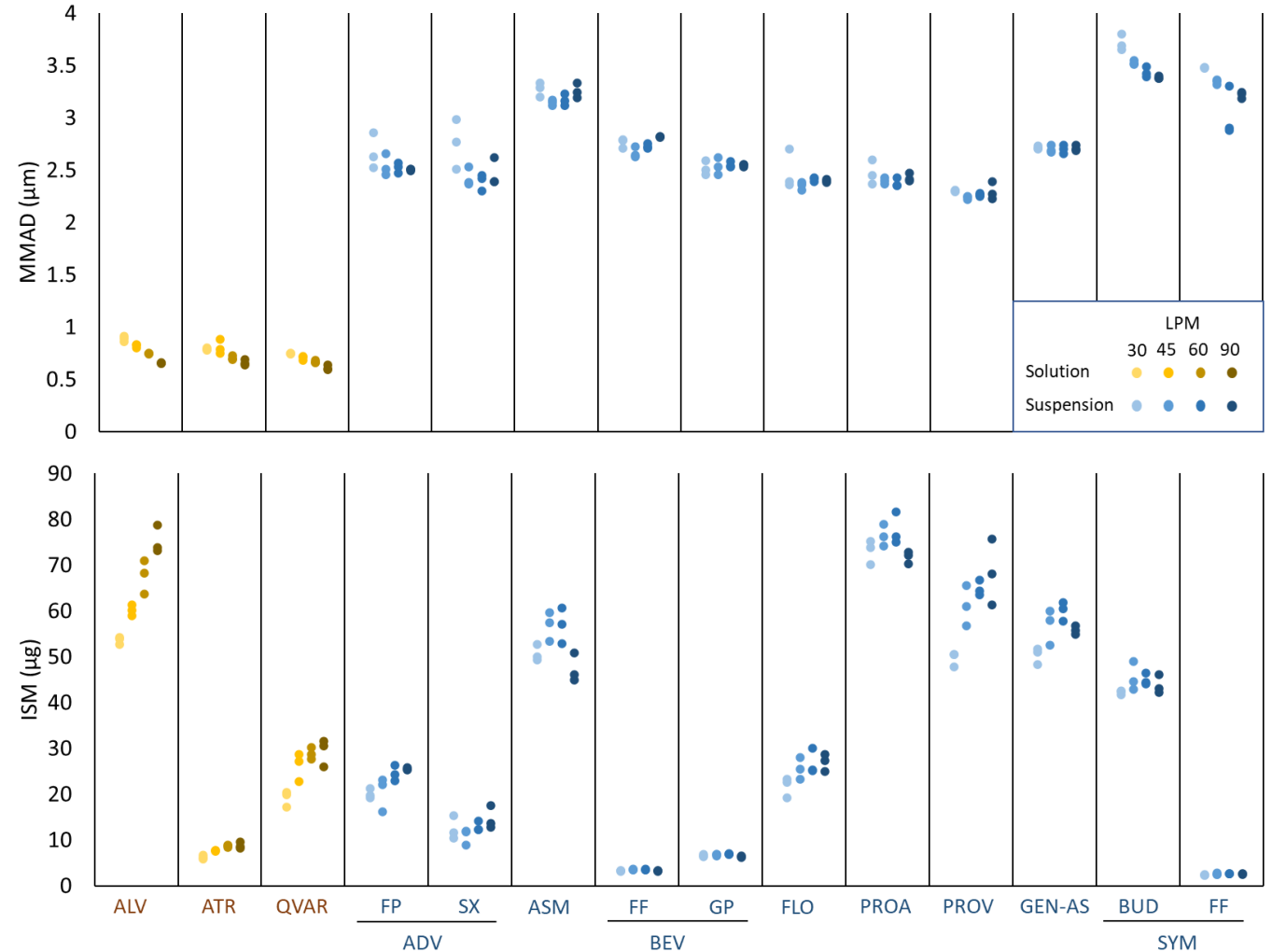
Results: FPF < 5 μm



- In case of **suspension** MDIs, the effects of flow rate depended on the product

Results: ISM and MMAD

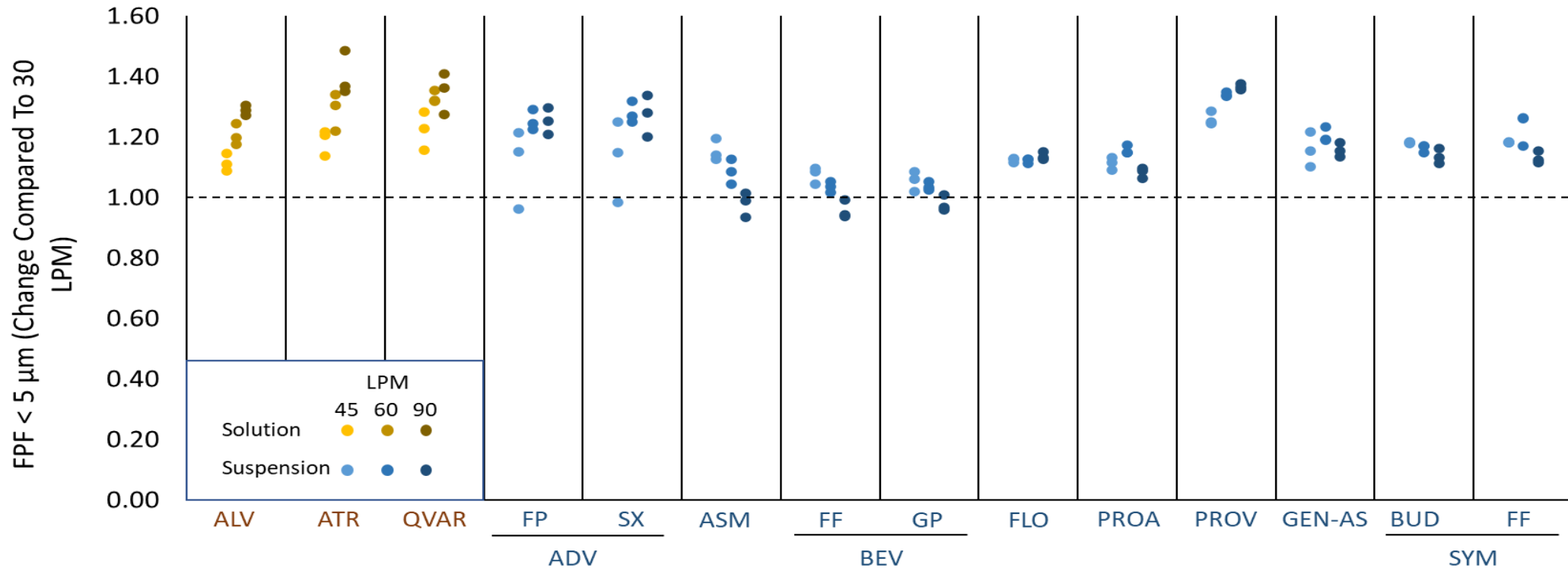
- The same trend with respect to flow rate was observed for **MMAD**, with respect to solution and suspension MDIs
- While a linear trend in **ISM** was observed for solution MDIs, it was not statistically significant



p-values from the linear regression model

Formulation type	Suspension	Solution
FPF < 5 µm	0.0274	1.00E-04
MMAD (µm)	0.0106	0.0048
ISM (µg)	0.5439	0.1853

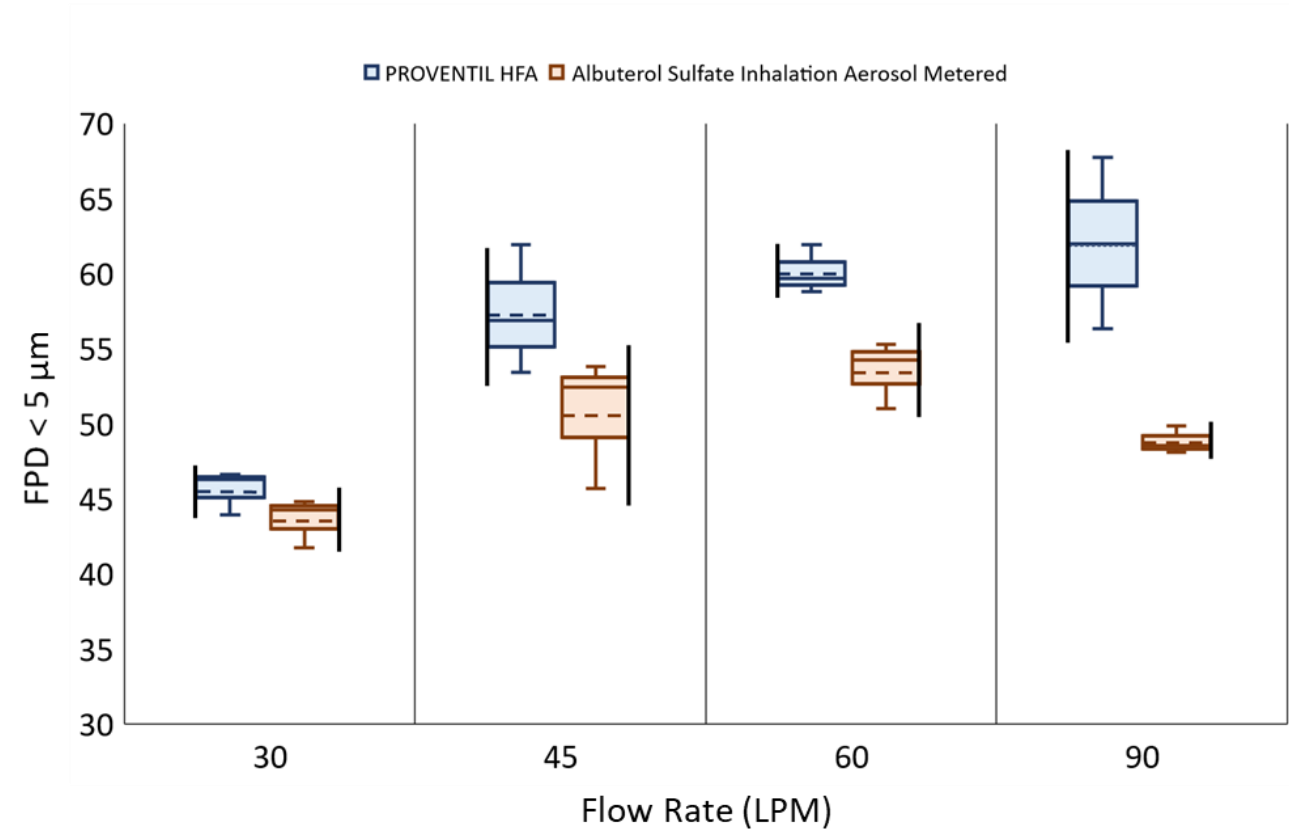
Results: FPF < 5 μm



- In case of **suspension MDIs**, no significant changes in FPF < 5 μm were found at flow rates higher than 45 LPM (e.g., 45 LPM vs. 60 LPM, 60 LPM vs. 90 LPM)

Results: PROVENTIL HFA and its generic

- Similar changes were observed in FPD<5 μm with flow rates up to 60 LPM.
- **Significant differences** in FPD< 5 μm at a flow rate of **90 LPM**.
- Additional studies are warranted to understand the relevance of APSD measurements at higher flow rates.



FPD: fine particle dose

Conclusions

- Inhalation flow rates showed significant effects on APSD parameters for **both solution and suspension MDIs**.
- While solution MDIs exhibited an almost **linear change** in FPF < 5 μm , ISM, and MMAD with increasing flow rate, most suspension MDIs showed **no significant effects** on these APSD parameters at higher flow rates.
- Additional studies are warranted to evaluate if MDI performance properties like APSD at higher airflow rates should be considered for the assessment of BE of solution MDIs.

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Questions?



Abhinav Mohan, PhD

ORISE Postdoctoral Fellow

Division of Therapeutic Performance, Office of Research and Standards

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Abhinav.Mohan@fda.hhs.gov

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