

In Vitro Scoping Study of a Dry Powder Inhaler Using Clinically Possible Abnormal Inhalation Profiles for Emitted Aerosol Aerodynamic Particle Size Distribution at Low Peak Inspiratory Flow Rates

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S U M M A R Y

Realistic breathing profiles attempting to mimic the treatment asthma exacerbation with a DPI, lacked sufficient “power” to properly break up the powder, a clinical concern for patients with weak inhalation.

INTRODUCTION

BACKGROUND

- SABA monotherapy provides short term relief of bronchoconstriction
- Lab-measured Inhalation profiles can indicate how the patient interacts with their inhaler (DPI)
- Peak inspiratory Flow Rate (PIFR) is viewed as diagnostically important

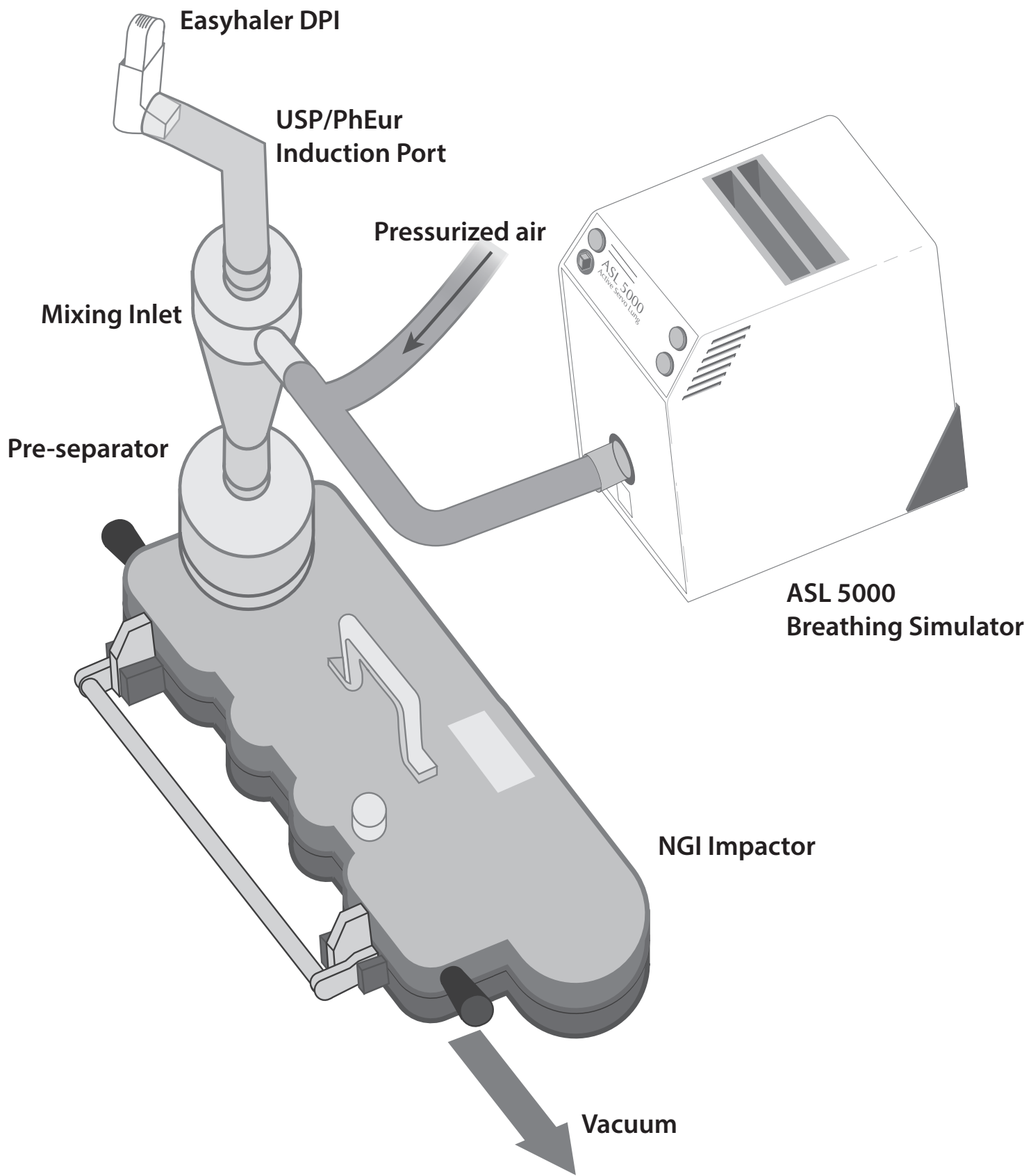
STUDY PURPOSE

- We evaluated delivery from a passive DPI with different inhalation profiles:
- PIFR was reduced by 10 L/min decrements from 60 to 40 L/min
- This process mimicked potential use by an asthmatic patient experiencing increasingly severe exacerbations.



MATERIALS & METHODS

- The performance of a salbutamol Easyhaler DPI assessed by Next Generation Impactor (NGI), and pre-separator
- Aerosol ex DPI entered a USP/ PhEur induction port followed by a Mixing Inlet (MI)
- MI enabled PIFR at the DPI mouthpiece to be controlled without changing the flow rate of the impactor
- Emitted aerosol APSD characterized by NGI with pre-separator at 60 L/min



METHODOLOGY

- n = 5 replicate measurements at each condition
- Inhalation flow profiles (Figure 1) created enabling the PIFR to be decreased as described previously
- Inhalation volume of 500cc chosen to mimic adult DPI use
- Salbutamol recovered quantitatively from all surfaces in the apparatus
- Fine particle mass (FPM_{<4.5µm}) and fine particle mass fraction (FPF_{<4.5µm}) assessed from the cumulative mass of API recovered from stages 2 to the MOC

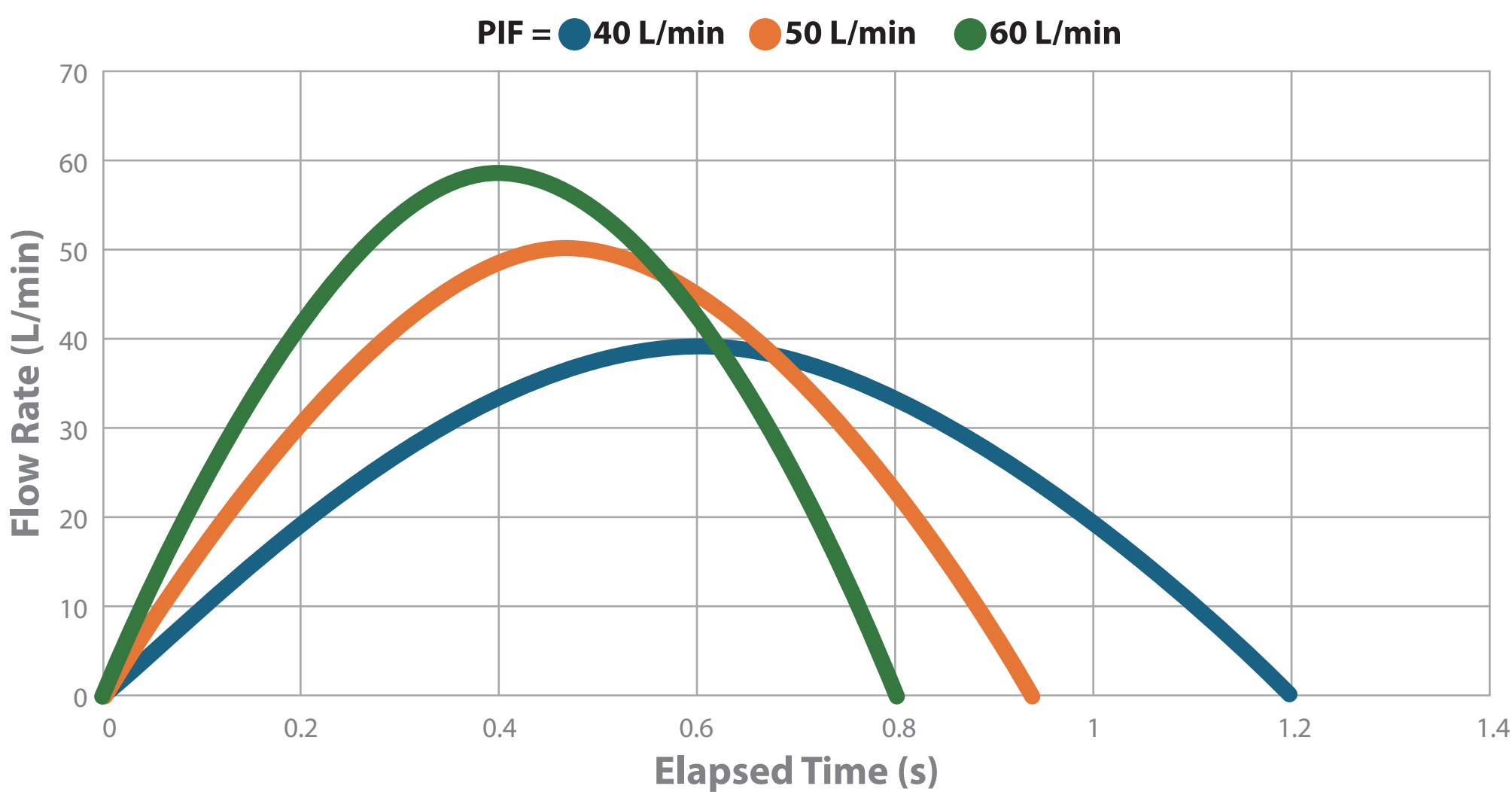
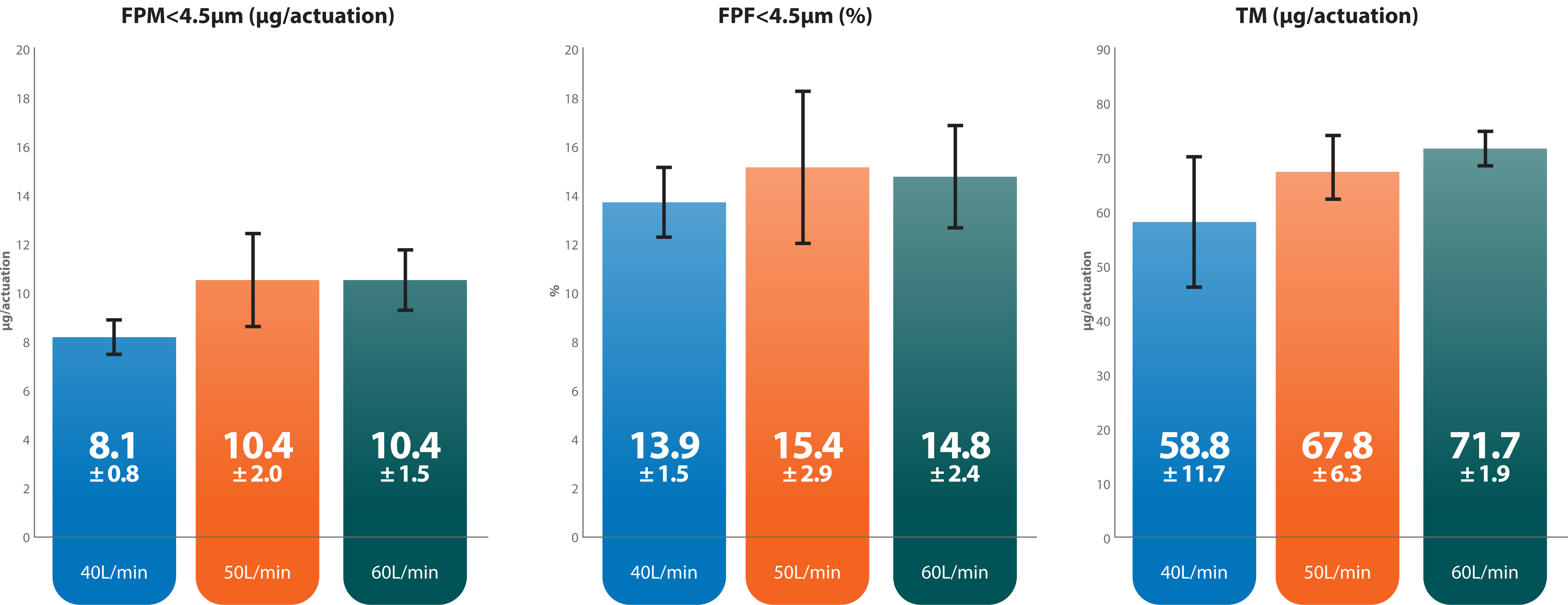


Figure 1
Inhalation Flow Rate-Time Profiles to Achieve Each PIFR

RESULTS

- These figures below show the NGI-Derived Metrics for Easyhaler DPI as a Function of PIFR



DISCUSSION

- There was an insignificant difference in TM or FPM_{<4.5µm} when comparing data at PIFR values of 50 vs. 60 L/min or 40 vs. 50 L/min ($p \geq 0.12$).
- FPF_{<4.5µm} was comparable at all three PIFR values (40, 50, and 60 L/min), again with an insignificant difference between them ($p \geq 0.05$).
- FPM_{<4.5µm} decreased slightly when from PIFR= 60 L/min to 40 L/min ($p = 0.03$).
- However, FPF_{<4.5µm} in all cases were much lower than anticipated for a nominal 100µg/actuation product.
- They were also smaller than equivalent values delivered by the equivalent salbutamol pMDI, which is patient effort-independent!

CONCLUSIONS

- The DPI delivered a significantly smaller FPM_{<4.5µm} than at all PIFRs expected, suggesting the realistic breathing profiles attempting to mimic an asthma exacerbation, lacked sufficient “power” to properly disaggregate the powder.
- This outcome is a clinical concern for patients experiencing a severe asthma exacerbation (who would have a weak inhalation)
 - Such users might not receive an adequate rescue dose with a single puff.
- Further considerations:
 1. The actual dose needed for a response may be small enough to be achieved with repeated inhalations,
 2. Using a combination (MART) therapy is often more effective for controlling exacerbations