Aerodynamic Particle Size Distribution Analysis of High Dose pMDIs using the Next Generation Impactor (NGI)

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INTRODUCTION

Development of the Next Generation Impactor, (NGI) by an industry consortium of 15 pharmaceutical companies was carried out to overcome some of the limitations observed in the current Andersen cascade impaction particle sizing technique. The NGI in particular was developed for the analysis of pressurised metered dose (pMDI) and dry powder inhalers (DPI) to allow:

- Easier and more efficient analysis
- Ease of Automation
- Provide more accurate stage cut-off's
- Improve inter-stage dynamics thereby limiting losses outside that impacted onto the surface of the collection cups

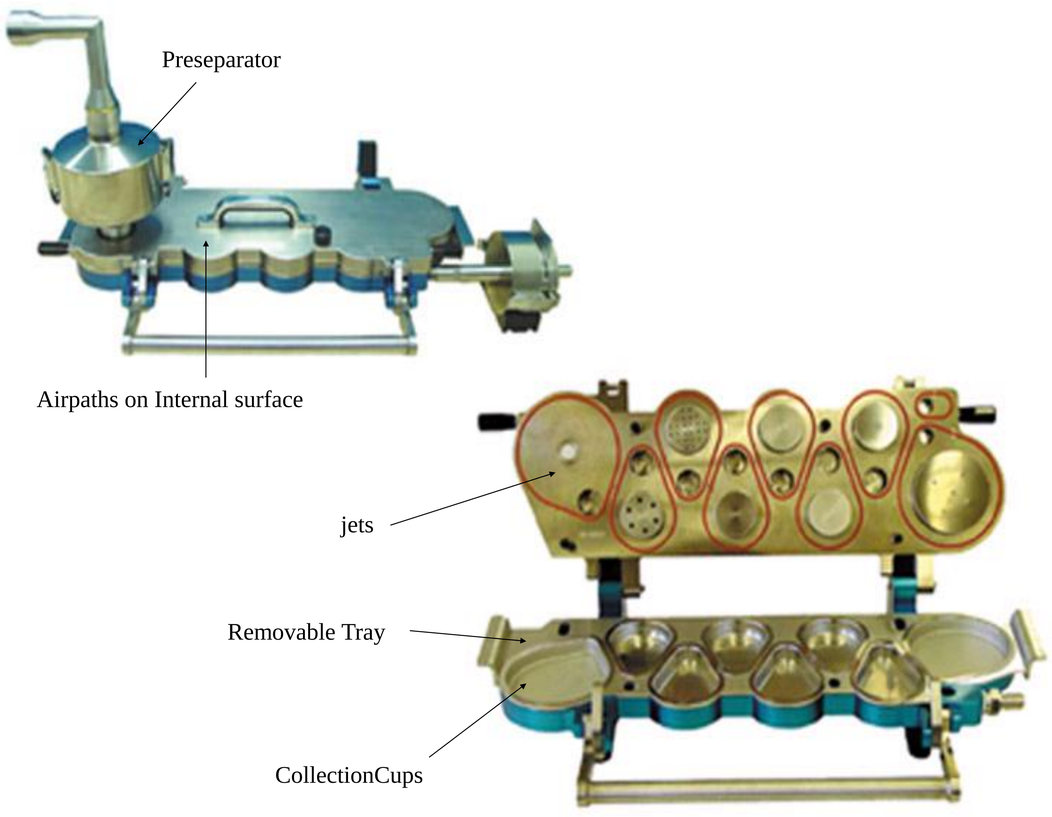

Figure 1: NGI Impactor Components

BACKGROUND

One of the current aims of the Inhalation Centre of Excellence, (ICE) is to produce a high dose inhaler product in the order of 10 mg/actuation. Analysis was performed using the NGI to benefit from the faster analysis times. However, relatively little was known about the NGI performance with high dose products and whether it would become overloaded with drug. As part of the study overloading effects in the NGI due to the high dosing was evaluated.

EXPERIMENTATION

The suitability of the NGI to receive high doses was evaluated by performing the following investigations:

1. Repetitive firing of a 160 µg/actuation product onto the NGI impactor to mimic both high and low loading on the impactor. (approximate loading range of 960 µg and 4800 µg)
2. Single actuation of a 10 mg/actuation product onto the NGI impactor.
3. Single actuation of 2 mg/actuation low density porous particles onto NGI Impactor.

For all of the above experiments an assessment of the recovery achievable from the collection cups was made, in addition the amount of drug retained in airpaths and jets were quantified.

RESULTS

1. HIGH AND LOW LOADING ON THE NGI IMPACTOR

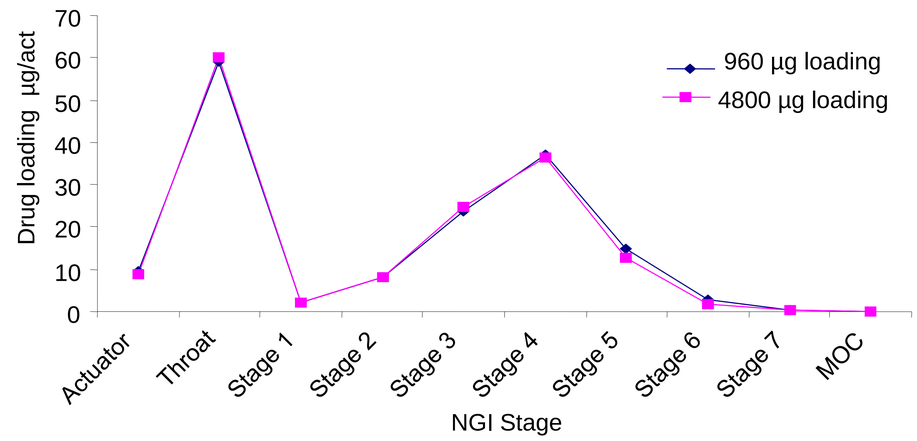

Figure 2: Effect on Impaction profile produced between high and low loading on the NGI

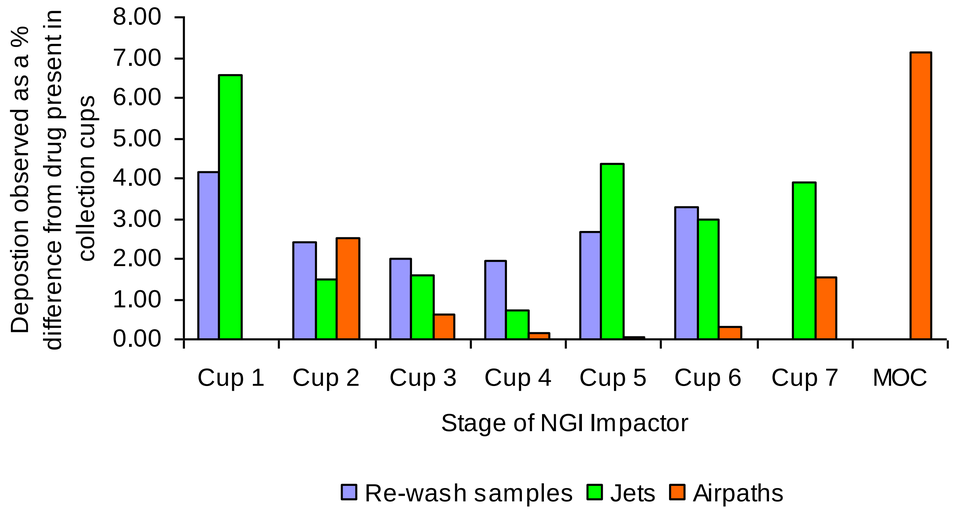

Figure 3: Deposition observed in the high loading (4800 µg) of the NGI Impactor

- Comparable impactor results produced for both high and low loading of the NGI.
- Deposition is highest in the jets of the NGI however this is < 10 % of the drug found in the cups.
- Deposition in jets as a total of drug impacted is < 1.6 %.
- > 95% of all drug is recovered in the first washing.

2. HIGH DOSE SAMPLES

- Increased jet deposition observed on collection of 10 mg/actuation product.
- Approximately 5 % of total drug remains on the jets.
- Deposition profile on the NGI is reproducible between samples.

3. LOW DENSITY HIGH DOSE POROUS PARTICLES

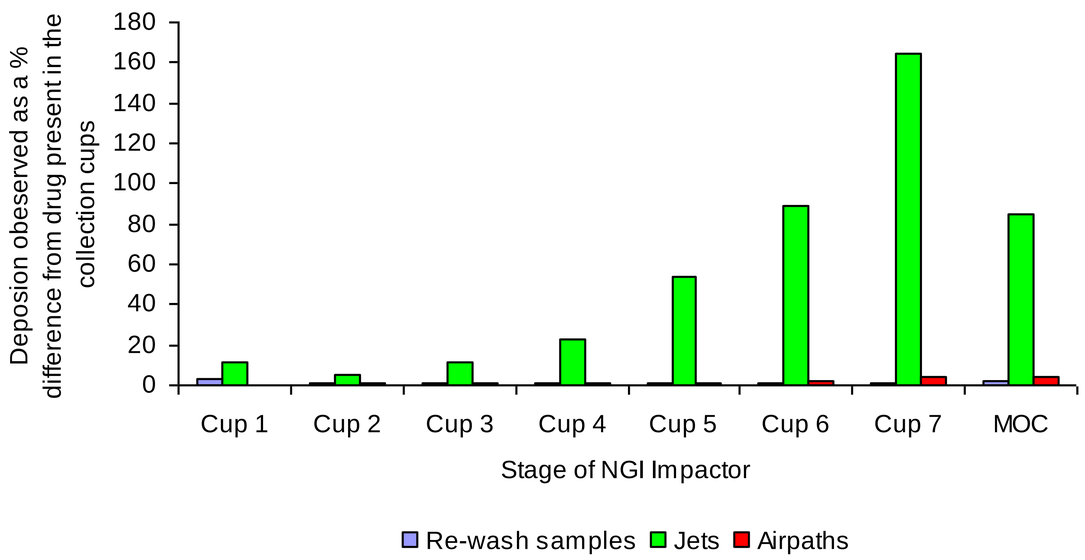

Figure 4: Deposition observed in the loading of the NGI Impactor with low density porous particles

- > 98% of drug impacted onto collection cups was recovered in the first wash.
- > 30 % of the total drug has impacted onto the jet surface
- Drug appears to be re-impacted on the jet surface above collection cups, (re-entrainment effects).
- < 1% of the total drug was impacted on the airpaths.
- Unexpected loading pattern observed on cup surface observed, (see figures 5 and 6).

COMMENTS

The low density porous particles may become re-entrained within the NGI due to:

- Low density particles have correspondingly low aerodynamic diameter and are more easily re-circulated through the NGI.
- Low density particles have different inertia and momentum through the impactor, hence a difference in the impaction profiles occurs.

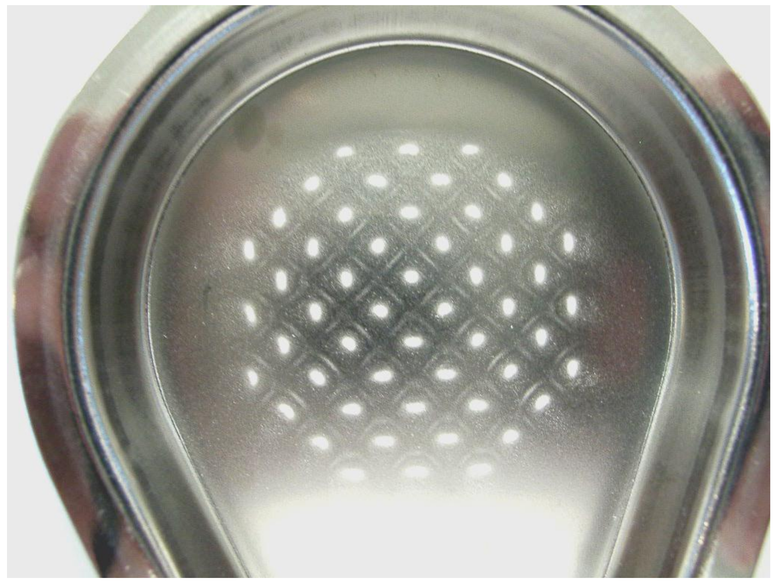

Figure 5 : Unexpected loading pattern – lines observed on plate between impaction areas

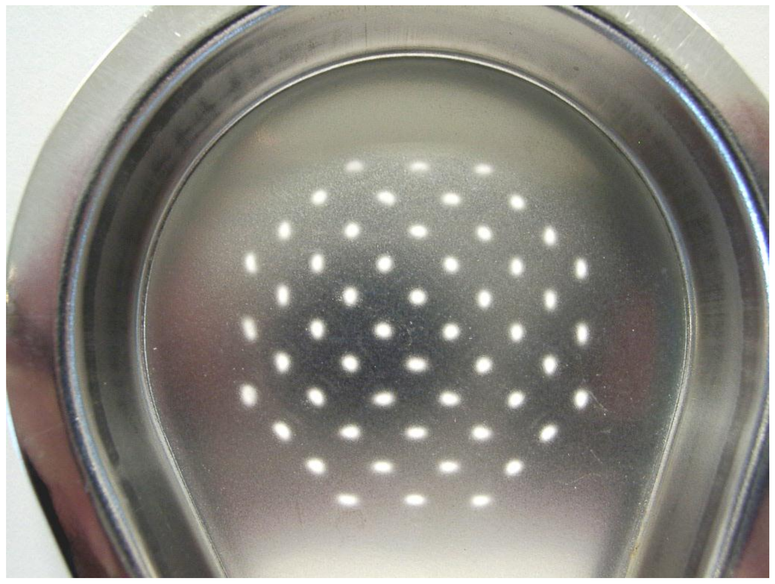

Figure 6 : Expected loading pattern

FURTHER WORK ON LOW DENSITY PARTICLES

Further investigation were performed on the low density particles using brij coating on the NGI cup surface.

Re-entrainment on the jet surface was found to be significantly reduced. <6 % of the total drug was found in the jets and airpaths of the NGI. Discussion of this work however is outside the scope of this poster.

CONCLUSIONS

- Multiple firing of low dose products onto the NGI produces comparable data, without any significant losses observed in either the jets or the air-paths.
- Increasing the dose leads to increased drug deposition in the jets.
- Low density particles appear to become re-impacted on the surface of the NGI and especially upon the jets.

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