Further developments of a mathematical model for simulation of Aerodynamic Particle Size Distributions on Cascade Impactors

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Introduction

There are many factors which can influence cascade impaction results[1,2] and much time is spent in the pharmaceutical industry troubleshooting unusual particle size distributions [3,4,5].

3M HealthCare Ltd in conjunction with the Mathematics Department, Loughborough University have developed a mathematical model which can be used to simulate the performance of the ACI (Andersen Cascade Impactor) for pharmaceutical inhaled products [6]. Since 2009, this model has been updated to operate for both the ACI and NGI (Next Generation Impactor).

Methodology

The model uses a Monte Carlo algorithm to select a statistically large number of particles, typically a million, with a particle size distribution defined by the MMAD (Mass Median Aerodynamic Diameter) and GSD (Geometric Standard Deviation) of the product, assuming a lognormal distribution. The model then takes each particle in turn and determines which plate the particle will impact on, assuming the stage has a perfect cut point (See Figure 1) and the size of its holes are normally distributed. The model then calculates the mass of particle deposits on the plate of each stage. The model profiles the deposition on the cascade impactor, and does not attempt to simulate Throat deposition or interstage losses. The features of the model are:

- Predicts filter and plate deposition on each stage of the ACI and NGI at a range of air flowrates.
- Allows input of nozzle size data and particle density enabling simulation of 'real' set-ups.

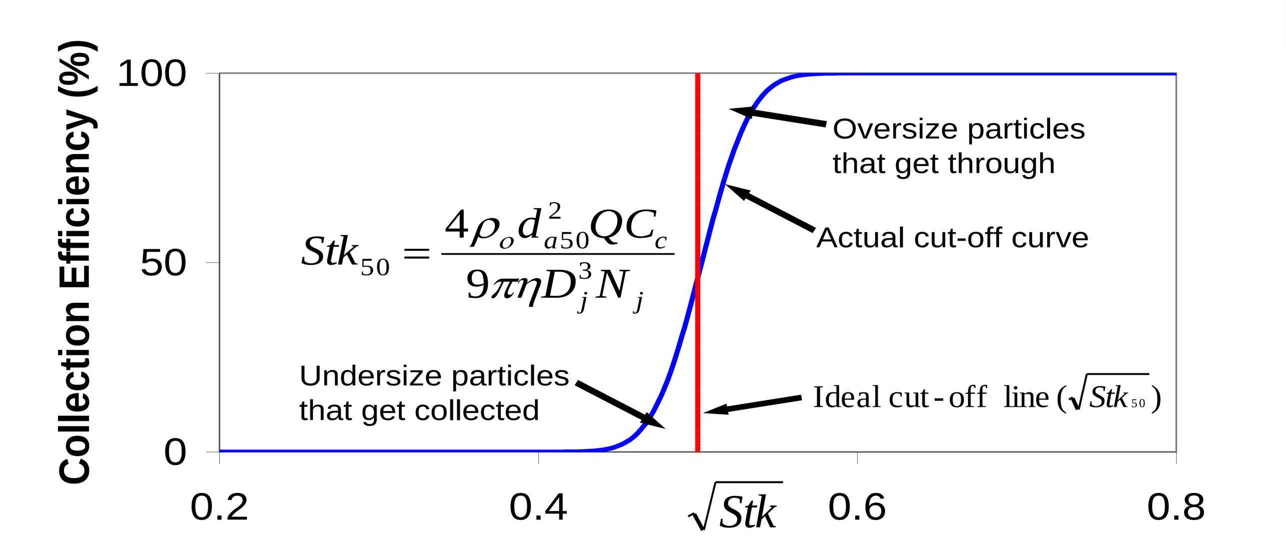

Figure 1. Pictorial representation of actual and ideal efficiency curves

Results and Discussion

The existing model [6] was updated to include the NGI and validation performed for a range of theoretical products (See Table 1) over a range of air flowrates. The model was validated by comparing the results to CITDAS Version 3.1, which is a commercially available software package from Copley Scientific Ltd. The comparison was performed by comparing the MMAD/GSD values entered into the model (to obtain the deposition profile) to the MMAD/GSD values obtained from CITDAS using the deposition profile generated by the model. Results in Figures 2 and 3 show good agreement to the level of accuracy normally used for reporting MMAD/GDSD values.

Case	MMAD (µm)	GSD
1	1.20	1.80
2	2.00	1.80
3	3.00	1.80
4	4.00	1.80
5	5.00	1.80
6	4.00	1.50
7	4.00	2.00
8	4.00	3.00
9	4.00	4.00

Table 1. Theoretical product case studies

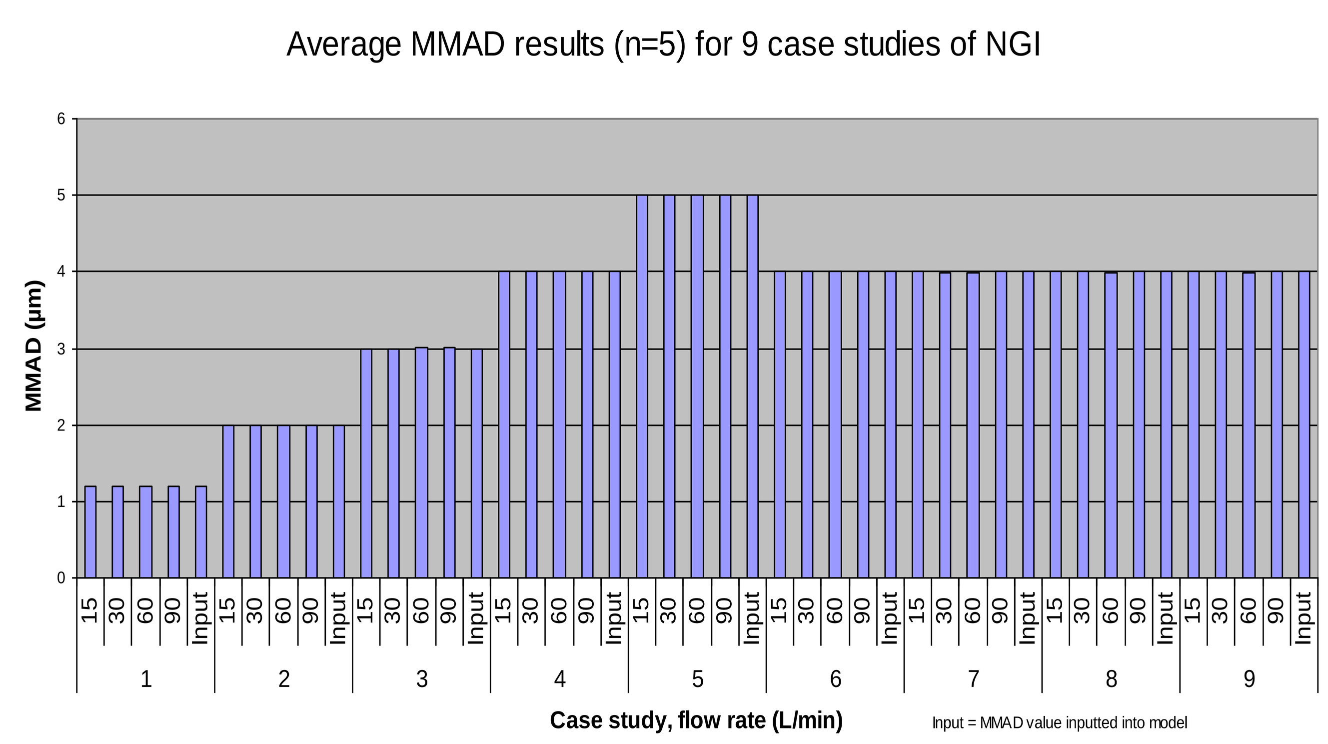

Figure 2. MMAD values for NGI Model versus CITDAS

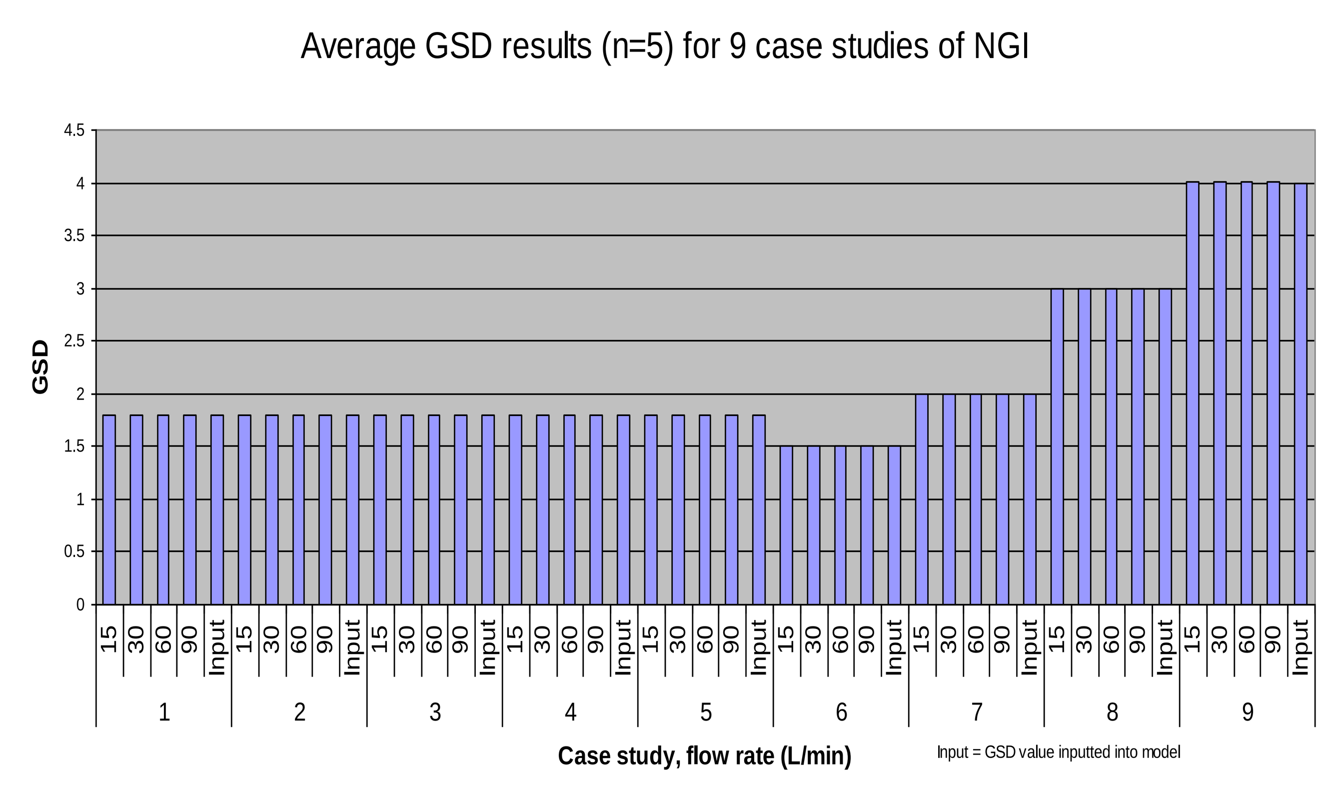

Figure 3. GSD values for NGI Model versus CITDAS

It is clear that the model is operating accurately, however there is still some error in the model. An assessment of the error attributable to the use of the random number generator was performed (See Figure 4). This shows that the routine use of 1 million particles is sufficient to minimise any stochastic error. A further assessment was made to understand whether this error was systematic or random in nature (See Figure 5). It is clear that the error is generally random and increases as GSD is increased; however the-maximum error observed in MMAD calculations (typically less than 0.5%), and GSD calculations (typically less than 0.8%) is acceptable for investigational purposes. The random nature of the error means that estimations would be improved by running multiple replicates.

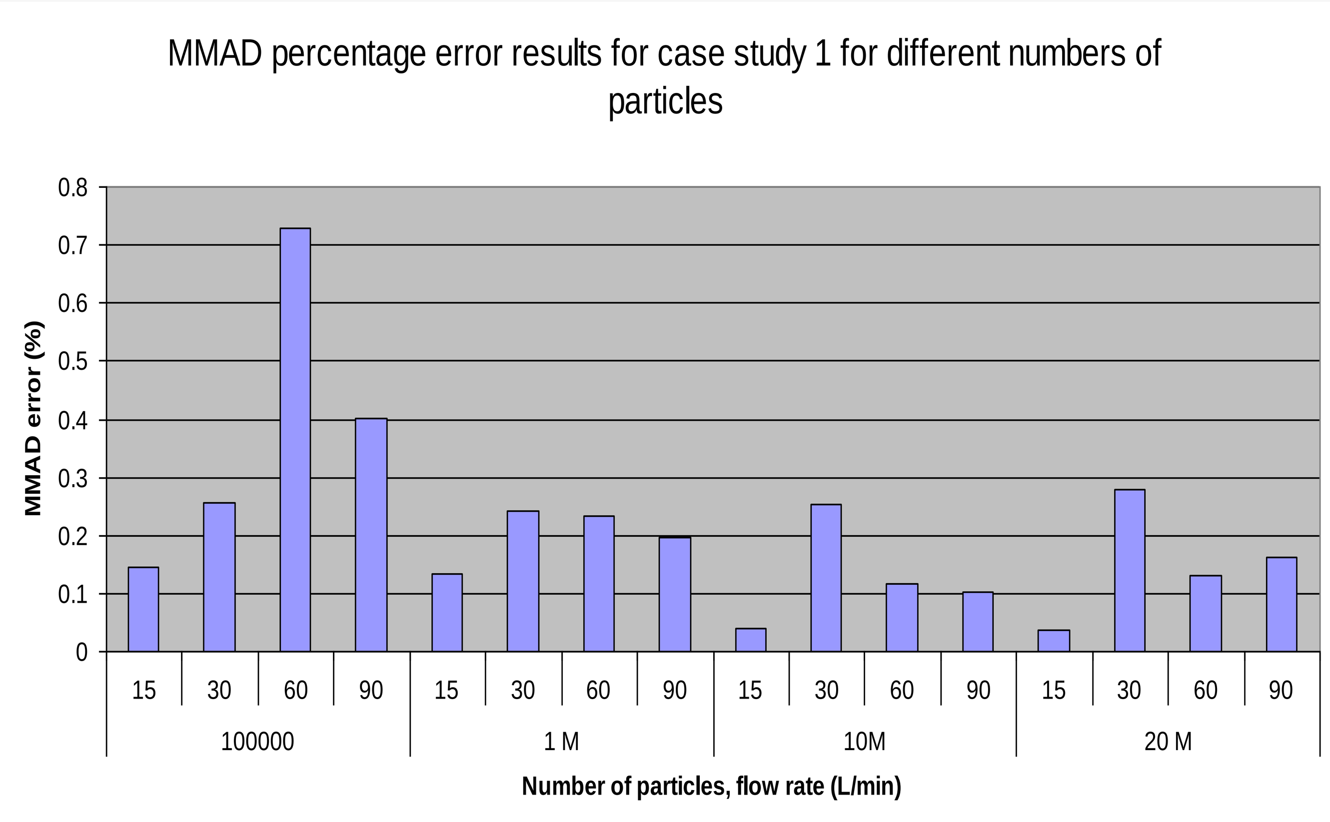

Figure 4. Error (%) in MMAD values for NGI Model versus CITDAS using increased particle number

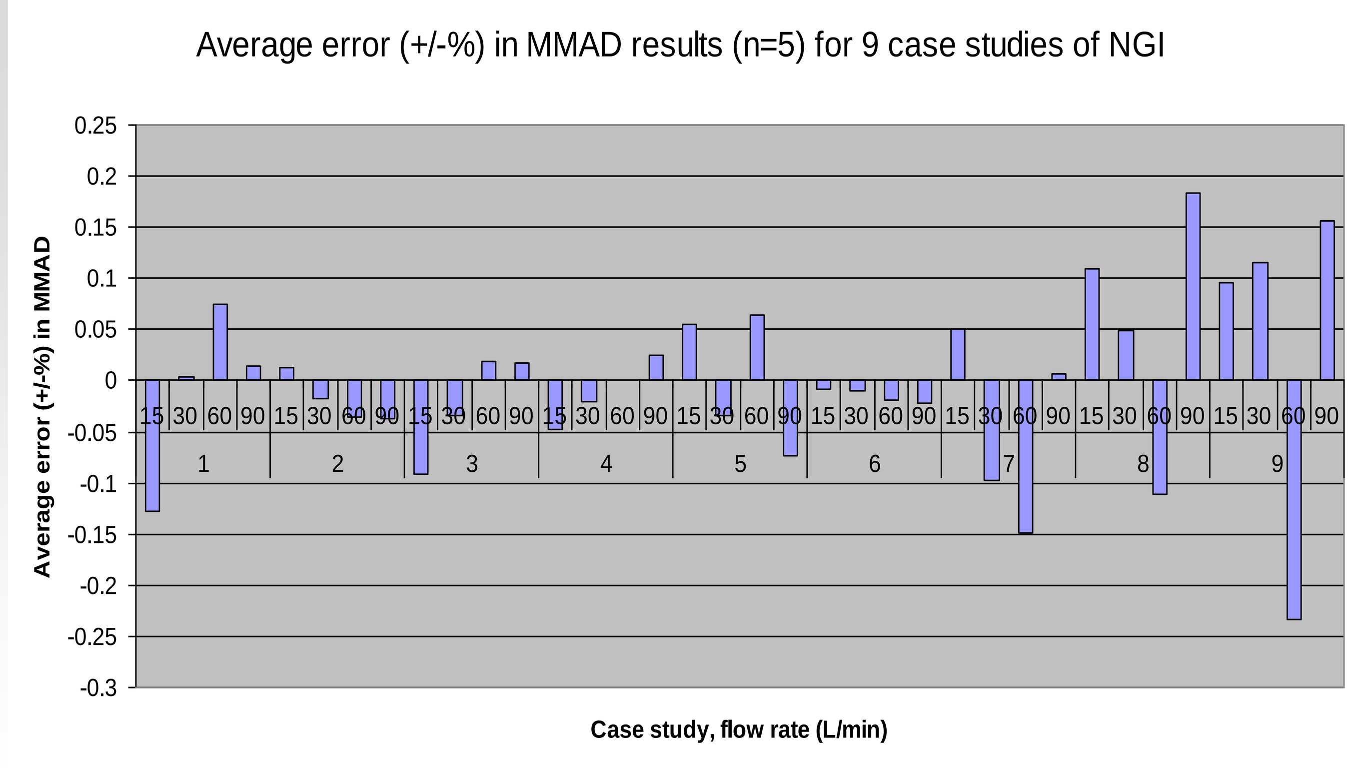

Figure 5. Error (%) in MMAD values for NGI Model versus CITDAS

Conclusions

A mathematical model has been developed by 3M HealthCare Ltd in conjunction with the Mathematics Department, Loughborough University which can be used to simulate the performance of the Andersen Cascade Impactor (ACI) and Next Generation Impactor (NGI) for pharmaceutical inhaled products. Some validation has been presented to demonstrate that the model is working with good accuracy.

It is considered that it can be a useful tool for trend analysis (rather than comparing to experimental data) and to evaluate ACI/flow meter calibration data [7].

Further work is ongoing, including evaluation of non-lognormal distributions, understanding of theoretical error and incorporating real-life analysis error.

Acknowledgement

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