Understanding the Transient Flow Behaviour of Abbreviated Impactors for Testing of DPIs

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EPAG European Pharmaceutical Aerosol Group www.epag.co.uk

1. Background/context of the research

- Abbreviated impactors (AIM): reduced NGI (rNGI), Fast Screening Impactor (FSI), Fast Screening Andersen (FSA).
- Two particle size fractions only: (i) above & (ii) below chosen aerodynamic cut point (D_{50}).
- Simple characterisation for quality control and for fast screening of candidate pMDI or DPI formulations in R&D.
- **Start-up kinetics of transient air flow may cause small differences in fine particle dose of breath-actuated DPI products measured by AIM apparatuses and full-stack impactors (NGI/ACI)** (Refs. [1]-[4]).

2. Study objectives

- Develop numerical model of start-up of air flow through AIM impactors.
- **Validate method by comparison of model predictions with preliminary experimental dataset reported in companion paper** (Ref. [7]).
- **Identify main factors controlling air flow rise time t_{90}.**

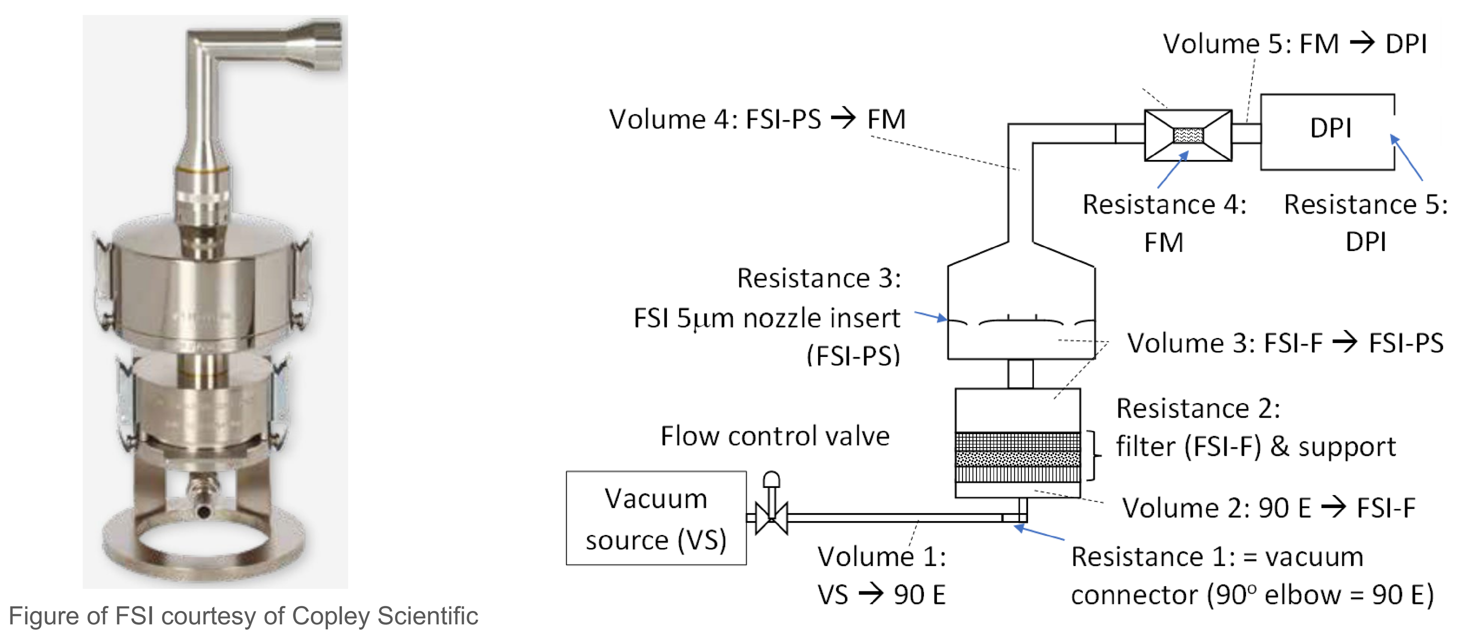

Figure 1 – Representation of FSI as system of chambers and resistances

3. Method

- Conceptual model (see Fig. 1): flow behaviour is studied through a system of chambers (e.g. USP-IP, pre-separator, filter holder) separated by concentrated resistances (impactor nozzles, DPI).
- Mathematical model: (i) rate of change of pressure P_i in chamber i as function of chamber volume P_i and mass flow rates $\dot{m}_i$ through resistances $\frac{dP_i}{dt} = \left(\frac{RT_\infty}{V_i}\right)(\dot{m}_i - \dot{m}_{i-1})$ (ii) pressure difference $P_i - P_{i-1}$ as function of mass flow rate and open area: linear losses (e.g. filter) $P_i - P_{i-1} = \frac{C_l}{A\rho}\dot{m}_i$ quadratic losses(e.g. nozzles) $P_i - P_{i-1} = \frac{C_q}{A^2\rho}\dot{m}_i^2$
- Non-dimensionalisation yields system of ordinary differential equations (ODEs) for non-dimensional chamber pressure vs. non-dimensional time.
- Numerical approach: system of ODEs is solved in Matlab(R).

4. Results & discussion

- System parameters for AIM and full-stack impactors obtained from impactor system chamber volumes and measured or estimated resistance P_i-P_{i-1}. (see Table 1).
- Processed model results: non-dimensional mass flow rate vs. non-dimensional time for FSI at steady state flow rate of 60 l/min (see Fig. 2).
- Monotonic increase of flow rate vs. time for all impactor systems.
- Rise time t_{90} for flow into the DPI inlet: (i) find t_{90}/t_{ref} = 1.36 corresponding to Q/Q_{ss} = 0.9.
- Model parameters for FSI → reference time t_{ref} = 96 ms → t_{90} = 130 ms.
- Table 2 gives model predictions of t_{90} for NGI, rNGI, ACI, FSI and FSA for steady state flow rates Q_{ss} = 30, 60 and 90 l/min.
- Figure 3 compares the model predictions of t_{90} with experimental data.
- Rise time t_{90} trends correlate with impactor volumes (see results in Tables 1 & 2).
- Rise time t_{90} decreases as flow rate increases. Ref [7] has shown that this is caused by the higher resistance of DPIs tested at low flow rates.

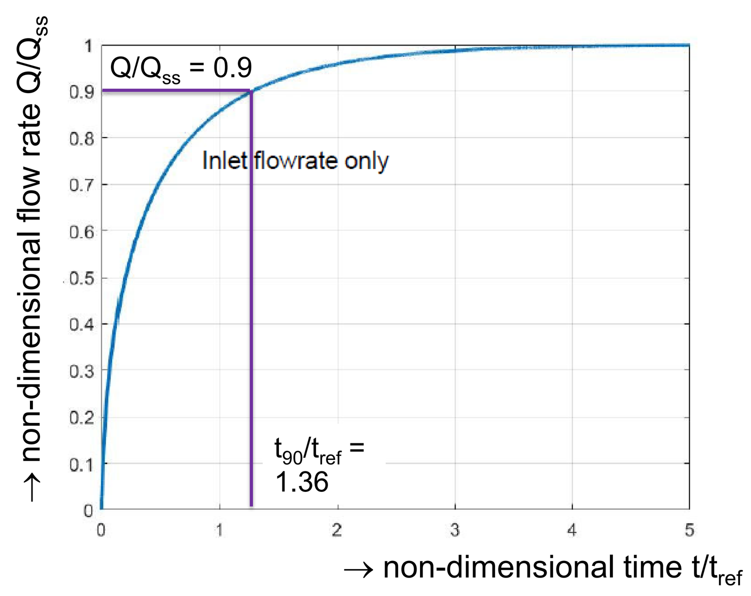

Figure 2 – Non-dimensional flow rate into DPI vs. non-dimensional time FSI - steady state flow rate 60 l/min

5. Conclusions

- Predictions show that rise time t_{90} is longest for rNGI and shortest for FSA and are related FSA < FSI ≈ ACI < NGI < rNGI (see Fig. 3).
- Effect of system volume and steady state flow rate: model correctly predicts trends of rise time t_{90} vs. impactor system volume & steady state flow rate.
- **Understanding: rise time t_{90} is proportional to the time to evacuate air from the impactor system volume to reduce the pressure by 4 kPa caused by the surrogate DPI resistance; this takes longer when the impactor system volume is larger or the flow rate is smaller.**
- Discrepancies model predictions & experiments: (i) uncertainties in system component volumes and ΔP, (ii) unknown experimental issues.
- Further work: resolve differences & complete system understanding (in progress).

Table 1. Impactor Volume and Model-Predicted Pressure Drop at Steady-State Conditions

Impactor volume (cm³)	1990	1980	1150	1180		630
Predicted steady-state pressure drop (kPa) across impactor system						
Q_{ss} (L/min)	**NGI**	**rNGI**	**FSI**	**ACI**		**FSA**
				28.3 l/min config.	**60.0 l/min config.**	**28.3 l/min config.**
30	6.9	8.3	5.6	10.0	6.1	5.3
60	15.6	19.1	7.6	26.4	10.6	6.7
90	31.5	38.3	10.2	56.4	17.7	8.1

Table 2. Predicted Time t_{90} (ms) to Reach 90% of Steady-State Air Flow Rate

Q_{ss} (L/min)	NGI	rNGI	FSI	ACI	FSA
30	456	489	249	252	147
60	266	302	131	153	77
90	212	244	93	101	54

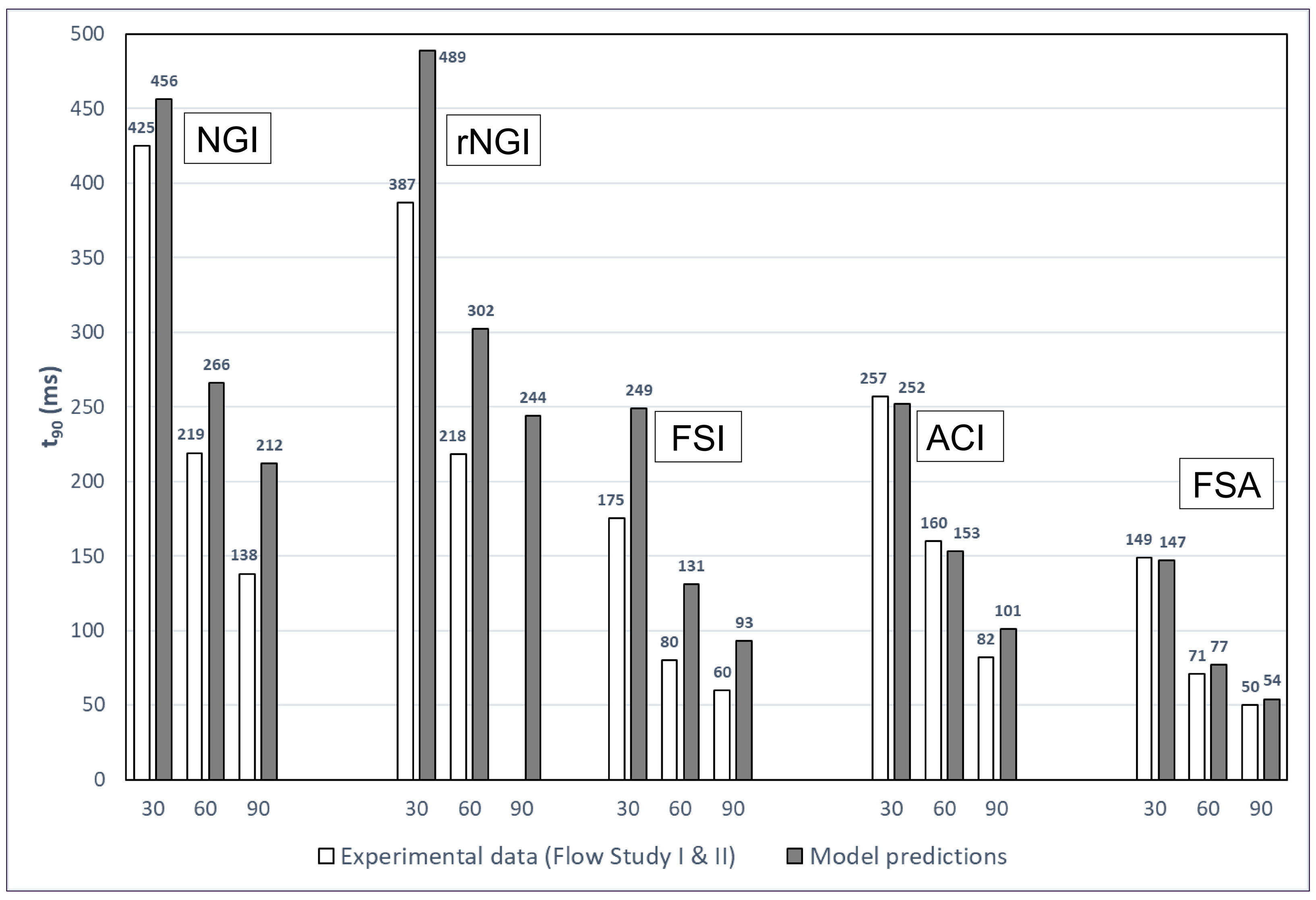

Figure 3 – Model Predictions and Experimental Measurements of Rise Time t_{90}

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