

Addressing Variations in Volume and Flow Resistance When Testing Dry Powder Inhalers With Full Resolution and Abbreviated Impactors

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Objective:

To determine the volume and resistance adjustments required to align the flow rate rise-time of the Fast Screening Impactor (FSI) with the Next Generation Impactor (NGI) when testing commercially available Dry Powder Inhaler (DPI) devices across varying flow rates, using a Volume and Resistance Compensator (VRC).

Background:

Abbreviated Impactor Measurement (AIM) offers an alternative testing approach for the research, development and quality control of DPIs. However, abbreviated impactors have been shown to result in differences in flow rate rise-time profiles compared to full-resolution impactors. This variation in rise-time is a recognised concern as it influences the actuation, dispersion, and aerosolisation of doses from DPI devices. The discrepancy arises from differences in volume and resistance between abbreviated and full-resolution impactors, affecting the consistency and reliability of test outcomes.



Volume and Resistance Compensator (VRC)

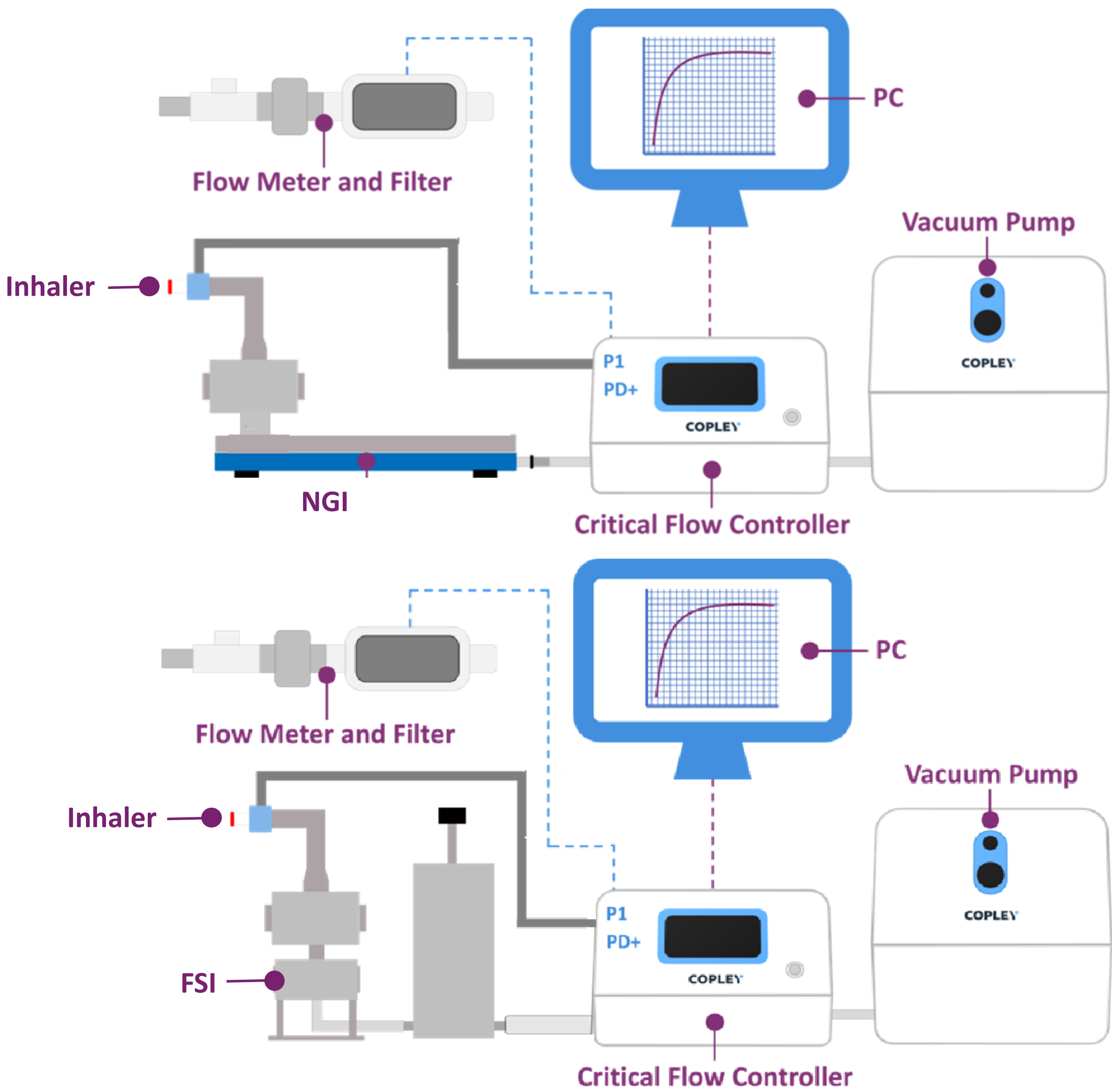
The VRC introduces additional volume and flow resistance between the dose collection device and the flow controller:

- A piston is used to adjust volume
- Choke plates are inserted to modify flow resistance

Adjustments can be made independently to accommodate various configurations of test apparatus.

Method

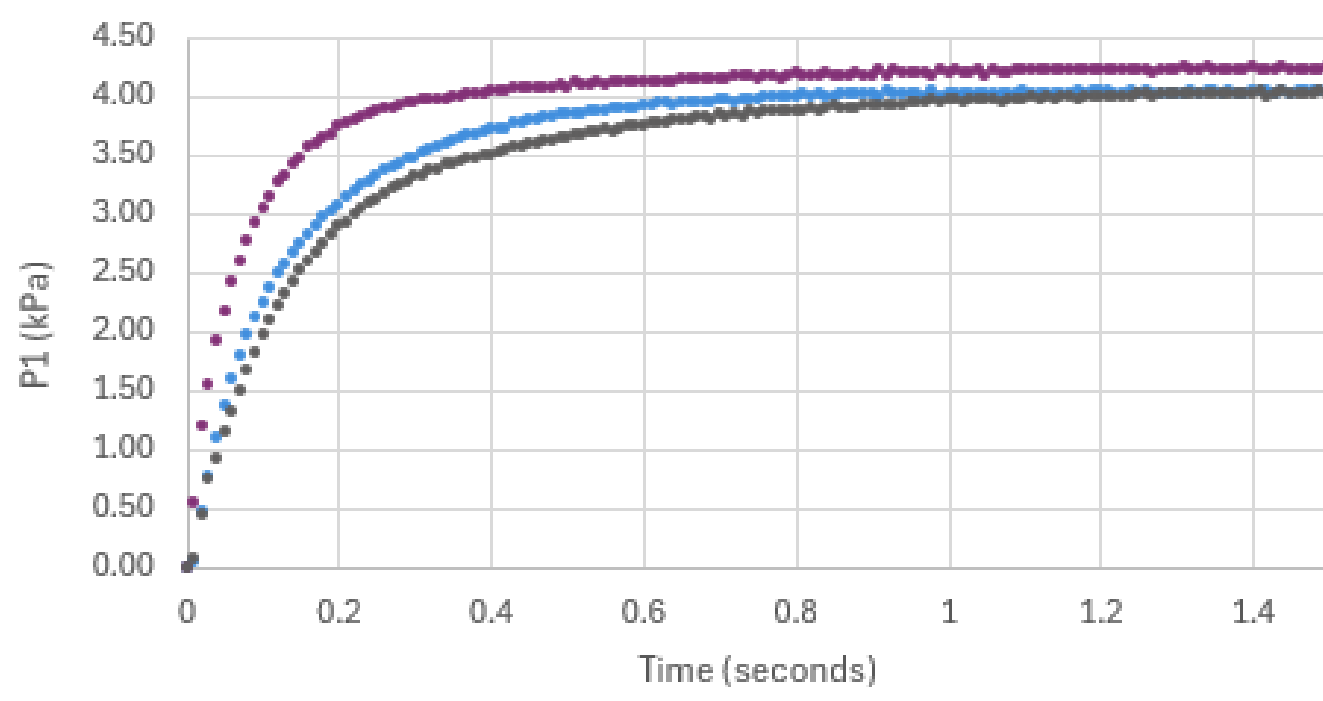
1. A test set-up was configured for evaluating aerodynamic particle size distribution (APSD) of a DPI, in accordance with compendial requirements, using an NGI, flow meter (DFM 2000), critical flow controller (TPK 100i-R) and vacuum pump (HCP6), see diagram below. (All equipment, Copley Scientific Ltd., Nottingham, UK.)
2. Three DPI devices were selected, each having high, medium and low resistance, and were tested at flow rates of 45, 60 and 90 L/min respectively, as required to generate a pressure drop (P1) of 4 kPa.
3. The flow resistance and flow rate rise-time of the system were determined using the critical flow controller and data logging software, with differential pressure recorded at 10 ms intervals.
4. The procedure was repeated using an FSI in place of the NGI, with appropriate inserts used to achieve a 5 µm cut-off at 45, 60, and 90 L/min, and the flow rate rise-time of each corresponding configuration compared.
5. A VRC was incorporated into the FSI set-up and the flow resistance and volume adjusted by inserting different choke plates and adjusting the volume setting.



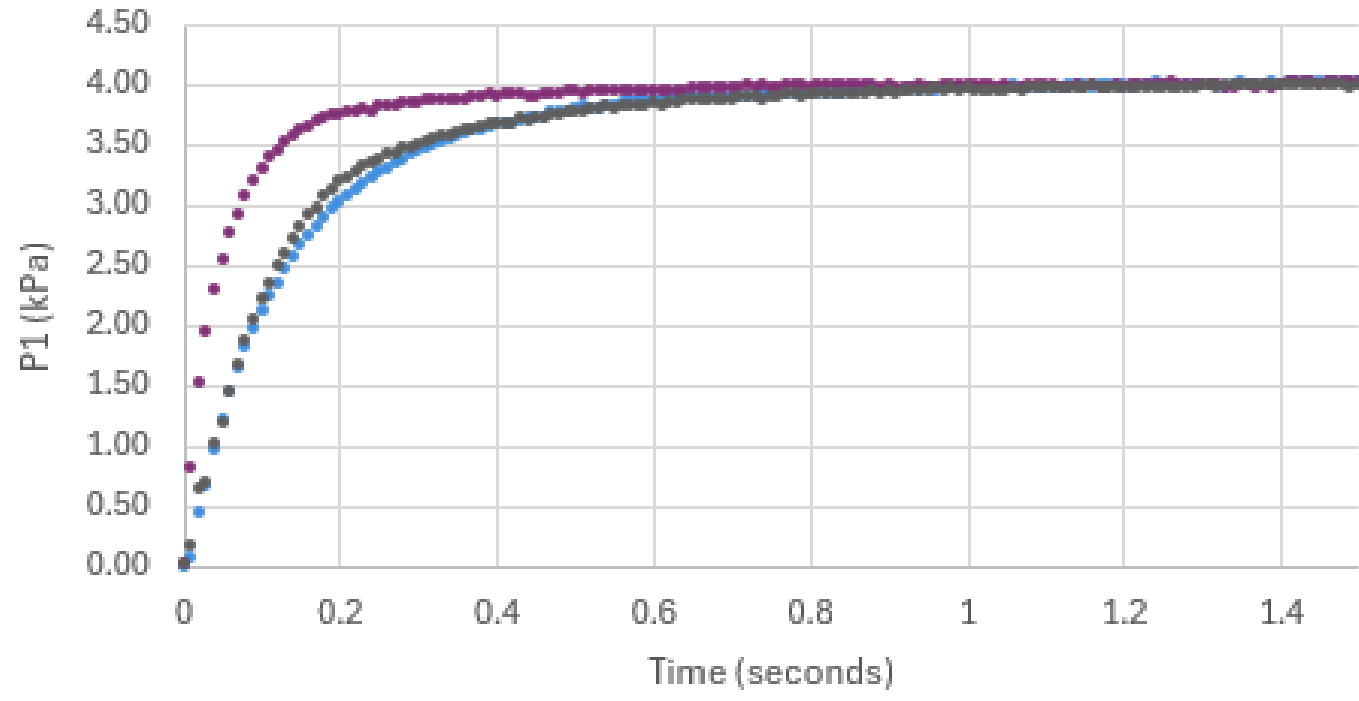
Schematic of the test set-ups for assessing flow rate rise-time profiles of full resolution NGI (top) and FSI with VRC (bottom).

Results

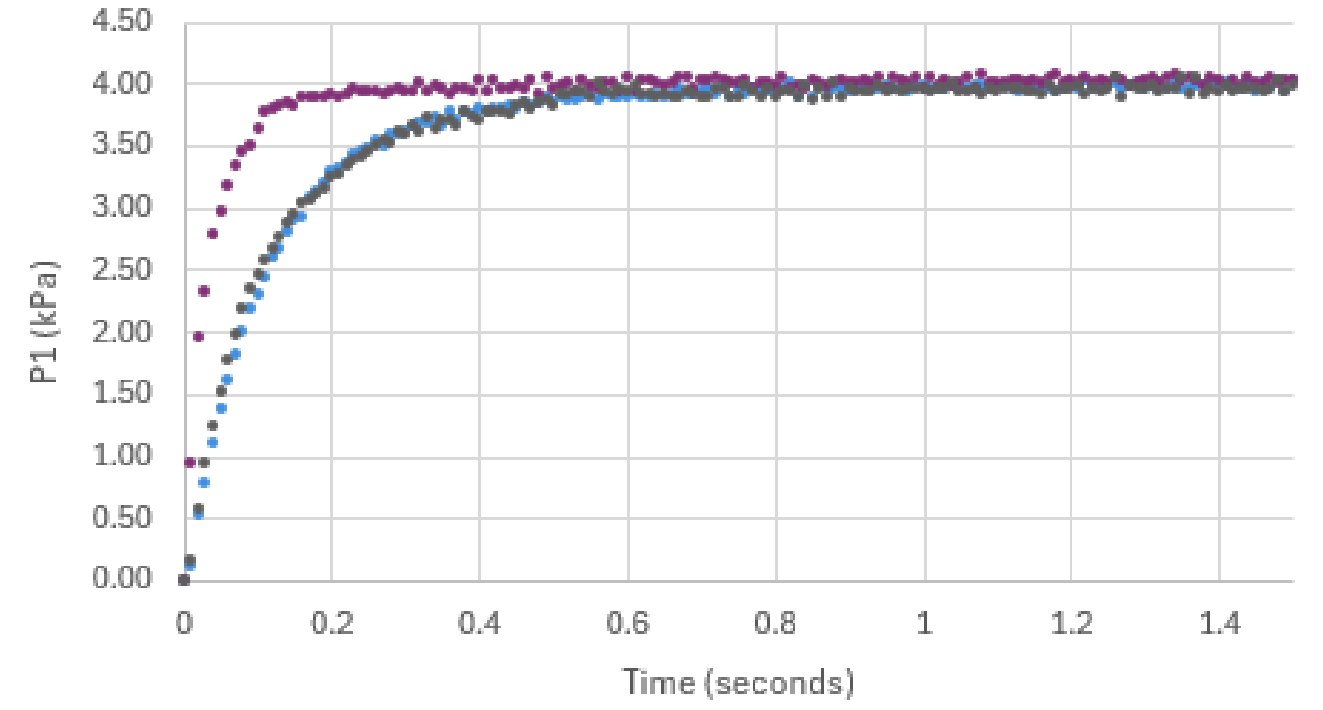
NGI, FSI and FSI+VRC at 45 L/min



NGI, FSI and FSI+VRC at 60 L/min



NGI, FSI and FSI+VRC at 90 L/min



Legend

- Blue = rise-time of NGI alone
- Purple = rise-time of FSI alone
- Grey = rise-time of the FSI+VRC

VRC choke plates and volumes required to match resistance and flow rate rise-times between NGI and FSI.

Device	Flow Rate at 4 kPa Pressure Drop Across Device (L/min) (Q)	Full Resolution Impactor			Abbreviated Impactor + VRC			
		Flow Resistance (kPa ^{0.5} minL ⁻²)	Rise-Time T ₉₀ (ms)	L/min Insert	Choke Plates	Flow Resistance (kPa ^{0.5} minL ⁻²)	VRC Volume (mL)	Rise-Time T ₉₀ (ms)
Low resistance	90	0.052	0.39	90	5 mm and 5 mm	0.053	600	0.35
Medium resistance	60	0.053	0.37	60	4 mm and 4.5 mm	0.052	600	0.35
High resistance	45	0.055	0.36	45	4 mm and 4 mm	0.056	600	0.37

Discussion

- By using different combinations of choke plates in the VRC, depending on the test flow rate, it is possible to adjust flow resistance to account for differences between NGI and FSI configurations.
- Flow resistance of NGI and FSI test configurations can be closely matched using a VRC (see table above).
- Significant difference in the flow rate rise-time for the NGI and FSI test configurations were observed (see graphs above).
- Flow rate rise-times of NGI and FSI test configurations can be matched by using a VRC to introduce an additional volume of 600 mL (see table and graphs).
- Interestingly, the VRC volume setting does not match the difference in physical volumes of the NGI and FSI.

Conclusion

Differences in flow resistance and volume between AIM apparatus and full-resolution impactors creates variations in transient flow conditions during initial activation of passive DPIs. By utilising a VRC, analysts can closely match flow rate rise-time profiles of AIM apparatus and NGI configurations. The volume and resistance adjustments provided by the VRC enhance the utility of AIM by aligning the parameters of the abbreviated and full-resolution test set-ups therefore balancing the benefits of streamlined DPI testing with improved correlation to the APSDs generated by full-resolution methods.