

# Efficiency of Valved Holding Chambers: Experimental Full Dose Assessment

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## Introduction / Objectives

- The **Valved Holding Chamber (VHC)** devices are used by patients **without** the **capacity** to properly **use** a pressurized Metered-Dose Inhaler (pMDI).
- VHC devices contribute to the **reduction** of the **oropharyngeal** spray **deposition**, while allowing the patient to **breathe normally**.
- The main objective is to experimentally **evaluate** eight commercially available VHC devices, through **two** distinct **Systems**.
- VHC efficiency was evaluated through the assessment of the **Emitted Dose**.

## Methods

### Devices

The experimental tests were performed using a commercial pMDI HFA-134a containing a Salbutamol formulation (**Ventolin**<sup>®</sup> from GlaxoSmithKline<sup>®</sup>) coupled with the **VHC device**. A total of 8 devices were assessed throughout this experimental study (see **Figure 1**).

(a) A2A Spacer<sup>®</sup> from Clement Clarke International<sup>®</sup>, (b) AeroChamber Plus<sup>®</sup> from Trudell Medical International<sup>®</sup>, (c) Volumatic<sup>®</sup> from Glaxo SmithKline<sup>®</sup>, (d) NebuChamber<sup>®</sup> from AstraZeneca<sup>®</sup>, (e) SpaceChamber Plus<sup>®</sup> from Medical Development International<sup>®</sup>, (f) Vortex<sup>®</sup> from PARI<sup>®</sup>, (g) Compact SpaceChamber Plus<sup>®</sup> from Medical Development International<sup>®</sup> and (h) OptiChamber Diamond<sup>®</sup> from Philips<sup>®</sup>.

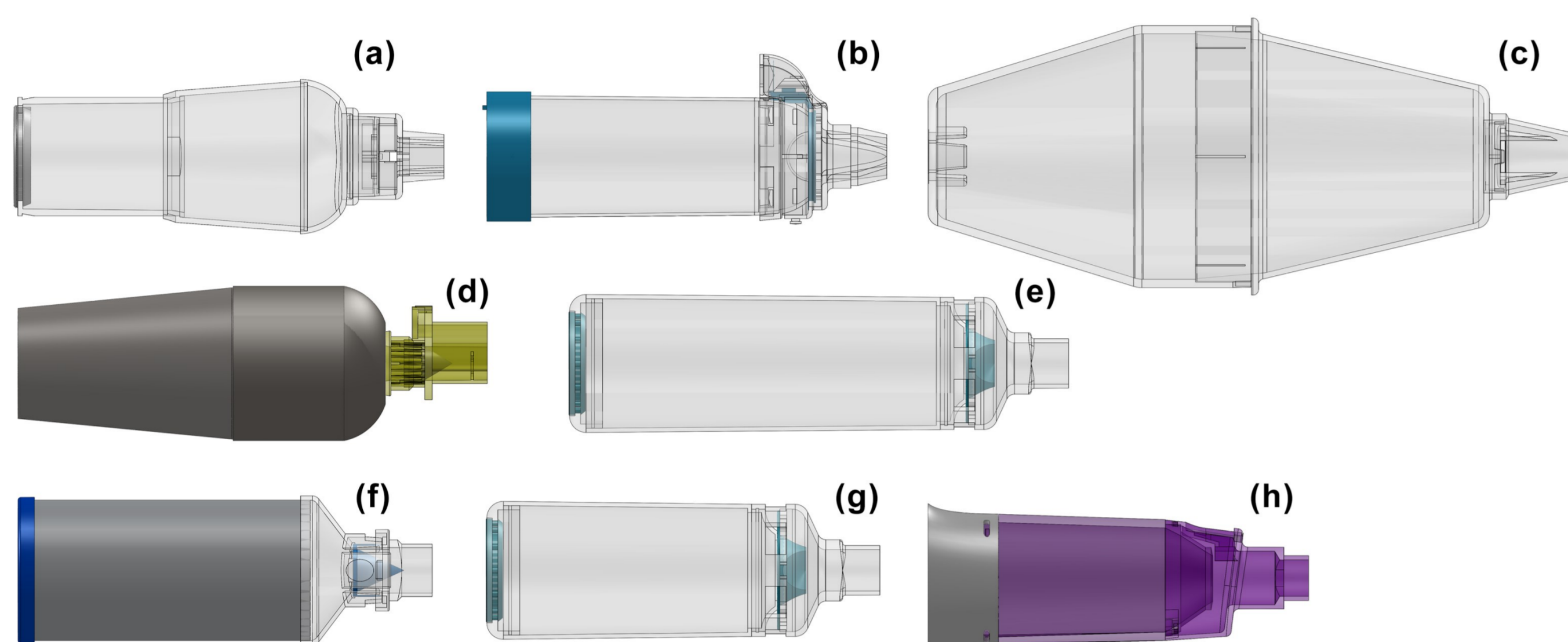


Figure 1. Geometric representation of the VHC devices evaluated.

### Experimental System

**Figure 2** depicts that the pMDI and the VHC were attached to a rubber adapter, fitted on the edge of an aluminum filter housing (containing a paper filter MN 1674 from Macherey-Nagel).

In **System 1**, this component was then coupled to a vacuum pump, which was calibrated to an output of 26 L/min. A flow meter was used to monitor the vacuum pump flow rate, which was controlled by a needle valve.

In **System 2**, the filter housing is directly connected to a breath machine, which is based in a closed-form cam-follower mechanism.

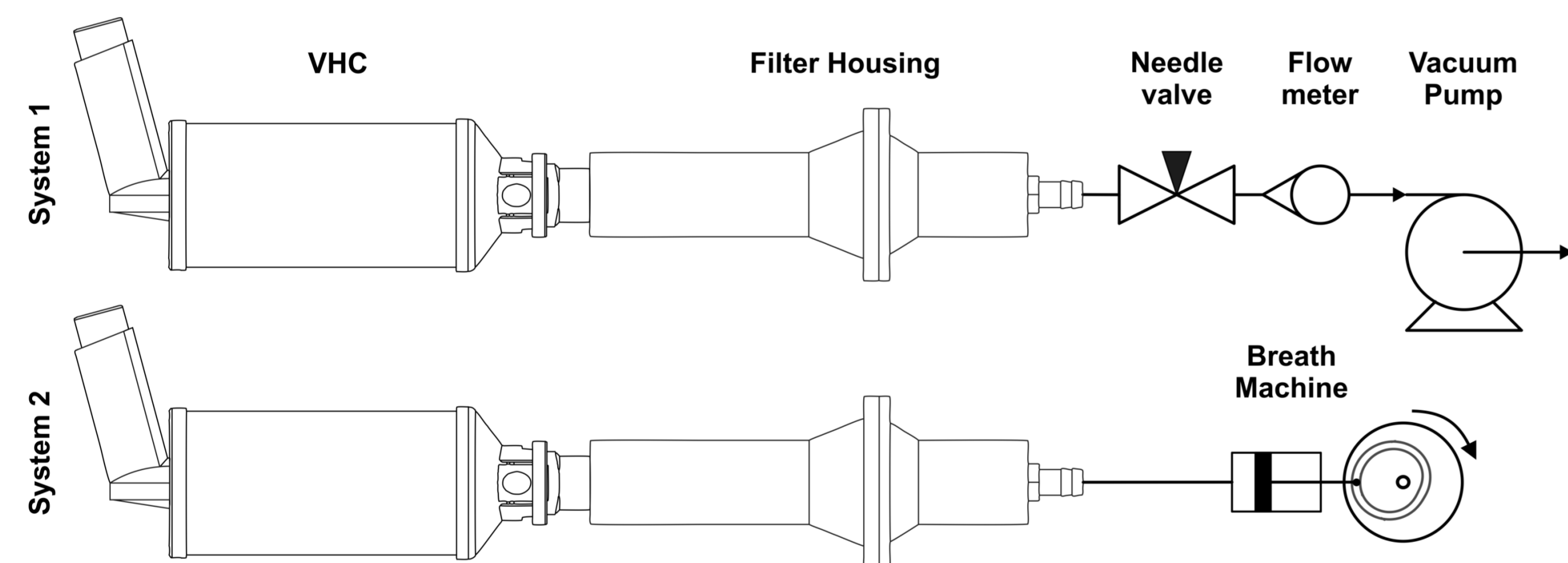


Figure 2. Schematic representation of the experimental systems.

### Breath Profile

A 7 yrs. old asthmatic child breathing profile was considered to be the study target, which was applied in the breath machine of **System 2**. The profile was defined by several literature data sources, along with a sinusoidal simplification: breathing frequency of **30 BPM**, duty cycle of **0.33** and tidal volume of **150 mL**. The breath profile used is represented in **Figure 3**.

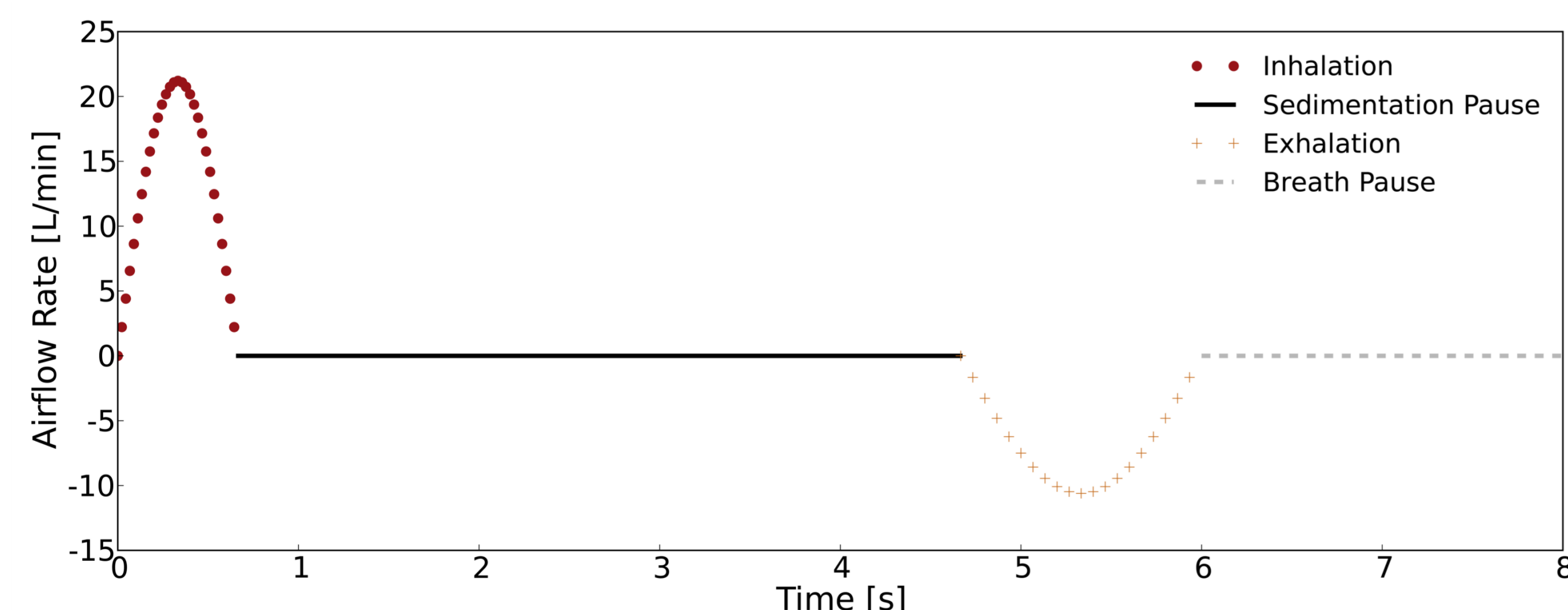


Figure 3. Asthmatic breath profile used in the experimental System 2.

The amplitude of the inspiratory sinus is **21 L/min**. A pause of 4 s after inspiration was added, to **allow** for the **sedimentation** of drug **particles** in the **lungs**. After the exhalation phase, a 2 s pause was intended to **simulate** the **poor coordination** of an asthmatic patient using a VHC device.

## Methods (cont.)

### Experimental Protocol

- VHC devices were **submerged** in an anionic soap solution (1:250) for a period of 1h and **dried** for at least 12h, prior to the experimental procedure.
- The pMDI canister was then **shaken** for 5 seconds and **fired** twice to **waste** in its original actuator. The canister was then placed in the **service actuator**, already **attached** to the VHC.
- In **System 1**, a total of 20 puffs were **discharged**, with **shaking** of the canister for 5 seconds **between** each puff.
- Prior to **shutting off the pump**, it was allowed a 30 seconds suction time starting from the last puff.
- In **System 2**, the actuations were made at the **beginning** of the **inspiratory phase** during 20 cycles, **shaking** the canister between puffs.
- A minimum of 3 repetitions of each test **were made**, in order to **reduce protocol errors** and increase the result's significance.
- Every **stage** of the System was **washed**, with NaOH 0.01M, into **volumetric flasks**: primarily, the **pMDI actuator** into a 25 ml flask, then the **VHC device** into a 100 ml flask and, finally, the **paper filter** and the **filter housing** into 50 ml flasks.
- To improve the drug solubility and its release from the paper filter, the solution was initially placed into an ultrasonic shaker for 10 min.
- The washing solutions **absorbance** ( $\lambda = 244 \text{ nm}$ ) was **measured** in triplicate by means of a **UV-Vis spectrophotometer** (UV-2401PC from Shimadzu Corporation<sup>®</sup>).
- Using a **calibration curve** of **known** absorbance for specific **concentrations** of **Salbutamol**, the washing solutions concentration was **estimated**, which allows the **determination** of **mass** retained in each stage.
- Values of the **total mass collected** in each test were also **determined** and used to **evaluate** the **accuracy** of the test. **Only** tests with mass recovery **between** 85% and 120% of the mass injected were considered as **valid**.

## Results

**Table 1** reports the experimental values obtained for **System 1** (i.e. at 26 L/min) and **System 2** (i.e. using a Breath Profile). Data is presented in terms of **Emitted Dose** (Ex-actuator) considering a dose base of 100 mcg salbutamol.

Table 1. Experimental data obtained for each VHC device.

VHC Device (Acronym)	Emitted Dose (Ex-actuator) [mcg]	
	26 [L/min]	Breath Profile
Volumatic <sup>®</sup> (VOL)	32.2 ± 2.4 (n=3)	16.1 ± 0.6 (n=3)
Compact SpaceChamber Plus <sup>®</sup> (CSCP)	36.8 ± 0.2 (n=3)	23.0 ± 1.2 (n=3)
A2A Spacer <sup>®</sup> (A2A)	38.1 ± 2.9 (n=3)	10.5 ± 1.1 (n=3)
OptiChamber Diamond <sup>®</sup> (OCD)	40.7 ± 0.6 (n=3)	20.8 ± 0.3 (n=3)
SpaceChamber Plus <sup>®</sup> (SCP)	41.9 ± 1.8 (n=4)	24.3 ± 0.4 (n=3)
NebuChamber <sup>®</sup> (NC)	46.3 ± 2.3 (n=4)	21.6 ± 0.8 (n=3)
AeroChamber Plus <sup>®</sup> (ACP)	46.9 ± 0.7 (n=3)	21.4 ± 0.1 (n=3)
Vortex <sup>®</sup> (V)	50.8 ± 1.8 (n=4)	18.2 ± 0.9 (n=4)

**Figure 4** depicts the results reported in **Table 1**, sorted in ascending order of Emitted Dose at 26 L/min.

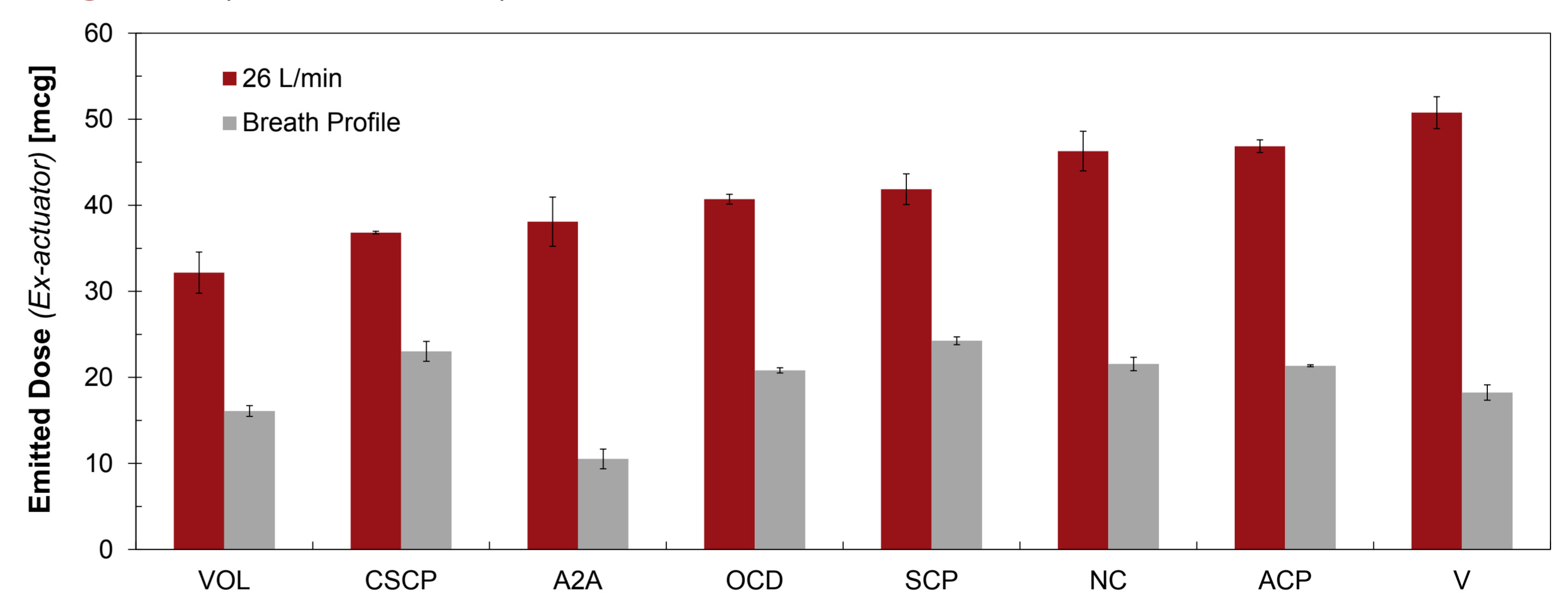


Figure 4. Graphical representation of the Emitted Dose (Ex-actuator) for the evaluated devices, on both systems.

- The result reported reveals that **V** has the **highest** Emitted Dose of the VHC at constant flow. Under the use of a unsteady flow the **SCP** is the device with **highest** Emitted Dose.

### Ranking as:

System 1: VOL < CSCP < A2A < OCD < SCP < NC < ACP < V  
System 2: A2A < VOL < V < OCD < ACP < NC < CSCP < SCP

- Vortex** is the **best** device at **constant flow** although the same is **not** verified under **unsteady flow**. This may arise from valve leakage.
- Longer VHC** body results in **higher** Emitted Dose. This can be concluded from comparing SCP with CSCP.
- Emitted Dose at unsteady flow is **1.6 – 3.6** times **lower** than at constant flow. Anti-static materials play a major role as the plume is on hold in the VHC body for a longer period.

## Conclusions

- Considering Emitted Dose results, the **Vortex** is the **best** VHC device at **constant flow** and the **SpaceChamber Plus** at **unsteady flow**.
- Body **length**, valve **design** and device **material** seems to be the **most** influential design characteristics.