

# 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® from GlaxoSmithKline®) coupled with the VHC device. A total of 8 devices were assessed throughout this experimental study (see Figure 1).

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

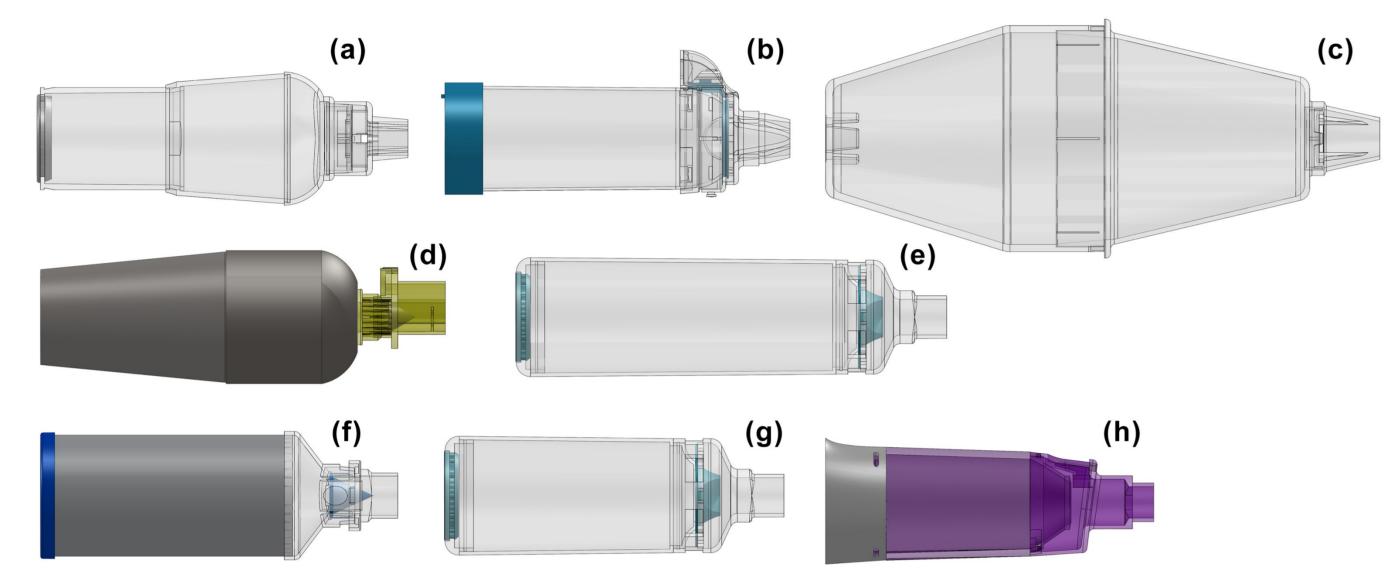


Figure 1. Geometric representation of the VHC devices evaluated.

#### **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 closedform cam-follower mechanism.

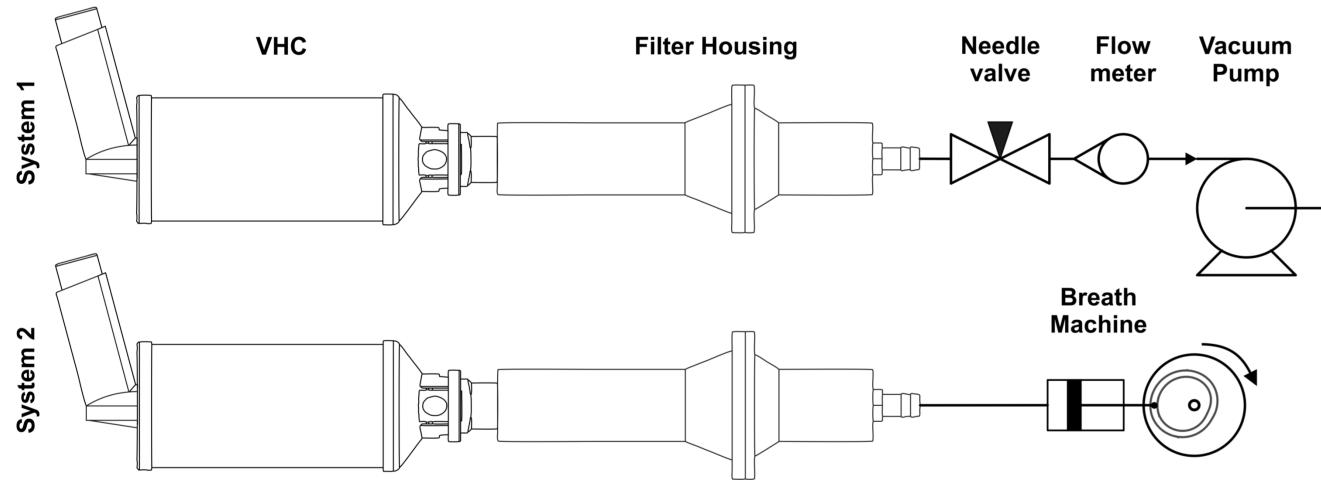


Figure 2. Schematic representation of the experimental systems.

# **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**.

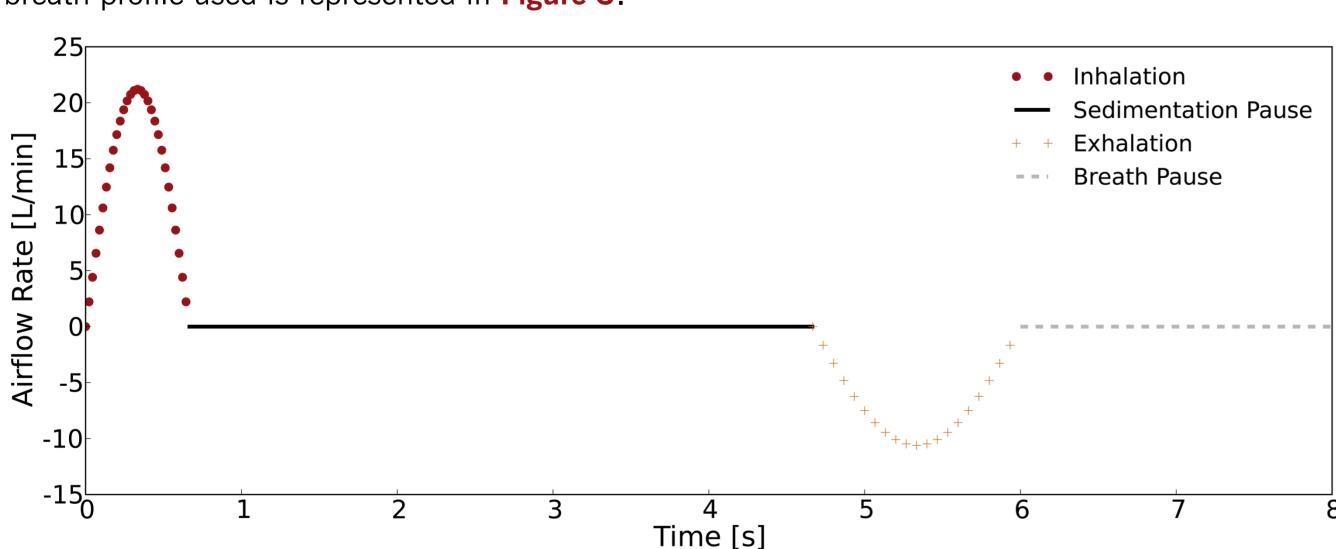


Figure 3. Asthmatic breath profile used in the experimental System 2.

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**

- 1. 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.
- 2. 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.
- 3. In System 1, a total of 20 puffs were discharged, with shaking of the canister for 5 seconds between each puff.
- 4. Prior to shutting off the pump, it was allowed a 30 seconds suction time starting from the last puff.
- 5. In System 2, the actuations were made at the beginning of the inspiratory phase during 20 cycles, shaking the canister between puffs.
- 6. A minimum of 3 repetitions of each test were made, in order to reduce protocol errors and increase the result's significance.
- 7. 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.
- 8. To improve the drug solubility and its release from the paper filter, the solution was initially placed into an ultrasonic shaker for 10 min.
- 9. The washing solutions absorbance ( $\lambda = 244$  nm) was measured in triplicate by means of a UV-Vis spectrophotometer (UV-2401PC from Shimadzu Corporation®).
- 10. 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.
- 11. 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® (VOL)	$32.2 \pm 2.4 (n=3)$	$16.1 \pm 0.6 (n=3)$
Compact SpaceChamber Plus® (CSCP)	$36.8 \pm 0.2 (n=3)$	$23.0 \pm 1.2 (n=3)$
A2A Spacer® (A2A)	$38.1 \pm 2.9 (n=3)$	$10.5 \pm 1.1 (n=3)$
OptiChamber Diamond® (OCD)	$40.7 \pm 0.6 (n=3)$	$20.8 \pm 0.3 (n=3)$
SpaceChamber Plus® (SCP)	$41.9 \pm 1.8 (n=4)$	$24.3 \pm 0.4 (n=3)$
NebuChamber® (NC)	$46.3 \pm 2.3 (n=4)$	$21.6 \pm 0.8 (n=3)$
AeroChamber Plus® (ACP)	$46.9 \pm 0.7 (n=3)$	$21.4 \pm 0.1 (n=3)$
Vortex® (V)	$50.8 \pm 1.8 (n=4)$	$18.2 \pm 0.9 (n=4)$

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

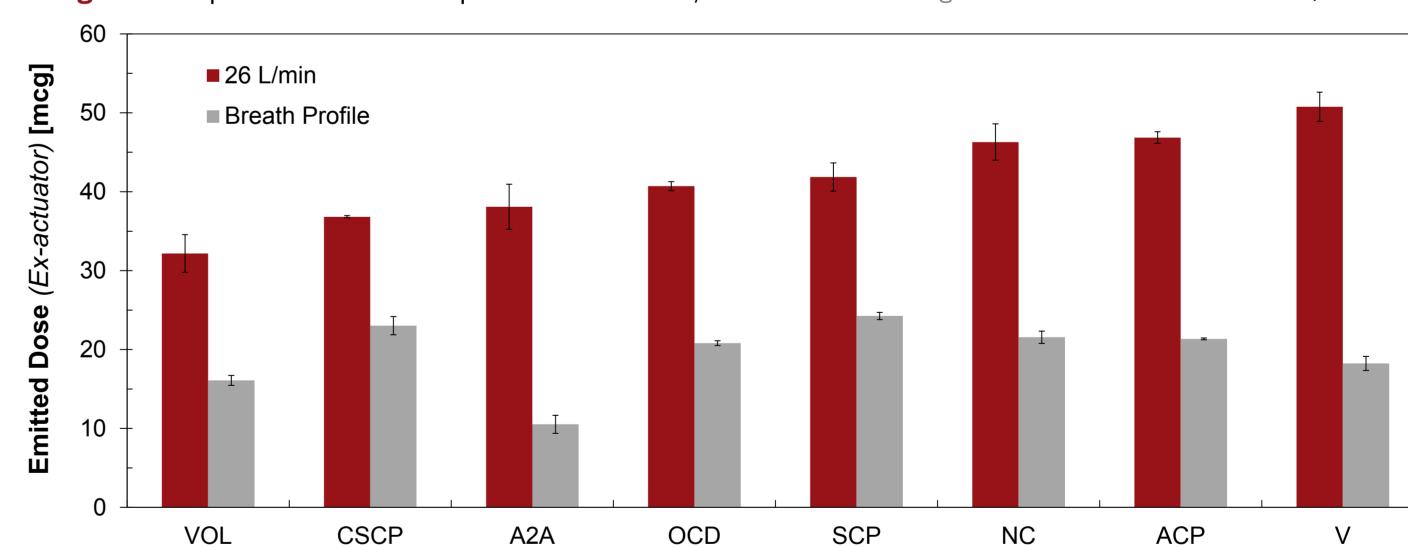


Figure 4. Graphical representation of the Emitted Dose (Ex-actuator) for the evaluated devices, on both systems.

- 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.