

Computational Modelling of Metering Chamber Refill in Pressurised Metered Dose Inhalers with Current and Next Generation Propellants

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Summary

The refill phase of pressurised Metered Dose Inhalers (pMDIs), which immediately follows actuation, remains significantly less studied compared to the actuation stage, where dose delivery and aerosol spray characteristics have typically been the focus. This study used Computational Fluid Dynamics (CFD) to analyse the transient behaviour of a capillary retention metering valve using both current (HFA-134a, HFA-227ea) and next-generation low Global Warming Potential (GWP) propellants (HFA-152a, HFO-1234ze(E)). The simulation captured transient data, including metering chamber pressure, temperature, and liquid fill percent over an initial 300 ms duration. Reopening of the metering chamber to the canister reservoir was included in the simulation and a Eulerian multiphase mixture method was employed. Results indicate clear differences between the filling performance of propellants. HFA-152a achieved the highest liquid fill level (88.3% at 300 ms), followed by HFA-134a (87.1%), HFO-1234ze(E) (75.9%), and HFA-227ea (65.7%).

The development of this model provides a framework for exploring metering valve geometries and a foundation for evaluating formulation-specific refill dynamics for capillary retention metering valves but can be easily extended to primeless metering valves. Ongoing and future work will include sensitivity analysis of model inputs and mesh optimisation to enhance simulation accuracy. Experimental data will be obtained from high-speed x-ray imaging to validate the transient metering chamber liquid fill level during refill.

Key Message

This study demonstrates the capability of CFD to resolve the transient refill dynamics of pMDI metering valves using current and next-generation low-GWP propellants, supporting the design of the next generation of environmentally sustainable pMDIs.

Introduction

The pMDI has been widely used since the 1950s for delivering aerosolised medication directly to the lungs. Initially relying on chlorofluorocarbons (CFCs), these devices underwent reformulation with the adoption of hydrofluoroalkanes (HFAs) such as HFA-134a and HFA-227ea following regulatory changes aimed at reducing the use of ozone-depleting substances. However, in response to further regulatory changes, the industry faces a second major transition towards propellants with significantly lower GWP. Propellants such as HFA-152a and HFO-1234ze(E) are promising alternatives that offer much lower environmental impact from a GWP standpoint while possessing the necessary physicochemical properties for effective drug delivery [1].

At present, the majority of pMDI research has focussed on the actuation phase, with studies addressing aerosolisation and dose delivery. The refilling event inside the metering valve, which occurs immediately after actuation and ensures the metering chamber is filled with the next dose, has remained relatively understudied despite playing a critical role in ensuring consistent dosing. Prior experimental work has explored internal flow behaviour using optically transparent external componentry and high-speed imaging, leading to observations of cavitation during the refill process [2]. Further observations have shown that dose retention can be adversely affected by thermal gradients and subsequent cavitation, leading to partial loss of prime or inconsistent fill volumes [3]. As a result of these observations, simulating the flow behaviour inside the metering chamber presents an interesting opportunity for further study.

During the refill process, cavitation can occur when the local pressure within the liquid propellant drops below its saturation vapour pressure, leading to the formation of vapour bubbles [4]. Therefore, it may be important to incorporate a cavitation mechanism into metering chamber filling CFD models, which can be achieved using mass transfer models based on the Rayleigh-Plesset equation [5]. Appropriate models enable the prediction of mass transfer between phases, making them suitable for simulating cavitation and two-phase flow within pMDI metering valves. Therefore, this study presents a CFD-based approach to investigate the refill dynamics of four propellants (HFA-134a, HFA-227ea, HFA-152a, and HFO-1234ze(E)) within a capillary retention metering valve. The aim of the study was to quantify the influence of propellant selection on refill rate, and metering chamber pressure and temperature evolution, providing data to support the design of the next generation of environmentally sustainable pMDIs.

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Experimental Methods

Software and Hardware

The CFD simulations were carried out using Ansys Fluent 25R1. The geometry of the metering valve and associated fluid flow path was created using SOLIDWORKS 2023. Thermophysical properties for each propellant were obtained from the NIST REFPROP v10.0 library [6] and implemented into the simulation as Real Gas Property (RGP) files. All simulations were performed on the University of Hertfordshire's High-Performance Computing (HPC) facility.

Geometry, Mesh, Boundary Conditions and Model Setup

The computational domain, as illustrated in Figure 1, replicated the internal flow path from the pressurised canister to the metering chamber within a capillary retention metering valve. A high-quality unstructured polyhedral mesh with boundary layer refinement was used to capture the geometry. The inlet was specified as a pressure inlet, set to the saturated vapour pressure for each propellant at 20°C, with a liquid volume fraction of 1.0. The metering chamber was initialised at atmospheric pressure and its corresponding saturation temperature, containing only pure vapour (vapour volume fraction of 1.0), representing conditions immediately following actuation. Mesh motion was implemented to simulate the inlet opening during the metering valve's return.

A Eulerian multiphase mixture model was used to solve the continuity, momentum and energy equations for the mixture, and the volume fraction equation for the secondary phase [7] including cavitation effects [8]. Surface tension effects were enabled within the simulation and modelled by adding a source term to the momentum equation [9]. Adaptive time stepping was used throughout the simulations to ensure both numerical stability and efficiency. The solver automatically adjusted time step size to maintain a global Courant number below 0.5, allowing for accurate resolution of cavitation behaviour during refill.

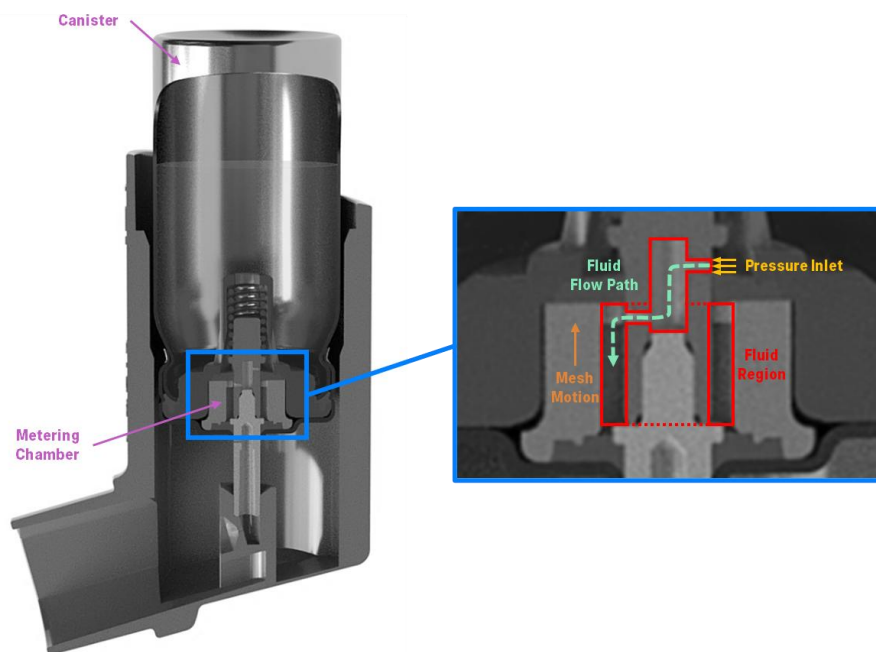


Figure 1 - Simulation Setup Diagram Indicating Components and Boundary Conditions

Results and Discussion

The data discussed within this section is presented in Figure 2, Figure 3, Figure 4, Figure 5, and Table 1. At the start of the simulation, the metering chamber is isolated from the pressurised canister, containing saturated vapour at atmospheric pressure – representing conditions immediately after actuation. As the inlet began to open, a high-pressure differential between the canister and metering chamber initiated rapid in-flow of propellant. This early stage of filling was dominated by cavitation and flashing, with a corresponding rapid increase in metering chamber pressure and temperature. By 22.5 ms (25% inlet opening), HFA-152a exhibited the fastest initial refill, achieving 9.7% fill. HFA-227ea, by comparison, achieved only 6.4% fill. These early differences reflect the influence of vapour pressure and liquid density; HFA-152a's relatively high vapour pressure and lowest density resulted in faster volumetric flow into the metering chamber.

As the inlet opened to 50% (37.5 ms), refill continued across all propellants despite a reduction in pressure gradient. HFA-152a maintained a higher liquid fill percentage (24.3%), followed by HFA-134a (22.6%), HFO-1234ze(E) (19.6%), and HFA-227ea (17.0%). At this stage, the mass transfer mechanism was observed to follow a gradual transition from flashing and cavitation to mostly liquid in-flow. Beyond 52.5 ms (75% inlet opening), further inlet area increases had diminishing influence on the overall volume flow rate, and flow became primarily pressure-gradient driven.

By 300 ms the refill rate had reduced significantly; however, despite convergence in metering chamber pressure to the upstream saturated vapour pressure of the canister, a small residual pressure gradient remained, suggesting filling would continue beyond the simulated time duration until the pressure gradient reaches zero. At the end of the simulation HFA-152a achieved the highest liquid fill level (88.3%), closely followed by HFA-134a (87.1%), with HFO-1234ze(E) at 75.9% and HFA-227ea at 65.7%. Interestingly, although HFA-134a has the highest saturated vapour pressure, the lower saturated vapour pressure of HFA-152a was counteracted by its lower density, subsequently resulting in a slightly faster refill rate. Overall, the simulation data demonstrates that refill performance correlates strongly with the saturated vapour pressure and density of the liquid propellant inside the canister. These differences in refill rate can be compensated for by adjusting metering valve geometry, such as the inlet diameter, to maintain consistent metering chamber refill performance across propellants; therefore, ensuring rapid refill during typical patient use and consistent dosing with subsequent actuations.

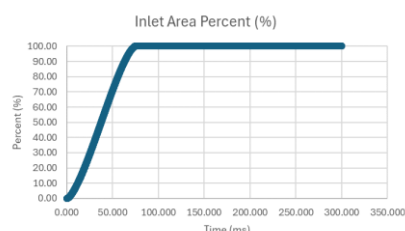


Figure 2 - Inlet Area Percent (%) - Time Plot

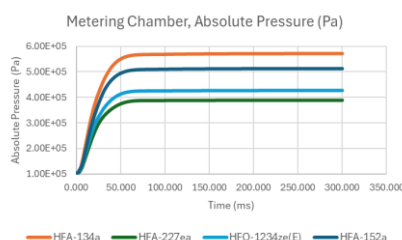


Figure 3 - Metering Chamber, Absolute Pressure (Pa) - Time Plot

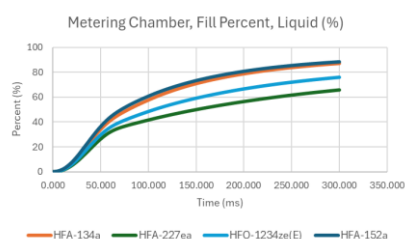


Figure 4 - Metering Chamber, Fill Percent, Liquid (%) - Time Plot

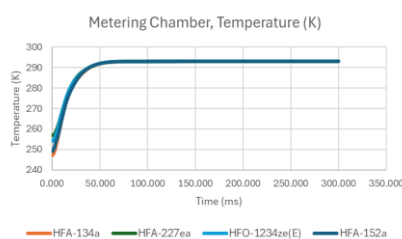


Figure 5 - Metering Chamber, Temperature (K) - Time Plot

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Table 1 - Simulation Model Numerical Data

Stage	Propellant	Metering Chamber, Temperature (K)	Metering Chamber, Absolute Pressure (Pa)	Metering Chamber, Fill Percent, Liquid (%)
Inlet, 25% Open (t = 22.5 ms)	HFA-134a	281.52	3.91E+05	8.7
	HFA-227ea	283.10	2.78E+05	6.4
	HFO-1234ze(E)	282.99	3.06E+05	7.5
	HFA-152a	281.24	3.49E+05	9.7
Inlet, 50% Open (t = 37.5 ms)	HFA-134a	289.33	5.07E+05	22.6
	HFA-227ea	289.67	3.48E+05	17.0
	HFO-1234ze(E)	289.72	3.83E+05	19.6
	HFA-152a	289.56	4.59E+05	24.3
End of Simulation (t = 300 ms)	HFA-134a	293.08	5.71E+05	87.1
	HFA-227ea	293.08	3.89E+05	65.7
	HFO-1234ze(E)	293.09	4.27E+05	75.9
	HFA-152a	293.09	5.13E+05	88.3

Conclusion

This study demonstrated the application of CFD to model the refill dynamics of pMDIs immediately following actuation. By simulating four propellants, HFA-134a, HFA-227ea, HFA-152a, and HFO-1234ze(E), the study highlighted significant differences in refill behaviour that was attributed to differences in their saturated vapour pressure and liquid density. These differences in refill rate can be compensated for by adjusting metering valve geometry, such as the inlet diameter, to maintain consistent metering chamber refill performance across propellants; therefore, ensuring rapid refill during typical patient use and consistent dosing with subsequent actuations.

Among the propellants studied, HFA-152a exhibited the fastest refill, reaching 88.3% fill by 300 ms, followed closely by HFA-134a at 87.1%, and HFO-1234ze(E) at 75.9%. In contrast, HFA-227ea demonstrated the slowest refill rate, reaching 65.7% fill by 300 ms, which was attributed to its lowest saturated vapour pressure and highest liquid density.

Overall, this study provided information that supports the design of the next generation of environmentally sustainable pMDIs. Furthermore, the developed simulation model provides a foundation for exploring additional parameters such as metering chamber and inlet geometry, and formulation-specific refill dynamics. Although the current simulation model focusses on capillary retention metering valves, its principles can be extended to alternative designs, including primeless metering valves. Ongoing and future work will include sensitivity analysis of model inputs and mesh optimisation to enhance simulation accuracy. Experimental data will be obtained from high-speed x-ray imaging to validate the transient metering chamber liquid fill level during refill.

References

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