Computational Fluid Dynamics Model Validation of Spray Characteristics from a Suspension-Based Pressurized Metered-Dose Inhaler

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Abstract

Computational fluid dynamics (CFD) models provide a powerful, cost-effective approach for investigating impact of emitted spray characteristics on pressurized metered dose inhaler (pMDI) efficiency by simulating complex flow and transport phenomena. This study aims to evaluate the effects of plume characteristics on drug deposition using CFD models. As a first step, we conducted a validation study to ensure model accuracy. We simulated and analyzed the plume angle and plume width from a suspension-based pMDI, comparing the results with particle image velocimetry (PIV) data of sprayed particles [1]. The validated models establish a basis for improving predictive capabilities, enabling more accurate assessments of drug transport in the respiratory tract, guiding the development of more effective inhaler designs, and aiding with bioequivalence recommendations for generic drug products.

Introduction

Pressurized metered dose inhalers (pMDIs) are among the most common and effective devices for delivering aerosolized medications to patients with respiratory diseases such as asthma and chronic obstructive pulmonary diseases. Their therapeutic effectiveness depends heavily on the characteristics of the emitted spray, including spray patterns and velocity of sprayed particles, which influence drug particle transport, deposition within the airways, and ultimately clinical efficacy. As inhaler design continues to evolve, a deeper understanding of these spray characteristics is essential for improving performance and optimizing patient outcomes.

While parameters, such as plume width and plume angle, can be measured optically, velocity profiles play a crucial role in determining the trajectory and fate of drug particles as they move through the mouth-throat and into the lung regions. To evaluate these key features, we developed a CFD model and validated it against PIV experiments, which provide both geometric and velocity information about the spray. The PIV method was chosen specifically for its ability to capture the dynamic behavior of the spray plume, offering critical data that go beyond static measurements and enable a more accurate representation of drug delivery processes.

Directly simulating the internal spray formation within the pMDI device is computationally expensive due to the complexity of multiphase flow and atomization processes. Furthermore, the plume dynamics—such as velocity distribution and geometric spread—are strongly dependent on the design of the inhaler itself. Instead of attempting to replicate the full internal dynamics, this study adopts a more efficient approach by using empirical plume characteristics obtained from experiments as boundary conditions for the CFD model. This allows us to focus computational resources on simulating the downstream transport and deposition of drug particles in the respiratory tract, while still accounting for device-specific spray behavior.

The validated CFD model presented here serves two important purposes. First, it provides confidence in the prediction accuracy of plume geometry and velocity using the developed CFD method. Second, it provides a piece to a framework that may eventually be used for answering questions related to the performance and bioequivalence of generic pMDI drug products. When complete, this framework will contribute to both regulatory science and inhalation drug product development.

Materials and Methods

PIV Experimental Data
Particle velocity measurements in the aerosol plume were obtained from particle image velocimetry (PIV) experiments reported by Crosland et al. [1]. Details on the methods in Crosland et al. [1] are presented here to provide the full context of what these data represent in comparison to CFD predictions. In that study, salbutamol sulfate (i.e., albuterol sulfate) pMDIs were actuated repeatedly in quiescent air. At various time delays post-actuation, a PIV system captured two-dimensional instantaneous velocity flow fields in the vertical (sagittal) plane. Two commercially available pMDIs—Ventolin HFA (GlaxoSmithKline Inc.) and ratio-Salbutamol HFA (Ratiopharm Inc.)—were tested, using hydrofluoroalkane-134a (HFA-134a) as the propellant.

CFD Simulation Setup
CFD simulations were performed using ANSYS Fluent 2023 R2 (ANSYS, Inc.). The simulation domain mimicked the experimental setup with an open airspace modeled as an enclosure extending from the pMDI mouthpiece, as shown in Figure 1. Mesh generation was performed using ANSYS Fluent Meshing 2023 R2 with gradient density. Mesh independence was tested using 1.5 million cells, 3.5 million cells, and 6 million cells, and the final simulation was done using 3.5 million cells. Timestep convergence was verified through timestep variation studies with step sizes of 25, 50, and 100 μs. Additional verification included testing the effect of varying domain size and particle number density.

Velocity boundary conditions for both the continuous and discrete phases were informed by PIV measurements taken 1 mm downstream of the mouthpiece exit. These time-resolved velocity profiles were used to match initial jet momentum in the simulation. All other boundaries of the enclosure were treated as pressure outlets to simulate open-air discharge conditions

The continuous phase was solved using a pressure-based transient solver with the energy equation and a k-omega Reynolds-averaged Navier-Stokes turbulence model. Species transport was modeled for air and propellant species, where the propellant was HFA-134a. Sensitivity studies were conducted for air-to-propellant mixture ratios (ranging from 0 to 1), and plume temperatures (from -54°C to 6°C [2]) for both continuous and discrete phases. We did not find notable influence on CFD-PIV agreement.

A Lagrangian approach was employed for simulating the discrete phase (drug particles), with particles injected into the domain through the same mouthpiece exit. The injection profile used an external file containing nine discrete particle size bins derived from aerodynamic particle size distribution (APSD) data based on experimental results from a Next Generation Impactor (NGI) operating at 30 L/min.

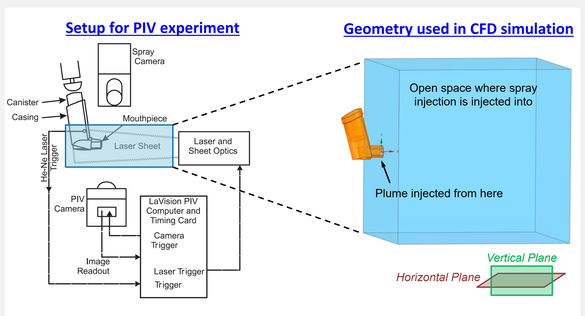


Figure 1. PIV experiment setup [1] and CFD simulation setup.

Results and Discussion

Extraction of Asymptotic Plume Profiles from PIV Data
Asymptotic expressions for the spatial and transient characteristics of plume sprayed near the exit of the pMDI mouthpiece were obtained by fitting simplified analytical expressions to PIV experimental data, as given in Figure 2.

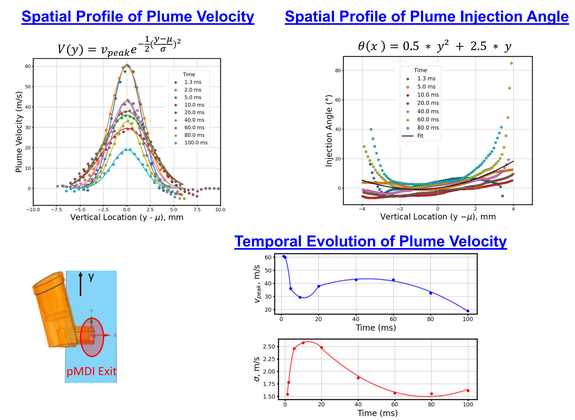
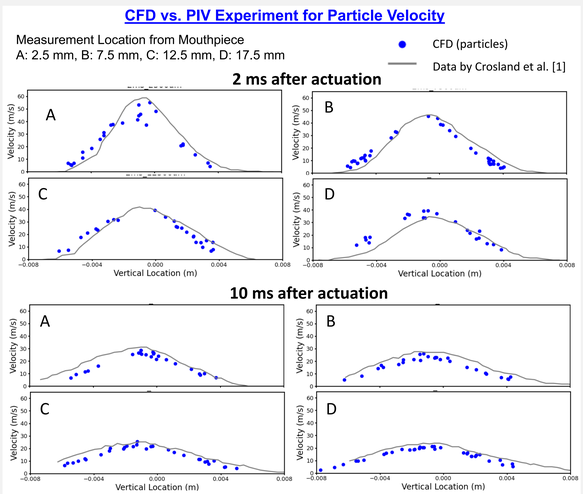


Figure 2. Empirical expressions for plume velocity and injection angle at the exit of the pMDI mouthpiece.

Validation of CFD with Experimental PIV Data
Comparisons between CFD-predicted particle velocities and experimental PIV data demonstrated reasonable agreement at four downstream locations: 2.5 mm, 7.5 mm, 12.5 mm, and 17.5 mm from the mouthpiece exit, as shown in Figure 3. The velocity profiles and their evolution along the plume axis were consistent with observed trends in the experimental dataset.



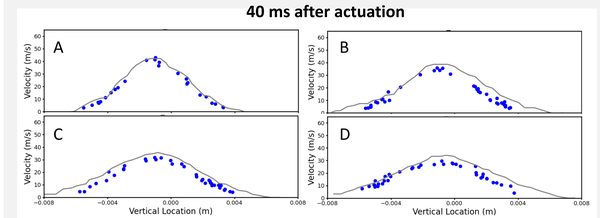


Figure 3. Comparison of vertical (radial) velocity profiles of sprayed particles measured by PIV and predicted by CFD at 2 ms, 10 ms, and 40 ms following pMDI actuation.

Prediction of Regulatory Plume Characteristics
The CFD model was used to compute plume characteristics recommended by the U.S. Food and Drug Administration (FDA) for evaluating bioequivalence between reference standard and test pMDI products. These include plume angle and plume width at 30 mm and 60 mm downstream from the pMDI exit, as provided in Figure 4.

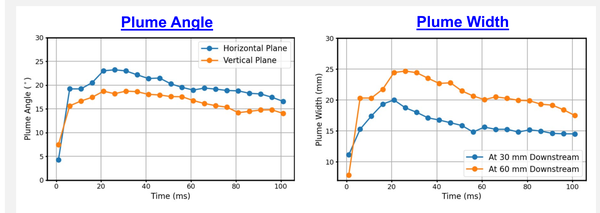


Figure 4. CFD predictions of plume angle and plume width (i.e., the length of major axis) at cross-sectional planes.

Conclusion

We developed a CFD model incorporating a multiphase transport framework to simulate drug particle dynamics in the plume generated by a pMDI. Empirical velocity and injection angle profiles near the pMDI exit were obtained from experimental data and used to define realistic boundary conditions for the CFD model. The model was validated through comparison with PIV-based particle velocity measurements at multiple downstream locations, showing good agreement. The CFD simulations predicted key plume characteristics recommended by the FDA for in vitro bioequivalence testing of generic inhalation products. The validated CFD model, together with the derived empirical injection profiles of plume, may be used for future investigations of aerosol transport and drug deposition patterns in pMDI-based drug delivery systems.

References

1. Crosland BM, Johnson MR, Matida EA. Characterization of the spray velocities from a pressurized metered-dose inhaler. J Aerosol Med Pulm Drug Deliv. 2009 Jun;22(2):85-97.
2. Brambilla G, Church T, Lewis D, Meakin B. Plume temperature emitted from metered dose inhalers. Int J Pharm. 2011 Feb 28;405(1-2):9-15.

This poster reflects the views of the authors and should not be construed to represent the FDA's views or policies.