Study of a Pressurized Metered-dose Inhaler Spray Parameters in Fluent™

Ricardo F. Oliveira, Senhorinha Teixeira, Luís F. Silva, José Carlos Teixeira and Henedina Antunes

Abstract— **The objective of this paper is to help fulfill the lack of information about the parameters needed to simulate a pressurized metered-dose inhaler (pMDI) spray (using a commercial computational fluid dynamics tool), providing future researchers the necessary information to study other pMDIs related devices, such as holding chambers. Following a previous bibliographic research about the characteristics of a pMDI spray, a further compilation was needed regarding the information to computationally define the spray in Fluent™. A very common drug asthma treatment (Ventolin®) was used in this study, with particles diameters going from 1.22 µm to 49.5 µm in a Rosin-Rammler distribution. The parameters were tested in Fluent™ (v6.3.26), using a three-dimensional "testbox" created especially for this purpose and meshed using the Gambit™ software (v2.2.30). The results showed that the selected parameters have produced a simulated spray very similar to the real one. It was also observed that the air behavior inside the "testbox" had a predictable response.**

Index Terms— **pressurized Metered-Dose Inhaler (pMDI), Spray, Fluent™, Discrete Phase Model (DPM), Computational Fluid Dynamics (CFD)**

I. Introduction

Pressurized metered-dose inhalers, pMDIs, are the most commonly used aerosol delivery device in the world [1-2]. They have been the backbone of inhalation therapy for asthma for approximately 50 years [3]. It was an idea of George Maison, a medical consultant at 3M Riker Laboratories in 1956, when he saw his daughter having difficulties using her hand bulb nebulizer [4]. This device was a revolution in the asthma treatment and its convenience has been recognized by patients and physicians. The pMDI contains 100-400 doses in a small and (very) portable device that can be easily kept in a pocket. The best feature of a pMDI device is that is always ready to be used, making it a magnificent example of an engineering solution.

The device incorporates a disposable canister (see Fig. 1) where the drug formulation is stored which can be replaced for a new one at any time. A pMDI combines an aluminum canister mounted in a plastic actuator [3, 5]. The four basic components that can be found in all pMDIs are: the formulation canister; the metering valve; the actuator, and the container [6].

The formulation is made up by the drug, the propellants and often contains surfactant and other excipients. The interaction of the formulation with the other pMDI components defines the final dosage form and characteristics.

The metering valve of a pMDI is a critical component in the effectiveness of the delivery system, due to the fact that its main functions are [1-3, 5-7]:

- to deliver, in an accurately and reproducibly form, a measured volume (20-100 µL), containing between 20 to 5000 µg of the dispersed drug,
- to form a propellant-tight seal for high pressure in the canister.

The actuator is normally a single piece produced by injection molding that consists of a mouthpiece, body and nozzle [2-3, 5-6, 8]:

- the mouthpiece is the interface part to the patient mouth;
- the body provides support for the canister;
- the nozzle has a very important role in controlling the atomization process, to guarantee a spray plume formation. The nozzle diameter interferes directly with the particles size distribution.

The canisters for a pMDI are typically made of aluminum and they are designed to be light, compact and strong to hold the high internal pressure of 3 to 5 atmospheres [3, 5]. Its regular capacity is around 15-30 mL [6].

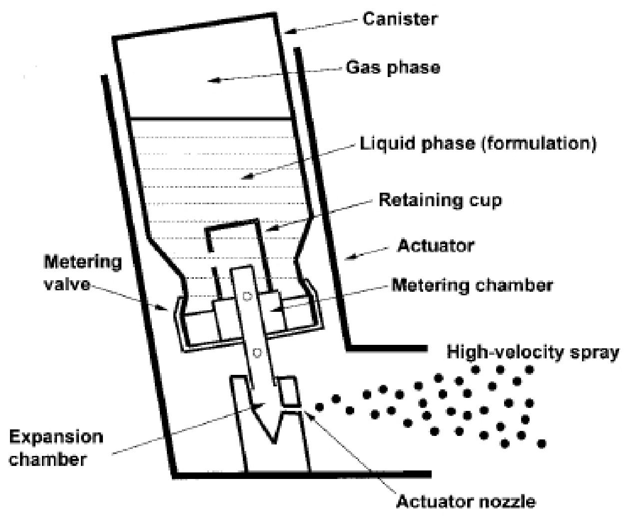

Figure 1 - pMDI schematic cross-section [5].

In this research work, the Ventolin® was used because it is one of the most common drugs used in developed countries to

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treat asthma in children and adults. It mainly consists of salbutamol, which is the most frequently prescribed short-acting β-agonist (SABA) [4, 9-10]. The pMDI actuator used was the one that is typically sold with the Ventolin®, both produced by the GlaxoSmithKline company.

The objective of the work herein reported is to highlight the configuration parameters that better fits the real-life case of a pMDI spray, using a commercially available CFD software, such as Fluent™ from ANSIS®.

Fluent™ is a CFD code based in the finite volume method, which was originally developed as a special finite difference formulation. Its numerical algorithm is based on three steps: first, there is a formal integration of the governing equations of fluid flow over all the control volumes of the solution domain; it is followed by the discretization that converts the integral equations into a system of algebraic equations and finally the solution of the algebraic equations by an iterative method [11-12].

Fluent™ also enables the simulation of particles with fluids using a second phase in a Lagrangian frame of reference, known as the Discrete Phase Model (or DPM) [13].

The results given by the CFD analysis are normally a realistic approximation of a real-life system. The user has a wide choice regarding the level of detail of the results, since it is possible to simulate any fluid that cannot be reproduced experimentally due to economical or physical reasons. These advantages makes the CFD software to be a very powerful tool in the engineering research field [11-12].

II. Methods and Configurations

A. *"Testbox" proprieties*

The "testbox" consists of a simple parallelepiped form with the dimensions of 0.1 x 0.1 x 0.15 (m) representing a sample of a room environment.

The solid was drawn in the Gambit™ software (from ANSIS®), that enables the drawing of 3D geometric forms, its mesh and the definition of different boundaries types [14].

The type of mesh used was the Hexahedral/Wedge Cooper scheme with 4 mm interval, resulting in a 3D computational grid with 23750 hexahedral elements and 26364 nodes. The quality report showed that mesh had a very good quality [14].

The spray injection point is located in the origin point (0,0,0), which is also the center point of a face (Fig. 2).

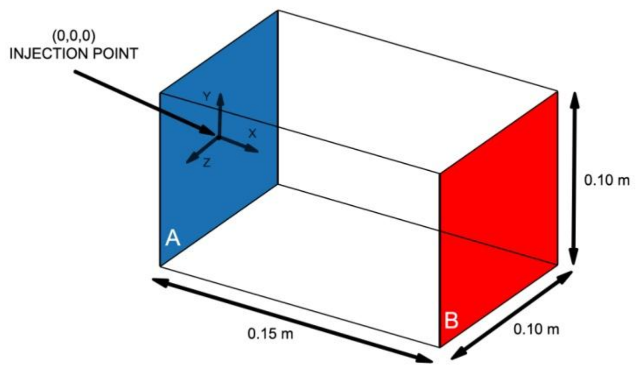

Figure 2 - A "testbox" representation. The blue plane (A) is the boundary condition Velocity Inlet and the red plane (B) is the boundary Outflow.

The boundary conditions were defined in two opposite faces, one as a Velocity Inlet, forcing air to move inside the "testbox" at 0.05 m/s and the other as an Outflow, enabling the air to move out or in freely. For the remaining four faces a symmetry boundary condition was assumed.

B. *Ventolin® proprieties*

As mentioned previously, the Ventolin® was used since it is a common SABA drug applied in the treatment of asthma with a pMDI. The characteristics of the Ventolin® are listed in Table I.

TABLE I - VENTOLIN® PROPERTIES.

Characteristic	Value	Refs.
Propellant	HFA 134a	[2, 15]
Salbutamol density (kg/m^3)	1230	[2]
Actuation dose (μg)	100	[15-17]
Actuation time (s)	0.1	[8]

C. *Particle diameter distribution in the spray*

Fluent™ allows the user to choose between three different particle diameter distributions [13]. For this project the Rosin-Rammler distribution model was used. This was also used by the laser diffraction particle sizer Malvern 2600, always showing a good experimental fit to the data. This experimental data provided the parameters needed to configure the dispersed phase injection in Fluent™ – see Table II.

TABLE II - PARTICLES DIAMETER DISTRIBUTION PARAMETERS.

Parameter	Value
Diameter distribution	Rosin-Rammler
Minimum diameter (μm)	1.22
Maximum diameter (μm)	49.5
Mean diameter (μm)	12.82
Spread parameter	1.44

D. *Spray configuration in Fluent™*

The spray parameters used to configure the Fluent™ software were obtained from various references though some caution is required.

The angle of the spray was considered to be 8º.

The spray particles were considered to be solid, instead of the well-known liquid droplets. The reason for this consideration is simple: when the drug exits the nozzle of the pMDI, it undergoes a flash evaporation. That can be defined as the instantaneous transformation of a liquid phase into a vapor phase due to a sudden decrease in pressure. Because this is an instantaneous process, it is assumed that no heat transfer between the gas and liquid phases [1, 6, 18].

The spray flow rate was determined with the information presented in Table I, dividing the dose over the duration of the spray.

Table III summarizes the main spray parameters used to configure the Fluent™ software.

E. *Mathematical models*

Fluent™ is a finite volume based code, which uses the integral form of the conservation equations as its starting point. The solution domain is divided into a finite number of contiguous control volumes and the conservation equations

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are applied to each one.

TABLE III - FLUENT™ SPRAY PARAMETERS.

Parameter	Value	Refs.
Spray type	solid-cone	[5, 13]
Angle (º)	8	
Velocity (m/s)	40	[5, 19]
Radius (m)	0.00025	[5, 8, 19]
Flow rate (kg/s)	$1e^{-6}$	

This method can be used with any type of grid (good for complex geometries) and it is perhaps the simplest to understand, which is why it is so popular among engineers [11].

1) Simulation of the air flow

The air flow inside the "testbox" was considered to be transient, incompressible, Newtonian and viscous turbulent. The turbulence model used was the standard k-ε model, since it is the most common, simple and well-known model of turbulence [11-13, 20].

The differential equations for mass and momentum were solved in a sequential manner, using the Semi-Implicit Method for Pressure-Linked Equations (SIMPLE) algorithm [11-13, 20].

The standard discretization scheme was used for the pressure and the second order upwind scheme for the momentum, turbulent kinetic energy and turbulent dissipation rate equations.

The convergence criterion used in the simulation had a value of 1E-5 for the continuity, x, y and z velocity, and for k and ε turbulence parameters.

The time step used in the simulation was 0.01 s, during 15 time steps with 300 iterations in each.

The gravitational acceleration was assumed 0 m/s^2 as a simplification, because the particle weight is negligible.

2) Simulation of particles flow and trajectories

The DPM model assumes spherical particles dispersed in the continuous phase. Fluent™ computes the trajectories of these discrete phase particles, as well as heat and mass transfer to/from them [13].

The Lagrangian discrete phase model in Fluent™ follows the Euler-Lagrange approach, where the fluid phase is treated as a continuum by solving the time-averaged Navier-Stokes equations, while the dispersed phase is solved by tracking a large number of particles through the calculated flow field. The particle trajectories are computed individually at specified intervals during the fluid phase calculation. The dispersed phase can exchange momentum, mass and energy with the continuous phase. This makes this approach appropriate to model and simulate spray dryers, coal and liquid fuel combustion and some particle-laden flows, but inappropriate for modelling liquid-liquid mixtures, fluidized beds, or any application where the volume fraction of the second phase is not negligible [13].

The parameters used to configure the DPM model menu in Fluent™ are listed in Table IV Different configuration parameters have been tested but these seemed to be the most appropriated in the simulation.

As the injection had a limited period in time (0.1 s), the unsteady particle tracking was used. Also the interaction with the continuous phase was included to approximate the simulation to the real event, because the velocity difference between the two phases is high.

TABLE IV - PARAMETERS FOR THE DPM MODEL.

Parameter	Value
Interaction with Continuous Phase	On
Unsteady Particle Tracking	On
Inject Particles at	Particle Time Step
Particle Time Step Size (s)	0.001
Drag Law	Spherical
Two-way coupling turbulence	On

The drag law used (spherical) is the most well-know law and is the one that better fits this model amongst the four different options available in Fluent™. The spherical drag law considers the particle as a sphere, which is an acceptable simplification for the drug particles that exit the pMDI nozzle [13, 18].

In the present calculations, the dynamic drag model was not used, as no models for droplet collision and break up were introduced [13].

The total number of particles streams injected during the simulation was approximately 41000.

III. RESULTS

The computational results are herein reported as images, obtained from the various types of the results view modes available in Fluent™, such as particle position and velocity. The data were obtained for various time steps of the simulation showing the time evolution of the process.

A. *Particles position*

In the particles position report, as presented in Fig. 3, it is possible to observe each particle velocity and position. The results show a good approximation to the real-life pMDI spray [8, 17].

The injection was started at 0.02 s, so in the first time steps only air at a constant inlet velocity (of 0.05 m/s) was calculated. This procedure appears to accelerate the convergence rate because it is advised to stabilize the air velocity field, before injecting the particles [13].

The results show that the particles reduce their injection velocity from 40 m/s to the air velocity of 0.05 m/s in a very short time.

B. *Air velocity pathlines*

The air velocity pathlines, as displayed in Fig. 4, were obtained for a symmetry plane (z=0) that splits the "testbox" in two equal parts, giving an idea how the air moves inside of the geometrical model considered.

The resulting images were taken from the air velocity magnitude, ranging from 0.05 to 0.11 m/s, and for the same time steps as the particles positions, so the influence of the particles in the air inside the "testbox" could be assessed.

At 0.02 s, the results show an increase of the air velocity, as well as a perturbation of the air velocity field. This effect is due to the momentum transferred from the fast moving droplets into the main flow. This effect is only observed in the vicinity of the spray.

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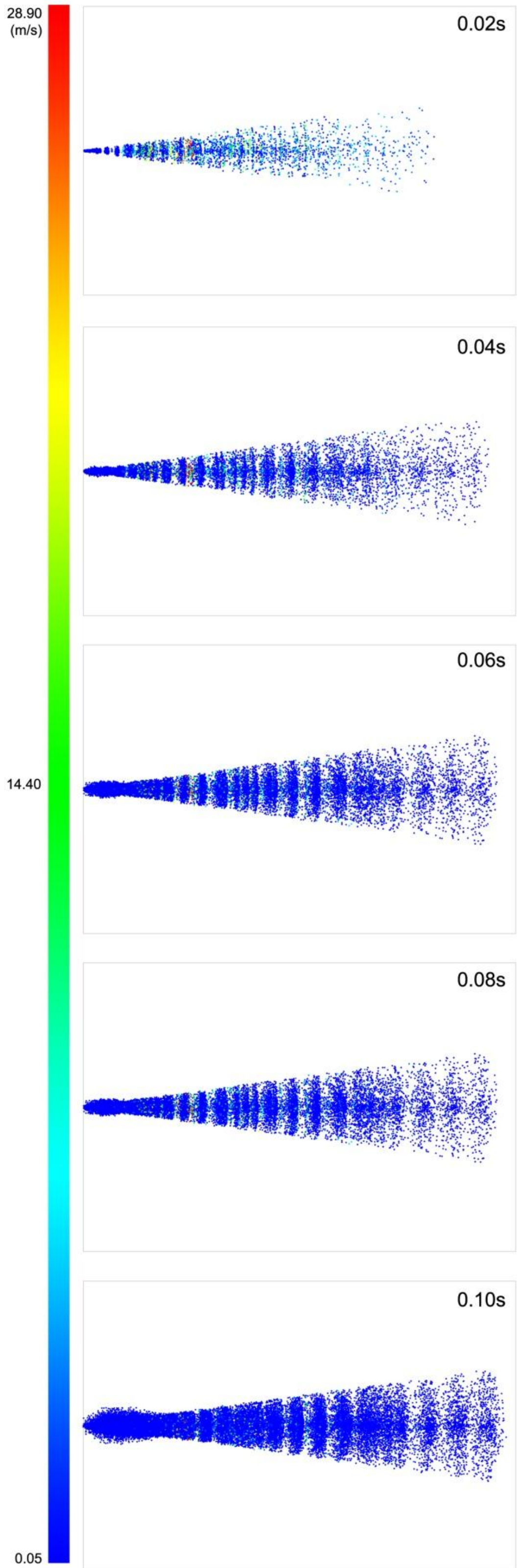

Figure 3 - Particles positions during the computational simulation, from 0.02 to 0.10 s. The scale represents the particles velocity magnitude in m/s.

It is also possible to correlate the location of the air acceleration zone with the position of the particles in the spray: as the particles move along the “testbox”, the air acceleration zone also moves along.

This acceleration of the air is caused by the contact of the particles (with a velocity of 40 m/s) with the air (with a velocity of 0.05 m/s), resulting in a decrease of the particles velocity until it becomes the same as the air velocity.

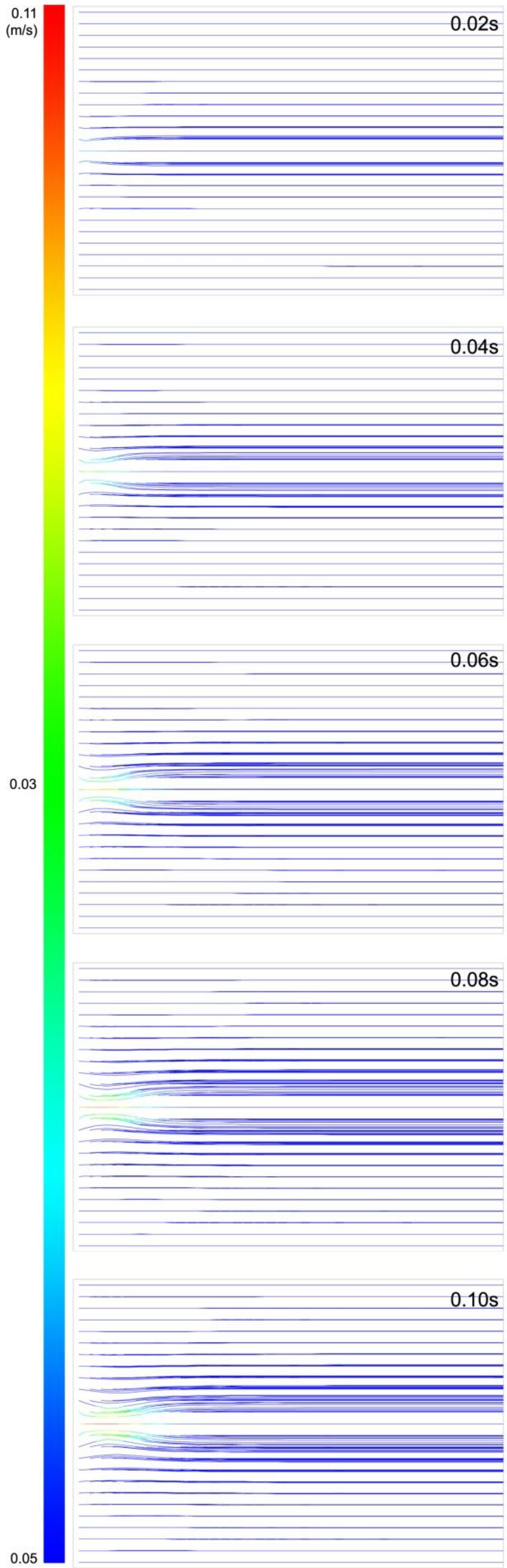

Figure 4 - Pathlines velocities of air inside the "testbox", from 0.02 to 0.10 s, obtained from a plane z=0 that splits the “testbox” in two equal parts. The scale is the velocity magnitude of air in m/s.

IV. Conclusions

The main conclusion from this study highlights the ability of the Fluent™ software to simulate a “real” pMDI spray.

The parameters determined can be used in different computational studies with particles and devices related to pMDI, such as holding chambers or spacers.

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Computational simulation is the cheapest and quickest method to study most of the problems and events of interest in the engineering field, having just the experimental testing procedures to validate the results or obtaining input parameters. Therefore, more experimental data should be obtained to create a more accurate and reliable simulation model.

The Fluent™ calculated the expected results in terms of particles behavior and their influence on the air.

The pMDI spray type can possibly be used in the configuration of any other type of aerosol spray with the same kind of nozzle, using other relevant input data.

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