

PRESSURISED METERED DOSE INHALER: CHIESI MODULITE®
Sauro Bonelli

CMC – Drug Product Development Department– Chiesi Farmaceutici S.p.A., Parma
S.Bonelli@chiesigroup.com

ABSTRACT

In pMDI inhalers, optimal lung delivery of active ingredients depends on a number of factors, including the device's configuration, the formulation, and the patient's ability to coordinate actuation and inhalation. The aim of the formulator is to produce a low speed aerosol with a defined particle size to ensure delivery to the desired part of the respiratory tract. Moreover, the relatively slow generation of the aerosol cloud facilitates coordination between inhaler activation and patient inhalation. With the Chiesi Modulite® technology platform, it is possible to achieve these objectives by conveniently modulating two independent formulation variables: the concentration of low volatility components in the formulation solution, and the actuator orifice diameter. Two minor variables, the solution vapour pressure and the metering valve chamber volume, also contribute toward defining optimal aerosol characteristics.

THE USE OF LOW VOLATILITY COMPONENTS

Lung deposition is determined mainly by the aerodynamic diameter of the aerosol particles. This is generally referred to as "mass median aerodynamic diameter" (MMAD), an index which defines aerodynamic diameter as the midway point with 50% of the mass of particles above and 50% below.

MMAD values ranging between 1 and 5 µm are generally considered suitable for lung deposition. Particles with an aerodynamic diameter close to 5 µm deposit in the larger and more central region of the airways (bronchi – bronchioles), whilst the particles with an aerodynamic diameter close to 1 µm reach the peripheral lung regions (alveoli).

A pMDI product in solution is essentially made up of a simple blend with an active ingredient, an HFA propellant, and ethanol as co-solvent. This type of formulation produces a rather low MMAD aerosol with values typically ranging between 0.8 and 1.2 µm, certainly capable of reaching the pulmonary alveoli. For deposition to occur in other parts of the lung, depending on the target area for the active ingredient, it may be necessary to generate a higher MMAD aerosol. The addition of a low volatility component to the solution such as glycerol or polyethylene glycol determines the

increase of the MMAD. A correlation between low volatility component concentration and MMAD has been defined.

EFFECT OF THE ACTUATOR NOZZLE DIAMETER

The fraction aerosol particles with an aerodynamic diameter lower than 5 µm is known as "Fine Particle Fraction" (FPF); these dimensional characteristics allow the particles to reach the lungs.

In pMDIs, it has been shown that the aerosol FPF generated by a product in solution depends mainly on the actuator orifice diameter, and to a lesser extent, on the metering chamber valve volume and propellant concentration.

Smaller diameter nozzles significantly increase aerosol FPF fraction thus reducing the FPF loss due to oropharyngeal deposition. This fact is a consequence of the creation of slower aerosol clouds that take longer to form. The slower spray velocity facilitates coordination between the patient's activating the inhaler and the patient's act of inhaling, thus reducing oropharyngeal deposition. Within the range of diameters investigated, the mass median aerodynamic diameter (MMAD) is influenced very little by actuator orifice diameter variations.

In conclusion, the defined correlations enable one to vary the two main aerosol performance indicators (MMAD and FPM) relatively independently. Adjusting formulation composition and selecting the most suitable device make it possible to modulate aerosol characteristics in relation to the desired pulmonary target