tube element according to any aspect or embodiment described herein for the reduction of the non-respirable dose and consequent potential oro-pharyngeal deposition of the dispensed aerosol formulation on actuation of the inhaler.

The presence of the tubular element according to the invention manipulates the airflow internal to the mouthpiece portion of the actuator, creating an area of low velocity immediately after the orifice aperture and altering the expansion dynamics of the flashing liquid emitted by the orifice which results in significant advantages over the prior art.

Among the main advantages one is the significant reduction in the non-respirable, coarse fraction of the emitted aerosol medicament via inertial impaction and retention in the actuator than in the oro-pharynx. Non respirable fraction is often associated with systemic side effects and oral candidiasis and dysphonia (in case of inhaled corticosteroid treatment).

In addition the presence of the tubular element has minimal, negligible impact on the particle size distribution (PSD) of the delivered particles having aerodynamic diameter lower than 9 μm. In fact the PSD observed in vitro using Andersen Cascade Impactor (ACI) fitted with a USP throat (Apparatus 1, United States Pharmacopoeia - USP34-NF29) is extremely comparable with that of a conventional actuator.

An actuator according to the invention, retaining the coarse dose on the tubular element wall via inertial impaction, may remove the requirement for add-on devices, spacers or holding chambers such as the Volumatic™ and AeroChamber Plus™, which prevent a large proportion of the coarse particles from the dose reaching the patient, but produce dramatically changes in the PSD with respect to "actuator only" products. This reduces the need to carry such ~~for~~ add-on devices which are cumbersome and is an additional factor considering patient compliance.

The so called "cold Freon effect", in which high-velocity aerosol hits

the back of the throat, causing hiccup and patients to stop inhaling prematurely, is minimised.

The patient generated airflow is identical to that generated in a conventional MDI actuator without the tubular element according to the invention. Duration of plume ~~formulation~~ and manner of patient use are also unaffected.

This kind of actuator is compatible with the pMDI aerosol formulation technology based on hydrofluoroalkane (HFA) propellants The aerosol formulation may be an aerosol solution formulation or an aerosol suspension formulation. The aerosol formulation may contain at least one active ingredient in a propellant or in a propellant/solvent system and, optionally, further excipients. In particular with solution formulation comprising an alcohol co-solvent an optional low volatility component such as glycerol may be present.

The performance of this kind of actuator through-can-life is consistent.

Any eventual deposits of the medicament in the tubular element or in the mouthpiece portion of the actuator may be removed through conventional washing techniques.

The above and other effects will be illustrated further with reference to exemplary embodiments described with reference to the drawings.

Brief description of the drawings

Reference will now be made, by way of example, to the accompanying drawings, in which:

Figure 1 is a schematic longitudinal sectional view of a conventional pressurised metered dose inhaler (pMDI) according to the prior art.

Figure 2 is a schematic longitudinal sectional view of a pMDI actuator of an embodiment of the invention.

Figure 3A is a schematic longitudinal sectional view of a pMDI actuator

Lipped Tubes (Fig. 20A): represented by parallel tubes consisting of various designs and features surrounding the exit orifice The lipped tubes consisted of a range of parallel tubes with either a lip of varied thickness (T), step length ~~(L)~~ (S) and a smooth or a stepped feature around the exit orifice;

Narrow Divergent Tubes (Fig. 20B): represented by non-parallel tubes with a narrow entrance orifice (d_1 = 1.50 ± 0.10mm) which fits into the frusto-conical aperture of the actuator orifice 8;

Wide Divergent Tubes (Figure 20C): represented by non-parallel tubes with a wide entrance orifice (d_1 = 4.50 ± 0.10mm) which fit externally, around the frusto-conical aperture of the actuator orifice 8;

Elliptical Tubes (Figure 20D): represented by elliptical shaped tubes with various internal features such as oval or circular section or with internal partial obstructed airflow features.

The actuator 1, the nozzle block 5, the tubular element 11 and /or the shaped cylindrical object 12 may be formed of different materials and with different specifications which are suited for their specific purposes. Examples of suitable materials include metal materials such as aluminium, aluminium alloy or stainless steel; but also plastic polymeric materials, such as thermoplastic resins, optionally UV curable, including different grades polypropylene (PP) the material of first choice in general for the pMDI actuators, polyethylene (i.e. HDPE, high density PE); fluorinated polymers such as polytetrafluoroethylene (PTFE); acrylonitrile-butadiene-styrene (ABS); polyacrylate such as polymethyl methacrylate (PMMA); polycarbonate (PC); polyamide (i.e. nylon); polyester such as polyethylene terephthalate (PET). Moreover the plastic polymeric materials may be coated with antistatic agents by means of a moulding or a coating process.

The lateral surface of the tubular element 11 may be continuous or in alternative, perforated by one or more holes of optimised shapes (for instance

an actuator according to any of any one of claim 1 to 10 and

a canister having a metering valve and containing a pressurised medicament formulation.

13. A metered-dose inhaler actuator comprising

a housing having a mouthpiece portion and a canister receiving portion configured to receive a canister,

a nozzle block disposed within the housing and defining a valve stem receptacle configured to receive a valve stem of the canister,

an orifice in fluid communication with the valve stem receptacle to propel the aerosol formulation towards the mouthpiece opening, and

a tubular element extending in the mouthpiece portion from the orifice aperture in a longitudinal axis aligned with a longitudinal axis of the actuator mouthpiece portion and coinciding with the orifice longitudinal axis.

14. A kit of parts comprising

an actuator for an aerosol inhalation device,

the shaped hollow cylindrical object of claim 11, and

an aerosol canister containing a pressurised medicament formulation.

~~15. The use of an actuator according to any one of claims 1 to 10 for the~~ reduction of the non-respirable dose ~~and~~ consequent potential oro-pharyngeal ~~deposition of the dispensed aerosol formulation on actuation of the inhaler.~~