

## THE EFFECT OF SURFACTANT CONCENTRATION ON THE SIZE OF AGING DROPLETS PRODUCED BY A METERED DOSE INHALER

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Surface active materials are employed for drug suspension and valve lubrication purposes in the preparation of metered dose inhalers (MDI) (Byron 1986). Their non-volatile nature will affect the evaporation rate of droplets leaving the MDI and the final particle size of surfactant coated drug. Both factors will influence the deposition pattern in the mouth and lung (Moren 1987). To explore these effects, three formulations were made by suspending  $2\text{mg ml}^{-1}$  salbutamol sulphate (volume mean diameter =  $2.5\ \mu\text{m}$ ) in 30:70 blend of propellants P11 and P12. Soya lecithin was included in drug-surfactant ratios of 1:0.5, 1:2 and 1:10. Using  $50\ \mu\text{l}$  valves, a common actuator and cylindrical extension tube, ten doses were discharged into an inertial impactor from a distance of 100, 200 and 300 mm. A single stage, which captured particles greater than  $3.3\ \mu\text{m}$  (Stage 3, Anderson model 1CFM) and a final filter were used. This reduced configuration had been shown to give the same cut off as the full assembly and SEM analysis of samples captured by the filter showed no particles greater than  $3.3\ \mu\text{m}$ . By avoiding the convoluted path in a conventional cascade impactor, its use ensures that particles captured at a particular distance from the actuator are of the same age.

Material on the actuator, extension tubes, stage 3 and filter was collected by washing with mobile phase and the amount of salbutamol sulphate analysed by HPLC. The total recovery was always more than 80% of the nominal dose.

Results given in the figure showed that for a given formulation there was no significant change in the deposition of particles less than  $3.3\ \mu\text{m}$  when using the three extension tubes. This indicates that the deeply respirable fraction of the cloud ( $< 3.3\ \mu\text{m}$ ) is established at a distance of 100 mm from the actuator and does not change at greater distances. Microscopy showed that most deposits were derived from droplets containing a single solid particle. However, increasing surfactant concentrations significantly reduced the respirable fraction and their inclusion should be at the lowest level possible compatible with suspension stability.

