Investigation Into The Effect Of Delay Times And Inspiration Volumes On The Particle Size Distribution Of Aerosol Droplets From A pMDI With A Spacer

C von Anrep*, F Chambers,

AstraZeneca R & D Charnwood, Pharmaceutical and Analytical R & D, Bakewell Rd, Loughborough, Leicestershire LE11 5RH England

INTRODUCTION

The Copley TPK-S is a modified variant of the original Copley TPK Critical Flow Controller designed by Copley Scientific for dose and Impactor testing of DPI's. In response to a request from AstraZeneca R&D Charnwood the TPK has been modified to incorporate a second timer which allows user programmable time delays to be set between inhaler actuation and dose/Andersen Cascade Impactor (ACI) sampling. Thus, the TPK-S can be used to control both inspiration delay times and effective inspiratory volume. Accurate control of these parameters is of great benefit in the field of pMDI/Spacer testing, especially when evaluating the performance of these devices as holding chambers.

This poster describes a study carried out to investigate the effect of varying the delay time and inspiration volumes on the particle size distribution using two different spacer types, and introduces the TPK-S as a device for controlling and setting different delay times.

INSTRUMENTATION

Andersen Cascade Impactor (ACI)

250 µg/act (Active) HFA pMDI

TPK-S Copley Scientific critical flow controller

Spacer A Plus Plastic Valved Spacer*

Spacer B Stainless steel Valved Spacer device*

(* Both spacer variants were pre-washed according to manufacturers instructions)

The TPK-S has been designed to evaluate the effect of introducing inspiration delay times on the fine particle dose received from a pMDI-Spacer combination by way of two timers controlling a solenoid valve.

- Timer 1 Controls the total airflow delivered to the impactor
- Timer 2 Controls a the delay time between pMDI actuation and the start of impactor sampling

Figure 1: The TPK-S with an Andersen Cascade Impactor (ACI)

EXPERIMENTAL

This investigation compared the results obtained using 4 and 1 litre inspiration volumes. The volume of air drawn through the impactor is limited by applying a test time, which is calculated using the following equation.

T= IV x 60 x Q-1

Where

T = Test time (seconds)

IV = Inspiration volume (L)

Q = Flow rate (28.3 L/min)

The particle size distribution from two HFA pMDI were determined by ACI analysis using both Spacer A and B both with a 2 and 5 second delay times and an inspiration volume of 4 litres. Spacer B was then tested to see if a reduction in inspiration volume from 4 litres to 1 litre affected the observed particle size distribution

The test conditions are summarised in Table 1.

Table 1: Test conditions

Spacer Type	Delay Time (seconds)	Forced Inspiration Volume (Litres)
Spacer A	5	4
	2	4
Spacer B	5	4
	2	4
	2	1

The the TPK-S was connected downstream of the ACI set up as shown in Figure 1, and the spacer/pMDI under test was connected to the ACI throat by way of suitable adapters.

RESULTS AND DISCUSSION

The amount of drug recovered from each stage is shown graphically in Figure 2, with the cumulative recovery shown in Figure 3.

Different particle size distributions are observed when testing the same product via the two spacer designs tested, with the most significant differences being observed in the throat. Spacer A shows virtually no deposition, whereas Spacer B shows significant deposition in the throat of up to 20 μg. Stages 3 and 4 also show significant increases in deposition with the Spacer B compared with Spacer A.

In all cases the TPK-S maintained accurate control of the user programmed times governing air flow volumes and delay times. A particularly important test was the 2 second delay, since previous studies with spacers have indicated that the bulk of the aerosol deposition in the spacer could occur within the first couple of seconds after actuation.

Figure 2: Amount of Drug Recovered for Each Stage

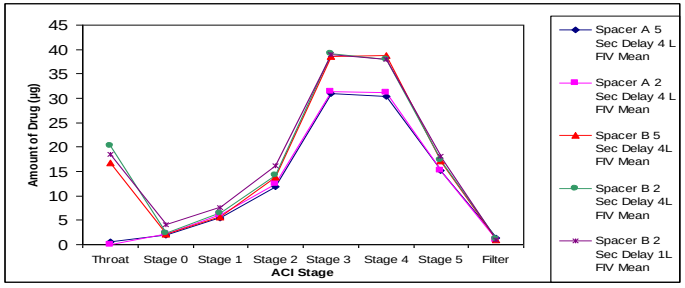
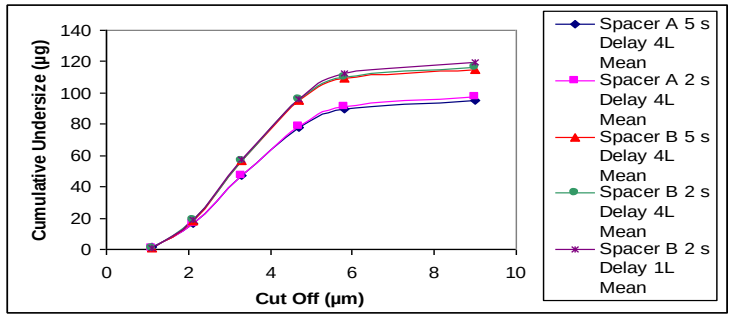


Figure 3: Cumulative Amount of Drug Recovered for Each Stage



- no change in particle size distribution is observed when the delay time is reduced from 5 seconds to 2 seconds.
- The particle size distribution also remains unchanged when the inspiration volume is reduced from
- 4 litres to 1 litre.
- The fine particle dose and fine particle fraction have been determined and are summarised in Table 2.
- The fine particle dose is approximately 20 μg higher when using a Spacer B in place of an Spacer A.

Table 2: Fine Particle Dose (FPD) Particles <4.5 μm

	Fine Particle Dose (μg)
Spacer A/5sec Delay/4Litre	78
Spacer A/2sec Delay/4Litre	79
Spacer B/5sec Delay/4Litre	95
Spacer B/2sec Delay/4Litre	97
Spacer B/2sec Delay/2Litre	96

CONCLUSION

This study has demonstrated that the TPK-S is a useful device for controlling airflow volumes and delay times and can be applied to pMDI/Spacer evaluations. The addition of the second timer means that short delay times between pMDI actuation and impactor sampling can be controlled precisely. Use of Timer 1 to control total airflow through the impactor gives the user the opportunity to study the effect of sampling the aerosol with different airflow volumes in conjunction with Spacer/pMDI combinations also.

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